OPTIMISING OUTCOMES FOR ANTIREFLUX AND HIATUS HERNIA SURGERY THROUGH RANDOMISED CONTROLLED TRIALS

David Ian Watson
MBBS, MD, FRACS, FAHMS

Discipline, Surgery
School of Medicine
Faculty of Medicine, Nursing and Health Sciences
Flinders University
Adelaide, South Australia

A thesis submitted in fulfillment of the requirement for the degree of Doctor of Philosophy (PhD) by published work

Submitted 20 June, 2015

This work is dedicated to my wife Claire,
my children James, Edward, Timothy and Abigail,
and my parents Mary and Ian

I am forever grateful to them for their tremendous support over many years, their patience with the challenges of my work, and the sacrifices they all made to enable the work in this thesis to be completed.

TABLE OF CONTENTS

SUMMARY

Gastro-oesophageal reflux is common and its treatment consumes significant health resources in Australia. Whilst most individuals with this problem are managed using medication, surgery is required when reflux is more severe. In the 1980's the "gold standard" surgical approach for reflux was the open Nissen fundoplication procedure. Whilst effective, Nissen fundoplication can be followed by troublesome side effects. To reduce the risk of side effects and improve overall outcome, various modifications to the Nissen procedure have been proposed.

Aiming to improve outcome following antireflux surgery a series of modifications to the Nissen fundoplication procedure were evaluated in eight prospective randomised controlled trials, conducted from 1993 to 2015. The modifications included laparoscopic surgery, non-division of the short gastric blood vessels, anterior hiatal repair, anterior 180 degree partial fundoplication, anterior 90 degree partial fundoplication, posterior partial fundoplication, and mesh repair for very large hiatus hernia. The trials addressed several questions:

- Can laparoscopic access reduce complications and speed recovery following Nissen fundoplication?
- Is division of the short gastric blood vessels necessary during Nissen fundoplication?
- Can an anterior 90 or 180 degree partial fundoplication achieve better outcomes following antireflux surgery than Nissen fundoplication?
- What type of partial fundoplication achieves the best overall outcome - anterior or posterior?
- Can dysphagia after Nissen fundoplication be reduced by anterior hiatal repair?
- Can mesh reinforcement of the oesophageal hiatus during repair of very large hiatus hernia reduce hernia recurrence?

The randomized trials demonstrated improved outcomes for antireflux surgery following appropriate technique changes. In particular;

- Laparoscopic Nissen fundoplication is followed by a quicker recovery, and less respiratory complications than open Nissen fundoplication, but offset by increased operating time. Reflux control and side effects are similar.

- Division of the short gastric blood vessels during laparoscopic Nissen fundoplication is unnecessary.
- Anterior hiatal repair is an effective technique during laparoscopic Nissen fundoplication and achieves outcomes which are at least as good as following posterior hiatal repair.
- Anterior 180 degree partial fundoplication achieves equivalent long term reflux symptom control and overall outcome satisfaction to Nissen fundoplication. At follow-up to 5 years anterior 180 degree partial fundoplication is followed by less side effects.
- Anterior 90 degree partial fundoplication achieves adequate reflux symptom control, less side effects and equivalent overall satisfaction compared to Nissen fundoplication at follow-up to 5 years, although more reflux symptoms are reported after anterior 90 degree partial fundoplication.
- At 12 months follow-up outcome satisfaction is similar for anterior 180 degree and posterior partial fundoplication. However, anterior partial fundoplication controls reflux symptoms less effectively, whereas posterior partial fundoplication is followed by more side effects.
- Posterior reinforcement of the hiatal repair with absorbable or non-absorbable mesh during laparoscopic repair of very large hiatus hernia does not reduce the early risk of hernia recurrence.

These randomized trials make a significant contribution to the evidence base underpinning surgery for gastro-oesophageal reflux and hiatus hernia. They support using the laparoscopic approach for antireflux surgery, simplifying the technique for Nissen fundoplication by not dividing the short gastric vessels, the wider use of anterior 180 degree partial fundoplication for the treatment of gastro-oesophageal reflux, and not using mesh for repair of large hiatus hernia. Future randomized trials provide an opportunity to refine other aspects of antireflux and hiatus hernia surgery.

DECLARATION

I certify that this thesis does not incorporate without acknowledgement any material previously submitted for a degree of diploma in any university; and that to the best of my knowledge and belief, does not contain any material previously published or written by another person, except where due reference has been made in the text.

David Ian Watson

PUBLICATIONS INCLUDED IN THIS THESIS

Randomised trial of laparoscopic vs. open Nissen fundoplication
Ackroyd R, Watson DI, Majeed AW, Troy G, Treacy PJ & Stoddard CJ. Randomised clinical trial of laparoscopic versus open Nissen fundoplication for gastro-oesophageal reflux disease. *Br J Surg* (2004) **91**:975-982.

Division vs. non-division of the short gastric blood vessels during Nissen fundoplication
Watson DI, Pike GK, Baigrie RJ, Mathew G, Devitt PG, Britten-Jones R & Jamieson GG. Prospective double blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg* (1997) **226**:642-652.

O'Boyle CJ, Watson DI, Jamieson GG, Myers JC, Game PA & Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication – a prospective double blind randomized trial with five year follow-up. *Ann Surg* (2002) **235**:165-170.

Yang H, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Randomized trial of division versus non-division of the short gastric vessels during laparoscopic Nissen fundoplication – 10 year outcomes. *Ann Surg* (2008) **247**:38-42.

Engström C, Jamieson GG, Devitt PG, Watson DI. Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of short gastric vessels during Nissen fundoplication. *Br J Surg* (2011) **98**:1063-1067.

Anterior vs. posterior hiatal repair during Nissen fundoplication
Watson DI, Jamieson GG, Devitt PG, Kennedy A, Ellis T, Ackroyd R, Lafullarde T, Game PA. A prospective randomized trial of laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair. *Arch Surg* (2001) **136**:745-751.

Wijnhoven BPL, Watson DI, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair: long-term results of a randomized trial. *Am J Surg* (2008) **195**:61-65.

Chew CR, Jamieson GG, Devitt PG, Watson DI. Prospective randomised trial of laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair – late outcomes. *World J Surg* (2011) **35**:2038-2044.

Anterior 180 degree partial fundoplication vs. Nissen fundoplication
Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M & Devitt PG. Prospective randomized double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg* (1999) **86**:123-130.

Ludemann R, Watson DI, Game PA, Devitt PG & Jamieson GG. Laparoscopic total versus anterior 180^0 fundoplication - five year follow-up of a prospective randomized trial. *Br J Surg* (2005) **92**:240-243.

Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180^0 partial fundoplication. *Br J Surg* (2008) **95**:1501-1505.

Broeders JA, Roks DJ, Jamieson GG, Devitt PG, Baigrie RJ, Watson DI. Five year outcome after laparoscopic anterior partial versus Nissen fundoplication - Four randomized trials. *Ann Surg* (2012) **255**:637-642.

Gatenby PAC, Bright T, Watson DI. Anterior 180 Degree Partial Fundoplication – How I do it. *J Gastrointest Surg* (2012) **16**:2297-2303.

Broeders, JA, Broeders EA, Watson DI, Devitt PG, Holloway RH, Jamieson GG. Objective Outcomes 14 Years after Laparoscopic Anterior 180˚ Partial versus Nissen Fundoplication - Results from a Randomized Trial. *Ann Surg* (2013) **258**:233-239.

Anterior 90 degree partial fundoplication vs. Nissen fundoplication with division of the short gastric blood vessels

Krysztopik RJ, Jamieson, GG, Devitt PG & Watson DI. A further modification of the Nissen fundoplication – 90^0 anterior fundoplication. *Surg Endosc* (2002) **16**:1446-1451.

Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin C, Martin IJG, Nathanson LK, Windsor J. Multicentre prospective double blind randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. *Arch Surg* (2004) **139**:1160-1167.

Woodcock SA, Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin CJ, Martin IJG, Nathanson LK, Windsor JA. Quality of life following laparoscopic anterior 90^0 versus Nissen fundoplication - results from a multicentre randomized trial. *World J Surg* (2006) **30**:1856-1863.

Nijjar RS, Watson DI, Jamieson GG, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin IJG, Nathanson LK, Windsor J. Five year follow-up of a multicentre double blind randomized clinical trial of laparoscopic Nissen vs. anterior 90^0 partial fundoplication. *Arch Surg* (2010) **145**:552-557.

Anterior 90 degree partial fundoplication vs. Nissen fundoplication without division of the short gastric blood vessels

Spence GM, Watson DI, Jamieson GG, Lally CJ & Devitt PG. Single centre prospective randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. *J Gastrointest Surg* (2006) **10**:698-705.

Watson DI, Devitt PG, Smith L, Jamieson GG. Anterior 90^0 partial vs Nissen fundoplication - 5 year follow-up of a single-centre randomized trial. *J Gastrointest Surg* (2012) **16**:1653-1658.

Anterior 180 degree partial fundoplication vs. posterior partial fundoplication
Daud WMBW, Thompson SK, Jamieson GG, Devitt PG, Martin IJG, Watson DI. Randomized controlled trial of laparoscopic anterior 180° partial vs. posterior 270° partial fundoplication. *ANZ J Surg* (2013) DOI: 10.1111/ans.12476. (published online).

Repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh
Watson DI, Thompson SK, Devitt PG, Smith L, Woods SD, Aly A, Gan S, Game PA, Jamieson GG. Laparoscopic repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh - a randomized controlled trial. *Ann Surg* (2015) **261**:282-289.

Koetje J, Irvine T, Thompson SK, Devitt PG, Woods SD, Aly A, Jamieson GG, Watson DI. Quality of life following repair of large hiatal hernia is improved but not influenced by use of mesh: Results from a randomized controlled trial. *World J Surg* (2015) **39**:1465-1473.

Wijnhoven BPL & Watson DI. Laparoscopic repair of a giant hiatus hernia - How I do it. *J Gastrointest Surg* (2008) **12**:1459-1464.

Late outcome following Nissen fundoplication
Lafullarde T, Watson DI, Jamieson GG, Myers JC, Game PA & Devitt PG. Laparoscopic Nissen fundoplication – 5 year results and beyond. *Arch Surg* (2001) **136**:180-184.

Kelly J, Watson DI, Chin K, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication – clinical outcomes at 10 years. *J Am Coll Surg* (2007) **205**:570-575.

Engström C, Cai W, Irvine T, Devitt PG, Thompson SK, Game PA, Bessell JR, Jamieson GG, Watson DI. Twenty years of experience with laparoscopic antireflux surgery. *Br J Surg* (2012) **99**:1415-1421.

Late outcome following anterior 180 degree partial fundoplication
Rice S, Watson DI, Lally CJ, Devitt PG, Game PA & Jamieson GG. Laparoscopic anterior 180-degree partial fundoplication - 5 year results and beyond. *Arch Surg* (2006) **141**:271-275.

Chen Z, Thompson SK, Jamieson GG, Devitt PG, Game PA, Watson DI. Anterior 180 degree partial fundoplication – a 16 year experience with 548 patients. *J Am Coll Surg* (2011) **212**:827-834.

Some components of the introduction and literature review included in this thesis have been published previously within a book chapter;

> Watson DI. Treatment of gastro-oesophageal reflux disease. In: Griffin SM, Raines SA & Shenfine J eds, *A Companion to Specialist Surgical Practice – Oesophagogastric Surgery (fifth edition)*. Elsevier Ltd., UK, 2014, pgs 241-268.

ACKNOWLEDGEMENTS

I am indebted to many people for their assistance with the studies and published papers which have been included in this thesis. I am grateful for their co-operation and willingness to help and contribute.

Professor Alan Johnson from the University of Sheffield provided invaluable mentoring when I worked with him as a Lecturer in his Department in 1993. He taught me to look beyond the obvious, and to ask questions. His experience with establishing and successfully completing randomized trials to evaluate new procedures provided me with the tools and understanding to commence and complete the randomized trials included in this thesis. He taught me to look beyond the obvious, and that good research can sometimes generate unexpected outcomes.

Professor Glyn Jamieson has always provided invaluable support and wise counsel, both when I worked with him at the Adelaide University and the Royal Adelaide Hospital from 1994 to 2002, and later after I moved to Flinders University from 2002. He has always been a great source of ideas. He helped me to keep asking questions, to consider the quality of the evidence underpinning clinical practice, and to look beyond what the "experts" were saying. Conversations and discussions in operating theatre tearooms, and during operating cases sparked many of the ideas that generated the trials included in this thesis.

I am grateful for the support of many other colleagues who were willing to contribute to the randomized trials by being willing to enroll their patients in the trials. I am particularly indebted to Professor Peter Devitt, Dr Robert Britten-Jones, Mr Philip Game, and Associate Professor Sarah Thompson at the Royal Adelaide Hospital; Dr Justin Bessell, Dr Susan Gan and Dr Tim Bright at Flinders Medical Centre; Dr Christopher Stoddard and Dr Roger Ackroyd at the Royal Hallamshire Hospital in Sheffield, UK; and Dr Ahmad Aly, Dr Simon Woods, Dr Ian Martin and other colleagues in Australia and New Zealand for their willingness to contribute to the trials. Without access to their patients the studies included in this thesis could not have been undertaken.

Invaluable funding for the randomized trials included in this thesis was provided by grants from the National Health and Medical Research Council (NHMRC) of Australia, the Royal Australasian College of Surgeons (RACS), and the South Australian Department of Health. This funding allowed a team of research nurses to be employed, and the nurses and others provided the support which underpinned the very high rate of clinical follow-up achieved across the last 2 decades.

I am specifically grateful for the help received from Dr Greg Pike, Ms Tanya Ellis, Ms Nicky Carney, Ms Carolyn Lally, Ms Lorelle Smith, Ms Marian Martin and Ms Lorraine Sheehan-Hennessy. Collectively they collected the clinical data in a "blinded" fashion across the various trials, and they entered data into the trial databases. Thank you also to Ms Jenny Myers, Mrs Nicky Carney and Mrs Jenny Globe who performed the manometric and pH studies used for objective assessment within these trials.

I am also indebted to my friends Dr Robert Baigrie, Cape Town, South Africa, and Professor Lars Lundell, Sweden for their willingness to share their original data sets from their randomized trials. These data sets were used for the combined data set analyses included in this thesis.

Approval for studies included in this thesis was provided by the Human Research Ethics Committees of the Royal Hallamshire Hospital, Sheffield, UK; the Royal Adelaide Hospital; the Southern Adelaide Clinical Human Research Ethics Committee (Flinders Medical Centre), and the local Research Ethics Committees for each hospital contributing patients to the multicenter trials. Over two decades there were many submissions to these committees, and the time spent considering these applications has been greatly appreciated.

Last but not least, I am forever grateful for the support from my wife Claire and my children James, Edward, Timothy and Abigail. They have all shown considerable patience with me and the demands of my work. They have supported me and loved me, and they have made many sacrifices, without which the work underpinning this thesis would not have been completed.

CONTRIBUTIONS TO CONJOINT WORK UNDERTAKEN AND INCLUDED IN THE PUBLISHED PAPERS IN THIS THESIS

The randomised trials and other outcome studies included in this thesis were all conceived and led by me, in collaboration with colleagues at the Royal Adelaide Hospital and Flinders Medical Centre in Adelaide, South Australia, and the Royal Hallamshire Hospital in Sheffield, UK. For all studies included in this thesis I -

- Jointly conceived the study concept with the colleagues acknowledged below
- Led the development and wrote the protocol for all trials
- Led, wrote, and managed all Ethics committee submissions
- Led, wrote, submitted and managed the 4 research grant applications that funded the randomized trials and other supporting infrastructure
- Coordinated the management of all trials
- Contributed substantially to the recruitment of participants in each trial
- Conducted the data analysis and wrote the initial publications for 6 of the 8 trials
- Led the publication of all other papers included in this thesis as senior and corresponding author, supervised the data analysis, and led the editing of all published papers.

Specific contributions to each study were:

Randomised trial of laparoscopic vs. open Nissen fundoplication

Ackroyd R, Watson DI, Majeed AW, Troy G, Treacy PJ & Stoddard CJ. Randomised clinical trial of laparoscopic versus open Nissen fundoplication for gastro-oesophageal reflux disease. Br J Surg (2004) ***91****:975-982.*

I jointly conceived the concept of this study with Dr Chris Stoddard and Professor Alan Johnson in 1993. I led the development, wrote the protocol and Ethics submission for this trial. I coordinated the management of this trial in 1993, and recruited the first 42 patients. After 1993, the trial was managed to completion by Dr Jon Treacy, Dr Ali Majeed and Dr Roger Ackroyd. Ms Gill Troy performed the oesophageal motility studies. I undertook an interim data analysis, and Dr Ackroyd undertook the final data analysis which underpinned the publication. Dr Ackroyd wrote the first draft of the paper. I edited the first draft before other authors edited my revised draft.

Division vs. non-division of the short gastric blood vessels during Nissen fundoplication

Watson DI, Pike GK, Baigrie RJ, Mathew G, Devitt PG, Britten-Jones R & Jamieson GG. Prospective double blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. Ann Surg (1997) ***226****:642-652.*

O'Boyle CJ, Watson DI, Jamieson GG, Myers JC, Game PA & Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication – a prospective double blind randomized trial with five year follow-up. Ann Surg (2002) ***235****:165-170.*

Yang H, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Randomized trial of division versus non-division of the short gastric vessels during laparoscopic Nissen fundoplication – 10 year outcomes. Ann Surg (2008) ***247****:38-42.*

Engström C, Jamieson GG, Devitt PG, Watson DI. Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of short gastric vessels during Nissen fundoplication. Br J Surg (2011) ***98****:1063-1067.*

I jointly conceived the concept of this study with Professor Glyn Jamieson in 1994. I led the trial development, and wrote the protocol and Ethics submission for this trial. I coordinated the management of this trial. Professor Glyn Jamieson, Dr Robert Britten-Jones, Professor Peter Devitt and Dr Philip Game all contributed patients to this trial. Dr George Mathew and Dr Robert Baigrie assisted me with recruitment of patients at the Royal Adelaide Hospital. Dr Greg Pike undertook the "blinded" clinical follow-up in the early stages after the trial, before research nurses were employed to complete the follow-up in a blinded fashion. Ms Jennifer Myers performed the oesophageal motility studies. For the 6 month outcome paper, I undertook the data analysis, wrote the first draft of this paper, and led publication submission. For the 5 year and 10 year outcome papers, I directly supervised surgical trainees - Dr Colm O'Boyle and Dr Huiqi Yang, who undertook the data analysis at those time points. Dr O'Boyle and Dr Yang wrote the first drafts of the papers reporting 5 and 10 year outcomes. I edited these first drafts to the submitted papers, and handled the papers as senior and corresponding author.

For the paper reporting analysis of combined Adelaide and Swedish data sets, I conceived the study design and worked with Dr Cecilia Engström to merge the data sets. Dr Cecilia Engström undertook the initial data analysis, and wrote the first draft

of the paper. I edited this first draft to the submitted paper, undertook some additional data analysis, and handled the papers as senior and corresponding author.

Anterior vs. posterior hiatal repair during Nissen fundoplication

Watson DI, Jamieson GG, Devitt PG, Kennedy A, Ellis T, Ackroyd R, Lafullarde T, Game PA. A prospective randomized trial of laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair. Arch Surg (2001) ***136****:745-751.*

Wijnhoven BPL, Watson DI, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair: long-term results of a randomized trial. Am J Surg (2008) ***195****:61-65.*

Chew CR, Jamieson GG, Devitt PG, Watson DI. Prospective randomised trial of laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair – late outcomes. World J Surg (2011) ***35****:2038-2044.*

I jointly conceived the concept of this study with Professor Glyn Jamieson in 1997. I led the trial development, wrote the protocol and Ethics submission for the trial, and coordinated the management of the trial. Professor Glyn Jamieson, Professor Peter Devitt and Dr Philip Game contributed patients to this trial. Dr Andrew Kennedy, Dr Roger Ackroyd and Dr Thierry Lafullarde assisted me with recruitment of patients at the Royal Adelaide Hospital. Ms Tanya Ellis coordinated the "blinded" clinical follow-up in this trial and Ms Jennifer Myers performed the oesophageal motility studies. For the 6 month outcome paper, I undertook the data analysis, wrote the first draft of this paper, and led publication submission. For the 5 year and 10 year outcome papers, I directly supervised surgical trainees - Dr Bas Wijnhoven and Dr Carolyn Chew, who undertook the data analysis at those time points. Dr Wijnhoven and Dr Chew wrote the first drafts of the papers reporting 5 and 10 year outcomes. I edited these first drafts to the submitted papers, and handled the papers as senior and corresponding author.

Anterior 180 degree partial fundoplication vs. Nissen fundoplication

Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M & Devitt PG. Prospective randomized double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg (1999) ***86****:123-130.*

Ludemann R, Watson DI, Game PA, Devitt PG & Jamieson GG. Laparoscopic total versus anterior 180^0 fundoplication - five year follow-up of a prospective randomized trial. Br J Surg (2005) ***92****:240-243.*

Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180^0 partial fundoplication. Br J Surg (2008) ***95****:1501-1505.*

Broeders JA, Roks DJ, Jamieson GG, Devitt PG, Baigrie RJ, Watson DI. Five year outcome after laparoscopic anterior partial versus Nissen fundoplication - Four randomized trials. Ann Surg (2012) ***255****:637-642.*

Gatenby PAC, Bright T, Watson DI. Anterior 180 Degree Partial Fundoplication – How I do it. J Gastrointest Surg (2012) ***16****:2297-2303.*

Broeders, JA, Broeders EA, Watson DI, Devitt PG, Holloway RH, Jamieson GG. Objective Outcomes 14 Years after Laparoscopic Anterior 180˚ Partial versus Nissen Fundoplication - Results from a Randomized Trial. Ann Surg (2013) ***258****:233-239.*

I jointly conceived the concept of this study and developed the surgical technique for laparoscopic Anterior 180 degree partial fundoplication with Professor Glyn Jamieson in 1995. I led the trial development, wrote the protocol and Ethics submission for this trial, and coordinated the management of this trial. Professor Glyn Jamieson, Dr Robert Britten-Jones, Professor Peter Devitt and Dr Philip Game all contributed patients to this trial. Dr Nick Davies and Dr Mark Richardson assisted me with recruitment of patients at the Royal Adelaide Hospital. Dr Greg Pike undertook the "blinded" clinical follow-up in the early stages after the trial, before research nurses were employed to complete the follow-up. Ms Jennifer Myers performed the oesophageal motility studies. For the 6 month outcome paper, I undertook the data analysis, wrote the first draft of this paper, and led publication submission. For the 5 year and 10 year outcome papers, I directly supervised surgical trainees - Dr Robert Ludemann and Dr Wang Cai, who undertook the data analysis at those time points. Dr Ludemann and Dr Cai wrote the first drafts of the papers reporting 5 and 10 year outcomes. I edited these first drafts to the submitted papers, and handled the papers as senior and corresponding author.

For the paper reporting analysis of combined Adelaide and Cape Town, South Africa data sets, I conceived the study design and worked with Dr Joris Broeders to merge the data sets. Dr Broeders undertook the data analysis, and wrote the first draft of the paper. I edited this first draft to the submitted paper, and handled the papers as senior and corresponding author.

The long term objective outcome study was also conceived by me. The protocol and detailed study design was refined by Dr Joris Broeders. Dr Broeders also performed the oesophageal function studies, conducted the data analysis, and wrote the first draft of the paper. I edited this first draft to the submitted paper, and substantially rewrote the paper to its final form.

The technique description paper was conceived by me, and written as an invited paper for the Journal of Gastrointestinal Surgery. The first draft of this paper was written by Dr Piers Gatenby with my assistance and the assistance of Dr Tim Bright. I edited the first draft to the submitted paper, provided all of the figures which illustrated the technique, and handled the paper as senior and corresponding author.

Anterior 90 degree partial fundoplication vs. Nissen fundoplication with division of the short gastric blood vessels

Krysztopik RJ, Jamieson, GG, Devitt PG & Watson DI. A further modification of the Nissen fundoplication – 90^0 anterior fundoplication. Surg Endosc (2002) ***16****:1446-1451.*

Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin C, Martin IJG, Nathanson LK, Windsor J. Multicentre prospective double blind randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. Arch Surg (2004) ***139****:1160-1167.*

Woodcock SA, Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin CJ, Martin IJG, Nathanson LK, Windsor JA. Quality of life following laparoscopic anterior 90^0 versus Nissen fundoplication - results from a multicentre randomized trial. World J Surg (2006) ***30****:1856-1863.*

Nijjar RS, Watson DI, Jamieson GG, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin IJG, Nathanson LK, Windsor J. Five year follow-up of a multicentre double blind randomized clinical trial of laparoscopic Nissen vs. anterior 90^0 partial fundoplication. Arch Surg (2010) ***145****:552-557.*

I led the development of the surgical technique for laparoscopic Anterior 90 degree partial fundoplication with Professor Glyn Jamieson in 1998. The trial protocol was developed in collaboration with surgeons from all Australian States and New Zealand

at meetings of the International Society for the Diseases of the Esophagus Australasian Section (IsDEAS) meetings in 1998 and 2000. I led the trial development, wrote the protocol and Ethics submissions, sourced funding, and coordinated the management of this trial. 15 surgeons (authors of the papers) each contributed up to 10 patients to this trial. For the 6 month outcome paper, I undertook the data analysis, wrote the first draft of this paper, and led publication submission. For the quality of life paper, I supervised Dr Sean Woodcock who analysed the data and wrote the first draft. I edited the first draft to the submitted paper, and handled this paper as senior and corresponding author. For the 5 year outcome paper, I supervised Dr Raj Nijjar (surgical trainee) who undertook the data analysis at that time point. Dr Nijjar wrote the first draft of the 5 year outcome paper, and I edited this draft to the submitted paper, and handled the paper as senior and corresponding author.

Anterior 90 degree partial fundoplication vs. Nissen fundoplication without division of the short gastric blood vessels

Spence GM, Watson DI, Jamieson GG, Lally CJ & Devitt PG. Single centre prospective randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. J Gastrointest Surg (2006) ***10:****698-705.*

Watson DI, Devitt PG, Smith L, Jamieson GG. Anterior 90^0 *partial vs Nissen fundoplication - 5 year follow-up of a single-centre randomized trial. J Gastrointest Surg (2012)* ***16****:1653-1658.*

I led the development of the second laparoscopic Anterior 90 degree partial fundoplication trial in 2002, wrote the protocol and Ethics submission, sourced funding, and coordinated the management of this trial. Professor Glyn Jamieson and Professor Peter Devitt also contributed patients to this trial. For the 6 month outcome paper, I supervised Dr Gary Spence, who undertook the data analysis, and wrote the first draft of this paper. I edited the first draft to the submitted paper, and handled this paper as senior and corresponding author. For the 5 year outcome paper, I undertook the data analysis, wrote the first draft of this paper, and led journal submission and publication.

Anterior 180 degree partial fundoplication vs. posterior partial fundoplication
Daud WMBW, Thompson SK, Jamieson GG, Devitt PG, Martin IJG, Watson DI. Randomized controlled trial of laparoscopic anterior 180° partial vs. posterior 270° partial fundoplication. ANZ J Surg (2014) DOI: 10.1111/ans.12476. (published online).

I led the development of the trial of Anterior 180 degree vs. Posterior partial fundoplication. This was conceived at a meeting of the International Society for the Diseases of the Esophagus Australasian Section (IsDEAS) in 2004, and the protocol was developed from discussions at this meeting. I wrote the final protocol and Ethics submissions, sourced funding, and coordinated the management of this trial. Professor Glyn Jamieson, Professor Peter Devitt. A/Professor Sarah Thompson, and Dr Ian Martin also contributed patients to this trial. Ms Lorelle Smith led the research nurses who collected the clinical follow-up data. For the outcome paper, I supervised Dr Najmi Daud, who undertook the data analysis, and wrote the first draft of this paper. I edited the first draft to the submitted paper, and handled this paper as senior and corresponding author.

Repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh
Watson DI, Thompson SK, Devitt PG, Smith L, Woods SD, Aly A, Gan S, Game PA, Jamieson GG. Laparoscopic repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh - a randomized controlled trial. Ann Surg (2015) ***261****:282-289.*

Koetje J, Irvine T, Thompson SK, Devitt PG, Woods SD, Aly A, Jamieson GG, Watson DI. Quality of life following repair of large hiatal hernia is improved but not influenced by use of mesh: Results from a randomized controlled trial. to World J Surg (2015) ***39****:1465-1473.*

Wijnhoven BPL & Watson DI. Laparoscopic repair of a giant hiatus hernia - How I do it. J Gastrointest Surg (2008) ***12****:1459-1464.*

I led the development of the mesh repair trial. The concept was developed at a meeting of the International Society for the Diseases of the Esophagus Australasian Section (IsDEAS) in 2004, and the protocol was developed following discussions at this meeting. I wrote the protocol and Ethics submissions, sourced funding, and coordinated the management of this trial. Professor Glyn Jamieson, Professor Peter Devitt. A/Professor Sarah Thompson, Dr Simon Woods and Dr Ahmad Aly also

contributed patients to this trial. Ms Lorelle Smith led the research nurses who collected the clinical follow-up data. For the clinical and objective outcome paper, I undertook the data analysis, wrote the first draft of the paper, submitted paper, and handled this paper as corresponding author. For the quality of life paper, I supervised Dr Jan Koetje who analysed the data and wrote the first draft. I edited the first draft to the submitted paper, and handled this paper as senior and corresponding author.

The technique description paper was conceived by me, and written as an invited paper for the Journal of Gastrointestinal Surgery. The first draft of this paper was written by Dr Bas Wijnhoven. I edited the first draft to the submitted paper, provided all of the figures which illustrated the technique, and handled the paper as senior and corresponding author.

Late outcome following fundoplication

Lafullarde T, Watson DI, Jamieson GG, Myers JC, Game PA & Devitt PG. Laparoscopic Nissen fundoplication – 5 year results and beyond. Arch Surg (2001) ***136****:180-184.*

Rice S, Watson DI, Lally CJ, Devitt PG, Game PA & Jamieson GG. Laparoscopic anterior 180-degree partial fundoplication - 5 year results and beyond. Arch Surg (2006) ***141****:271-275.*

Kelly J, Watson DI, Chin K, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication – clinical outcomes at 10 years. J Am Coll Surg (2007) ***205****:570-575.*

Chen Z, Thompson SK, Jamieson GG, Devitt PG, Game PA, Watson DI. Anterior 180 degree partial fundoplication – a 16 year experience with 548 patients. J Am Coll Surg (2011) ***212****:827-834.*

Engström C, Cai W, Irvine T, Devitt PG, Thompson SK, Game PA, Bessell JR, Jamieson GG, Watson DI. Twenty years of experience with laparoscopic antireflux surgery. Br J Surg (2012) ***99****:1415-1421.*

For the late outcome studies, I jointly conceived the concept of these studies with Professor Glyn Jamieson and Professor Peter Devitt. I established the database and follow-up processes that underpinned the outcomes reported in these papers, and sourced funding for the research nurses who conducted the clinical follow-up. My colleagues at the Royal Adelaide Hospital and Flinders Medical Centre contributed patients to the database that underpinned these studies. For each of these outcome

papers, I directly supervised the first authors who were surgical trainees. These trainees undertook the initial data analysis and wrote the first drafts of the papers reporting late outcomes. I undertook additional data analyses as required, edited the first drafts to the submitted papers, and handled the papers as senior and corresponding author.

FUNDING

The randomized trials included in this thesis were supported by research grants funded by the National Health and Medical Research Council (NHMRC) of Australia and the Royal Australasian College of Surgeons (RACS).

1. The Royal Australasian College of Surgeons Research Foundation - $12,000 (November 1994) for: Optimising the Results of Laparoscopic Anti-reflux Surgery (Investigator; DI Watson).

2. RACS Section of Upper GI/HPB Surgery / Astra Pharmaceuticals Upper GI Surgery Research Grant - $20,000 (1999) for Multicentre randomised trial of laparoscopic Nissen fundoplication versus anterior fundoplication for gastro-oesophageal reflux. (Investigators; D Watson et al).

3. National Health and Medical Research Council Competing Extended Project Grant (157986) - $275,923 (2001-2005) for: Randomised controlled trials of laparoscopic techniques for antireflux surgery (Investigators; DI Watson & GG Jamieson).

4. John Mitchell Crouch Fellowship, Royal Australasian College of Surgeons - $55,000 (2003)

5. National Health and Medical Research Council Competing Project Grant (375111) - $1,027,382 (2006-2010) for: Randomised controlled trials of laparoscopic techniques for antireflux surgery. (Investigators; DI Watson, GG Jamieson, CJ Martin, G Smith).

6. National Health and Medical Research Council Competing Project Grant (1022722) - $712,100 (2012-2016) for: Long term follow-up of randomised controlled trials for laparoscopic antireflux surgery. (Investigators; D Watson, G Jamieson, P Devitt, S Thompson).

PORTIONS OF WORK SUBMITTED FOR RESEARCH HIGHER DEGREES AT OTHER UNIVERSITIES

Preliminary data from the randomised trials of laparoscopic vs. open Nissen fundoplication, division vs. non-division of the short gastric blood vessels during Nissen fundoplication, and Anterior 180 degree partial vs. Nissen fundoplication were included in my earlier thesis entitled “Improving outcomes following surgery for gastro-oesophageal reflux disease”. This was awarded the degree of Doctor of Medicine (MD) in 1998 in the University of Adelaide. The papers pertinent to this earlier work are included in the current thesis to ensure that the relevant randomized trials are fully described. Papers included in the current thesis complete the recruitment for these trials, and extend the follow-up of participants for up to 10 more years.

The publication “Broeders, JA, Broeders EA, Watson DI, Devitt PG, Holloway RH, Jamieson GG. Objective Outcomes 14 Years after Laparoscopic Anterior 180˚ Partial versus Nissen Fundoplication - Results from a Randomized Trial. *Ann Surg* (2013) 258:233-239.” was included in a PhD thesis entitled Laparoscopic antireflux surgery - Indications, techniques and physiological effects” which was awarded by Utrecht University, the Netherlands, in 2011 to Dr Joris Broeders. Whilst Dr Broeders led the data analysis for this study, the work used data collected across a 16 year period under my supervision, I devised and proposed this study, and co-wrote the published paper.

SECTION 1

BACKGROUND - SURGERY FOR GASTRO-OESOPHAGEAL REFLUX AND HIATUS HERNIA

Gastro-oesophageal reflux is common, affecting between 10% and 40% of the population of most Western countries, and the treatment of reflux consumes significant health care resources (*Thompson WE 1982, Watson and Lally 2009*). A recent study from South Australia, revealed that 17% of the adult population currently consume medication for the treatment of reflux symptoms, and 10% of the population consume proton pump inhibitor medication either regularly or on an ad hoc basis to manage reflux symptoms (*Watson and Lally 2009*). Gastro-oesophageal reflux disease is caused by excessive reflux of gastric contents into the oesophageal lumen. Pathological reflux is usually associated with symptoms such as heartburn, upper abdominal pain and/or the regurgitation of gastric contents into the oropharynx.

Gastro-oesophageal reflux is associated with a range of contributing factors, and a multifactorial aetiology is likely. First is hiatus herniation, which is found in approximately half of individuals who undergo surgical treatment (*Watson, Pike et al. 1997, Watson, Jamieson et al. 1999*). This results in widening of the angle of His, effacement of the lower oesophageal sphincter and loss of the assistance of positive intra-abdominal pressure acting on the lower oesophagus. Second is the reduced lower oesophageal sphincter pressure, which is often found, although in many patients with reflux the resting lower oesophageal sphincter pressure is normal. Reflux in these patients results from an excessive number of transient lower oesophageal sphincter relaxation events (*Ireland, Holloway et al. 1993*). Other factors that might contribute to the genesis of reflux include abnormal oesophageal peristalsis (which causes poor clearance of refluxed fluid) and delayed gastric emptying.

The treatment of reflux is usually incremental, commencing with various levels of medical measures, surgery being reserved for patients with more severe disease, who either fail to respond adequately to medical treatment or who do not wish to take lifelong medication. Non-operative therapy treats the effects of reflux, but as the underlying reflux problem is not actually corrected, therapy for most patients must be continued indefinitely (*Dent 1990*). Surgical procedures, however, aim to be curative, preventing reflux by reconstructing an antireflux valve at the gastro-oesophageal junction (*Ireland, Holloway et al. 1993, Watson, Mathew et al. 1997*). Surgery has tended to be reserved for patients with complicated reflux disease or those with very severe symptoms. However, since the introduction of laparoscopic surgical approaches in the early 1990's some surgeons advocate utilising surgery at earlier stages in the course of reflux disease.

1.1 Non-surgical treatment for gastro-oesophageal reflux

A variety of simple measures might be helpful for the management of patients who experience mild reflux symptoms. These include simple antacids, the avoidance of precipitating factors such as spicy foods, and the avoidance of alcohol. Additional measures include weight loss (when appropriate), avoiding cigarette smoking, modification of the timing and quantity of meals (e.g. avoiding going to bed with a full stomach), and raising the bed head. Unfortunately, these measures are rarely effective for patients with moderate to severe gastro-oesophageal reflux disease, and most individuals who present for surgery cannot be adequately treated with these measures.

The first effective non-operative treatment for reflux was the development of the histamine type 2 (H_2)-receptor antagonists that reduced the production of acid by the stomach. These medications relieved or reduced mild to moderate reflux symptoms in some individuals (*Bate, Keeling et al. 1990*). However, with the development of proton-pump inhibitors, H_2-receptor antagonists are now rarely used as first-line medical therapy.

Proton-pump inhibitors (omeprazole, lanzoprazole, pantoprazole, rabeprazole and esomeprazole) were introduced into clinical practice in the late 1980s (*Dent 1990*). Proton-pump inhibitors are more effective for the relief of symptoms and achieve better healing of oesophagitis than H_2-receptor antagonists. However, patients with higher grades of oesophagitis have a higher failure rate with these medications (*Hetzel, Dent et al. 1988*), and some patients who initially achieve good symptom control go on to develop breakthrough symptoms at a later date, usually requiring an increased dose of medication to maintain symptom control. It is presumed that failure is due to inadequate acid suppression, although in some cases the presence of bile or duodenal fluid in the refluxate may play a role. In patients who respond well to proton-pump inhibitors, symptoms usually recur rapidly (sometimes in less than 24 hours) following cessation of medication, and for this reason lifelong medical treatment is likely to be required, unless surgery is performed. Some patients require escalating dosages of proton-pump inhibitors to control their symptoms. Overall, approximately 70% of individuals with moderate to severe symptoms of gastro-oesophageal reflux are satisfied with the symptom control achieved using proton pump inhibitor medication, but up to 85% still experience symptoms whilst using medication (*Chey, Mody et al.*

2009). Hence, a significant number of individuals with moderate to severe reflux symptoms continue to experience significant symptoms of reflux despite consuming regular proton-pump inhibitor medication, and many of these are candidates for surgery.

1.2 Surgical treatment for gastro-oesophageal reflux

The principle underlying the surgical management of gastro-oesophageal reflux disease is the creation of a mechanical antireflux barrier between the oesophagus and stomach. This works independently of the composition of the refluxate. Whilst medical therapy is effective in relieving symptoms for many patients with acid reflux, only surgery achieves effective control of duodeno-gastro-oesophageal reflux.

1.2.1 Selection of patients for antireflux surgery

Patients who undergo anti-reflux surgery should have objective evidence of reflux; i.e. erosive oesophagitis on endoscopy or excessive acid reflux demonstrated by 24-hour pH monitoring, and other conditions such as achalasia should be excluded by oesophageal manometry. However, none of the tests for reflux are sufficiently reliable to base all preoperative decisions on their outcome (*Waring, Hunter et al. 1995*), and some patients with troublesome reflux have either a normal 24-hour pH study or no evidence of oesophagitis at endoscopy (and, very occasionally, both). Hence, the tests must be interpreted in the light of the patient's clinical presentation, and a final recommendation for surgery must be based on all available clinical and objective information (*Waring, Hunter et al. 1995*). Impedance monitoring (in combination with pH monitoring) has been used more recently to measure "volume" reflux, although the additional information obtained from this investigation only occasionally influences surgical decision making (*Francis, Goutte et al. 2011*).

Patients selected for surgery generally fall into two groups: (1) patients who have failed to respond (or have responded only partially) to medical therapy; (2) patients whose symptoms are fully controlled by medications, but who do not wish to continue with medication throughout their lives. The first group represents the large majority of patients presenting for surgery, whereas the latter group are less common, and more likely to be younger patients who face decades of acid suppression to alleviate their symptoms. The response to surgery is usually more certain if the patient has had a good response to acid suppression in the past, or at least has had some symptom relief from medication. In patients who have had no response to proton-pump inhibitors,

particularly those presenting with atypical symptoms, their symptoms are often due to something other than reflux, despite concurrent objective evidence of reflux (which can be asymptomatic). Such patients will usually not benefit from antireflux surgery.

Barrett's oesophagus in itself is probably not an indication for antireflux surgery, rather it is evidence that the patient has gastro-oesophageal reflux disease. Patients with Barrett's oesophagus who have reflux symptoms should be selected for surgery on the basis of their symptoms and their response to medications, not simply be because they have a columnar-lined oesophagus (*Farrell, Smith et al. 1999*). There is currently no evidence to support the contention that antireflux surgery reduces the risk of Barrett's oesophagus progressing to cancer.

Other less common indications for antireflux surgery include reflux with respiratory complications. For example, when gastro-oesophageal regurgitation spills over into the respiratory tree, this can cause chronic respiratory illness, such as recurrent pneumonia, asthma or bronchiectasis. As the predominant action of proton-pump inhibitors is to block acid secretion, and the volume of reflux is not greatly altered, and these individuals will often benefit from surgery.

Other problems such as halitosis, chronic cough, chronic laryngitis, chronic pharyngitis, chronic sinusitis and loss of enamel on teeth are sometimes attributed to gastro-oesophageal reflux. On occasions such problems do arise in refluxing patients, but these problems in isolation are not reliable indications for surgery, and whether or not these symptoms will be relieved following surgery is often unpredictable (*Ratnasingam, Irvine et al. 2011*).

1.2.2 Medical versus surgical therapy

The issue of the most appropriate treatment for gastro-oesophageal reflux disease has been the subject of disagreement between surgeons and gastroenterologists, although most would agree that a single management strategy is unlikely to be appropriate for all patients. Eight randomised trials *(Behar, Sheahan et al. 1975, Spechler 1992, Ortiz, Martinez de Haro et al. 1996, Lundell, Miettinen et al. 2000, Lundell, Miettinen et al. 2001, Parrilla, Martinez de Haro et al. 2003, Mahon, Rhodes et al. 2005, Anvari, Allen et al. 2006, Mehta, Bennett et al. 2006, Attwood, Lundell et al. 2008, Lundell, Attwood et al. 2008, Lundell, Miettinen et al. 2009, Anvari, Allen et al. 2011, Goeree, Hopkins et al. 2011*) have been reported that have investigated the issue of medical vs.

surgical therapy, although five of these were completed or commenced before the availability of both laparoscopic antireflux surgery or proton pump inhibitor medication. In general, the protocol for each of these trials entailed recruiting patients who had reflux symptoms that were well controlled by medical therapy. For the latter trials this entailed complete symptom control with a proton pump inhibitor at trial commencement, and patients with uncontrolled symptoms were excluded. Hence, the surgical groups in these trials excluded the patients who represent the majority of those currently selected for surgery, i.e. patients with a poor response to a proton-pump inhibitor.

The first large trial was reported in 1992 by Spechler et al (*Spechler 1992*). Two hundred and forty seven patients (predominantly men) were randomised to either continuous medical therapy with a H_2 blocker, medical therapy for symptoms only or an open Nissen fundoplication. Overall patient satisfaction was highest following surgery at 1 and 2 years follow-up. However, neither the surgical approach nor the medical treatment investigated is now considered to be optimal. The longer-term outcomes from this study were published in 2001, with median follow-up of approximately 7 years and with proton-pump inhibitors now used for the medically treated patients (*Spechler, Lee et al. 2001*). Follow-up was not complete and only 37 (45%) surgical patients were available for late follow-up, with 23% of the original surgical group lost to follow-up, and 32% died during follow-up. The later results did, however, show reasonable outcomes in both the medically and surgically treated groups. However, 62% of the surgical patients consumed some form of antireflux medication at late follow-up, although when these medications were ceased in both the study groups the surgical group had significantly less reflux symptoms than the medical group, suggesting that most of the surgical patients did not actually need the medications.

In 2003 Parrilla et al *(Parrilla, Martinez de Haro et al. 2003*) reported a randomised trial that randomised 101 patients with Barrett's oesophagus. Medical therapy was initially a H_2 blocker and later a proton-pump inhibitor. A satisfactory clinical outcome was achieved at 5 years follow-up in 91% of each group, although medical treatment was associated with a poorer endoscopic outcome. Progression to dysplasia was similar in both groups.

In 2000 Lundell and colleagues (*Lundell, Miettinen et al. 2000, Lundell, Miettinen et al. 2001, Lundell, Miettinen et al. 2009*) reported a trial of proton-pump inhibitor medication vs. open antireflux surgery. Three hundred and ten patients were randomised, and antireflux surgery achieved a better outcome at up to 3 years follow-up. Later reports of 7 years follow-up in 228 patients, and 12 years follow-up in 124, confirmed that surgery still achieved better reflux control than medication, although dysphagia and various wind-related side-effects were more common after fundoplication (*Lundell, Miettinen et al. 2007, Lundell, Miettinen et al. 2009)*.

Rhodes et al reported the first randomised trial to compare proton-pump inhibitor medication with laparoscopic Nissen fundoplication; 217 patients were enrolled. Surgery was followed by less oesophageal acid exposure 3 months after treatment, and better symptom control at 12 months (*Cookson, Flood et al. 2005, Mahon, Rhodes et al. 2005, Mehta, Bennett et al. 2006*). A similar study from Anvari et al enrolled 104 patients into a trial of proton-pump inhibitor therapy vs. laparoscopic Nissen fundoplication (*Anvari, Allen et al. 2006, Anvari, Allen et al. 2011, Goeree, Hopkins et al. 2011*). Follow-up at 12 months and 3 years demonstrated better control of reflux and better quality of life in the patients who underwent surgery.

In 2009, Lundell et al (*Lundell, Miettinen et al. 2009*) reported the outcomes for a further multicentre of laparoscopic Nissen fundoplication vs. esomeprazole proton pump inhibitor therapy (20-40 mg per day). This trial, which was funded by the pharmaceutical company that provided the medical therapy, enrolled 554 patients and outcomes at up to 3 years have been reported. Similar success rates of approximately 90% were reported for each treatment.

The results from all of these randomized trials support the application of surgery for the treatment of gastro-oesophageal reflux, and potentially a wider role in the management of reflux in proton pump inhibitor dependent patients with symptoms that are well controlled by medication.

1.2.3 Pros and cons of antireflux surgery

Surgery has some significant advantages over medical management for the treatment gastro-oesophageal reflux disease. The operation actually cures the problem, i.e. stops gastric contents from refluxing into the oesophagus. Hence patients treated by surgery

should be able to eat whatever foods they choose, lie flat and bend over without reflux occurring, and importantly they do not need to take any tablets.

A disadvantage, however, is the morbidity associated with the operation. Whilst laparoscopic surgery reduces the pain associated with the open operation, most patients have difficulty in swallowing in the immediate postoperative period, although in the great majority this is only temporary *(Watson, Jamieson et al. 1996*). Most patients also feel full quickly after eating even small meals, and this often leads to some postoperative weight loss *(Watson, Pike et al. 1997*). In patients who are overweight at the time of surgery (the majority!) this is sometimes seen as an advantage. This restriction on meal size usually disappears within the first 6 to 12 months.

Because fundoplication often produces a one-way valve, swallowed air that has passed into the stomach usually cannot pass back through the valve. Thus, patients may not be able to belch effectively after surgery, especially in the first 6 to 12 months (*Ackroyd, Watson et al. 1999*). This probably applies more to patients who undergo a Nissen (total) fundoplication. For similar reasons, all patients will be unable to vomit after an effective procedure. As swallowed gas is often not belched effectively, the majority of patients are also aware of increased passage of wind after the procedure (*Gotley, Smithers et al. 1996*). Despite these possible disadvantages, the overwhelming majority of patients (approximately 90%) claim that the disadvantages are far outweighed by the advantages of the operation *(Trus, Laycock et al. 1996, Watson, Jamieson et al. 1996, Watson, Pike et al. 1997, Watson, Jamieson et al. 1999*).

1.3 Fundoplication for gastro-oesophageal reflux

The fundoplication introduced by Nissen in 1956, or some variant of it, remains the most commonly performed antireflux operation in the world today. Total fundoplications, such as the Nissen, or partial fundoplications, whether anterior or posterior, probably all work in a similar fashion (*Watson, Mathew et al. 1997, Watson, Mathew et al. 1998*), and that fashion is almost certainly mechanical rather than physiological, based on the creation of a flap valve. It has been demonstrated that all of these procedures are effective when constructed using bench-top models, i.e. ex vivo (*Watson, Mathew et al. 1997*). The principles of fundoplication are to mobilise the lower oesophagus, wrap the fundus of the stomach, either partially or totally,

around the oesophagus, and then stabilise the new anatomy long term. When the oesophageal hiatus is enlarged, it is narrowed by sutures to prevent paraoesophageal herniation postoperatively and also to prevent the wrap being pulled up into the chest.

1.3.1 Mechanisms of action of antireflux operations

The proposed mechanisms of action of an antireflux operation include:

1. The creation of a floppy valve by maintaining close apposition between the abdominal oesophagus and the gastric fundus - as intragastric pressure rises the intra-abdominal oesophagus is compressed by the adjacent fundus. This mechanism is independent of the basal pressure at the gastro-oesophageal junction.
2. Exaggeration of the flap valve at the angle of His.
3. Increase in the basal pressure in the vicinity of the lower oesophageal sphincter, generated by the fundoplication.
4. Reduction in the triggering of transient lower oesophageal sphincter relaxations.
5. Reduction in the filling capacity of the gastric fundus, thereby speeding proximal and total gastric emptying.
6. Prevention of effacement or stretching of the lower oesophagus (which effectively weakens the lower sphincter).

As the procedures even ex vivo work (*Watson, Mathew et al. 1997*), it is likely that the first two mechanisms account for the efficacy of the majority of antireflux procedures. The increase in lower oesophageal sphincter pressure following surgery is probably not critical, and in some partial fundoplication procedures there is very little increase in pressure, yet reflux is well controlled *(Watson, Jenkinson et al. 1991, Watson, Jamieson et al. 1999*).

The various different antireflux operations all have their advocates. However, no one procedure yields perfect results, i.e. 100% cure of reflux and no side-effects. As published reports can be found that support every known procedure, it is better to consider results from randomised trials when assessing the merits of these procedural variants rather than relying on uncontrolled outcomes reported by advocates of a single procedure.

1.3.1.1 Nissen fundoplication

The Nissen fundoplication is the most commonly performed antireflux operation worldwide. Nissen originally described a procedure that entailed mobilisation of the oesophagus from the diaphragmatic hiatus, reduction of any hiatus hernia into the abdominal cavity, preservation of the vagus nerves and mobilisation of the posterior gastric fundus around behind the oesophagus without dividing the short gastric vessels, and suturing of the posterior fundus to the anterior wall of the fundus using non-absorbable sutures, thereby achieving a complete wrap of stomach around the intra-abdominal oesophagus (*Nissen 1956*). The original fundoplication was 5 cm in length and an oesophageal bougie was not used to calibrate the wrap.

Because this procedure was associated with an incidence of persistent postoperative dysphagia, gas bloat syndrome and an inability to belch, the procedure has been progressively modified in an attempt to improve the long-term outcome. Most surgeons agree that calibration of the wrap with a large (52 Fr) intraoesophageal bougie, and shortening the fundoplication to 1–2 cm in length, reduces the risk of side effects (*DeMeester, Bonavina et al. 1986*). Furthermore, whilst the need for routine hiatal repair was uncertain in the era of open surgery, most surgeons routinely include this step during laparoscopic antireflux surgery. Omission of this step is associated with a higher incidence of postoperative hiatal herniation (*Watson, Jamieson et al. 1995*). The hepatic branch of the vagus nerve is also usually preserved during this procedure to stabilise the fundoplication, and preserve pyloric innervation.

However, controversy exists about the need to divide the short gastric vessels to achieve full fundal mobilisation. The so-called floppy Nissen procedure described by Donahue and Bombeck relies on extensive fundal mobilization (*Donahue PE 1977*). On the other hand, the modification of the Nissen fundoplication using the anterior fundal wall alone, also first described by Nissen and Rossetti (*Nissen 1956, Rossetti and Hell 1977*), does not require short gastric vessel division to construct the fundoplication. This simplifies the dissection, although more judgement and experience might be required to select the correct piece of stomach for construction of a sufficiently loose fundoplication. Both procedures have their advocates, and good results (90% good or excellent long-term outcomes) have been reported for both variants *(Rossetti and Hell 1977, DeMeester, Bonavina et al. 1986*). Nevertheless, strong opinions are held about whether the short gastric vessels should be divided or

not, and this controversy was heightened around the time that laparoscopic fundoplication techniques were introduced.

1.3.1.2 Posterior partial fundoplication

A variety of fundoplication operations have been described in which the fundus is wrapped around the back of the oesophagus, with the aim of reducing the possible side-effects of total fundoplication which probably result from over-competence of the cardia, i.e. dysphagia and gas-related problems. Toupet described a posterior partial fundoplication in which the fundus is passed behind the oesophagus and sutured to the left lateral and right lateral walls of the oesophagus, as well as to the right diaphragmatic pillar, creating a 270° posterior fundoplication (*Toupet 1963*). A similar procedure was described by Lind et al (*Lind JF 1965*). This entails a 300° posterior fundoplication, which is constructed by suturing the fundus to the oesophagus at the left and right lateral positions, and additionally anteriorly on the left, leaving a 60° arc of oesophageal wall uncovered. The hiatus is repaired if necessary.

1.3.1.3 Anterior partial fundoplication

Several anterior partial fundoplication procedures have been described, and all purport to reduce the incidence of dysphagia and other side-effects. The Belsey Mark IV procedure, popular in thoracic practice up the early 1990's entails a 240° anterior partial fundoplication that was performed through a left thoracotomy approach (*Belsey 1977*). The distal oesophagus is mobilised, sutured to the gastric fundus and sutured to the diaphragm. Any hiatus hernia is repaired, and the anterior two-thirds of the abdominal oesophagus is covered by the fundoplication The open thoracic access required is associated with significant morbidity, and for this reason this procedure fell from favour following the arrival of abdominal approaches to antireflux surgery. A minimally invasive thoracoscopic approach has been described (*Nguyen, Schauer et al. 1998*), although clinical outcomes have not been reported, and this procedure is rarely performed.

The Dor procedure is an anterior hemi-fundoplication that involves suturing of the fundus to the left and right sides of the oesophagus (*Dor, Humbert et al. 1967*). The Dor procedure is commonly used in combination with an abdominal cardiomyotomy for achalasia as it is unlikely to cause dysphagia, and it reduces the risk of gastro-oesophageal reflux following cardiomyotomy.

An anterior 120 degree fundoplication has also been described (*Watson, Jenkinson et al. 1991*). This entails reduction of any hiatus hernia, posterior hiatal repair, suture of the posterior oesophagus to the hiatal pillars posteriorly, suture of the fundus to the diaphragm to accentuate the angle of His, and creation of an anterior partial fundoplication by suturing the fundus to the oesophagus on the right anterolateral aspect. Satisfactory medium-term reflux control following open surgery has been reported for this procedure, and also a low incidence of gas-related problems. However, published laparoscopic experience is more limited.

This thesis reports the results from prospective randomised trials of laparoscopic anterior 180° partial fundoplication and laparoscopic anterior 90° partial fundoplication vs. Nissen fundoplication (*Watson, Jamieson et al. 1999, Watson, Jamieson et al. 2004, Ludemann, Watson et al. 2005, Spence, Watson et al. 2006, Cai, Watson et al. 2008, Nijjar, Watson et al. 2010*). The full details and rationale underpinning these approaches will be detailed later. The anterior 180° fundoplication procedure entails hiatal repair, suture of the distal oesophagus to the hiatal rim and construction of an anterior fundoplication that is sutured to the oesophagus and the hiatal rim on the right and anteriorly. Sutures between the left oesophagus and the adjacent fundus are often omitted when performing this procedure. The anterior 90° partial fundoplication procedure entails hiatal repair, posterior oesophagopexy, narrowing of the angle of His, and construction of a limited anterior fundoplication that covers the left anterolateral aspect of the oesophagus.

1.3.1.4 Hill procedure

Hill described a procedure that is often regarded as a gastropexy rather than a fundoplication (*Hill 1967*). However, it also plicates the cardia and when examined endoscopically the intragastric appearances are similar to an anterior partial fundoplication. The procedure entails suturing the anterior and posterior phreno-oesophageal bundles to the pre-aortic fascia and the median arcuate ligament. Whilst excellent results have been reported by Hill and colleagues (*Aye, Hill et al. 1994*), it has not been applied widely because most surgeons have difficulty understanding the anatomical principles and, in particular, the so-called phreno-oesophageal bundles are not clear structures. Hill also emphasised the need for intraoperative manometry. This is not widely available, limiting the dissemination of his technique.

1.3.1.5 Collis procedure

The Collis procedure is proposed for patients with a large hiatus hernia in whom the oesophagogastric junction cannot be reduced below the diaphragm; i.e. a shortened oesophagus (*Jobe, Horvath et al. 1998*). The frequency of this situation in current practice is controversial, with significant disagreement between surgeons who apply this procedure frequently vs. those that virtually never use this option. The Collis procedure entails the construction of a tube of gastric lesser curve to recreate an abdominal length of "oesophagus", around which a fundoplication can then be constructed. Laparoscopic and thoracoscopic techniques for this procedure have been described (*Swanstrom, Marcus et al. 1996, Johnson, Oddsdottir et al. 1998*). A disadvantage of this procedure is that the gastric tube does not have peristaltic activity and furthermore it can secrete acid. This probably contributes to a poorer overall success rate for this procedure, along with the end-stage nature of the reflux disease that led to the choice of this procedure in the first place.

1.3.2 Laparoscopic antireflux surgery

Laparoscopic Nissen fundoplication was first reported in 1991 (*Dallemagne, Weerts et al. 1991, Geagea 1991*) and rapidly established itself as the procedure of choice for reflux disease, with the vast majority of antireflux procedures now performed laparoscopically. Long-term clinical follow-up has been reported more recently in several large series (*Cowgill, Gillman et al. 2007, Kelly, Watson et al. 2007*). These series confirm that laparoscopic Nissen fundoplication is effective, and that 10 years after surgery it achieves an excellent clinical outcome in at least 85–90% of patients. However, several complications and side effects seen in the open surgical era remain an issue following laparoscopic fundoplication, and some issues which appear to be unique to the laparoscopic approach have also been described, including hiatal stenosis and a higher incidence of post-operative hiatus hernia (*Watson, Jamieson, Mitchell et al. 1995, Watson, Jamieson, Devitt et al. 1995*).

Dysphagia in the early recovery period following fundoplication is seen in most individuals, and persists in the longer term in a smaller proportion of individuals who have undergone surgery. The proportion of individuals reporting dysphagia probably varies with the duration of follow-up time and between different procedure types (*Engstrom, Cai et al. 2012*). Recurrent reflux also develops in some individuals, and its prevalence also increases with longer follow-up and varies between different procedures (*Engstrom, Cai et al. 2012*). Other problems include bloating and

flatulence symptoms, which also vary with length of follow-up and the procedure type. Overall, up to 10% of patients appear to be dissatisfied with their outcome following antireflux surgery. This dissatisfaction can arise following recurrent gastro-oesophageal reflux, because of a complication of the original surgery, or because of persistent side effects.

Because the Nissen fundoplication procedure appears to be associated with a higher risk of postoperative dysphagia, gas bloat and other gas-related symptoms, the relative merits of Nissen vs. various partial fundoplication variants have been debated for many years. It appears that the Nissen procedure produces an over-competent gastro-oesophageal junction, and this probably contributes to the problems of dysphagia and gas bloat (*DeMeester, Bonavina et al. 1986, Watson, Pike et al. 1997*). On the other hand, it has been suggested that partial fundoplications reduce the risk of over-competence, but perhaps at the expense of a less durable antireflux repair (*Toupet 1963, Watson, Jenkinson et al. 1991, Watson, Jamieson et al. 1999)*. Prospective randomised trials of Nissen vs. partial fundoplication have now been performed, including the trials described in this thesis, and these will be discussed in context later.

It is also important to realize that dysphagia following fundoplication is not always directly associated with the fundoplication or a technical error in its construction. Early laparoscopic Nissen fundoplication case series reported an incidence of "hiatal stenosis" or a tight diaphragmatic hiatus, a situation resulting in a tight ring of scar tissue encircling the distal oesophagus (*Watson, Jamieson et al. 1995*). Furthermore, revision surgery undertaken for dysphagia following laparoscopic Nissen fundoplication more often addresses a tight oesophageal hiatus, and rarely a tight fundoplication (*Watson, Jamieson et al. 1999*). This highlights the potential for the method of hiatal repair to contribute to post-fundoplication dysphagia, and suggests that modifying the techniques used for hiatal repair might also be considered to reduce the risk of post-fundoplication dysphagia.

Steps that have been recommended to reduce the risk of side effects and complications following fundoplication, whilst not compromising the efficacy of reflux control, include:

- Undertake the surgery using a laparoscopic approach
- Perform a short, loose Nissen fundoplication
- Calibrate the fundoplication using an intra-oesophageal bougie

- Anchor the fundoplication to the diaphragm using “pexy” sutures
- Divide the short gastric blood vessels when constructing a Nissen fundoplication
- Perform a partial fundoplication - anterior or posterior
- Do not over tighten the oesophageal hiatus during hiatal repair

1.4 Large hiatus hernia

Patients undergoing surgery for a very large hiatus hernia often present with a different clinical scenario to those presenting for antireflux surgery. Whilst many individuals report symptoms of troublesome gastro-oesophageal reflux, the dominant presentation in many individuals is with mechanical symptoms associated with rotation and twisting of the stomach, rather than conventional reflux symptoms. This presentation can entail episodes of chest pain, vomiting and dysphagia, as well as acute presentations with gastric volvulus in a subgroup of individuals. Some patients present with anaemia, but few other symptoms. Work-up requires assessment of anatomy, and this is best achieved using radiological studies such as barium meal examination or CT scan. As a rough rule of thumb, 50% or more of the stomach within the chest is associated with a significant risk of mechanical symptoms, and if this scenario is seen in younger patients (less than 60 years old) surgery can be recommended even if symptoms are not present. All fit symptomatic older patients should be considered for surgical repair.

Laparoscopic approaches to surgery for very large hiatus hernia are now standard clinical practice. In the early days of laparoscopic antireflux surgery this problem represented less than 10% of the antireflux surgery and hiatus hernia repair caseload (*Engstrom, Cai et al. 2012*). However, as laparoscopic techniques for repair have become more reliable, surgeons have been referred more patients with very large hiatus hernias, and in recent years the number of patients with this problem has increased to comprise approximately 50% of the laparoscopic antireflux surgery workload in countries like Australia (*Engstrom, Cai et al. 2012*), perhaps partly offset by less operations for gastro-oesophageal reflux.

In the 1990’s, the standard approach to laparoscopic repair of very large hiatus hernias entailed complete dissection of the hernia sac from the mediastinum, hiatal repair with sutures and a fundoplication (*Edye, Salky et al. 1998, Watson, Davies et al. 1999*). Whilst good clinical outcomes were reported following laparoscopic repair, with clinical success rates of approximately 90% described *(Edye, Salky et al. 1998, Watson, Davies et al.*

1999), later studies utilising barium meal radiology follow-up identified that sutured repair is followed by radiological recurrence rates of approximately 25-30%, although only a few of these individuals actually develop symptoms from the recurrent hernia or require further surgery (*Aly, Munt et al. 2005*). Nevertheless, concern remains that patients with an asymptomatic recurrence could develop problems later.

Mesh repair has been suggested as a strategy to prevent hernia recurrence, as it applies the principles of groin hernia repair, i.e. tension-free repair with prosthetic reinforcement, and it is technically straightforward to perform laparoscopically. Whilst good results have been reported from case series of mesh repair, some surgeons have been concerned that the potential advantages of mesh repair might be offset by the risk of the mesh eroding into the esophageal lumen, and other complications (*Frantzides, Carlson et al. 2010*). Difficulties also occur when assessing the outcomes of mesh repair, as there is great variability between mesh types and configurations, and little standardization of surgical techniques.

Three previously reported randomized trials have examined the impact of mesh repair of the esophageal hiatus, two in the context of very large hiatus hernia (*Frantzides, Madan et al. 2002, Granderath, Schweiger et al. 2005, Oelschlager, Pellegrini et al. 2006, Oelschlager, Pellegrini et al. 2011*). In one study, Frantzides et al enrolled 72 patients to undergo repair with sutures vs. a piece of polytetrafluoroethylene mesh and the results at median 2.5 years follow-up showed a reduction in hernia recurrence from 22% to 0% (*Frantzides, Madan et al. 2002*). In a second study, Oeschlager et al reported 6 month outcomes from a multicenter trial of 108 patients who underwent repair with sutures vs. an absorbable mesh, and hernia recurrence was reduced from 24% to 9% (*Oelschlager, Pellegrini et al. 2006*). Later follow-up, however, revealed no outcome differences (*Oelschlager, Pellegrini et al. 2011*). Currently there is ongoing uncertainty about the preferred technique for repair of very large hiatus hernia, with surgeons disagreeing about whether or not to use mesh, and if mesh is used, what type of mesh and what configuration is optimal. Further randomized trials are needed to inform this debate.

1.5 The need for better evidence

Unfortunately, the perfect operations for the treatment of gastro-oesophageal reflux or repair a large hiatus hernia are yet to be described. For antireflux surgery, the issues that must be considered include the risk of recurrent reflux vs. side effects, and for hiatus hernia repair the critical issue is the risk of hernia recurrence vs. side effects or

complications. By refining technique, all surgeons hope to improve outcomes, but how can this be done in an evidence based manner?

When assessing the evidence pertinent to the different surgical approaches to antireflux surgery and hiatus hernia surgery, it is apparent that much of the evidence cited to support different approaches is sourced from uncontrolled case series (*Dallemagne, Weerts et al. 1996, Trus, Laycock et al. 1996, Cowgill, Gillman et al. 2007*), or case series compared to historical controls (*Donahue PE 1977, DeMeester, Bonavina et al. 1986, Hunter, Swanstrom et al. 1996*). The risk of bias in these studies is significant, and the evidence from these studies rates poorly in the evidence based medicine hierarchies. Furthermore, as many studies report only short term outcomes, the placebo effect can introduce an additional risk of bias. In sham endoscopy vs. endoscopic antireflux procedure trials reported a decade ago, the placebo effect was shown to persist for at least 6 months, with sham procedures relieving reflux symptoms in up to 50% of individuals at short term follow-up (*Rothstein, Filipi et al. 2006, Schwartz, Wellink et al. 2007*)! Hence, when deciding how to best undertake surgery for reflux and hiatus hernia, evidence from well conducted randomized controlled trials, with long term follow-up, is needed to underpin sound decision making.

1.6 Aims

The studies included in this thesis address the need for higher quality evidence and represent a series of randomized controlled trials undertaken across a period of 22 years. These trials aimed to identify the best operation for the surgical treatment of gastro-oesophageal reflux disease, and for repair of hiatus hernia, i.e. an operation with a low rate of complications and adverse outcomes, and excellent long term reflux control. To do this the trials systematically and incrementally evaluated proposed improvements in surgical technique. These trials address modifications to procedures which aimed to improve the overall outcome following surgery for gastro-oesophageal reflux and hiatus hernia by reducing surgical morbidity, and reducing the risk of side effects and other adverse outcomes following fundoplication, whilst still achieving good long term control of gastro-oesophageal reflux, and stable post-surgical anatomy.

The trials were designed to answer the following questions:

- Can laparoscopic surgical access for Nissen fundoplication improve outcome by reducing the risk of complications and speeding recovery?

- Can the outcomes following Nissen fundoplication be improved? Approximately 10% of patients have a less than optimal outcome following this procedure.
- Is division of the short gastric blood vessels during Nissen fundoplication necessary?
- An anterior partial fundoplication achieves effective reflux control in patients undergoing surgery for achalasia, and also in individuals with reflux and very poor oesophageal motility. Can an anterior partial fundoplication outperform the Nissen fundoplication and achieve good results in all patients undergoing surgery for reflux?
- What type of partial fundoplication achieves the best balance between control of reflux and minimization of side effects - anterior vs. posterior partial?
- As conventional hiatal repair with posterior placement of sutures might contribute to dysphagia following Nissen fundoplication, can the risk of dysphagia be reduced by repairing the hiatus in front of the oesophagus; i.e. anteriorly?
- Can mesh reinforcement of the oesophageal hiatus during repair of very large hiatus hernia reduce the risk of hernia recurrence?

1.7 Hypotheses tested in randomised controlled trials

1) The laparoscopic approach to Nissen fundoplication is followed by quicker recovery and a reduced risk of complications compared to open Nissen fundoplication.
2) Division of the short gastric blood vessels during Nissen fundoplication is followed by a lower incidence of post-fundoplication dysphagia.
3) Anterior hiatal repair during Nissen fundoplication is followed by a lower incidence of post-fundoplication dysphagia, compared to posterior hiatal repair.
4) Anterior 180 degree partial fundoplication is followed by a lower incidence of dysphagia and other side effects, but equivalent reflux control, compared to Nissen fundoplication.
5) Anterior 90 degree partial fundoplication is followed by a lower incidence of dysphagia and other side effects, but equivalent reflux control, compared to Nissen fundoplication.

6) Anterior 180 degree partial fundoplication is followed by a lower incidence of dysphagia and other side effects, but equivalent reflux control compared to Posterior partial fundoplication.
7) Mesh reinforcement of sutured hiatal repair of very large hiatus hernia is followed by a reduced risk of hernia recurrence.

SECTION 2

RANDOMISED TRIALS FOR ANTIREFLUX SURGERY AND HIATUS HERNIA

Randomised trials

Randomised trials addressing the following issues were conducted;

1) Laparoscopic vs. open Nissen fundoplication
2) Division vs. non-division of the short gastric blood vessels during Nissen fundoplication
3) Anterior vs. posterior hiatal repair during Nissen fundoplication
4) Anterior 180 degree partial fundoplication vs. Nissen fundoplication
5) Anterior 90 degree partial fundoplication vs. Nissen fundoplication (2 trials)
6) Anterior 180 degree partial fundoplication vs. Posterior partial fundoplication
7) Repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh

2.1 Laparoscopic vs. open Nissen fundoplication

Ackroyd R, Watson DI, Majeed AW, Troy G, Treacy PJ & Stoddard CJ. Randomised clinical trial of laparoscopic versus open Nissen fundoplication for gastro-oesophageal reflux disease. *Br J Surg* (2004) **91**:975-982.

This randomized trial compared laparoscopic vs. open Nissen fundoplication. The paper reported clinical and objective outcomes at 12 months follow-up.

Randomized trial

Randomized clinical trial of laparoscopic *versus* open fundoplication for gastro-oesophageal reflux disease

R. Ackroyd, D. I. Watson, A. W. Majeed, G. Troy, P. J. Treacy and C. J. Stoddard

Department of Surgery, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK
Correspondence to: Mr R. Ackroyd (e-mail: roger.ackroyd@sth.nhs.uk)

Background: **The aim of this study was to compare laparoscopic and open Nissen fundoplication for gastro-oesophageal reflux disease in a randomized clinical trial.**
Methods: **Ninety-nine patients were randomized to either laparoscopic (52) or open (47) Nissen fundoplication. Patients with oesophageal dysmotility, those requiring a concurrent abdominal procedure and those who had undergone previous antireflux surgery were excluded. Independent assessment of dysphagia, heartburn and patients' satisfaction 1, 3, 6 and 12 months after surgery was performed using multiple standardized clinical grading systems. Objective measurement of oesophageal acid exposure and lower oesophageal sphincter pressure before and after surgery, and endoscopic assessment of postoperative anatomy, were performed.**
Results: **Operating time was longer in the laparoscopic group (median 82 *versus* 46 min). Postoperative pain, analgesic requirement, time to solid food intake, hospital stay and recovery time were reduced in the laparoscopic group. Perioperative outcomes, postoperative dysphagia, relief of heartburn and overall satisfaction were equally good at all follow-up intervals. Reduction in oesophageal acid exposure, increase in lower oesophageal sphincter tone and improvement in endoscopic appearances were the same for the two groups.**
Conclusion: **The laparoscopic approach to Nissen fundoplication improved early postoperative recovery, with an equally good outcome up to 12 months.**

Presented to a meeting of the Association of Upper Gastrointestinal Surgeons, Portsmouth, UK, September 2003, and published in abstract form as *Gut* 1994; **35**(Suppl 2): S15

Paper accepted 24 February 2004

Published online 14 May 2004 in Wiley InterScience (www.bjs.co.uk). **DOI:** 10.1002/bjs.4574

Introduction

Antireflux surgery is the treatment of choice for moderate to severe gastro-oesophageal reflux disease, particularly in patients with reflux symptoms that have not responded fully to medical therapy, or who do not wish to continue medication indefinitely. The most commonly performed procedure is the Nissen 360° fundoplication, with long-term success achieved in around 90 per cent of patients[1–3].

Over the past decade, the development of laparoscopic techniques has changed the way in which antireflux surgery is performed, with the perceived advantages of a minimally invasive approach making fundoplication more acceptable. This may have contributed to the increase in the number of patients undergoing fundoplication in many countries. Although in the open surgical era, surgery was often reserved for patients with complicated reflux or very severe symptoms, the introduction of laparoscopic approaches may have resulted in a tendency to operate at an earlier stage[4].

Non-randomized comparisons of open and laparoscopic fundoplication have suggested that the incidence of postoperative complications may be reduced and the length of postoperative hospital stay shortened with the laparoscopic approach, although the procedure takes longer[5,6]. Furthermore, the efficacy of reflux control appears to be similar for the two approaches.

Seven randomized trials comparing laparoscopic total fundoplication with an open surgical equivalent have been published as full papers[7–13]. Although follow-up in these studies was generally short, the differences between open and laparoscopic approaches were of lesser magnitude than

those noted in the earlier non-randomized studies. The trials have demonstrated that the laparoscopic approach may improve short-term outcome.

Longer-term outcomes from laparoscopic case series have also been reported recently, with success rates of approximately 90 per cent at 5–8 years[14,15]. Despite this, some surgeons believe that this approach may lead to a higher incidence of postoperative problems, in particular dysphagia. A recent randomized comparison of open *versus* laparoscopic fundoplication was terminated early because of a higher incidence of problems in the laparoscopic group[13].

Further evaluation of the outcome of laparoscopic procedures for gastro-oesophageal reflux against that of traditional open surgery is therefore warranted. The aim of this study was to compare the outcome of open and laparoscopic Nissen fundoplication in a randomized clinical trial.

Patients and methods

Patients undergoing antireflux surgery for gastro-oesophageal reflux disease were randomized to undergo either laparoscopic or open fundoplication. Informed consent was obtained from all participants and randomization was performed in the operating theatre by opening one of 120 previously sealed opaque envelopes, after the commencement of general anaesthesia. The envelopes were prepared and shuffled before the study and were then selected at random by the surgeon before each procedure. The study protocol was approved by the South Sheffield Research Ethics Committee and the study was conducted in accordance with the World Medical Association declaration of Helsinki (revised 1989).

All patients with proven gastro-oesophageal reflux disease who presented for primary antireflux surgery were considered for entry into the trial. Patients were excluded if they had an oesophageal motility disorder, required a concurrent abdominal procedure with fundoplication (such as cholecystectomy), or had undergone previous antireflux surgery. All patients underwent preoperative investigation by endoscopy, 24-h ambulatory pH monitoring and oesophageal manometry.

Laparoscopic Nissen fundoplication was performed as described previously[16,17]. Open surgery was performed via a standard upper midline incision. The procedure comprised dissection of the hiatal pillars, followed by full oesophageal mobilization and posterior hiatal repair. A tape was placed around the oesophagus in all patients to assist with oesophageal retraction and the short gastric vessels were not divided unless absolutely necessary to create a loose wrap. The anterior wall of the gastric fundus was pulled behind the oesophagus to create a loose fundoplication over a 52-Fr oesophageal bougie. Three 2/0 polypropylene interrupted sutures were used to secure the wrap, which was 1·5–2 cm in length. If a laparoscopic procedure was converted to an open operation owing to intraoperative difficulty, the fundoplication was constructed in exactly the same way. Surgeons were asked to rate the difficulty of the procedure on a scale of 1 (easy) to 10 (most difficult).

Patients in both groups were allowed to commence oral fluids on the evening of the day of surgery and soft solid food the next day. During the hospital stay, data were collected on analgesic usage, time at which liquid and semisolid oral intake was commenced, and early postoperative complications. To standardize postoperative analgesic use, epidural catheters were not allowed in either group. Discharge from hospital was allowed as soon as the patient was comfortable and felt able to manage at home. Patients were instructed to avoid bread and lumpy foods for the first 3–4 weeks after surgery and then gradually to increase the consistency of their diet.

Patients were interviewed before operation, and in a dedicated outpatient clinic 1, 3, 6 and 12 months after surgery by an experienced clinician using a structured questionnaire. Blinding to the treatment received was not attempted. At each visit it was determined whether the patient was still convalescent. The presence or absence of the following symptoms was sought: heartburn, epigastric pain, regurgitation, dysphagia to lumpy solids, soft solids and liquids, odynophagia, early satiety, inability to belch, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing and wheezing. A symptom score was used, which assessed the frequency, timing, intensity and duration of heartburn, epigastric pain and regurgitation. A frequency score of 1, 2 or 3 was used to indicate whether each symptom occurred less than once per week, on most days or every day respectively; daytime or nocturnal symptoms scored 1 each or 2 for both. Mild, moderate and severe symptoms scored 1, 2 and 3 respectively; symptoms for 5 min or less scored 1, symptoms for over 5 min scored 2. Using this system, a score of 0–30 was generated, where 0 indicated an absence of symptoms and 30 the presence of severe symptoms. At each visit, a record was made of bodyweight, medication being taken and any adverse events, and wounds were examined for any abnormality. Patients ranked the outcome of surgery using a modified Visick grading (*Table 1*) and were asked to score the outcome as excellent (complete recovery), good (minor problems), fair (major improvement but with

Table 1 Modified Visick grading

1	No symptoms
2	Mild symptoms easily controlled by simple measures such as avoiding certain foods or small meals etc.
3	Moderate symptoms not controlled by simple measures but not interfering with social or economic life
4	Moderate symptoms interfering with social or economic life
5	Symptoms as bad or worse than before operation

significant problems) or poor (minor or no improvement or deterioration).

Endoscopy, ambulatory 24-h pH monitoring and oesophageal manometry were performed approximately 3 months after surgery. Endoscopy specifically sought the presence of oesophagitis, Barrett's oesophagus or residual hiatus hernia. Ambulatory 24-h pH monitoring was carried out with a single-use antimony crystal probe (Mediplus, High Wycombe, UK) positioned 5 cm above the lower oesophageal sphincter as determined by oesophageal manometry and connected to a Flexilog™ 2000 datalogger (Oakfield Instruments, Witney, UK). The patient was encouraged to continue with normal activities over the 24 h. The percentage of time during which the pH was less than 4 and the total number of reflux episodes over 24 h were analysed.

Patients were fasted for 6 h before manometry and all medication known to affect oesophageal motility was ceased for 3 days beforehand. Oesophageal manometry was performed using an eight-lumen water-perfused catheter incorporating a sleeve sensor (Dentsleeve, Adelaide, Australia) with signals recorded on a Phoenix™ recording system (Albyn Medical, Dingwall, UK). The lower oesophageal sphincter (or high-pressure zone after fundoplication) was located by the station pull-through technique and the centre of the sleeve was positioned at the central point of the lower oesophageal sphincter. Each lumen of the catheter was connected in series with a pressure transducer and was constantly perfused with degassed distilled water at 0·5 ml/min by a low-compliance pneumohydraulic pump (Arndorfer Medical Specialties, Greendale, Wisconsin, USA). The resting lower oesophageal sphincter pressure was measured over 5 min, followed by measurement of the amplitude and propagation of primary peristalsis and residual relaxation pressure of the lower oesophageal sphincter, during ten swallows of 10-ml water boluses at least 30 s apart.

Statistical analysis

The primary clinical outcome measures were postoperative recovery and analgesic use, together with both short- and medium-term dysphagia and control of reflux symptoms. Before the trial it was determined that 84 patients (42 in each group) would be needed to demonstrate a 20 per cent difference in these outcome measures, at a significance level of $P < 0{\cdot}050$ and power of 90 per cent. To ensure that this was achieved, it was intended to recruit 100 patients, allowing for an estimated 20 per cent refusing the objective postoperative investigations. All analyses were performed on an intention-to-treat basis.

Values are presented as median (range). Data were analysed using SPSS® for Windows®, version 6.0 (SPSS, Chicago, Illinois, USA). χ^2 test or, where appropriate, Fisher's exact test was used to determine the significance of 2×2 contingency tables. Two-tailed Mann–Whitney U test was used to assess the significance of non-parametric data and unpaired Student's t test to determine the significance of data for which it was reasonable to assume a normal distribution (height and weight). $P < 0{\cdot}050$ was considered statistically significant.

Results

Between June 1993 and June 2000, 99 patients undergoing a 360° Nissen fundoplication were entered into the trial. Fifty-two patients were randomized to laparoscopic fundoplication and 47 to open fundoplication. Six patients were excluded because of the need to perform a concurrent cholecystectomy, 25 refused entry into the trial because they had a preference for a specific procedure, and ten were unwilling to participate in the follow-up protocol. Of the 99 patients entered, 97 (98 per cent) attended for follow-up 1 month after surgery, 87 (88 per cent) at 3 months, 77 (78 per cent) at 6 months and 81 (82 per cent) at 12 months. No patient withdrew from the study. It was not possible to contact all patients at each follow-up interval, as indicated in *Fig 1*.

The two groups were well matched for age, sex, height, weight, cigarette and alcohol consumption, type of employment, incidence of previous abdominal surgery and medication taken before surgery. The duration of preoperative symptoms was longer in the laparoscopic group (*Table 2*). Analysis of the presence or absence of preoperative symptoms revealed no significant differences (*Table 3*). The overall reflux symptom score was similar for each group (23 (0–30) for the laparoscopic group and 21 (9–29) for the open group; $P = 0{\cdot}731$), as was the preoperative Visick grade (*Table 4*).

Preoperative endoscopic grading of oesophagitis was similar; ten of 52 patients in the laparoscopic group and eight of 47 in the open group had complicated reflux disease, demonstrated by either Barrett's oesophagus

or stricture formation ($P = 0{\cdot}079$). The only difference between the groups was in the prevalence of a hiatus hernia (36 *versus* 22 patients respectively; $P = 0{\cdot}030$).

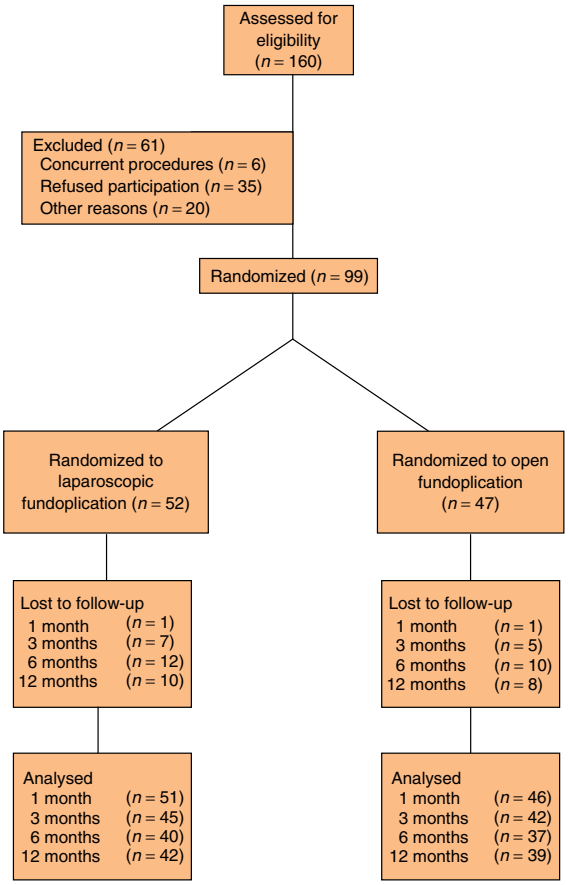


Fig. 1 Study flow diagram

Preoperative oesophageal manometric findings were similar. No significant differences were seen between the groups, except that the median residual relaxation lower oesophageal sphincter pressure was lower in the laparoscopic group (0·25 *versus* 0·50 cmH_2O; $P = 0{\cdot}046$). Twenty-four-hour ambulatory pH monitoring in all patients revealed no significant difference in either percentage exposure to an acid pH or the total number of reflux episodes.

Five surgeons were involved, all of whom were either experienced upper gastrointestinal consultants or trainees under direct supervision. All patients randomized to undergo open surgery underwent successful construction of a loose ('floppy Nissen') fundoplication. Five of 52 patients randomized to laparoscopic fundoplication had the procedure converted to an open operation, owing to obesity and fatty liver (two patients), intra-abdominal adhesions (one), bleeding (one) and equipment failure (one). These patients remained in the laparoscopic group for subsequent analysis.

Preoperative American Society of Anesthesiologists scores and the anaesthetic techniques used were similar in the two groups, as was the type and amount of intraoperative analgesia. The fundoplication was created in the same manner in all patients. The short gastric vessels were divided in one patient in the laparoscopic group and three in the open group to achieve a sufficiently loose wrap ($P = 0{\cdot}260$). A bougie was employed in all but one patient ($P = 0{\cdot}339$). The hiatus was repaired posteriorly in 49 patients and anteriorly in three patients in the laparoscopic group, compared with 42 posterior and five anterior repairs in the open group ($P = 0{\cdot}375$). The hiatus was repaired with a median of 2 (1–3) and 2 (0–3) sutures in the

Table 2 Patient demographics

	Laparoscopic ($n = 52$)	Open ($n = 47$)	P
Age (years)*	42·5 (23–71)	38 (21–69)	0·068‡
Sex ratio (M : F)	39 : 13	36 : 11	0·853†
Height (cm)*	173 (150–197)	170 (150–189)	0·854‡
Weight (kg)*	78·9 (43·0–103·1)	82·7 (44·0–110·0)	0·164‡
Cigarette smoker	16	12	0·563†
Alcohol consumer	39	36	0·853†
Previous surgery	13	15	0·575†
Duration of symptoms (months)*	72 (9–420)	48 (8–480)	0·020‡
Preoperative medication			0·070†
Proton pump inhibitor	51	42	
H_2 blocker	1	5	

*Values are median (range). †χ^2 test; ‡Mann–Whitney U test.

Table 3 Number of patients with each symptom before and after surgery

	Preop.		1 month		3 months		6 months		12 months	
	Laparoscopic ($n = 52$)	Open ($n = 47$)	Laparoscopic ($n = 51$)	Open ($n = 46$)	Laparoscopic ($n = 45$)	Open ($n = 42$)	Laparoscopic ($n = 40$)	Open ($n = 37$)	Laparoscopic ($n = 42$)	Open ($n = 39$)
Heartburn	48	45	11	2	2	0	1	0	1	3
Epigastric pain	39	45	6	4	4	1	5	2	3	4
Regurgitation	45	45	2	3	2	0	0	1	1	1
Dysphagia to lumpy solids	9	14	25	22	11	6	8	3	10	6
Dysphagia to soft solids	2	2	4	1	2	1	2	1	1	2
Dysphagia to liquids	5	3	2	2	2	1	0	0	0	1
Odynophagia	12	11	6	1	1	2	1	1	3	1
Postprandial fullness	22	21	14	20	7	8	11*	3	11	5
Inability to belch	0	0	6	5	2	3	4	2	3	2
Epigastric bloat	27	23	9	10	5	8	10	3	11	7
Anorexia	9	10	3	2	2	1	1	0	0	0
Nausea	17	15	2	5	0	1	1	1	2	1
Vomiting	16	17	2	4	0	1	1	0	0	2
Nocturnal cough	8	9	0	2	0	0	0	0	1	1
Nocturnal wheeze	4	6	0	1	0	0	0	0	1	0

*$P = 0{\cdot}036$ *versus* open (Fisher's exact test).

Table 4 Outcome scale and Visick grading

	Preop.		1 month		3 months		6 months		12 months	
	Laparoscopic ($n = 52$)	Open ($n = 47$)	Laparoscopic ($n = 51$)	Open ($n = 46$)	Laparoscopic ($n = 45$)	Open ($n = 42$)	Laparoscopic ($n = 40$)	Open ($n = 37$)	Laparoscopic ($n = 42$)	Open ($n = 39$)
Outcome										
Excellent	—	—	14	17	27	23	29	24	30	24
Good	—	—	31	22	14	17	9	9	8	11
Fair	—	—	4	7	3	1	2	4	4	3
Poor	—	—	2	0	1	1	0	0	0	1
Visick grade										
1	0	0	16	15	26	27	22	25	22	25
2	1	0	27	24	16	13	16	8	15	10
3	19	22	5	4	2	1	1	3	4	2
4	32	25	2	3	0	1	0	1	1	2
5	—	—	1	0	1	0	1	0	0	0

There were no significant differences between groups at equivalent follow-up intervals.

laparoscopic and open groups respectively ($P = 0{\cdot}680$). The fundoplication was constructed with a median of 3 (2–4) and 3 (3–4) sutures respectively ($P = 0{\cdot}499$).

The median operating time was 82 (40–197) min in the laparoscopic group and 46 (20–87) min in the open group ($P < 0{\cdot}001$). The corresponding median total operating theatre times were 110 (55–223) and 74 (30–108) min ($P < 0{\cdot}001$). The median operating time for laparoscopic fundoplication decreased from 92 (58–197) min for the first ten patients to 60 (40–119) min for the final ten. That for the open procedure was 44 (23–58) min for the first ten patients and 48 (20–61) min for the last ten. The median number of procedures performed by the surgeon before operating in the trial was 27 (2–200) and 26 (5–300) for the laparoscopic and open groups respectively ($P = 0{\cdot}734$). There was no difference in the surgeons' perception of operative difficulty between the groups; median difficulty gradings were 4 (1–10) for laparoscopic and 4 (1–9) for open surgery ($P = 0{\cdot}428$).

There was less postoperative wound pain in the laparoscopic group than in the open group (two of 52 *versus* 14 of 47; $P < 0{\cdot}001$), and less consumption of morphine, diclofenac and dihydrocodeine. The time from surgery to commencement of oral fluids was similar (both 1 (0–2) days; $P = 0{\cdot}084$), but time to commencement of solids was longer in the open group (2 (1–4) *versus* 2 (1–6) days;

$P = 0{\cdot}004$). Postoperative hospital stay (3 (2–6) *versus* 5 (2–11) days) and total hospital stay (4 (3–6) *versus* 5 (3–12) days) were longer in the open group ($P < 0{\cdot}001$). One patient in the laparoscopic group needed early reoperation for dysphagia, which was rectified by removing the most anterior hiatal repair suture. There were no deaths or major complications in either group. Postoperative atelectasis was seen in two patients in the laparoscopic group and five in the open group. Four patients in the laparoscopic group and six in the open group suffered postoperative urinary retention. One patient in each group suffered postoperative ileus that lasted more than 2 days. There was no significant difference in symptoms at discharge between the groups, other than a higher incidence of dysphagia in the laparoscopic group (to solids: 25 of 52 *versus* 13 of 47 patients; to liquids; four *versus* one; $P = 0{\cdot}028$ for both comparisons).

Patients undergoing open fundoplication took longer to return to normal physical activity or work. At 1 month, 26 of 51 patients in the laparoscopic group were still convalescent or not yet back at work, compared with 34 of 46 patients who had open surgery ($P = 0{\cdot}023$). The median time to return to work was shorter in the laparoscopic group, 4 (0–13) *versus* 7 (0–32) weeks ($P = 0{\cdot}002$).

A detailed analysis of the standardized clinical assessments is summarized in *Tables 3* and *4*. There were no differences between groups in the incidence of symptoms over the 12 months after surgery, with the exception of a higher incidence of postprandial fullness at 6 months in the laparoscopic group (*Table 3*). The ability of patients to relieve bloating and belch was no different between the groups. Outcomes were similar at all follow-up intervals, according to the outcome and modified Visick scales (*Table 4*). No patient complained of persistent wound pain, and no incisional or port-site hernia was noted.

Seventy-five patients (76 per cent) underwent a postoperative endoscopic examination, 42 in the laparoscopic group and 33 in the open group. Sixty-nine (70 per cent) underwent 24-h pH monitoring and oesophageal manometry, 38 and 31 in the laparoscopic and open groups respectively. The clinical outcomes in patients who agreed to postoperative investigation were similar to those in patients who declined.

Endoscopic examination revealed no residual oesophagitis or hiatus hernia in any patient in either group. Seven patients in the laparoscopic group and four in the open surgical group had evidence of Barrett's oesophagus, with no evidence of regression. All fundoplications appeared intact.

Twenty-four-hour pH monitoring demonstrated a similar outcome in each group; median acid exposure times (pH < 4) were 0·1 (0–5·5) and 0·4 (0–7·3) per cent for the laparoscopic and open groups respectively ($P = 0{\cdot}250$). The median number of reflux episodes was 1 (0–17) and 3 (0–27) respectively ($P = 0{\cdot}169$). One patient in each group had an acid exposure time of more than 4 per cent.

Oesophageal body motility variables were similar in both groups; the only significant difference was in the amplitude of distal oesophageal contractions, which was slightly lower in the laparoscopic group (70·5 (43–269) *versus* 80 (59–171) mmHg; $P = 0{\cdot}038$). Nine (0–10) of ten successful swallows were noted in each group ($P = 0{\cdot}539$), although oesophageal dysmotility, defined as fewer than eight of ten successful swallows, was noted in eight of 38 and 12 of 31 respectively ($P = 0{\cdot}180$).

Discussion

Despite the publication of several trials comparing open *versus* laparoscopic Nissen fundoplication, there remains controversy over which is the better approach. Different patient selection criteria, operative details, surgical experience and variations in postoperative assessment methodology are all confounding factors. This study provides further evidence to inform the debate.

Several small trials have demonstrated equivalent short-term reflux control, shortened postoperative hospital stay, longer operating times and a reduced incidence of complications after laparoscopic fundoplication[8,9,11,12]. In these studies, the hospital stay after open fundoplication was shorter than that in historical case series, suggesting that at least some of the apparent initial benefits of the laparoscopic approach may be related to general management changes, such as encouraging earlier oral intake and earlier discharge from hospital.

Larger studies have been reported by Laine *et al.*[7], Chrysos *et al.*[10] and Bais *et al.*[13] with 110, 106 and 103 patients entered respectively. All of these studies reported short-term outcome between 3 and 12 months. Hospital stay was shortened, with a more rapid return to work in the laparoscopic groups, at the expense of increased operating time. Effective reflux control was achieved by both approaches equally and two studies specifically noted that dysphagia was not influenced by the choice of surgical approach[7,10].

Conversely, Bais *et al.*[13] demonstrated some disadvantages for the laparoscopic approach. Follow-up was short (3 months) and the trial was stopped early because of an excess of adverse endpoints in the laparoscopic group, based primarily on 'whether or not patients had dysphagia' after surgery, although no definition of dysphagia was provided[18–20]. It has been argued that the

conclusions drawn were therefore misleading and several large series have reported that many patients who undergo laparoscopic Nissen fundoplication still suffer some dysphagia 3 months after surgery[4], which usually resolves with extended follow-up.

The two groups in the present study were well matched; the only significant preoperative differences related to duration of symptoms, the prevalence of hiatus hernia and lower oesophageal sphincter residual relaxation pressure. There was virtually no difference in terms of clinical outcome between the groups. The only variables that reached statistical significance were the frequency of dysphagia at the time of hospital discharge and postprandial fullness–early satiety at 6 months, both of which were more prevalent in the laparoscopic group.

The main advantage of the open procedure was the shorter operating and total theatre times, in keeping with other randomized studies[8,9,11,12]. It should be emphasized that the laparoscopic operating time decreased during the course of the study and that some of these procedures were undertaken relatively early in the surgeon's learning curve. A similar trend was observed with the rate of conversion to open operation. The majority of the conversions occurred early in the course of the study, which again may reflect relative surgical inexperience at the beginning of the trial.

The laparoscopic approach had several advantages over open fundoplication. Postoperative analgesia use was significantly less, as was the time to solid food intake following surgery. Length of hospital stay and the time to return to normal activity and/or employment were shorter in the laparoscopic group.

The two operations were equal in their ability to correct reflux symptoms, but longer-term follow-up is required to assess their durability. In the short term, laparoscopic Nissen fundoplication appears to be as effective as its open counterpart, and is associated with less postoperative pain and a quicker recovery. A laparoscopic operation should be regarded as the procedure of choice in the surgical management of chronic gastro-oesophageal reflux disease.

References

1 DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. *Ann Surg* 1986; **204**: 9–20.
2 Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. *World J Surg* 1977; **1**: 439–444.
3 Donahue PE, Samelson S, Nyhus LM, Bombeck CT. The floppy Nissen fundoplication. Effective long-term control of pathologic reflux. *Arch Surg* 1985; **120**: 663–668.
4 Watson DI, Jamieson GG. Antireflux surgery in the laparoscopic era. *Br J Surg* 1998; **85**: 1173–1184.
5 Rattner DW, Brooks DC. Patient satisfaction following laparoscopic and open antireflux surgery. *Arch Surg* 1995; **130**: 289–294.
6 Peters JH, Heimbucher J, Kauer WKH, Incarbone R, Bremner CG, DeMeester TR. Clinical and physiologic comparison of laparoscopic and open Nissen fundoplication. *J Am Coll Surg* 1995; **180**: 385–393.
7 Laine S, Rantala A, Gullichsen R, Ovaska J. Laparoscopic *versus* conventional Nissen fundoplication. A prospective randomized study. *Surg Endosc* 1997; **11**: 441–444.
8 Heikkinen T-J, Haukipuro K, Koivukangas P, Sorasto A, Autio R, Sodervik H *et al*. Comparison of costs between laparoscopic and open Nissen fundoplication: a prospective randomized study with a 3-month follow-up. *J Am Coll Surg* 1999; **188**: 368–376.
9 Perttila J, Salo M, Ovaska J, Gronroos J, Lavonius M, Katila A *et al*. Immune response after laparoscopic and conventional Nissen fundoplication. *Eur J Surg* 1999; **165**: 21–28.
10 Chrysos E, Tsiaoussis J, Athanasakis E, Zoras O, Vassilakis JS, Xynos E. Laparoscopic *versus* open approach for Nissen fundoplication. A comparative study. *Surg Endosc* 2002; **16**: 1679–1684.
11 Nilsson G, Larsson S, Johnsson F. Randomized clinical trial of laparoscopic *versus* open fundoplication: blind evaluation of recovery and discharge period. *Br J Surg* 2000; **87**: 873–878.
12 Luostarinen M, Virtanen J, Koskinen M, Matikainen M, Isolauri J. Dysphagia and oesophageal clearance after laparoscopic *versus* open Nissen fundoplication. A randomized, prospective trial. *Scand J Gastroenterol* 2001; **36**: 565–571.
13 Bais JE, Bartelsman JF, Bonjer HJ, Cuesta A, Go PM, Klinkenberg-Knol EC *et al*. Laparoscopic or conventional Nissen fundoplication for gastro-oesophageal reflux disease: randomized clinical trial. The Netherlands Antireflux Surgery Study Group. *Lancet* 2000; **355**: 170–174.
14 Lafullarde T, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG. Laparoscopic Nissen fundoplication – five-year results and beyond. *Arch Surg* 2001; **136**: 180–184.
15 Bammer T, Hinder RA, Klaus A, Klingler PJ. Five- to eight-year outcome of the first laparoscopic Nissen fundoplications. *J Gastrointest Surg* 2001; **5**: 42–48.
16 Watson DI, Jamieson GG, Devitt PG, Mathew G, Britten-Jones RE, Game PA *et al*. Changing strategies in the performance of laparoscopic Nissen fundoplication as a result of experience with 230 operations. *Surg Endosc* 1995; **9**: 961–966.
17 Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. *Ann Surg* 1994; **220**: 137–145.

18 Bloechle C, Mann O, Gawad KA, Izbicki JR. Gastro-oesophageal reflux disease. *Lancet* 2000; **356**: 69(Letter).
19 Gorecki PJ, Hinder RA. Gastro-oesophageal reflux disease. *Lancet* 2000; **356**: 70(Letter).
20 de Beaux AC, Watson DI, Jamieson GG. Gastro-oesophageal reflux disease. *Lancet* 2000; **356**: 71–72(Letter).
21 Franzen T, Andeberg B, Tibbling L, Johansson KE. A report from a randomized study of open and laparoscopic 360° fundoplication. *Surg Endosc* 1996; **10**: 582.

2.2 Division vs. non-division of the short gastric blood vessels during Nissen fundoplication

---

Watson DI, Pike GK, Baigrie RJ, Mathew G, Devitt PG, Britten-Jones R & Jamieson GG. Prospective double blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg* (1997) **226**:642-652.

This paper reported clinical and objective outcomes at 6 months (short term) follow-up from a randomized trial comparing laparoscopic Nissen fundoplication with vs. without division of the short gastric blood vessels.

O'Boyle CJ, Watson DI, Jamieson GG, Myers JC, Game PA & Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication – a prospective double blind randomized trial with five year follow-up. *Ann Surg* (2002) **235**:165-170.

This paper reported the 5 year (longer term) clinical outcomes from the same trial.

Yang H, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Randomized trial of division versus non-division of the short gastric vessels during laparoscopic Nissen fundoplication – 10 year outcomes. *Ann Surg* (2008) **247**:38-42.

This paper reported the 10 year (long term) clinical outcomes from the same trial.

Engström C, Jamieson GG, Devitt PG, Watson DI. Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of short gastric vessels during Nissen fundoplication. *Br J Surg* (2011) **98**:1063-1067.

This paper reported analysis of long term clinical outcomes (10-12 years follow-up) from a combined data set which included the patients enrolled in this trial, and a cohort from Sweden who were enrolled in a trial which used a similar protocol.

ANNALS OF SURGERY
Vol. 226, No. 5, 642–652

Prospective Double-Blind Randomized Trial of Laparoscopic Nissen Fundoplication With Division and Without Division of Short Gastric Vessels

David I. Watson, M.B., B.S., F.R.A.C.S., Gregory K. Pike, Ph.D.,
Robert J. Baigrie, M.D., F.R.C.S., George Mathew, M.S.,
Peter G. Devitt, M.S., F.R.C.S., F.R.A.C.S.,
Robert Britten-Jones, M.B., B.S., F.R.C.S., F.R.A.C.S.,
and Glyn G. Jamieson, M.S., F.A.C.S., F.R.A.C.S.

From the Royal Adelaide Centre for Endoscopic Surgery and the University Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia

Objective
To determine whether division of the short gastric vessels (SGVs) and full mobilization of the gastric fundus is necessary to reduce the incidence of postoperative dysphagia and other adverse sequelae of laparoscopic Nissen fundoplication.

Summary Background Data
Based on historical and uncontrolled studies, division of the SGVs has been advocated during laparoscopic Nissen fundoplication to improve postoperative clinical outcomes. However, this modification has not been evaluated in a large prospective randomized trial.

Methods
One hundred two patients with proven gastroesophageal reflux disease presenting for laparoscopic Nissen fundoplication were prospectively randomized to undergo fundoplication with (52 patients) or without (50 patients) division of the SGVs. Patients with esophageal motility disorders, patients requiring a concurrent abdominal procedure, and patients who had undergone previous antireflux surgery were excluded. Patients were blinded to the postoperative status of their SGVs. Clinical assessment was performed by a blinded independent investigator who used multiple standardized clinical grading systems to assess dysphagia, heartburn, and patient satisfaction 1, 3, and 6 months after surgery. Objective measurement of lower esophageal sphincter pressure, esophageal emptying time, and distal esophageal acid exposure and radiologic assessment of postoperative anatomy were also performed.

Results
Operating time was increased by 40 minutes (median 65 *vs.* 105) by vessel division. Perioperative outcomes and complications, postoperative dysphagia, relief of heartburn, and overall satisfaction were not improved by dividing the SGVs. Lower esophageal

sphincter pressure, acid exposure, and esophageal emptying times were similar for the two groups.

Conclusion

Division of the SGVs during laparoscopic Nissen fundoplication did not improve any clinical or objective postoperative outcome.

Laparoscopic techniques are being applied widely to the treatment of gastroesophageal reflux disease, with reports describing the outcome of many large series now published.[1-3] Before laparoscopic surgery, the Nissen 360° fundoplication was the most commonly performed procedure, although a smaller number of surgeons advocated the routine use of a partial fundoplication to minimize the risk of postoperative difficulties.[4,5] Nevertheless, the Nissen procedure has been the most widely accepted and applied, achieving long-term success in approximately 90% of patients.[6,7] To reduce the risk of postoperative problems such as dysphagia, this procedure has been progressively modified during the last 20 years from that originally described by Nissen. Operative modifications advocated have included routine repair of the esophageal hiatus, shortening of the fundoplication's length, and division of the short gastric vessels (SGVs).[6,8,9] None of these modifications have been assessed in a prospective randomized trial.

With the advent of laparoscopic fundoplication, the finer details of surgical technique have become more controversial. Because the laparoscopic technique does not eliminate all complications and is still associated with a low incidence of poor longer-term outcomes, many surgeons have expressed concern that time-honored rules have been broken to facilitate the application of laparoscopic techniques.[2,10,11] Analysis of some initial series appears to confirm this: some published results have improved after altering laparoscopic techniques to avoid initial shortcuts.[11-13]

Arguably, the most controversial issue is whether the SGVs should be divided to minimize the likelihood of dysphagia.[6,10,13] Good results have been reported at both laparoscopic and open surgery with and without division of these vessels.[1,2,14,15] Many of the proponents of laparoscopic division of the SGVs did not divide these vessels while they were learning laparoscopic Nissen fundoplication; subsequently, they divided them and then compared their early and late experience.[11,13] Because of the inherent problem of a learning curve bias associated with such an analysis, the outcome in the latter group is usually better, leading to the conclusion that the SGVs should always be divided. Other surgeons, however, argue that they have achieved equally good results without dividing these vessels.[14,15]

To determine whether division of the SGVs and full mobilization of the gastric fundus is necessary to reduce the risk of postoperative dysphagia and other adverse sequelae, we undertook a prospective double-blind randomized trial of division *versus* no division of the SGVs during laparoscopic Nissen fundoplication.

METHODS

Participant Assignment

Patients undergoing laparoscopic Nissen fundoplication for gastroesophageal reflux disease were randomized to undergo fundoplication with or without division of the SGVs. Informed consent was obtained from all participants. Randomization was performed by opening one of 120 sealed opaque envelopes and occurred in the operating room after general anesthesia had been induced. A research officer not directly involved in the trial prepared the envelopes before the study; the envelopes were selected by a departmental secretary, at a surgeon's request.

Patient Selection and Preoperative Investigation

All patients with proven gastroesophageal reflux disease who presented for primary antireflux surgery by the laparoscopic technique were considered for entry into this trial. Patients were excluded from consideration only if they had an esophageal motility disorder that precluded a 360° fundoplication, required a concurrent abdominal procedure at the same time as fundoplication (*e.g.*, cholecystectomy), or had undergone previous antireflux surgery. All patients underwent preoperative investigation with esophageal manometry and endoscopy. Preoperative manometric testing also included an acid reflux provocation test and Bernstein test. Twenty-four-hour pH monitoring was performed routinely for patients who did not

Supported by the Royal Australasian College of Surgeons Research Foundation.

Address reprint requests to Mr. David I. Watson, Consultant Surgeon, University Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia; phone: +618 82225516; fax: +618 82225896.

Accepted for publication July 19, 1996.

have unequivocal reflux disease demonstrated by preliminary endoscopic and manometric studies. Most patients also underwent preoperative barium meal X-ray examination.

Operating Technique

Laparoscopic Nissen fundoplication was performed using a previously described technique.[1,16] In brief, this consisted of dissection of the hiatal pillars followed by full esophageal mobilization and routine posterior hiatal repair. If the SGVs were to be divided, this was performed next. Vessels were dissected, secured by metal clips, and divided. Division usually commenced at the level of the inferior pole of the spleen and progressed superiorly along the greater curvature of the stomach until the left pillar of the hiatus was seen. Division of the SGVs was considered adequate if the superior part of the gastric fundus could be brought loosely around the esophagus for construction of the fundoplication.

If the SGVs were not divided, the anterior wall of the gastric fundus was pulled behind the esophagus for construction of the fundoplication. Occasionally, when the SGVs had not been divided, the first piece of fundus selected appeared tight. By repositioning instruments and grasping an adjacent piece of fundus, a much looser wrap could be constructed. Care was taken to ensure that the completed fundoplication was not tight by having a 52 Fr bougie within the abdominal esophagus. Three or four 2/0 Prolene interrupted sutures were used to secure the wrap, which was 1.5 to 2 cm long.

If the laparoscopic procedure was converted to an open procedure because of intraoperative difficulties, the SGVs were still divided or not divided according to the randomization schedule, with the patient remaining in the trial.

Postoperative Care

Nasogastric tubes were not used in any patients. Patients were allowed oral fluids on the evening of the day of surgery and soft solid food the next day. Discharge from the hospital was encouraged after the second postoperative day. Patients were instructed to avoid bread and lumpy foods for 3 to 4 weeks after surgery, and then to increase the consistency of their diet gradually. A barium meal examination was usually obtained on the second postoperative day to detect any problems amenable to early laparoscopic reintervention (*e.g.*, acute paraesophageal hernia, tight fundoplication, or hiatus).

Masking

Patients did not know whether their SGVs had been divided during laparoscopic fundoplication. Because they had no direct access to case notes or trial records, and both laparoscopic procedures used identical operative wounds, all remained unaware of the exact procedure for the duration of the trial follow-up period. Although operating surgeons were aware of the exact procedure performed, all follow-up was obtained by a scientific officer who was blinded to the randomization of each patient. Because he was not involved in the initial surgery, he remained unaware of the allocated group for each patient throughout the follow-up period. Participant data were entered into a computerized database by another research assistant who was not involved in direct patient follow-up. Final data analysis was performed independently by both the scientific officer and a surgeon investigator.

Table 1. DYSPHAGIA SCORE

1	Water
2	Milk (or thin soup)
3	Custard (or yoghurt or pureed fruit)
4	Jelly
5	Scrambled egg (or baked beans or mashed potato)
6	Baked fish (or steamed potato or cooked carrot)
7	Bread (or pastries)
8	Apple (or raw carrot)
9	Steak (or pork or lamb chop)

The presence of any dysphagia for each liquid or solid substance is first determined and scored; dysphagia always = 1 point, sometimes = 1/2 point, never = 0 points. A score from 0 (no dysphagia) to 45 (severe dysphagia) is then determined by multiplying the score for each substance by the adjacent line number, and then summing all nine lines.

Clinical Follow-Up

Patients were interviewed before surgery and then 1, 3, and 6 months after surgery by a scientific officer using a structured questionnaire. Although longer-term follow-up will be sought, it is unavailable for reporting in this paper. The presence or absence of each of the following symptoms was sought: heartburn, epigastric pain, regurgitation, dysphagia for lumpy solids, soft solids, and liquids, odynophagia, early satiety, inability to belch, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing, and wheezing. The ability to relieve bloating and whether a normal diet was being consumed were also determined.

Heartburn was scored using a visual analog scale (0 = no heartburn, 10 = severe heartburn). Dysphagia was scored by several methods. Visual analog scales (0 = no dysphagia, 10 = total dysphagia) were independently applied for solids and liquids, as well as a previously validated score[17] (0 = no dysphagia, 45 = severe dysphagia) that combines information about difficulty swallowing 9 types of liquids and solids (Table 1). This latter

Table 2. MODIFIED VISICK GRADING

1	No symptoms
2	Mild symptoms easily controlled by simple care such as avoiding certain foods or small meals, etc.
3	Moderate symptoms not controlled by simple care but not interfering with social or economic life
4	Moderate symptoms interfering with social or economic life
5	Symptoms as bad or worse than preoperatively

score was reversed from that originally described so that the numerical score increased with the severity of dysphagia. Overall outcome was determined using three further scales. Patients ranked the outcome of surgery using a modified Visick grading (Table 2) and were asked to score the outcome as excellent, good, fair, or poor (Table 3). An overall assessment of satisfaction with the operative outcome was scored by a further visual analog scale (0 = dissatisfied, 10 = satisfied).

Objective Follow-Up

Objective investigation with esophageal manometry, 24-hour pH monitoring, barium meal examination, and a radionuclide esophageal emptying study were performed 3 to 4 months after surgery. The investigation assessed lower esophageal sphincter function, control of reflux, postsurgical anatomy, and the presence of any postsurgical esophageal obstruction caused by a tight wrap or any other cause.

Esophageal Manometry

Patients fasted for 6 hours before each study, and all medications affecting esophageal motility were discontinued 3 days earlier if necessary. Esophageal manometry was performed using an eight-lumen water-perfused catheter incorporating a sleeve sensor (Dent Sleeve, Adelaide, Australia) with signals recorded on a polygraph chart recorder (Model 7D; Grass Instrument Company, Peabody, MA). The lower esophageal sphincter (or postfundoplication high-pressure zone) was located by the station pull-through technique, and the center of the sleeve was positioned at the central point of the lower esophageal sphincter. Each lumen of the catheter was connected in series with a pressure transducer (Stratham P231D; Gould, Oxnard, CA) and was constantly perfused with degassed distilled water at 0.5 mL/min by a low-compliance pneumohydraulic pump (Arndorfer Medical Specialities, Greendale, WI). The resting lower esophageal sphincter pressure was measured over a 5-minute period, followed by measurement of the amplitude and propagation of primary peristalsis and residual relaxation pressure of the lower esophageal sphincter during 10 swallows of 5-mL water boluses.

Table 3. OUTCOME ASSESSMENT

Excellent	Complete recovery
Good	Major improvement with minor problems
Fair	Major improvement with still significant problems or adverse effects
Poor	Minor or no improvement or deterioration

Ambulatory 24-Hour pH Monitoring

A glass pH probe (Radiometer, Copenhagen, Denmark) was positioned 5 cm above the lower esophageal sphincter measured by esophageal manometry and was connected to a Digitrapper (Synectics Medical, Stockholm, Sweden). The patient was encouraged to continue with normal activities for 24 hours. The results were analyzed for the percentage of time during which pH was <4 and for the correlation between reflux symptoms and measured reflux events.

Radionuclide Esophageal Emptying Study

This test measured esophageal emptying of three swallows of a solid meal of cooked ground beef containing 10 to 12 MBq of 99m-technetium sulfur colloid dispersed in egg white. Esophageal emptying was measured as the average time taken for 95% of each of three 10-g solid boluses to clear from the esophagus. The normal emptying time for this test is 7 to 93 seconds.

Barium Swallow Examination

Swallowed radiopaque barium contrast was used to image the distal esophagus, fundoplication, and stomach. Imaging determined any gross delay in esophageal emptying, the site of the fundoplication (abdominal *vs.* thoracic), the presence or absence of any paraesophageal herniation, and any abnormal distortion of gastric anatomy. Prone oblique views were obtained specifically to examine for paraesophageal herniation.

Statistical Analysis

The primary clinical outcomes the trial was designed to evaluate were postoperative dysphagia and control of reflux symptoms. Before the trial began, it was determined that 84 patients (42 per group) would be needed to demonstrate a 20% difference in these outcome measures, at a significance level of $p < 0.05$ and power of

Table 4. PREOPERATIVE PARAMETERS: MEAN (95% CONFIDENCE INTERVAL)

	Vessels Not Divided	Vessels Divided	Value
Number of patients	50	52	
Age (yr)	46.7 (42.7, 50.8)	45.3 (41.8, 48.8)	0.50
Sex	31M; 19F	31M; 21F	0.84
Height (cm)	170 (167, 173)	172 (169, 175)	0.39
Weight (kg)	83.5 (79.4, 87.5)	84.5 (80.0, 88.9)	0.74
Cigarette smoker (%)	20	12	0.38
Alcohol consumed (%)	67	66	1.00
Previous abdominal surgery (%)	38	40	0.84
Duration of symptoms (yr)	9.1 (6.7, 11.5)	8.2 (5.6, 10.8)	0.38
Preoperative medications (%)			
Omeprazole	68	66	0.83
H2 blocker	78	84	0.44
Cisapride	18	20	0.80

90%. To ensure that this was achieved, we decided to recruit 100 patients, allowing for an estimated 20% of all patients who would refuse the objective postoperative investigations. All analyses were performed on an intent-to-treat basis, with all patients remaining in their initial allocated group for this analysis.

Before the trial began, we decided to publish the initial outcomes and results of postoperative testing (this paper) after all patients had been followed for an initial 6-month period. This period was considered adequate to allow the assessment of any differences in the incidence of postoperative dysphagia between the two groups. Medium- to long-term outcomes are more important for determining the efficacy of reflux control and will be reported after follow-up has matured further.

All data was entered into a computerized database (Filemaker Pro version 2.0; Claris, Santa Clara, CA) and analyzed using a commercially available statistical package (InStat version 2.01; GraphPad Software, San Diego, CA). Fisher's exact test was used to determine the significance of 2×2 contingency tables. A two-tailed Mann-Whitney test was used to assess the significance of nonparametric data sets and an unpaired Student's t test to determine the significance of data sets where it was reasonable to assume a parametric distribution (height and weight). Statistical significance was accepted at $p < 0.05$. Unless otherwise stated, all data are reported as the percentage of the total patients in each group, or as the mean (95% confidence intervals [CI]).

Ethical Approval

The protocol for this study was approved by the Royal Adelaide Hospital Human Research Ethics Committee, and the study was conducted in accordance with the World Medical Association Declaration of Helsinki (revised 1989) and the National Health and Medical Research Council of Australia's guidelines on human experimentation.

RESULTS

From May 1994 to October 1995, 102 patients undergoing a laparoscopic 360° Nissen fundoplication were entered into the trial. Fifty patients were randomized to undergo fundoplication without SGV division and 52 to undergo division of these vessels. During the same period, 38 further patients underwent a laparoscopic Nissen fundoplication performed by surgeons contributing patients to this study. Three of these patients were excluded because of the need to perform a concurrent abdominal procedure (cholecystectomy in two, highly selective vagotomy in one). The remaining 35 patients refused entry into the trial because they had a preference for a specific procedure to be performed or were unwilling to participate in the follow-up protocol. Of the 102 patients entered, 98 (96%) were available for follow-up 1 month after surgery, 99 (97%) at 3 months, and 100 (98%) at 6 months. Although prospectively collected follow-up data were unavailable for a few patients at the specific follow-up intervals, no patient elected to withdraw from the study. Missing data were the result of an inability to contact patients at the specific follow-up intervals. Only 2 patients could not be contacted 6 months after surgery; 1 of them had decided to emigrate to Greece.

Preoperative Assessment

Both groups were similar in age, sex, height, weight, cigarette and alcohol consumption, incidence of previous abdominal surgery, duration of symptoms, and medications consumed before surgery (Table 4). Analysis of the

Table 5. SUMMARY OF PREOPERATIVE AND POSTOPERATIVE SYMPTOMS (%)

	Preoperative		1 mo After Operation		3 mo After Operation		6 mo After Operation	
	Not Divided	Divided	Not Divided	Divided	Not Divided	Divided	Not Divided	Divided
Heartburn	94	88	8	8	4	6	6	10
Epigastric pain	57	56	38	50	31	37	29	18
Regurgitation	90	88	29	26	19	14	14	6
Odynophagia	27	16	10	14	13	8	4	4
Early satiety	37	30	85	90	63	69	41	49
Epigastric bloat	59	44	50	50	33*	55*	35	41
Anorexia	4	6	21	16	8	6	8	2
Nausea	27	16	21	16	2	10	10	2
Vomiting	22	26	4	10	0	0	2	0
Nocturnal cough	39	40	15	14	8	14	12	6
Nocturnal wheeze	16	20	8	10	4	12	8	4
Can relieve bloat	79	79	52	50	63	59	65	57
Unable to belch	0	0	48	42	46	51	38	53
Eats normal diet	55	78	48	48	85	84	92	88

* There were no significant differences demonstrated between trial groups ($p > 0.05$ at all follow-up intervals), except epigastric bloat 3 months after operation ($p = 0.043$, Fisher's exact test).

presence or absence of preoperative symptoms (Table 5), as well as the assessment of heartburn using the visual analog scale (Table 6), revealed no significant differences. A significant proportion of patients in each group experienced preoperative dysphagia to some extent, with an incidence of 43% in the division group, and 52% in the non-division group, when assessed using the dysphagia score (Table 7). Although different methods of scoring dysphagia elicited slightly different rates, there was no clinically or statistically significant difference between the two groups. Preoperative Visick grading was also similar for each group (Table 8)

Endoscopic grading of esophagitis before surgery was similar, with 12 (24%) of the nondivision group and 10 (19%) of the division group having complicated reflux disease, demonstrated by either Barrett's esophagus or stricture formation ($p = 0.80$). A hiatus hernia was seen before surgery in 24 (48%) of the nondivision group *versus* 28 (54%) of the division group ($p = 0.67$). Barium meal examination was performed before surgery in 30 patients in the nondivision group and 32 in the division group. A hiatus hernia was demonstrated in 16 (53%) and 18 (56%) examinations, respectively.

Preoperative esophageal manometry outcomes (Table 9) were similar. No statistically significant differences were seen between the groups, although the mean resting lower esophageal sphincter resting pressure was lower in the nondivision group (6.3 *vs.* 8.3 mm Hg, $p = 0.08$).

Twenty-four-hour ambulatory pH monitoring was performed in 22 patients in the nondivision group and 24 in the division group. The mean percentage exposure to an acid pH <4 was 10.0% (6.4% to 13.7%) and 10.3% (6.1% to 14.5%), respectively ($p = 0.68$).

Surgery

Surgery was performed by one of seven surgeons. All patients randomized to the nondivision group had a loose fundoplication successfully fashioned without resorting to vessel division. One patient randomized to undergo

Table 6. ASSESSMENT OF HEARTBURN BY VISUAL ANALOGUE SCALE: MEAN (95% CONFIDENCE INTERVAL)

	Vessels Not Divided	Vessels Divided	p Value
Preoperative	4.8 (3.7, 5.8)	3.7 (2.8, 4.7)	0.18
1 mo after operation	0.21 (−0.10, 0.51)	0.20 (−0.01, 0.41)	0.88
3 mo after operation	0.11 (−0.11, 0.32)	0.47 (−0.06, 0.98)	0.63
6 mo after operation	0.33 (−0.03, 0.69)	0.48 (−0.04, 1.00)	0.75

Table 7. DYSPHAGIA ASSESSMENT: PERCENTAGE OF TOTAL OR MEAN (95% CONFIDENCE INTERVAL)

	Preoperative		1 mo After Operation		3 mo After Operation		6 mo After Operation	
	Not Divided	Divided	Not Divided	Divided	Not Divided	Divided	Not Divided	Divided
Dysphagia for								
Lumpy solids (%)	31	36	56	56	48	49	33	29
Soft solids (%)	4	8	17	16	8	13	2	2
Liquids (%)	6	2	15	18	13	10	6	16
Visual analogue scale								
Solids	1.7 (0.9, 2.5)	2.5 (1.5, 3.4)	3.4 (2.6, 4.2)	3.2 (2.4, 4.0)	2.2 (1.4, 3.0)	2.1 (1.3, 2.7)	1.4 (0.8, 2.0)	1.3 (0.7, 1.9)
Liquids	0.74 (0.1, 1.4)	0.78 (0.2, 1.3)	1.4 (0.6, 2.3)	0.9 (0.4, 1.4)	0.60 (0.06, 1.2)	0.61 (0.2, 1.1)	0.39 (−0.07, 0.9)	0.48 (0.1, 0.8)
Dysphagia score								
Overall result	9.5 (5.5, 13.6)	7.6 (4.5, 10.8)	14.5 (10.8, 18.2)	13.5 (10.2, 16.8)	8.3 (5.1, 11.5)	7.9 (5.2, 10.5)	4.8 (2.4, 7.2)	4.6 (2.3, 6.9)
Scored 0 only (%)	48	57	26	27	43	39	63	61

No tests for significance between groups at comparable follow-up intervals were significant ($p > 0.05$ at all follow-up intervals).

division did not have the SGVs divided because intraoperative anesthetic difficulties meant it was necessary to complete the procedure as rapidly as possible. This patient remained in the division group for subsequent analysis. One patient in the division group sustained an intraoperative perforation of the anterior gastric wall because of an injury from a grasping instrument. This was successfully repaired laparoscopically.

Three to eight SGVs (median, five) were divided between metal clips when required. There was some variation in the number of vessels clipped by different surgeons, with some using electrocautery and others clips for smaller vessels. Bleeding sufficient to impair visibility was encountered during SGV division in 3 patients (6%). This was overcome in all instances, with no need for conversion to open surgery. However, the laparoscopic procedure in 4 (8%) of the patients in the division group was converted to open surgery during esophageal dissection. The reasons for conversion were obesity and liver hypertrophy in two patients, large hiatus hernia in one patient, and the inability to manipulate an instrument safely behind the esophagus because of periesophagitis in one patient. All procedures in the nondivision group were successfully completed laparoscopically.

Table 8. OUTCOME, SATISFACTION, AND VISICK GRADING

	Preoperative		1 mo After Operation		3 mo After Operation		6 mo After Operation	
	Not Divided	Divided	Not Divided	Divided	Not Divided	Divided	Not Divided	Divided
Outcome (%)								
Excellent	NA	NA	17	14	23	19	29	25
Good	NA	NA	60	60	64	67	59	69
Fair	NA	NA	23	24	11	12	10	4
Poor	NA	NA	0	2	2	2	2	2
Visick grade (%)								
1	0	0	11	12	23	15	25	23
2	0	0	53	46	60	70	57	69
3	26	29	25	30	11	9	10	2
4	74	71	11	8	4	4	6	4
5	0	0	0	4	2	2	2	2
Satisfaction score								
Mean score	NA	NA	8.3	7.9	8.7	8.5	8.5	8.6
95% CI	NA	NA	7.6, 8.9	7.2, 8.6	8.2, 9.2	7.8, 9.1	7.8, 9.2	8.0, 9.2

NA = not applicable; CI = confidence interval.
No tests for significance between groups at comparable follow-up intervals were significant ($p > 0.05$ at all follow-up intervals).

Table 9. ESOPHAGEAL MANOMETRY RESULTS: % OF TOTAL OR MEAN (95% CONFIDENCE INTERVAL)

	Vessels Not Divided	Vessels Divided	p Value
Preoperative			
Number of propagated swallows*	9.1 (8.6, 9.6)	8.7 (7.9, 9.4)	0.92
Peristaltic amplitude	66.8 (55.3, 78.4)	62.8 (51.1, 74.5)	0.59
% patients with normal peristalsis	89	82	0.39
LES resting pressure (mm Hg)	6.3 (4.5, 8.1)	8.3 (6.2, 10.3)	0.08
LES nadir pressure (mm Hg)	0.52 (0.27, 0.78)	1.06 (0.46, 1.66)	0.46
Resting LOSP < 10 mm Hg (%)	79	66	0.18
Postoperative			
Number of propagated swallows*	7.8 (6.6, 9.1)	8.2 (7.1, 9.3)	0.44
Peristaltic amplitude	60.5 (45.2, 75.7)	79.8 (61.7, 97.9)	0.14
% patients with normal peristalsis	68	72	1.00
LES resting pressure (mm Hg)	24.5 (20.1, 28.9)	20.9 (17.1, 24.7)	0.23
LES nadir pressure (mm Hg)	13.3 (9.4, 17.3)	11.0 (8.4, 13.6)	0.46
Resting LOSP < 10 mm Hg (%)	0	10	0.25

LES = lower esophageal sphincter; LESP = lower esophageal sphincter pressure.
* Swallowing was assessed from 10 wet swallows.

Operating time varied from 35 to 170 minutes (mean 70.6, median 65, CI 63.0 to 78.1) when the vessels were not divided and 59 to 215 minutes (mean 107.9, median 105, CI 99.0 to 116.8; $p < 0.0001$) when the vessels were divided. The corresponding operating room times were 60 to 185 minutes (mean 95.2, median 91, CI 87.5 to 102.9) and 75 to 245 minutes (mean 132.7, median 135, CI 121.7 to 143.8; $p < 0.0001$). Operating surgeons were asked to rate the difficulty of the operative procedure using a scale from 1 to 10. Procedures in which the SGVs were divided (mean score 6.0, CI 5.5 to 6.6) were perceived to be more difficult than when the vessels were not divided (mean score 4.7, CI 4.1 to 5.4; $p = 0.0072$)

Early Hospital Outcomes

The periods between surgery and the commencement of oral fluids and solids and the length of postoperative hospital stay were unaltered by division of the SGVs (Table 10). The incidence of postoperative complications was also unaffected by vessel division (Table 11). Most of the complications were minor and did not affect later outcomes. However, two patients in the nondivision group required laparoscopic revision on the second and fourth postoperative days for acute postoperative paraesophageal herniation. In both instances, a hernia was discovered at a routine barium meal examination on the second postoperative day, facilitating early diagnosis and laparoscopic repair. Three patients in the division group also required surgical revision during the follow-up period. One patient with severe dysphagia underwent laparoscopic reexploration on the fifth postoperative day. The problem in this instance—tight closure of the diaphragmatic esophageal hiatus despite calibration of the closure with a 52 Fr bougie—was rectified by removing the top hiatal suture. The second patient underwent a laparotomy 6 hours after the initial procedure for bleeding caused by slippage of a clip previously placed across a divided SGV. The third patient had persistent severe postoperative dysphagia caused by fibrous stenosis of the esophageal hiatus. Twelve weeks

Table 10. EARLY HOSPITAL OUTCOMES: MEAN (95% CONFIDENCE INTERVAL)

	Vessels Not Divided	Vessels Divided	p Value
Postoperative stay (days)	3.75 (3.16, 4.34)	3.93 (3.35, 4.52)	0.56
Median	3	3	
Days to oral fluids	1.16 (0.80, 1.51)	1.37 (1.03, 1.71)	0.31
Median	1	1	
Days to solids	2.27 (1.82, 2.73)	2.50 (2.16, 2.84)	0.15
Median	2	2	

Table 11. THIRTY-DAY COMPLICATIONS

	Vessels Not Divided	Vessels Divided	p Value
Urinary retention	1	0	
Minor respiratory	0	2	
Ileus (>2 days)	3	2	
Paraesophageal hernia	2	0	
Bleeding short gastric vessel	0	1	
Tight hiatal repair	0	1	
In hospital fall	1	0	
Total number of patients	7 (14%)	6 (12%)	0.77

later, the hiatus was widened at open surgery, relieving the swallowing difficulty. One patient in the nondivision group and two in the division group also required early flexible esophagoscopy for disimpaction of a bolus food obstruction caused by inappropriate early consumption of large lumps of meat.

Patients undergoing division of the SGVs took an average 1.5 weeks longer to return to normal physical activity, possibly because of the conversion of 4 of the procedures to open operations (mean 4.6 weeks (3.4, 5.8) *vs.* 6.3 weeks (4.6, 7.9); p = 0.064).

One- to 6-Month Postoperative Clinical Outcome

A detailed analysis of the outcome of the blinded standardized clinical assessment is summarized in Tables 5, 6, 7, and 8. No differences between groups in the incidence of assessed symptoms were seen at any stage of the initial 6-month follow-up period, with the exception of a higher incidence of epigastric bloating 3 months after surgery in the division group (see Table 5). The ability of patients to relieve symptoms of bloat and their ability to belch were not altered by dividing the SGVs. The incidence and severity of heartburn, as assessed by the visual analog scale, were also identical (see Table 6). Outcomes were similar at all follow-up intervals when assessed by the visual analog satisfaction score, the outcome scale, and the modified Visick scale (see Table 8). Similarly, the incidence and severity of dysphagia assessed 1, 3, and 6 months after laparoscopic Nissen fundoplication were not altered by division of the SGVs (see Table 7). No trend toward improvement in the overall outcome after division of the SGVs could be demonstrated by careful analysis of the different symptom scores.

Objective Postoperative Investigations

Eighty patients (78%) underwent a postoperative esophageal emptying study, 66 (65%) a barium swallow examination, 56 (55%) esophageal manometry, and 46 (45%) postoperative 24-hour pH monitoring. The clinical outcomes in patients who underwent postoperative investigation were similar to the outcomes in the patients who declined investigation.

In the division group, barium swallow examination revealed a small asymptomatic paraesophageal hernia in 4 patients (12%) and delayed emptying of barium from the esophagus in 2 patients (6%). None of these appearances were evident in patients in the nondivision group, except in one patient with delayed esophageal emptying. In all but 1 patient in the nondivision group, the fundoplication lay completely within the abdominal cavity; in 7 patients (21%) in the division group, the wrap partly straddled the diaphragm. No fundoplications in either group migrated fully into the thoracic cavity. All fundoplications appeared to be constructed correctly using gastric fundus, irrespective of operative technique.

Esophageal manometry outcomes after surgery are summarized in Table 9. Esophageal body motility parameters were similar, but mean lower esophageal sphincter resting and nadir pressures were 3.6 and 2.3 mmHg higher, respectively, in the nondivision group; however, this difference failed to reach statistical significance. Twenty-four-hour pH monitoring demonstrated normalization of acid exposure times in all but three patients (one in the nondivision group and two in the division group). All these patients had minimally elevated acid exposure times, and none had any symptom of gastroesophageal reflux.

The mean esophageal emptying time, measured by the radionuclide method, was 109 seconds (86, 132) in the nondivision group and 127 seconds (103, 151; p = 0.26) in the division group. In the division group, 44% of patients had a normal emptying time, compared with 49% in the nondivision group (p = 0.82).

DISCUSSION

Although approximately 90% of patients who undergo a Nissen fundoplication using conventional open techniques achieve good long-term relief of reflux symptoms with no significant postoperative sequelae,[6,7] a few patients develop at least one adverse outcome.[1,6,7] The surgical literature contains many papers that discuss the issues of postfundoplication dysphagia, gas bloat, and recurrent gastroesophageal reflux.[7,18,19] Because of these potential problems, Nissen's original total fundoplication has been progressively modified by calibrating the wrap with a large intraesophageal bougie, shortening the fundoplication length from 5 to 1 to 2 cm, and gaining full mobilization of the gastric fundus by dividing the SGVs.[6,8]

Division of SGVs during open Nissen fundoplication has been advocated in reports from DeMeester et al.[6] and

Donahue et al.[8] It has been suggested that this maneuver reduces the incidence of postoperative dysphagia and enables greater relaxation of the lower esophageal sphincter region during swallowing. Although persuasively argued, scientific data establishing this have been lacking. For instance, Donohue et al.[8] studied an uncontrolled series of 77 patients followed for an average of 4.1 years, with objective manometric follow-up in only 19 (25%). DeMeester et al.[6] studied a nonrandomized series of 100 patients, of whom 36 underwent postoperative manometric assessment.[6]

All modifications to Nissen's original operation have been introduced and advocated without supporting evidence from any controlled clinical trials. This has led to divergent opinions about whether modifications such as SGV division really do reduce the incidence of postoperative dysphagia.[6,7,8,13–15] Assessment outside prospective controlled trials often results in the comparison of different groups of patients who undergo surgery by different surgeons at different stages in their experience. This introduces the possibility of unintentional bias and means that conclusions from such studies should be seen as hypotheses to be tested.

The technique used for Nissen fundoplication in our department has changed over time.[1,20] Initially, we performed an extensive mobilization of the gastric fundus at open surgery. However, this procedure was modified to a fundoplication performed without dividing the SGVs at open surgery. Our anecdotal impression was that after open surgery, the incidence of postoperative dysphagia was not increased by omitting SGV division. Consequently, when laparoscopic Nissen fundoplication was first performed in our department in 1991, the SGVs were not divided. Our initial impression was that the incidence of dysphagia may have been higher after the laparoscopic technique.[16] Because of this, we began to divide the SGVs during laparoscopic fundoplication. This was done before beginning this randomized trial, ensuring that the technique for SGV division was standardized and all learning difficulties were overcome.

Good clinical outcomes have been reported after total fundoplication, both with and without SGV division, using both open and laparoscopic techniques.[1,2,6–8,14,15] Rossetti and Hell,[7] in a report on the 20-year outcomes of 875 patients who underwent fundoplication without division of the SGVs, found that 87.5% had achieved a good or excellent outcome. At follow-up of 1 to 13 years (mean 45 months), DeMeester et al.[6] reported that 91% of patients who underwent SGV division achieved a good or excellent outcome.

Published outcomes of laparoscopic fundoplication are all short term. However, Anvari et al.[14] and Geagea[15] have described substantial experience with Nissen fundoplication without vessel division, reporting dysphagia rates of 5.4% and 0%, respectively. This compares with the initial experience of Hinder et al.,[2] who advocated routine division of the SGVs, in which 23% of 198 patients experienced dysphagia at early follow-up. Peters et al.,[21] who also routinely divide these vessels, reported a 9.4% incidence of dysphagia 3 months after surgery in their initial 34 patients undergoing laparoscopic Nissen fundoplication.

The difficulty encountered when comparing these studies is that different procedures are performed by different surgeons, who may be at different stages in their experience. These problems are compounded by the use of different patient selection criteria and variation in postoperative assessment methodology. Personal follow-up obtained by an operating surgeon may elicit outcomes different from those obtained independently by a nonsurgeon investigator. In our earlier experience,[1] as well as that of Anvari et al.[14] and Geagea,[15] nearly all patients were offered the laparoscopic approach, whereas Peters and DeMeester[10] have recently advocated a more selective approach, excluding patients with Barrett's esophagus and esophageal stricture from consideration. These selection differences are likely to affect the incidence of postoperative dysphagia.

The double-blind prospective randomized trial reported in this paper minimizes the risk of bias inherent in the nonrandomized studies and retrospective reviews published previously. A significantly higher rate of postoperative manometric and other objective investigations was achieved than in these nonrandomized studies.[6,8]

The current trial demonstrated no significant differences between the study groups. Although some minor differences in individual dysphagia scores are apparent, when all criteria used for dysphagia assessment are considered together, the overall results reveal no trend toward an improved outcome in either group, nor any significant difference in lower esophageal sphincter pressure, esophageal emptying time, or barium meal outcome. It might be argued that a trend of difference favoring division of the SGVs has been established between the groups in certain parameters measured at 6 months (*e.g.*, dysphagia for lumpy solids [33% in the non division group *vs.* 29% in the division group], lower esophageal sphincter pressure [24.5 in the non division group *vs.* 20.9 mm Hg in the division group], lower esophageal sphincter nadir pressure [13.3 in the non division group *vs.* 11.0 mm Hg in the division group]) and that these figures may have reached significance in a larger study. Nevertheless, the other dysphagia scores and patient satisfaction were clearly comparable between the two groups, and esophageal emptying was quicker in the nondivision group. If there is any difference, it is likely to be marginal. The overall outcome scores also were not influenced by division of the SGVs. In terms of minimizing the incidence

of postoperative dysphagia, the construction of a loose wrap is probably more important than whether the SGVs are divided.

Outcomes may vary between surgeons with different levels of expertise and experience; indeed, our experience with laparoscopic fundoplication without division of the SGVs may not reflect the experience of other surgeons, especially during their initial learning curve. To achieve an acceptable outcome, the fundoplication must be constructed loosely when not dividing the SGVs. Nevertheless, this study has demonstrated that a sufficiently loose fundoplication can be constructed, irrespective of the status of the SGVs.

The ability of patients to belch after surgery was not improved by dividing the SGVs. Although approximately 40% to 50% of patients claimed they could not belch 6 months after surgery, this apparently high incidence reflects the supercompetent valve produced by the Nissen fundoplication. Other work from our department suggests that effective belching is unlikely after the Nissen procedure.[22] Patients who claim they can belch usually report esophageal belching rather than true gastroesophageal reflux of gas.

Dividing the SGVs was associated with an increase of about 40 minutes in operating time, resulting in increased expense and technical difficulty. The one patient who required early reintervention for bleeding demonstrates the added potential for intraoperative and postoperative hemorrhage that follows division of these vessels.

After short-term clinical follow-up at 6 months and objective investigation 3 to 4 months after surgery, this trial has failed to show any reduction in the incidence or severity of dysphagia after division of the SGVs during laparoscopic Nissen fundoplication. Early correction of reflux symptoms was identical between the groups, but longer-term follow-up will be needed to assess the durability of each operation and the incidence of recurrent reflux. At present, we conclude that division of the SGVs during laparoscopic Nissen fundoplication is indicated only in the uncommon circumstance that a loose wrap of fundus cannot be constructed.

Acknowledgments

The authors thank Mr. P.A. Game and Mr. R.S. Williams, who contributed patients to this study; Dr. M. Gabb, for her assistance with postoperative radiologic studies; and Mrs. L. Mackness, Ms. N. Ascott, Ms. T. Ellis, and Mrs. C. Bates-Brownsword, for their invaluable organizational and logistical support.

References

1. Watson DI, Jamieson GG, Devitt PG, et al. Changing strategies in the performance of laparoscopic Nissen fundoplication as a result of experience with 230 procedures. Surg Endosc 1995; 9:961–966.
2. Hinder RA, Filipi CJ, Wetscher G, et al. Laparoscopic Nissen fundoplication is an effective treatment for gastroesophageal reflux disease. Ann Surg 1994; 220:472–483.
3. McKernan JB, Champion JK. Laparoscopic antireflux surgery. Am Surg 1995; 61:530–536.
4. Lind JF, Burns CM, MacDougall JT. "Physiological" repair for hiatus hernia-manometric study. Arch Surg 1965; 91:233–237.
5. Watson A, Jenkinson LR, Ball CS, Barlow AP & Norris TL. A more physiological alternative to total fundoplication for the surgical correction of resistant gastro-oesophageal reflux. Br J Surg 1991; 78:1088–1094.
6. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease: evaluation of primary repair in 100 consecutive patients. Ann Surg 1986; 204:9–20.
7. Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. World J Surg 1977; 1:439–44.
8. Donahue PE, Samelson S, Nyhus LM, Bombeck T. The floppy Nissen fundoplication. Effective long-term control of pathological reflux. Arch Surg 1985; 120:663–668.
9. DeMeester TR, Stein HJ. Minimizing the side effects of antireflux surgery. World J Surg 1992; 16:335–336.
10. Peters JH, DeMeester TR. Early experience with laparoscopic Nissen fundoplication. *In* Szabo Z, Lewis JE, Fantini GA, eds. Surgical Technology International IV. San Francisco: Universal Medical Press; 1995:109–113.
11. Laycock WS, Trus TL, Hunter JG. New technology for the division of short gastric vessels during laparoscopic Nissen fundoplication. Surg Endosc 1996; 10:71–73.
12. Swanstrom LL, Pennings JL. Laparoscopic control of short gastric vessels. J Am Coll Surg 1995; 181:347–351.
13. Dallemagne B, Weerts JM, Jehaes C, Markiewicz S. Causes of failures of laparoscopic antireflux operations. Surg Endosc 1996; 10:305–310.
14. Anvari M, Allen C, Borm A. Laparoscopic Nissen fundoplication is a satisfactory alternative to long-term omeprazole therapy. Br J Surg 1995; 82:938–942.
15. Geagea T. Laparoscopic Nissen–Rossetti fundoplication. Surg Endosc 1994; 8:1080–1084.
16. Jamieson GG, Watson DI, Britten-Jones R, et al. Laparoscopic Nissen fundoplication. Ann Surg 1994; 220:137–145.
17. Dakkak M, Bennett JR. A new dysphagia score with objective validation. J Clin Gastroenterol 1992; 14:99–100.
18. Leonardi HK, Crozier RE, Ellis FH. Reoperation for complications of the Nissen fundoplication. J Thorac Cardiovasc Surg 1981; 81:50–56.
19. Rieger NA, Jamieson GG, Britten-Jones R, Tew S. Reoperation after failed antireflux surgery. Br J Surg 1994; 81:1159–1161.
20. Lundell L, Myers JC, Jamieson GG. The effect of antireflux operations on lower oesophageal sphincter tone and postprandial symptoms. Scand J Gastroenterol 1993; 28:725–731.
21. Peters JH, Heimbucher J, Kauer WKH, et al. Clinical and physiologic comparison of laparoscopic and open Nissen fundoplication. J Am Coll Surg 1995; 180:385–393.
22. Jamieson GG, Tew S, Holloway R, Ferguson S. Can patients belch after anti-reflux surgery? *In* Proceedings of the Sixth World Congress of the International Society for Diseases of the Esophagus Milan, Italy, 1995, p. 93 (abstract).

THIS MONTH'S FEATURE

ANNALS OF SURGERY
Vol. 235, No. 2, 165–170

Division of Short Gastric Vessels at Laparoscopic Nissen Fundoplication

A Prospective Double-Blind Randomized Trial With 5-Year Follow-Up

Colm J. O'Boyle, MD, FRCS, David I. Watson, MD, FRACS, Glyn G. Jamieson, MS, FRCS, FACS, FRACS, Jennifer C. Myers, BSc, Philip A. Game, FRCS, FRACS, and Peter G. Devitt, MS, FRCS, FRACS

From the University of Adelaide Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia

Objective
To determine whether division of the short gastric vessels at laparoscopic fundoplication confers long-term clinical benefit to patients.

Summary Background Data
Dividing the short gastric vessels during surgery for gastroesophageal reflux is controversial. This prospective randomized study was designed to determine whether there is a benefit in terms of patient outcome at a minimum of 5 years after primary surgery.

Methods
Between May 1994 and October 1995, 102 patients undergoing a laparoscopic Nissen fundoplication were randomized to have their short gastric vessels either divided or left intact. By September 2000, 99 (50 no division, 49 division) patients were available for follow-up, and they all underwent a detailed telephone interview by an independent and masked investigator.

Results
There were no significant differences between the groups at 5 years of follow-up in terms of the incidence of epigastric pain, regurgitation, odynophagia, early satiety, inability to belch, anorexia, nausea, vomiting, nocturnal coughing, and nocturnal wheezing. There was also no difference between the groups in the incidence of heartburn when determined by either yes/no questioning or a 0-to-10 visual analog scale. There was no difference between the groups in terms of the incidence and severity of dysphagia determined by yes/no questioning, 0-to-10 visual analog scales, or a composite dysphagia score. There was a significantly increased incidence of flatus production and epigastric bloating and a decreased incidence of ability to relieve bloating in patients who underwent division of the short gastric vessels.

Conclusions
Division of the short gastric vessels during laparoscopic Nissen fundoplication does not improve any measured clinical outcome at 5 years of follow-up and is associated with an increased incidence of "wind-related" problems.

Although the first laparoscopic antireflux procedure was performed almost a decade ago,[1] division of the short gastric vessels during laparoscopic Nissen fundoplication remains a controversial issue. The rationale behind dividing these vessels, and thereby fully mobilizing the gastric fundus, is to facilitate the fashioning of a loose "floppy" total fundoplication, a procedure said to be associated with a lower likelihood of a tight wrap and associated postoperative dysphagia and gas bloat. Proponents of division of the short gastric vessels generally report good results when they compare current patient cohorts in whom they undertook division of the short gastric vessels with their earlier experience (or that of other surgeons) when they did not divide the vessels. However, conclusions drawn from this analysis can be subject to the influence and bias of a learning curve.[2] On the other hand, other surgeons have reported good outcomes for patients undergoing total fundoplication in whom the short gastric vessels were not divided.[3]

Because of this controversy, in May 1994 we commenced a prospective randomized trial of division versus no division of the short gastric vessels in patients undergoing a laparoscopic Nissen fundoplication procedure. The early out-

Correspondence: David I. Watson, MD, University of Adelaide Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia.
E-mail: david.watson@adelaide.edu.au
Accepted for publication August 7, 2001.

comes from this trial have been published,[4] with clinical follow-up up to 6 months after surgery showing no significant difference in outcome between the two groups of patients, apart from operating time. These findings supported the proposition that division of the short gastric vessels was unnecessary for the performance of a laparoscopic Nissen fundoplication. Similar outcomes have been reported by Luostarinen and Isolauri[5] from a randomized trial of 50 patients undergoing open Nissen fundoplication and Blomqvist et al[6] from a randomized trial of 99 patients undergoing laparoscopic Nissen fundoplication. At the time of reporting the early outcomes for our trial, however, it was inappropriate to extrapolate the trial's short-term outcomes to long-term follow-up. For this reason we are now reporting the clinical outcome of our original trial with longer-term follow-up of at least 5 years in all of the original patients.

METHODS

From May 1994 to October 1995, 102 patients undergoing a laparoscopic 360° Nissen fundoplication were entered into a randomized trial of division versus no division of the short gastric vessels. Fifty patients were randomized to undergo fundoplication without short gastric vessel division and 52 to undergo division of these vessels. Full details of the methods used in the trial have been reported previously.[4] Between July and October 2000, when follow-up was at least 5 years for every patient, we obtained long-term clinical follow-up by interviewing the original patients using a structured questionnaire. This questionnaire was applied using a telephone interview, with the interview conducted by a surgeon (C.O'B.) who was not involved in the previous study. Further, he was unaware of the operation that had been performed.

Patient Selection and Surgical Technique

All patients entered into this trial underwent a laparoscopic Nissen fundoplication for objectively proven gastroesophageal reflux disease. Patients were excluded if they had an esophageal motility disorder that was at the time deemed to preclude a 360° fundoplication, if they required a concurrent abdominal procedure, or if they had undergone previous antireflux surgery. Randomization was carried out after the patient was anesthetized in the operating room.

Laparoscopic Nissen fundoplication was performed using a previously described technique.[7,8] The short gastric vessels were divided after being secured with metal clips. Division was undertaken from the lower margin of the spleen, proximally to the left pillar of the hiatus. In addition, attachments between the fundus and the undersurface of the diaphragm were routinely divided. The posterior attachments of the fundus were divided only when needed to achieve adequate fundal mobilization. Division was considered complete if the fundus of the stomach could be brought loosely around the esophagus, and the apex of the fundus could be used to construct the fundoplication. If the short gastric vessels were not divided, the anterior wall of the gastric fundus was pulled behind the esophagus, and the anterior fundus, not the apex, was used for the fundoplication.

A loose 1.5- to 2-cm wrap was fashioned with a 52F bougie sited within the abdominal esophagus for the purpose of calibration, for both techniques. If conversion to an open procedure was necessary, the randomization schedule was followed and the patients remained in the trial in the group to which they were originally allocated.

Follow-Up

All patients were unaware of the status of their short gastric vessels after surgery, and follow-up was performed by a surgeon investigator who was also unaware of the status of the vessels. Clinical follow-up was performed at least 5 years after the original surgical procedure. The clinical questionnaire applied was the same as that described in our previous report.[4] The presence of each of the following symptoms was sought: heartburn; epigastric pain; regurgitation; dysphagia for lumpy solids, soft solids, and liquids; odynophagia; early satiety; inability to belch; epigastric bloating; anorexia; nausea; vomiting; nocturnal coughing; and nocturnal wheezing. Patients were also asked whether their heartburn was controlled, whether they could relieve bloating after eating, and whether their diet was normal. An additional question inquiring whether patients passed excessive flatus was also asked during the late follow-up interview.

Heartburn, dysphagia for solids, and dysphagia for liquids were also scored using separate visual analog scales (0 = no symptoms, 10 = severe symptoms). Dysphagia was scored using a previously validated dysphagia score[9] (0 = no dysphagia, 45 = severe dysphagia). Patients were asked to rank the outcome of their surgery using a modified Visick grading (range 1–5, good outcome = 1 or 2) and whether they regarded the outcome of their surgery to be excellent, good, fair, or poor. Overall satisfaction with the surgical outcome was also assessed using a visual analog scale (0 = dissatisfied, 10 = satisfied). Formal evaluation using pH monitoring or esophageal manometry was not undertaken at 5 years of follow-up. The earlier outcomes of these studies were reported previously.[4]

Statistical Analysis

All analyses were performed on an intent-to-treat basis, with all patients remaining in their initial allocated group for this analysis. Data were entered into a dedicated database (FileMaker Pro version 4; Claris Corp., Santa Clara, CA) and analyzed using statistical software (Instat version 2.01; Graphpad Software, San Diego, CA). The chi-square test was used to determine the significance of 2×2 contingency

tables, and the Fisher exact test was applied as appropriate where numbers were small. A two-tailed Mann-Whitney test was used to assess differences between sets of nonparametric data.

RESULTS

Between May 1994 and October 1995, 102 patients who underwent a laparoscopic Nissen fundoplication at the Royal Adelaide Hospital were entered into this trial. Long-term follow-up was obtained for all patients. Three patients were not able to provide detailed clinical follow-up. Two had died of causes unrelated to their original surgery: a 37-year-old woman with diabetes died after an insulin overdose at 12 months, and a 63-year-old man died after esophagectomy performed for severe dysplasia in Barrett's epithelium at 13 months after surgery. A 69-year-old woman suffered a cerebrovascular accident 4 years after her fundoplication and could not communicate sufficiently to answer the follow-up questionnaire. Hence, 99 patients (vessels divided in 50, not divided in 49) completed the detailed clinical questionnaire 60 to 76 months after the original surgery (mean follow-up 68 months).

Both study groups were well matched for all preoperative factors previously reported: physical, demographic, preoperative clinical symptoms, grade of endoscopic esophagitis, presence of a hiatus hernia, and esophageal manometry and pH study outcomes.[4] During the initial 6 months of follow-up, two patients in the nondivision group required laparoscopic repair of a postoperative paraesophageal hernia, whereas three patients in the division group also underwent reoperation; one required laparotomy 6 hours after surgery for bleeding from a short gastric vessel, one patient required laparoscopic correction of a tight hiatal repair on postoperative day 5, and a further patient required open surgical revision for tight scarring at the esophageal hiatus 12 weeks after surgery.

Late reoperations (beyond 6 months) were performed in three patients because of failure of the original procedure. In the nondivision group a patient required open revision at 11 months for recurrent reflux resulting from a "slipped" Nissen fundoplication. In the division group dysphagia from a tight hiatus (hiatal stenosis)[8] led to open revision with widening of the esophageal hiatus at 9 months in one patient, and a further patient with recurrent reflux underwent successful laparoscopic correction of a "slipped" Nissen fundoplication at 6 years. In addition to these procedures, a further three patients underwent repair of a port-site hernia at 2, 4, and 6 years after surgery (two in the nondivision group, one in the division group). Eight patients (three in the nondivision group, five in the division group) also underwent endoscopy with dilatation for dysphagia. Six of these patients required a single dilatation only, whereas two patients required subsequent dilatations (both patients in the nondivision group).

At late follow-up there were no significant differences between the groups for the symptoms of epigastric pain, regurgitation, odynophagia, early satiety, inability to belch, anorexia, nausea, vomiting, nocturnal coughing, and nocturnal wheezing (Table 1). However, there was a significant difference in the incidence of flatus production, the occurrence of epigastric bloating, and a decreased ability to relieve bloating by belching, with a less satisfactory outcome in the group who underwent division of the short gastric vessels.

There was no difference in the incidence of heartburn when estimated empirically by a yes/no question or by the visual analog scale (Table 2). Although 18% (not divided) and 12% (divided) of patients reported the presence of at least occasional heartburn when asked the yes/no question, only five (three in the nondivision group, two in the division group) scored this symptom as greater than 5 of 10 on the visual analog scale. Most patients scored more than 5 of 10 before surgery. Nine patients (9%) were taking acid suppressive medication at the time of assessment (six in the nondivision group, three in the division group). Five of these patients (two in the nondivision group, three in the

Table 1. SYMPTOMS

	Preoperative		Late Postoperative Follow-Up	
	Not divided	Divided	Not divided	Divided
Heartburn	94%	88%	18%	12%
Epigastric pain	57%	56%	36%	35%
Regurgitation	90%	88%	4%	10%
Odynophagia	27%	16%	12%	16%
Early satiety	37%	30%	48%	51%
Epigastric bloat	59%	44%	48%	71%*
Anorexia	4%	6%	2%	6%
Nausea	27%	16%	12%	16%
Vomiting	22%	26%	4%	0%
Nocturnal cough	39%	40%	14%	12%
Nocturnal wheeze	16%	20%	8%	6%
Can relieve bloat	79%	79%	60%	39%†
Unable to belch	0%	0%	36%	47%
Eats normal diet	55%	78%	90%	82%
Increased flatus	Not applicable		70%	88%‡

No significant differences between trial groups ($P > .05$ at all follow-up intervals except * $P = .02$, † $P = .04$, ‡ $P = .03$ at late follow-up, Fisher exact test.

Table 2. ASSESSMENT OF HEARTBURN BY VISUAL ANALOG SCALE

	Vessels Not Divided	Vessels Divided	*P* Value
Preoperative	4.8 (3.7–5.8)	3.7 (2.8–4.7)	.18
≥5 years after surgery	1.1 (0.4–1.8)	1.0 (0.4–1.6)	.88

Figures expressed as mean (95% confidence intervals).

Table 3. DYSPHAGIA ASSESSMENT

	Preoperative		Late Postoperative	
	Not divided	Divided	Not divided	Divided
Dysphagia for				
Lumpy solids	31%	36%	36%	31%
Soft solids	4%	8%	12%	12%
Liquids	6%	2%	12%	10%
Visual analog scale				
Solids	1.7 (0.9–2.5)	2.5 (1.5–3.4)	2.2 (1.5–2.9)	2.8 (2.0–3.6)
Liquids	0.7 (0.1–1.4)	0.8 (0.2–1.3)	1.1 (0.5–1.7)	1.5 (0.8–2.2)
Dysphagia score				
Overall result	9.5 (5.5–13.6)	7.6 (4.5–10.8)	8.9 (6.2–11.6)	10 (7–13)
Scored 0 only	48%	57%	31%	34%

Figures are either percentage of total or mean (95% confidence intervals).
No tests for significance between groups at comparable follow-up intervals were significant ($P > .05$ at all follow-up intervals).

division group) had no recurrence of heartburn symptoms, and one reported minimal heartburn only (score 1 of 10 on visual analog scale). These patients had been prescribed medications by their general practitioner for a variety of symptoms unrelated to their previous reflux problem, and a further patient had developed a gastric ulcer. Only two patients were actually taking medication for reflux disease. One was taking 40 mg omeprazole per day for severe heartburn. This patient was also taking a nonsteroidal anti-inflammatory agent for arthritis. The other patient was taking ranitidine for moderate heartburn symptoms that, despite the need for medication, had been markedly improved by surgery.

Table 4. OUTCOME, SATISFACTION, AND VISICK GRADING

	Preoperative		Late Postoperative	
	Not divided	Divided	Not divided	Divided
Outcome				
Excellent	NA	NA	36%	37%
Good	NA	NA	42%	41%
Fair	NA	NA	14%	20%
Poor	NA	NA	8%	2%
Visick grade				
1	0%	0%	44%	27%
2	0%	0%	32%	43%
3	26%	29%	16%	14%
4	74%	71%	2%	10%
5	0%	0%	6%	6%
Satisfaction score				
Mean score	NA	NA	7.9	8.1
95% confidence interval	NA	NA	7.0–8.8	7.4–8.8

No tests for significance between groups at comparable follow-up intervals were significant ($P > .05$ at all follow-up intervals).

There was no difference between the groups in the incidence or severity of dysphagia when estimated by yes/no questions, visual analog scales, or the composite dysphagia score (Table 3). Of the patients who reported dysphagia to solids when asked the yes/no question, only five described dysphagia sufficient to require major dietary modification (two in the nondivision group, three in the division group; composite dysphagia score >30/45) at late review. Of the 10 patients who had a composite dysphagia score of more than 22.5 of 45, 7 had undergone division of the short gastric vessels ($P = .19$).

The overall outcome at late follow-up is summarized in Table 4. There was no overall difference between the groups in general patient satisfaction with the outcome of surgery. Five patients were not satisfied with the late outcome of their surgery. Four of these patients were in the nondivision group. One was not satisfied because she had required revision for a "slipped" Nissen at 9 months, and although she actually had minimal symptoms at late follow-up, she believed that the surgery had not corrected the additional symptom of a sore throat. Two patients (one in each group) offered recurrent heartburn as the predominant reason for their dissatisfaction, and two further patients (both in the nondivision group) were unhappy about postoperative dysphagia that had necessitated dilatation.

DISCUSSION

Nissen fundoplication, whether performed laparoscopically or by an open technique, involves the creation of a circumferential fundal wrap around the distal esophagus. To reduce the risk of postoperative problems, it is thought that this should be constructed loosely, with many surgeons advocating routine division of the short gastric vessels to fully mobilize the gastric fundus, thereby facilitating the formation of a loose "floppy" wrap.[10,11] However, Nissen's original procedures and Rossetti's subsequent modification

achieve a similar effect without division of the short gastric vessels.[12]

Findings from case series that compare outcome with data from historical trials have been used to support the argument for routine division of the short gastric vessels during both open and laparoscopic Nissen fundoplication.[10,11] Protagonists of division argue that dysphagia rates and reoperation rates are lower if the vessels are divided. However, because outcome data from historical controls whose vessels were left intact were used to support this conclusion,[13] there is a significant risk that the findings of these studies were influenced by a learning curve bias, where experience-related improvement in outcomes falsely conveys benefit for vessel division. Similarly, retrospective analyses of reasons for failure after laparoscopic Nissen fundoplication have also been used to advocate vessel division. These studies have usually compared earlier experience with a later series of patients, when numerous modifications to the original procedure have been introduced with time.[14,15]

Using similar methodology, some other surgeons have shown no benefit for patients undergoing division of the short gastric vessels during Nissen fundoplication. In a recent multicenter analysis of 1,470 patients, Pessaux et al[16] compared the outcomes of Nissen (n = 655), Rossetti (n = 423), and Toupet (n = 392) procedures. Short gastric vessel division provided no clinical benefit in terms of complications, reoperation rate, or dysphagia at various time intervals up to 2 years after surgery. Many authors report good outcomes from extensive experiences with Nissen fundoplication without division of the short gastric vessels.[3,17,18]

To resolve the question of whether division of the short gastric vessels is necessary, data from prospective randomized trials are required. The outcome of these studies should not be influenced by the problem of learning curve bias. The early report from our trial[4] and those of Luostarinen et al[5] and Blomqvist et al[6] are the only randomized trials that have addressed this issue. Luostarinen et al randomized 50 patients undergoing an open Nissen fundoplication to have their short gastric vessels either divided or left intact. At median follow-up of 36 months, no clinical outcome differences were seen between the two techniques for the problem of dysphagia, ability to belch, amount of flatus passed, or gas bloat symptoms. However, there was a significantly increased incidence of recurrent sliding hiatus hernia, as well as a trend toward a greater incidence of a defective wrap and recurrent reflux symptoms in the group of patients who had undergone division of the short gastric vessels. Blomqvist et al randomized 99 patients and found that division of the short gastric vessels conferred no outcome benefit at 1 year after surgery. The only significant difference between both techniques was the finding of a longer operating time for vessel division. Further, two patients required urgent early reoperation for complications directly related to vessel division.

The results of our trial, similar to those reported by the above authors, show no benefit from dividing the short gastric vessels. In our earlier report with 6 months of follow-up[4] we could not show any statistically significant outcome differences between the two groups, with the exception of longer operating time in the group of patients randomized to undergo vessel division. However, there was a trend toward an increased incidence of epigastric bloating (41% vs. 35%) and inability to relieve bloating (43% vs. 35%) in the division group.[4] At late follow-up this trend has persisted, and there is now an approximately 20% greater incidence of epigastric bloating and inability to relieve bloating in the division group. The rate of excess flatus production, which was not asked about in the original study, is high in both groups, but more so in the division group at late follow-up. We found this surprising, because most surgeons would expect that division of the short gastric vessels would guarantee a loose, floppy wrap that would be more amenable to the escape of gas, and therefore would hypothesize that vessel division would be associated with less wind retention and less flatus production per rectum. This raises the possibility that mechanisms other than the apparent "tightness" of the wrap are responsible for these postfundoplication problems.

It is known that the belch reflex originates when stretch receptors in the fundus of the stomach are stimulated.[19] One possible explanation of our findings is that division of the short gastric vessels is dividing the afferent nerves responsible for this reflex. The argument that it is not the degree of tightness of the wrap is supported by the fact that in this study there was no difference in the incidence of recurrent heartburn or dysphagia between the groups at late follow-up. The fact that only 5% of patients overall reported significant heartburn suggests that both variants of the Nissen fundoplication achieve effective long-term control of reflux.

At 6 months there was no difference between the groups for all measurements of dysphagia. This is also true at late follow-up. Interestingly, and perhaps somewhat disappointingly, there appears to have been some deterioration in the dysphagia scores for the same patient group compared with our previously reported data from 6 months of follow-up. This appears to be contrary to the belief that dysphagia after Nissen fundoplication continues to improve with time. However, the overall level of dysphagia at late follow-up in this report was not much greater than that identified before surgery in both study groups. Also, dysphagia of a degree spoiling the outcome was uncommon.

The reliability of the clinical data collected in this trial and the method of collection are important issues to consider when determining the validity of conclusions drawn from the trial. We have sought to reduce the risk of bias in data collection by ensuring that a single masked investigator asked each patient a standardized set of questions, and by applying a previously validated dysphagia score.[9] It could be argued that the interviews should have been undertaken in person rather than by telephone, but this was impractical given that the geographic mobility of the Australian popu-

lation has resulted in at least 20% of the trial patients moving more than 1,000 km away from our hospital. Only the use of telephone interviews enabled us to achieve 100% follow-up. For these reasons, we believe that we have avoided the potential for bias inherent in incomplete follow-up, lack of blinding, and follow-up by the operating surgeon. The further potential problem of learning curve bias was minimized by commencing the trial after our overall experience with laparoscopic Nissen fundoplication exceeded 200 procedures.

It could be argued that more reliable follow-up would have been obtained if pH monitoring or esophageal manometry were performed at the 5-year follow-up point. However, we have previously reported that the results of these studies do not correlate well with clinical outcome after laparoscopic Nissen fundoplication,[20] and technical success judged by these tests or judged by the operating surgeon does not always equate to clinical success as determined by the individual patient. Hence the clinical outcome, as determined by the patient, is likely to be more useful as a measure of success than the outcome of physiologic testing or other parameters.

A further area in which this trial can be criticized is the issue of posterior fundal mobilization. In our study, not all patients undergoing division of the short gastric vessels had the posterior fundal attachments divided. Nevertheless, a recent randomized trial of Nissen fundoplication with division of the short gastric vessels and posterior versus no posterior fundal mobilization has not shown any benefit for complete fundal mobilization.[21] Further, in the randomized study of Blomqvist et al,[6] where no division of short gastric vessels was compared with complete fundal mobilization, again no difference in outcome was found.

Data from our trial have now shown no benefit for division of the short gastric vessels during laparoscopic Nissen fundoplication at both short- and long-term follow-up. This study, in association with data reported previously, suggests that short gastric vessel division lengthens the procedure, adds complexity and expense, and is followed by a higher incidence of "wind" problems. On the basis of these findings, we believe it is unnecessary to divide the short gastric blood vessels routinely during laparoscopic Nissen fundoplication.

References

1. Dallemagne B, Weerts JM, Jehaes C, et al. Laparoscopic Nissen fundoplication: preliminary report. Surg Laparosc Endosc 1991; 1:138–143.
2. Watson DI, Jamieson GG, Baigrie RJ, et al. Laparoscopic surgery for gastro-oesophageal reflux: beyond the learning curve. Br J Surg 1996; 83:1284–1287.
3. Anvari M, Allen C. Laparoscopic Nissen fundoplication: two-year comprehensive follow-up of a technique of minimal paraesophageal dissection. Ann Surg 1998; 227:25–32.
4. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. Ann Surg 1997; 226: 642–652.
5. Luostarinen ME, Isolauri JO. Randomized trial to study the effect of fundic mobilization on long-term results of Nissen fundoplication. Br J Surg 1999; 86:614–618.
6. Blomqvist A, Dalenback J, Hagedorn C, et al. Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication. J Gastrointest Surg 2000; 4:493–500.
7. Jamieson GG, Watson DI, Britten-Jones R, et al. Laparoscopic Nissen fundoplication. Ann Surg 1994; 220:137–145.
8. Watson DI, Jamieson GG, Devitt PG, et al. Changing strategies in the performance of laparoscopic Nissen fundoplication as a result of experience with 230 operations. Surg Endosc 1995; 9:961–966.
9. Dakkak M, Bennett J. A new dysphagia score with objective validation. J Clin Gastroenterol 1992; 14:99–100.
10. Donahue PE, Samelson S, Nyhus LM, et al. The floppy Nissen fundoplication. Effective long-term control of pathologic reflux. Arch Surg 1985; 120:663–668.
11. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. Ann Surg 1986; 204:9–20.
12. Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. World J Surg 1977; 1:439–444.
13. Patti MG, Arcerito M, Feo CV, et al. An analysis of operations for gastroesophageal reflux disease: identifying the important technical elements. Arch Surg 1998; 133:600–607.
14. Dallemagne B, Weerts JM, Jehaes C, et al. Causes of failures of laparoscopic antireflux operations. Surg Endosc 1996; 10:305–310.
15. Hunter JG, Swanstrom L, Waring JP. Dysphagia after laparoscopic antireflux surgery. The impact of operative technique. Ann Surg 1996; 224:51–57.
16. Pessaux P, Arnaud J, Ghavami B, et al. Laparoscopic antireflux surgery: comparative study of Nissen, Nissen-Rosetti, and Toupet fundoplication. Surg Endosc 2000; 14:1024–1027.
17. Geagea T. Laparoscopic Nissen-Rossetti fundoplication. Surg Endosc 1994; 8:1080–1084.
18. Zaninotto G, Molena D, Ancona E. A prospective multicenter study on laparoscopic treatment of gastroesophageal reflux disease in Italy: type of surgery, conversions, complications, and early results. Study Group for the Laparoscopic Treatment of Gastroesophageal Reflux Disease of the Italian Society of Endoscopic Surgery (SICE). Surg Endosc 2000; 14:282–288.
19. Wyman JB, Dent J, Heddle R, et al. Control of belching by the lower oesophageal sphincter. Gut 1990; 31:639–46.
20. Mathew G, Watson DI, Myers JC, et al. Oesophageal motility before and after laparoscopic Nissen fundoplication. Br J Surg 1997; 84: 1465–1469.
21. Richardson MA, Smith GS, Baladas HG, et al. Laparoscopic fundoplication: a randomised control trial of division of the short and posterior vessels vs division of short gastric vessels alone [abstract]. Aust NZ J Surg 2000; 70:A92.

RANDOMIZED CONTROLLED TRIALS

Randomized Trial of Division Versus Nondivision of the Short Gastric Vessels During Laparoscopic Nissen Fundoplication

10-Year Outcomes

Huiqi Yang, MD, David I. Watson, MD, FRACS,* Carolyn J. Lally, RN, RM,*† Peter G. Devitt, MS, FRCS, FRACS,† Philip A. Game, MS, FRCS, FRACS,† and Glyn G. Jamieson, MS, FRACS†*

Background: Although laparoscopic Nissen fundoplication is an effective procedure for the treatment of gastroesophageal reflux, in some patients it is followed by troublesome side effects, such as dysphagia, abdominal bloating, and inability to belch. It has been claimed that dividing the short gastric blood vessels during laparoscopic Nissen fundoplication minimizes the risk of these problems. We have previously reported the 6-month and 5-year outcomes from a randomized trial, which have shown no advantages after division of these vessels. In this study, we determined the longer-term (10 years) outcomes from this trial.

Methods: From May 1994 to October 1995, 102 patients with gastroesophageal reflux disease who underwent a laparoscopic Nissen fundoplication were entered into this randomized trial (vessels divided in 50, not divided in 52). At 10-year follow-up, 88 patients provided clinical follow-up information. Follow-up was obtained by telephone interview conducted by an independent and blinded investigator who applied a standardized questionnaire.

Results: At 10-year follow-up no significant differences between the 2 groups could be identified. Heartburn, dysphagia, and overall satisfaction were similar for both study groups.

Conclusions: The 10-year clinical outcomes from this trial have shown no benefit for division of the short gastric vessels during laparoscopic Nissen fundoplication.

(*Ann Surg* 2008;247: 38–42)

Laparoscopic Nissen fundoplication is widely regarded to be the gold standard for the surgical treatment of gastroesophageal reflux disease. The total fundic wrap achieves very effective control of reflux, although it can be followed by some troublesome side effects, such as dysphagia, gas bloat, and inability to belch.[1–3] To minimize the risk of developing these side effects, Nissen's procedure has been modified in a variety of ways. One of these modifications has been the introduction of routine division of the short gastric blood vessels.[4] It has been claimed that this step is followed by a lower risk of dysphagia, gas bloat, and other side effects.[4,5] However, some surgeons claim that an equally good outcome can be achieved without dividing these vessels.[6]

After the introduction of laparoscopic techniques for Nissen fundoplication, this aspect of antireflux surgery became particularly controversial, and strong arguments were made for routine division of the short gastric vessels.[7,8] For this reason, in 1994 we commenced a prospective double-blind randomized trial of division versus no division of the short gastric blood vessels during the laparoscopic Nissen fundoplication. We have reported the 6-month and 5-year outcomes from this trial in previous publications.[9,10] At these follow-up intervals, the clinical and objective outcomes were similar, and we concluded that division of short gastric vessels is not necessary during laparoscopic Nissen fundoplication. It is now more than 10 years since we closed the recruitment phase in this trial, and in our current article we have determined the clinical outcomes at 10-year follow-up.

METHODS

From May 1994 to October 1995, 102 patients with gastroesophageal reflux disease who underwent a laparoscopic Nissen fundoplication were entered into this randomized trial. Fifty patients were randomized to undergo a 360° fundoplication with division of the short gastric blood vessels, and 52 were randomized to undergo a similar fundoplication without division of these vessels. The protocol and full details for this trial have been

From the *Flinders University Department of Surgery, Flinders Medical Centre, Bedford Park, South Australia; and †University of Adelaide Discipline of Surgery, Royal Adelaide Hospital, Adelaide, South Australia.
Supported by the National Health and Medical Research Council of Australia (Project Grant Number 375111).
Reprints: David I. Watson, MD, FRACS, Flinders University Department of Surgery, Room 3D211, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia. E-mail: david.watson@flinders.edu.au.

ISSN: 0003-4932/08/24701-0038
DOI: 10.1097/SLA.0b013e31814a693e

described in a previous report.[10] In our current study we determined the 10-year clinical outcomes of this trial. Follow-up information was obtained by telephone interview using a standardized questionnaire. Interviews and data analysis were conducted in a blinded fashion by investigators who were not involved in the original recruitment of patients.

Patients were considered for entry into the trial if they were determined to be suitable to undergo a laparoscopic Nissen fundoplication operation. All patients were diagnosed with gastroesophageal reflux disease and had either endoscopic evidence of ulcerative esophagitis or abnormal esophageal pH monitoring. Patients were excluded if they had an esophageal motility disorder, which precluded a 360° fundoplication, if they required a concurrent abdominal procedure at the same time as the fundoplication, or if they had undergone a previous antireflux procedure.

The technique for laparoscopic Nissen Fundoplication has been described previously.[11] A loose 1.5–2-cm wrap was constructed with a 52F bougie in the abdominal esophagus. If short gastric vessels were to be divided, they were secured by metal clips and divided (ultransonic shears were not available when the surgery in this trial was undertaken). Division of the vessels began at the level of lower margin of spleen and continued proximally to the angle of His and the left pillar of the esophageal hiatus, so that the fundus of stomach was fully mobilized. If short gastric vessels were not to be divided, the anterior wall of gastric fundus was pulled behind the esophagus, manipulated until the loosest part was identified, and this was then used to construct a loose wrap.

A telephone interview using a standardized questionnaire was used for the 10-year follow-up. The presence of various clinical symptoms were determined using yes/no questions: heartburn, epigastric pain, regurgitation, dysphagia for lumpy solids, soft solids and liquids, odynophagia, early satiety, inability to belch, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing, and wheezing. The ability to relieve bloating and whether a normal diet was being consumed were also determined. Heartburn, dysphagia for solids and liquids were also assessed using visual analogue scales (0 = no symptom, 10 = severe symptom). A composite dysphagia score which assessed the ability to swallow 9 different liquid and solid substances was also applied (0 = no dysphagia, 45 = total dysphagia).[12] Patients were also asked to assess outcome of operation using a modified Visick grading (range 1–5, good outcome = 1 or 2), a visual analogue satisfaction scale (0 = unsatisfied, 10 = satisfied), and to rank the outcome of operation as excellent, good, fair, or poor. These symptom scoring systems have all been described elsewhere.[9] Routine objective investigation using esophageal manometry, 24-hour pH monitoring, and endoscopy was not undertaken at 10-year follow-up.

All analyses were performed on an intention-to-treat basis, with all patients remaining in their initial allocated group for analysis. Data were entered into a computer database (FileMaker Pro version 8.5; FileMaker Inc, http://www.filemaker.com) and were analyzed using statistical software (Instat version 3; Graphpad Software, San Diego, CA). Fisher exact test was used to determine the significance of 2×2 contingency tables, and a 2-tailed Mann-Whitney U test was used to assess differences between nonparametric data sets.

RESULTS

From May 1994 and October 1995, 102 patients who underwent a laparoscopic Nissen fundoplication were enrolled in this trial. At 10-year follow-up, 3 patients were lost to follow-up, and 2 patients refused follow-up. Hence, there were 97 (95%) patients for whom an outcome could be determined. Six patients died during follow-up. None of these deaths were related to the original Nissen fundoplication procedure. Three patients were also unable to provide detailed clinical information at 10-year follow-up because of dementia (2) or the effects of a cerebrovascular accident (1). Hence, detailed clinical follow-up was available at 10 years from 88 patients (vessels divided in 44, not divided in 44).

The preoperative, operative, and early postoperative details for the 2 study groups were similar. These results have been reported previously.[9,10] Four patients who were randomized to undergo division of the short gastric vessels had a procedure which was converted to an open operation, whereas all procedures in the nondivision group were completed laparoscopically. The mean operating time for the nondivision group was 71 minutes versus 108 minutes for the division group ($P < 0.0001$).

During the 10-year follow-up period, 13 patients (5 in nondivision group, 8 in division group) underwent a further operation for either recurrent reflux or a problem, which can be attributed to the original fundoplication. Eight of these procedures were undertaken within 6 months of the original operation: 3 patients in nondivision group (1—severe dysphagia, 2—paraesophageal hiatus hernia) and 5 in division group (dysphagia—4, bleeding short gastric blood vessel—1). Five further operations were undertaken during later follow-up: 2 patients in the nondivision group (postprandial pain because of bilobed stomach—1, dysphagia—1) and 3 patients in the division group (paraesophageal hiatus hernia—1, dysphagia because of a tight hiatus—1, recurrent reflux because of slipped fundoplication—1). Only 2 of the reoperations were undertaken beyond the 5-year follow-up time point.

At 10-year follow-up, there were no significant differences in most of the symptoms reported by each group of patients (Table 1). Patients in the nondivision group were more likely to be able to relieve symptoms of abdominal bloating by belching ($P = 0.05$).

The outcome for heartburn is summarized in Table 2. No significant differences between the study groups were identified. Thirteen (15%) patients (4 in the division group and 9 in the nondivision group) were taking proton pump inhibitor medication at 10-year follow-up. The outcome for dysphagia at 10 years is summarized in Table 3. No significant differences were seen. Overall outcome is summarized in the Table 4. The majority of patients in both groups were satisfied with their clinical outcome at 10 years. There were no significant differences between the 2 groups.

TABLE 1. Pre- and Postoperative Symptoms Assessed by Yes/No Questions

	Preoperative		10-Year Postoperative	
	Not Divided (%)	Divided (%)	Not Divided (%)	Divided (%)
Heartburn	94	88	18	11
Epigastric pain	57	56	22	24
Regurgitation	90	88	17	9
Odynophagia	27	6	15	6
Early satiety	37	30	29	44
Epigastric bloating	59	44	64	66
Anorexia	4	6	17	9
Nausea	27	16	10	21
Vomiting	22	26	5	3
Nocturnal cough	39	40	20	24
Nocturnal wheeze	16	20	10	9
Can relieve bloating	79	79	80	61
Unable to belch	0	0	32	41
Eats normal diet	55	78	89	91

No significant differences demonstrated between trial groups (ie, $P > 0.05$ for all comparisons).

DISCUSSION

Whether division of the short gastric blood vessels during Nissen fundoplication can contribute to a better postoperative outcome with fewer postoperative side effects, has been a controversial issue for many years.[4–6] Some surgeons argue that division of these vessels allows a looser antireflux wrap to be constructed, resulting in a lower incidence of postoperative dysphagia and gas bloat.[4,5] On the other hand, other reports claim that the division of the short gastric vessels does not influence the clinical outcome.[13,14] However, most of the studies which have investigated this issue have compared the outcomes of operations performed by different surgeons at different stages in their surgical experience, and such analyses are less reliable than the outcomes from prospective randomized trials.[9,10,13,14]

The results from 4 prospective randomized trials (including our study) of Nissen fundoplication with versus without division of the short gastric blood vessels have now been published, and none of these have supported routine division of the short gastric vessels.[9,10,13–15] However, late outcomes beyond 5-year follow-up are yet to be reported. Hence, one aim of our current study was to determine whether division of the short gastric blood vessels influences long-term clinical outcome.

The 6-month and 5-year follow-up outcomes from our trial have been published previously and no significant benefit from dividing the short gastric vessels was demonstrated.[9,10] At 5-year follow-up, patients who underwent division of the short gastric vessels were more likely to report epigastric bloating (71% vs. 48%) and be unable to relieve bloating by belching (61% vs. 40%). However, at 10-year follow-up, this difference was not as obvious. There was no significant difference in the incidence of epigastric bloating (66% vs. 64%) although patients who underwent vessel division were less able to relieve bloating by belching (39% vs. 20%, $P = 0.05$). At 10-year follow-up, there were no significant difference between the study groups for either incidence or severity of dysphagia, heartburn, or overall satisfaction. These outcomes were identical to the outcome of earlier follow-up.

In recent years, the majority of randomized and nonrandomized studies have reported similar outcomes to our trial.[13–17] In a study of 138 patients, Sato et al[16] analyzed the effect of short gastric vessel division on postoperative dysphagia. They reported that laparoscopic Nissen fundoplication with or without division of short gastric vessel achieved a similar outcome. Their research suggested that patient selection and accurate construction of the fundoplication were more important factors in minimizing postoperative dysphagia.

In a manometry-based study from a Swedish randomized trial,[18] the manometric outcomes for 12 patients who underwent division of the short gastric vessels were compared with 12 patients who did not. At 1-year follow-up no significant differences were found, except more transient

TABLE 2. Dysphagia Assessment

	Preoperative		10-Year Postoperative	
	Not Divided (%)	Divided (%)	Not Divided (%)	Divided (%)
Dysphagia for				
Lumpy solids	31	36	34	44
Soft solids	4	8	10	15
Liquids	6	2	17	14
Visual analogue scale				
Solids	1.7 (0.9–2.5)	2.5 (1.5–3.4)	2.3 (1.6–3.0)	2.5 (1.7–3.2)
Liquids	0.74 (0.1–1.4)	0.78 (0.2–1.3)	1.5 (0.9–2.2)	1.2 (0.6–1.9)
Dysphagia score				
Overall result	9.5 (5.5–13.6)	7.6 (4.5–10.8)	10.6 (7.1–14.1)	10.9 (7.7–14.0)
Scored 0 only	48	57	34	20

Figures are expressed as either percentage of total or mean (95% confidence intervals). No tests for significance between groups at comparable follow-up intervals were significant (ie, $P > 0.05$ for all comparisons).

TABLE 3. Overall Outcome of Surgery

	Preoperative		10-Year Postoperative	
	Not Divided (%)	Divided (%)	Not Divided (%)	Divided (%)
Outcome				
Excellent	NA	NA	44	50
Good	NA	NA	46	35
Fair	NA	NA	5	9
Poor	NA	NA	5	6
Visick grade				
1	0	0	27	29
2	0	0	61	53
3	26	29	10	12
4	74	71	2	6
5	0	0	0	0
Satisfaction score				
Mean score	NA	NA	7.9	8.3
95% CI	NA	NA	7.0–8.9	7.5–9.0

No tests for significance between groups at comparable follow-up intervals were significant (ie, $P > 0.05$ at all follow-up intervals).

NA indicates not applicable; CI, confidence interval.

TABLE 4. Assessment of Heartburn Using 0–10 Visual Analog Scale

	Vessels Not Divided	Vessels Divided	*P*
Preoperative	4.8 (3.7–5.8)	3.7 (2.8–4.7)	0.18
10-yr postoperative	1.7 (0.9–2.5)	1.1 (0.6–1.6)	0.73

Figures expressed as mean (95% confidence intervals).

lower esophageal sphincter relaxations were recorded in the group whose vessels were not divided, suggesting that preservation of the vessels led to better maintenance of the ability to vent air from the stomach.

Huntington et al examined the geometry involved in the construction of a laparoscopic Nissen fundoplication by measuring individual variations in fundic length.[19] Their findings also suggested that division of short gastric vessels was not necessary in many patients. This study suggested that tension on the antireflux wrap, rather than division of the short gastric vessels, was the crucial factor for achieving a satisfactory clinical outcome. However, postoperative symptoms and objective outcomes were not determined in this study.

Potential bias is minimized in a randomized trial and the results of trials such as ours should be more reliable than other nonrandomized trials and case series. Furthermore, our trial is the first prospective randomized trial to report long-term (10-year) follow-up. The data in this study was collected by a "blinded" research team, which applied standardized questionnaires, and the analysis of the data was not performed by the original surgeons who contributed to the trial. In a further attempt to minimize bias, this trial was commenced after more than 200 laparoscopic Nissen fundoplication procedures had been undertaken in our department.

In our current report, we have only evaluated the clinical outcome. Although, objective outcomes from tests such as esophageal manometry and pH monitoring would have provided additional information, such data was not available, and our previous experience, and that of others, is that compliance with objective follow-up is always incomplete, whereas a concerted effort can be made to obtain near complete clinical data. In addition, in previous research we have only shown poor (if any) correlations between objective outcomes and clinical symptoms after Nissen fundoplication.[20] Therefore, from the patient's perspective, clinical symptoms are more crucial in providing clinically useful information about the success of this surgical procedure.

In addition to the question, which was specifically addressed in our trial, the outcome data also provides further information about the longer-term (10 years) outcome for patients who have undergone a laparoscopic Nissen fundoplication. Nearly 90% of patients had a good or excellent clinical outcome at 10-year follow-up, only 15% were taking proton pump inhibitor medication, and further surgical intervention beyond 5 years was uncommon. These outcomes are similar to those seen in a larger cohort of patients from our institution who were followed clinically for 10–14 years after a Nissen fundoplication.[21] Contrasting these good outcomes, is the report from Spechler et al,[22] which describes long-term follow-up of patients enrolled in a randomized trial of open Nissen fundoplication versus medication for reflux. This study reported that 62% of surgically treated patients used proton pump inhibitor medication at mean 9.1-year follow-up. However, it should be recognized that the follow-up in the study by Spechler et al was incomplete. They obtained long-term outcomes from only 37 surgically treated patients, ie, approximately 25% of the original study group. Our studies, however, have achieved much more complete clinical follow-up (95%) in larger groups of patients, and these results could better reflect the long-term outcome after laparoscopic Nissen fundoplication for gastroesophageal reflux.

In conclusion, the long-term (10 years) outcomes of our randomized trial and the earlier outcomes from other studies[13–15] have not shown any benefit for division of the short gastric blood vessels during laparoscopic Nissen fundoplication. For this reason, we consider that routine division of these vessels is unnecessary. In addition, the longer-term outcome for patients undergoing laparoscopic Nissen fundoplication is excellent.

ACKNOWLEDGMENTS

The authors thank Ms. Tanya Ellis (database management), Ms. Nicola Ascott (finding "lost" patients), and Ms. Lorraine Sheehan-Hennessy (conducting the telephone interviews). Their contributions ensured that near complete clinical follow-up was available for analysis.

REFERENCES

1. Negre JB. Post-fundoplication? *Ann Surg.* 1983;198:698–700.
2. Luostarinen M, Isolauri J, Laaitinen J, et al. Fate of Nissen fundoplication after 20 years. A clinical, endoscopical and functional analysis. *Gut.* 1993;34:1015–1020.

3. Perdikis G, Hinder RA, Lund RJ, et al. Laparoscopic Nissen fundoplication: where do we stand? *Surg Laparosc Endosc*. 1997;7:17–21.
4. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastro-esophageal reflux disease. *Ann Surg*. 1986;204:9–20.
5. Donahue PE, Samuelson S, Nyhus LM, et al. The floppy Nissen fundoplication. Effective long-term control of pathologic reflux. *Arch Surg*. 1985;120:663–668.
6. Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. *World J Surg*. 1977;1:439–444.
7. Richardson WS, Hunter JG. Laparoscopic floppy Nissen fundoplication. *Am J Surg*. 1999;177:155–157.
8. Davis RE, Awad ZT, Filipi CJ. Technical factors in the creation of a "floppy" Nissen fundoplication. *Am J Surg*. 2004;187:724–727.
9. O'Boyle CJ, Watson DI, Jamieson GG, et al. Division of short gastric vessels at laparoscopic Nissen fundoplication. A prospective double-blind randomized trial with 5-year follow-up. *Ann Surg*. 2002;235:165–170.
10. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg*. 1997;226:642–652.
11. Jamieson GG, Watson DI, Britten-Jones R, et al. Laparoscopic Nissen fundoplication. *Ann Surg*. 1994;220:137–145.
12. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol*. 1992;14:99–100.
13. Loustarinen MES, Isolauro JO. Randomized trial to study the effect of fundic mobilization on long-term results of Nissen fundoplication. *Br J Surg*. 1999;86:614–618.
14. Blomqvist A, Dalenback J, Hagedorn C, et al. Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication. *J Gastrointest Surg*. 2000;4:493–500.
15. Chrysos E, Tzortzinis A, Tsiaoussis J, et al. Prospective randomized trial comparing Nissen to Nissen-Rossetti technique for laparoscopic fundoplication. *Am J Surg*. 2001;182:215–221.
16. Sato K, Award ZT, Filipi CJ, et al. Causes of long-term dysphagia after laparoscopic Nissen fundoplication. *JSLS*. 2002;6:35–40.
17. Felix VN, Yogi I, Perini M, et al. Surgical treatment of the non-complicated gastroesophageal reflux: fundoplication without division of the short gastric vessels. *Arq Gastroenterol*. 2002;39:93–97.
18. Engstrom C, Blomqvist A, Dalenback J, et al. Mechanical consequences of short gastric vessel division at the time of laparoscopic total fundoplication. . 2004;8:442–447.
19. Huntington TR, Danielson L. Variation in fundic dimensions with respect to short gastric vessel division in laparoscopic fundoplication. *Surg Endosc*. 2001;15:76–79.
20. Mathew G, Watson DI, Myers JC, et al. Oesophageal motility before and after laparoscopic Nissen fundoplication. *Br J Surg*. 1997;84:1465–1469.
21. Kelly J, Watson DI, Chin K, et al. Laparoscopic Nissen fundoplication—clinical outcomes at 10 years. *J Am Coll Surg*. 2007;205:570–575.
22. Spechler SJ, Lee E, Ahnen D, et al. Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial. *JAMA*. 2001;285:2331–2338.

Meta-analysis

Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of the short gastric vessels during Nissen fundoplication

C. Engström[1,3], G. G. Jamieson[2], P. G. Devitt[2] and D. I. Watson[3]

[1]Department of Surgery, Sahlgrenska University Hospital, Göteborg, Sweden, and [2]Adelaide University Discipline of Surgery, Royal Adelaide Hospital, and [3]Flinders University Department of Surgery, Flinders Medical Centre, Adelaide, South Australia, Australia
Correspondence to: Dr C. Engström, Department of Surgery, Sahlgrenska University Hospital, S-413 45 Göteborg, Sweden
(e-mail: cecilia.engstrom@surgery.gu.se)

Background: **Randomized trials suggest that division of the short gastric vessels during Nissen fundoplication is unnecessary. Some trials report an increased risk of gas bloat symptoms following division of the short gastric vessels. In this study long-term follow-up data from the two largest randomized clinical trials of division *versus* no division of the short gastric vessels during laparoscopic Nissen fundoplication were combined to determine whether there were differences in late outcome.**

Methods: **Patients with gastro-oesophageal reflux disease who underwent primary laparoscopic antireflux surgery and were included in two previously reported randomized trials were studied. Of 99 patients enrolled in the Swedish study and 102 in the Australian study, the short gastric vessels were divided in 104 and left intact in 97. Data sets were combined and late clinical outcomes analysed.**

Results: **At 10–12 years' follow-up (mean 11·5 years) clinical data were obtained from 170 patients (86 with vessels divided, 84 undivided). Statistical analysis of the combined data set showed no significant differences in symptoms of heartburn or dysphagia, ability to belch or vomit, and use of antisecretory medications. Division of the short gastric vessels was associated with a higher rate of bloating symptoms (72 *versus* 48 per cent; $P = 0{\cdot}002$).**

Conclusion: **Division of the short gastric vessels is followed by a slightly poorer clinical outcome at late follow-up after Nissen fundoplication. Surgeons should avoid dividing these vessels when undertaking a laparoscopic Nissen fundoplication.**

Paper accepted 22 March 2011
Published online 27 May 2011 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.7563

Introduction

The treatment of gastro-oesophageal reflux disease has changed over the past two decades with the development of both laparoscopic fundoplication techniques and more effective medical therapy. Various types of fundoplication have been introduced in the hope of minimizing the risk of postoperative side-effects such as dysphagia or gas bloat symptoms. Randomized controlled trials evaluating technical aspects of the operation have been undertaken, involving open and laparoscopic surgery, partial *versus* total wraps, and anterior *versus* posterior wraps[1–4].

In some parts of the world, such as Australia, the number of antireflux operations is increasing[5], whereas in others concern about the risk of long-term side-effects following surgery has led to a decline in the number of patients undergoing fundoplication. For example, in Sweden the number of antireflux operations declined from 17·5 per 100 000 inhabitants in 1998 to 11 per 100 000 in 2005[6].

It important to understand how best to achieve good outcomes. Better preoperative investigation with new technologies such as impedance and high-resolution oesophageal manometry might improve patient selection for surgery. For those undergoing operation, however, the nature of the procedure and quality of surgery may be critical.

There has been much argument about the need to divide the short gastric vessels to mobilize fully the gastric fundus during Nissen fundoplication. This manoeuvre allows a floppier wrap to be constructed, although five randomized

trials have failed to demonstrate any advantages of full mobilization of the fundus[7–11]. Two of these trials showed a significantly increased rate of bloating symptoms in patients undergoing division of the short gastric vessels[7,8], and a further trial showed a trend towards increased bloating that did not reach statistical significance[9]. The present study involved a meta-analysis of the original data sets from the Australian and Swedish randomized trials, to identify any outcome differences in the longer term between patients undergoing laparoscopic Nissen fundoplication with or without division of the short gastric vessels.

Methods

Data sets from two previously reported randomized trials of division *versus* non-division of the short gastric vessels during laparoscopic Nissen fundoplication were combined[8,9]. A meta-analysis of late follow-up from the original data sets was performed. The local clinical research ethics committees at both institutions approved the original study protocols. Informed consent to participate in the trials, including long-term follow-up, was obtained from each patient. Trial protocols and 5–10-year follow-up within these trials have been reported previously[12–14].

Both trials used a similar protocol and included patients with proven chronic gastro-oesophageal reflux disease who presented for primary laparoscopic Nissen fundoplication. All patients underwent surgery in either Adelaide, South Australia, or Göteborg, Sweden. The Australian patients were randomized in the operating room after commencing anaesthesia, and the Swedish patients were randomized in the ward the day before the surgical procedure. Randomization was carried out for the Swedish cohort using a computer program, taking into consideration the severity and duration of disease, sex, age and body mass index of each patient. For the Australian cohort, randomization was undertaken using a closed envelope method with no stratification.

Surgical technique

The technique for laparoscopic Nissen fundoplication used in each centre has been described in detail elsewhere[8,9]. The hiatus was repaired posteriorly, and the short gastric vessels were divided according to the randomization schedule. In both countries short gastric vessel division also included dissection of all tissues between the posterior portion of the stomach and the left hiatal pillar, starting at the level of the inferior pole of the spleen and progressing upwards along the greater curvature of the stomach. If the short gastric vessels were not divided, the anterior wall of the fundus was pulled behind the oesophagus and manipulated until its loosest part was identified. This was then used to construct a loose wrap. To ensure that the completed fundoplication was tension-free, a 52-Fr bougie was placed across the gastro-oesophageal junction during construction of the wrap. In Sweden the wrap was sutured by three interrupted polyester sutures and made approximately 1·5 cm long. In Australia three polypropylene sutures were used to construct a wrap of similar length.

Symptom assessments

A standardized questionnaire was used in both countries to obtain clinical follow-up information, and many questions were identical in both trials. Data from the common questions were combined into a single data set and analysed. Questionnaires were completed by telephone interview or mail. Reasonable attempts were made to identify and obtain late follow-up clinical data from patients who had previously been 'lost to follow-up'. In both countries, the collection of clinical data and subsequent analysis were conducted in a similar fashion. The interviewers undertaking follow-up were not involved in the original surgery, and were blinded to the operation actually undertaken.

Questions available for analysis included yes/no responses addressing heartburn, dysphagia and bloating in Australian patients, and a grading scale addressing the same symptoms in Swedish patients. In the Swedish group the data were reinterpreted into the Australian yes/no framework (none or mild, no; moderate or severe, yes). In both groups bloating was defined as the sensation of abdominal swelling of any type, and the presence or absence of this symptom was determined by the individual patient. In both the Swedish and the Australian patients the ability to belch and vomit, and any use of antisecretory medication were determined using yes/no responses. The ability to belch included belching achieved by each patient, and this definition encompassed both oesophageal and gastric belching. Patients were asked a secondary question to determine whether the act of belching relieved any abdominal bloating symptoms.

A previously validated composite dysphagia score ranging from 0 to 45 was used in both trials[15]. This assessment entailed a score that combined information about any difficulties swallowing nine types of liquid and solid. In the Swedish study the symptom of dysphagia for solid foods was also assessed using a score from 0 to 3 (0, no symptoms; 1, mild; 2, moderate; 3, severe symptoms). An

analogue dysphagia score ranging from 0 (no dysphagia) to 10 (severe dysphagia) used in the Australian study was reinterpreted to fit the Swedish score (score 0 the same in both systems; score 1–3, 4–6 and 7–10 in the Australian study equivalent to scores 1, 2 and 3 respectively in the Swedish study).

Statistical analysis

Trial data sets were combined and the two study groups defined according to their original randomization. Data analysis was then performed on an intention-to-treat basis. For comparison between groups, Fisher's exact test was used for dichotomous variables. The Mantel–Haenszel χ^2 exact test was used for non-ordered categorical variables.

Results

Of 99 patients enrolled in the original Swedish trial, the short gastric vessels were divided in 52 and left intact in 47. Of these, 82 had clinical data available at 10–12 years of follow-up (42 in the division group and 40 in the non-division group). Of 102 patients enrolled in the Australian trial, 52 were randomized to short gastric vessel division and 50 to leaving these vessels intact. Detailed information was available at 10–12 years' follow-up from 88 of these patients, 44 in each group.

Overall, late clinical follow-up data were available for 170 (84·6 per cent) of 201 patients at 10–12 years' follow-up. Nineteen of the other 31 patients (9·5 per cent of those randomized) died during follow-up, all from causes unrelated to the original antireflux surgery[13,14]. The remaining 12 patients (6·0 per cent) had moved abroad or were lost to follow-up. Outcome at 10–12 years was therefore known for 189 patients (94·0 per cent).

Mean(s.d.) follow-up was 11·5(0·9) years for the 86 patients in the division group and 11·7(0·7) years for the 84 randomized to leaving the vessels intact. The mean age of the patients at time of surgical treatment was 49·0 and 48·9 years respectively. Some 43 per cent of the division group were women, compared with 42 per cent of the non-division group. There were no significant demographic differences between patients randomized to vessel division *versus* non-division.

At late follow-up there was no significant difference in reflux symptoms between the two groups: 89 per cent of patients in the division group and 82 per cent in the non-division group answered no to the heartburn question ($P = 0{\cdot}290$). There were also no significant differences between study groups for dysphagia (*Fig. 1*); 20 per cent of the division group and 17 per cent of the non-division group reported severe problems with swallowing (dysphagia grade 3; $P = 0{\cdot}460$). The mean composite dysphagia score was 11·3 in the division group and 8·7 in non-division group ($P = 0{\cdot}298$). Some 54 per cent of patients in the division group and 54 per cent in the non-division group reported that they could belch normally ($P = 0{\cdot}527$), and 10 and 7 per cent respectively claimed to be able to vomit ($P = 0{\cdot}746$). Significantly more patients reported abdominal bloating in the group randomized to division of the short gastric blood vessels (72 *versus* 48 per cent; $P = 0{\cdot}002$). Antisecretory medication was used by 18 per cent in the division group and 22 per cent in the non-division group ($P = 0{\cdot}525$).

Twenty-three (11·4 per cent) of the 201 patients underwent reoperation within the 12-year follow-up period. Those who underwent reoperation continued in follow-up and were scored as treatment failures in the intention-to-treat analysis. Eleven patients (5·5 per cent) underwent reoperation within the first 6 months of the original operation, with no difference between groups ($P = 0{\cdot}218$). Eight reoperations (7·7 per cent) were undertaken in the division group (5 for dysphagia, 2 for bleeding short gastric vessels, 1 for gastric perforation) compared with three (3 per cent) in the non-division group (1 for dysphagia, 2 for paraoesophageal herniation).

From 6 months to 5 years of follow-up, eight further patients (4·0 per cent) underwent revision surgery, six (5·8 per cent) in the division group (4 for recurrent reflux, 1 for paraoesophageal herniation, 1 for dysphagia) compared with two (2 per cent) in the non-division group (1 for persistent dysphagia, 1 for a bilobular stomach resulting in chronic gastric obstruction). Four patients underwent

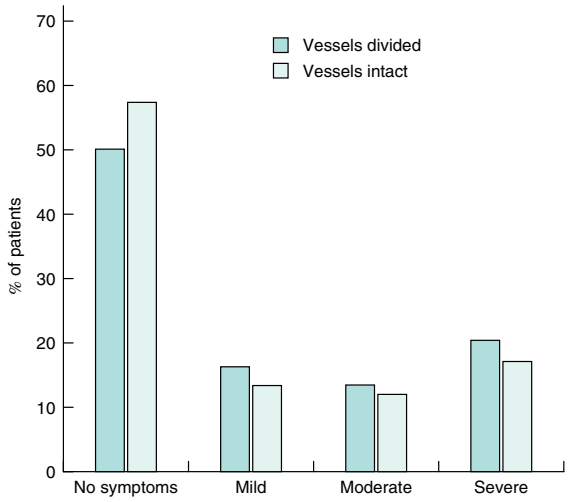


Fig. 1 Dysphagia scores at late follow-up

reoperation between 5 and 12 years, all for troublesome dysphagia (2 in each group). Overall, 16 patients in the division group (15·4 per cent) and seven (7 per cent) in the non-division group underwent revisional surgery during the whole follow-up period ($P = 0{\cdot}079$).

Discussion

The first description of a fundoplication was published by Nissen in 1956[16]. It soon became apparent that the procedure was associated with troublesome side-effects in some patients, and modifications were introduced to reduce their incidence. DeMeester and colleagues[17] suggested three modifications to the original technique to reduce the risk of dysphagia and bloating. These were the use of using a large intraoesophageal bougie, shortening the length of the fundoplication, and mobilizing the gastric fundus to facilitate construction of a very loose fundoplication. The principal study supporting these ideas was non-randomized, involving 100 patients. Follow-up was determined using actuarial statistics, rather than genuine long-term follow-up. This and other non-randomized studies have advocated short gastric vessel division during Nissen fundoplication[18,19].

There are now five published randomized clinical trials that have evaluated division of the short gastric blood vessels during Nissen fundoplication. All reported no difference in postoperative reflux control or dysphagia rates[7–11]. Four of these five trials evaluated the outcome 'bloating', and in three studies bloating was more common following division of the short gastric blood vessels[7,8,11]. Although there have been two meta-analyses of these five randomized trials, follow-up was relatively short at the time of the meta-analyses.

An aim of the present analysis was to combine two original data sets to achieve better statistical power, and to address fully the long-term symptomatic outcomes, including reflux symptoms, and side-effects such as dysphagia and various 'wind-related' problems. Protocols for both original randomized trials were virtually identical and late follow-up rates were high, allowing outcome to be determined for 94·0 per cent of patients, 10–12 years after their original surgery.

A weakness of this approach, however, was that some clinical data collection tools were different in the two trials. To deal with this, only data collected in a similar way were considered; where that was not feasible, some responses were reinterpreted into common categories to create a common data set. A further limitation was that objective outcomes from oesophageal function tests such as pH monitoring or endoscopy were not available.

It might be argued that the rate of dysphagia was higher than usual. This probably reflects the way dysphagia was scored in the original trials. There is no agreed standard method for assessing this symptom, and the rate of dysphagia reported in various clinical studies reflects the scoring system used, the questions applied and who asked the questions.

Analysis of the combined data set reinforces the findings in each trial of no differences in symptoms of heartburn or dysphagia, but significant differences in bloating problems. These data suggest that the short gastric vessels should not be divided, and that the long-term outcome following Nissen fundoplication is actually worse if these vessels are divided. This is a very different conclusion from that drawn by many non-randomized studies and different from the general consensus held by surgeons in some parts of the world. What is clear from the present analysis, however, is that long-term reflux control is not jeopardized by leaving the short gastric vessels intact during Nissen fundoplication. Furthermore, if the vessels are divided, more time is spent in the operating room[8,9], patients are subjected to an increased risk of perioperative bleeding from the divided short gastric vessels, and there is an increased risk of postoperative abdominal bloating symptoms in the longer term.

How might abdominal bloating be aggravated by dividing the short gastric blood vessels? In a previous study in which a subsample of patients selected randomly from the Swedish study was evaluated by detailed manometric assessment, patients with intact short gastric vessels following Nissen fundoplication had more transient lower oesophageal relaxations after gastric distension than those in whom the short gastric vessels were divided[20]. It is possible that venting gas from the stomach might be easier following Nissen fundoplication if the short gastric vessels were left untouched. One might also speculate that, during division of the attachments between the fundus of the stomach and the spleen, and/or mobilization of the posterior part of the proximal gastric fundus, branches of the vagus nerve innervating the gastric fundus are disrupted and this might adversely affect gastric function, thereby leading to bloating.

The combined results of two randomized clinical trials have shown no statistical differences in long-term control of reflux symptoms or dysphagia in patients undergoing Nissen fundoplication with or without division of the short gastric blood vessels. Bloating side-effects are more common in patients in whom the short gastric vessels have been divided, and this problem persists at longer-term follow-up.

Acknowledgements

Ms Tanya Ellis assisted with database access in Adelaide. Bent Bengtsson provided statistical support. Dr Hans Lönroth and Dr Jan Dalenbäck performed the operations on the Swedish patients, and Dr Philip Game contributed patients to the Australian study. Professor Lars Lundell initiated the original Swedish randomized clinical trial. The authors declare no conflict of interest.

References

1 Lundell L, Abrahamsson H, Ruth M, Ryder L, Lönroth H, Lobe L. Long-term results of a prospective randomized comparison of total fundic wrap (Nissen–Rossetti) or semifundoplication (Toupet) for gastroesophageal reflux. *Br J Surg* 1996; **83**: 830–835.
2 Salminen PT, Hiekkanen HI, Rantala AP, Ovaska JT. Comparison of long-term outcome of laparoscopic and conventional Nissen fundoplication: a prospective randomized study with an 11-year follow-up. *Ann Surg* 2007; **246**: 201–206.
3 Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg* 1999; **86**: 123–130.
4 Hagedorn C, Jönson C, Lönroth, Ruth M, Thune A, Lundell L. Efficacy of an anterior as compared with posterior laparoscopic partial fundoplication: result of a randomized clinical trial. *Ann Surg* 2003; **238**: 189–196.
5 Jay AP, Watson DI. Changing work patterns for benign upper gastrointestinal and biliary disease; 1994–2007. *ANZ J Surg* 2010; **80**: 519–525.
6 Statens beredning för medicinsk utvärdering (SBU). *Dyspepsi och reflux. En systematisk litteraturöversikt.* SBU-rapport nr 185. SBU: Stockholm, 2007.
7 Luostarinen ME, Koskinen MO, Isolauri JO. Effect of fundal mobilisation in Nissen–Rossetti fundoplication on oesophageal transit and dysphagia. A prospective, randomised trial. *Eur J Surg* 1996; **162**: 37–42.
8 Watson DI, Pike GK, Baigrie RJ, Mathew G, Devitt PG, Britten-Jones R *et al*. Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg* 1997; **226**: 642–652.
9 Blomqvist A, Dalenbäck J, Hagedorn C, Lönroth H, Hyltander A, Lundell L. Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication. *J Gastrointest Surg* 2000; **4**: 493–500.
10 Farah JF, Grande JC, Goldenberg A, Martinez JC, Lupinacci RA, Matone J. Randomized trial of total fundoplication and fundal mobilization with or without division of short gastric vessels: a short-term clinical evaluation. *Acta Cir Bras* 2007; **22**: 422–429.
11 Chrysos E, Tzortzinis A, Tsiaoussis J, Athanasakis H, Vassiliakis J, Xynos E. Prospective randomized trial comparing Nissen to Nissen–Rossetti technique for laparoscopic fundoplication. *Am J Surg* 2001; **182**: 215–221.
12 O'Boyle CJ, Watson DI, Jamieson GG, Myers J, Game PA, Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication: a prospective double-blind randomized trial with 5-year follow-up. *Ann Surg* 2002; **235**: 165–170.
13 Yang H, Watson DI, Lally C, DeWitt P, Game P, Jamieson GG. Randomized trial of division *versus* nondivision of the short gastric vessels during laparoscopic Nissen fundoplication. *Ann Surg* 2008; **247**: 38–42.
14 Mardani J, Lundell L, Lönroth H, Dalenbäck J, Engström C. Ten-year results of a randomized clinical trial of laparoscopic total fundoplication with or without division of the short gastric vessels. *Br J Surg* 2009; **96**: 61–65.
15 Dakkak M, Bennet JR. A new dysphagia score with objective validation. *J Clin Gastroenterol* 1992; **14**: 99–100.
16 Nissen R. Eine Einfache Operation zür Beeinflussung der Reflux Oesophagitis. *Schweiz Med Wochenschr* 1956; **85**: 590–592.
17 DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. *Ann Surg* 1986; **204**: 9–20.
18 Wills VL, Hunt DR. Dysphagia after antireflux surgery. *Br J Surg* 2001; **88**: 486–499.
19 Laycock WS, Trus TL, Hunter JG. New technology for the division of short gastric vessels during laparoscopic Nissen fundoplication. A prospective randomized trial. *Surg Endosc* 1996; **10**: 71–73.
20 Engström C, Blomqvist A, Dalenbäck J, Lönroth H, Ruth M, Lundell L. Mechanical consequences of short gastric vessel division at the time of laparoscopic total fundoplication. *J Gastroenterol* 2004; **8**: 442–447.

2.3 Anterior vs. posterior hiatal repair during Nissen fundoplication

---

Watson DI, Jamieson GG, Devitt PG, Kennedy A, Ellis T, Ackroyd R, Lafullarde T, Game PA. A prospective randomized trial of laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair. *Arch Surg* (2001) **136**:745-751.

This paper reported the clinical and objective outcomes at 6 months (short term) follow-up from a randomized trial comparing laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair.

Wijnhoven BPL, Watson DI, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair: long-term results of a randomized trial. *Am J Surg* (2008) **195**:61-65.

This paper reported the 5 year (longer term) clinical outcomes from the same trial.

Chew CR, Jamieson GG, Devitt PG, Watson DI. Prospective randomised trial of laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair – late outcomes. *World J Surg* (2011) **35**:2038-2044.

This paper reported the 10 year (long term) clinical outcomes from the same trial.

ORIGINAL ARTICLE

A Prospective Randomized Trial of Laparoscopic Nissen Fundoplication With Anterior vs Posterior Hiatal Repair

David I. Watson, MD, FRACS; Glyn G. Jamieson, MS, FRACS, FRCS; Peter G. Devitt, MS, FRCS, FRACS; J. Andrew Kennedy, MD, FRCS; Tanya Ellis, BSc; Roger Ackroyd, MD, FRCS, FRCS(Edin); Thierry Lafullarde, MD; Philip A. Game, MB, BS, FRCS, FRACS

Hypothesis: The technique used for repair of the esophageal hiatus during laparoscopic Nissen fundoplication can influence the likelihood of postoperative dysphagia.

Design: A prospective double-blind randomized control trial.

Setting: A university teaching hospital.

Participants: A total of 102 patients with proven gastroesophageal reflux disease, undergoing a laparoscopic Nissen fundoplication were randomized to undergo fundoplication with either anterior (47 patients) or posterior (55 patients) repair of the diaphragmatic hiatus. Patients were excluded for the following reasons: they had esophageal motility disorders, required a concurrent abdominal procedure, had undergone previous antireflux surgery, or had very large hiatus hernias.

Interventions: Laparoscopic Nissen fundoplication with anterior vs posterior hiatal repair.

Main Outcome Measures: Independent assessment of dysphagia, heartburn, patient satisfaction, and other symptoms 1, 3, and 6 months following surgery, using multiple standardized clinical grading systems. Objective measurement of lower esophageal sphincter pressure, esophageal emptying time, distal esophageal acid exposure, and endoscopic assessment of postoperative anatomy and esophageal mucosa.

Results: Symptoms of postoperative dysphagia, relief of heartburn, and overall satisfaction 6 months after surgery were not influenced by the hiatal repair technique. However, to achieve a similar incidence of dysphagia, more patients who initially underwent posterior hiatal repair required a second surgical procedure (6 vs 0 patients). The hiatal repair technique did not affect the likelihood of early postoperative paraesophageal herniation.

Conclusion: Anterior suturing of the hiatus appears to be at least as good in the short-term as posterior suturing as a method of narrowing the hiatus during laparoscopic Nissen fundoplication.

Arch Surg. 2001;136:745-751

From the University of Adelaide Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia.

SINCE THE EARLY 1990s, the status of laparoscopic antireflux surgery has moved from experimental to routine, with large experiences now reported by many centers.[1-3] Furthermore, the outcome in the majority of patients undergoing such surgery is good, with relief of reflux symptoms and few adverse effects in about 90% of patients.[1,4-6] However, some patients develop problems following fundoplication.[6] Problems due to hiatal herniation after surgery are now less common because hiatal repair has become routine during laparoscopic Nissen fundoplication in most centers,[7,8] but some patients still experience troublesome dysphagia following fundoplication. Recently reported randomized trials have suggested that the problem of dysphagia might be reduced following anterior partial fundoplication,[6] while routine division of the short gastric vessels has not been demonstrated to be of benefit.[9,10]

Previously, we have described the problem of postoperative hiatal stenosis. This causes dysphagia from narrowing of the diaphragmatic hiatus, due to excessive perihiatal scar tissue formation, which highlights the fact that in some patients postoperative dysphagia can be due to a problem at the hiatus, despite a technically correct total fundoplication.[11] In addition, we have observed that postoperative barium swallow x-ray films usually demonstrate anterior displacement of the distal esophagus following Nissen fundoplication, and it is possible that this angulation could contribute to dysphagia fol-

PATIENTS AND METHODS

PARTICIPANT ASSIGNMENT

Patients undergoing laparoscopic Nissen fundoplication for gastroesophageal reflux disease were randomized to undergo fundoplication with either anterior or posterior repair of the diaphragmatic hiatus. Informed consent was obtained from all participants, and randomization occurred in the operating theater by opening 1 of 120 previously sealed envelopes after the commencement of general anesthesia. Preparation of the envelopes was undertaken before the study by an independent research officer, and envelopes were randomly selected by a departmental secretary at a surgeon's request. No patients were withdrawn from the study following randomization.

PATIENT SELECTION AND PREOPERATIVE INVESTIGATION

Patients with proven gastroesophageal reflux disease, who presented to the University Department of Surgery at the Royal Adelaide Hospital, Adelaide, South Australia, for primary antireflux surgery by a laparoscopic technique were considered for entry. Patients were excluded from consideration if they had an esophageal motility disorder, which precluded a total fundoplication; they required a concurrent abdominal procedure at the same time as fundoplication; they had undergone previous antireflux surgery; or if they had a large hiatus hernia (ie, containing more than 50% of the stomach or >10 cm in length). All patients underwent preoperative investigation with esophageal manometry and endoscopy. Twenty-four–hour pH monitoring was only performed in patients who did not have unequivocal reflux disease demonstrated by preliminary endoscopy in association with typical reflux symptoms of retrosternal burning discomfort and/or acid regurgitation.

OPERATIVE TECHNIQUE

Laparoscopic Nissen fundoplication was performed using a previously described technique.[12] This comprised dissection of the hiatal pillars, followed by full esophageal mobilization. The hepatic branch of the vagus nerve was always preserved, and the short gastric vessels were divided in only 5 patients. The hiatus was repaired in front (anterior) or behind the esophagus (posterior), according to the randomization. If assigned to posterior repair, the hiatus was repaired using interrupted 2-0 monofilament nonabsorbable sutures before constructing the fundoplication, and if assigned to anterior repair, the hiatus was repaired after the fundoplication was constructed. The different sequence of steps facilitated the technical performance of the surgery. With both hiatal repair techniques, the hiatus was closed so that the closure was adequate but not tight. This was determined by assessing the degree of narrowing while a 52F bougie was sited within the esophageal lumen. The repair was evaluated further by placing a closed laparoscopic grasping instrument between the repaired hiatal rim and the esophagus (which was distended by the bougie) to ensure that the repair was not too tight.

The anterior wall of the gastric fundus was pulled behind the esophagus and a 1.5- to 2.0-cm loose total fundoplication was constructed, while a 52F bougie was sited within the abdominal esophagus. Three nonabsorbable interrupted sutures were used to secure the wrap. If the laparoscopic procedure was converted to an open procedure due to intraoperative difficulties, the randomization schedule was still followed and the patient remained in the trial.

POSTOPERATIVE CARE

Nasogastric tubes were not used and patients were allowed oral fluids after the operation that evening and soft solid food the next day. Discharge from the hospital was encouraged after the second day after surgery. A barium meal examination was routinely obtained on the second day after surgery to detect any problems requiring early laparoscopic reintervention (eg, acute paraesophageal hernia, tight fundoplication, or hiatus). This is our usual clinical practice.

MASKING

Whether the hiatus was repaired in front or behind the esophagus was concealed from all patients, and all remained unaware of the exact procedure for the duration

lowing fundoplication. This anatomical change could be due, at least in part, to posterior repair of the hiatus. Since anterior repair of the hiatus tends to push the esophagus posteriorly, thus keeping its axis straight, we hypothesized that anterior hiatal repair might be associated with less postoperative dysphagia. To test this hypothesis, we have undertaken a prospective double-blind randomized trial of anterior vs posterior hiatal repair during laparoscopic fundoplication.

RESULTS

From July 21, 1997, to October 29, 1999, 102 patients were entered into this trial. Forty-seven patients were randomized to undergo a total fundoplication with anterior hiatal repair, and 55 were randomized to undergo posterior repair. Fifty-two additional patients underwent a laparoscopic antireflux procedure during this same period. Of these patients, 27 were excluded from the trial because they had a very large hiatal hernia, 12 were excluded because of poor esophageal motility, 3 underwent a concurrent cholecystectomy, and 1 had undergone a previous antireflux procedure. Only 9 patients who were eligible for enrollment into the trial refused entry.

Of these patients, 96 (94%) were able to be interviewed 1 month after surgery, 96 (94%) at 3 months, and 99 (97%) at 6 months. Although prospectively collected follow-up data were not available for a few patients at the specific follow-up intervals, no patient elected to withdraw from the study, and missing data were due to an inability to contact a small number of patients at the specific follow-up intervals. Only 1 patient could not be in-

of follow-up. While operating surgeons were aware of the procedure performed, follow-up was obtained by a scientific officer (T.E.) who was blinded to the randomization of each patient. Since she was not involved in the initial surgery, she remained unaware of the allocated group for each patient throughout follow-up.

CLINICAL FOLLOW-UP

Patients were interviewed before surgery and then 1, 3, and 6 months after surgery by the scientific officer, using a structured questionnaire. Longer-term follow-up is being sought at yearly intervals, but these data are not available in this article. The presence or absence of each of the following symptoms was determined: heartburn; epigastric pain; regurgitation; dysphagia for lumpy solids, soft solids, and liquids; odynophagia; early satiety; inability to belch; epigastric bloating; anorexia; nausea; vomiting; nocturnal coughing and wheezing; increased passage of flatus; and diarrhea. The ability to relieve bloating and whether a normal diet was being consumed were also determined. Heartburn was also scored using a visual analog scale (0=no heartburn, 10=severe heartburn).

Dysphagia was scored by several methods. Visual analog scales (0=no dysphagia, 10=total dysphagia) were independently applied for solids and liquids, as well as a previously validated and described score[9,13] (0=no dysphagia, 45=severe dysphagia), which combines information about difficulty swallowing 9 types of liquids and solids. Overall outcome was determined using 3 further scales. Patients ranked the outcome of surgery using a previously described modified Visick grading[9] and were also asked to score the outcome as excellent, good, fair, or poor. An overall assessment of satisfaction with the operative outcome was scored by a visual analogue scale (0=dissatisfied, 10=satisfied).

OBJECTIVE FOLLOW-UP

Objective investigation with esophageal manometry, 24-hour pH monitoring, endoscopy, and a radionuclide esophageal emptying study were performed 3 to 4 months following surgery. Investigation sought to assess lower esophageal sphincter function, control of reflux, and postsurgical anatomy. The technique used for all studies has been described previously.[9] The esophageal emptying study measured emptying of 3 swallows of a solid meal, with the emptying time deemed to be the average time taken for 95% of each bolus to clear from the esophagus (normal time, 7-93 seconds).

STATISTICAL ANALYSIS

The primary clinical outcome, which the trial was designed to evaluate, was postoperative dysphagia. Before commencement, it was determined that 84 patients (42 in each group) would be needed to demonstrate a 20% difference in this outcome measure, at a significance level of $P<.05$ and power of 90%. To ensure that this was achieved, it was intended that 100 patients would be recruited. All analyses were performed on an intention-to-treat basis, with all patients remaining in their initially allocated group for this analysis. Before commencing, it was intended to publish the initial outcomes and results of postoperative testing once all patients had been followed up for an initial 6-month period. This period should be adequate to allow for the assessment of any differences in the incidence of postoperative dysphagia between the 2 trial groups. Medium- to long-term outcomes will be reported once follow-up has matured.

All data were entered onto a computerized database (Filemaker Pro, version 4.0; Claris Corporation, Santa Clara, Calif) and analyzed using a commercially available statistical package (InStat, version 2.01; GraphPad Software, San Diego, Calif). The Fisher exact test was used to determine the significance of 2×2 contingency tables. A 2-tailed Mann-Whitney U test was used to assess the significance of continuous data sets. Statistical significance was accepted at $P<.05$. Unless otherwise stated, all data are reported as the percentage of the total patients in each group or as the mean (95% confidence interval [CI]).

ETHICAL APPROVAL

The protocol for this study was approved by the Royal Adelaide Hospital Human Research Ethics Committee, and the study was conducted in accordance with the World Medical Association declaration of Helsinki (revised 1989), and the National Health and Medical Research Council of Australia's guidelines on human experimentation.

terviewed at all follow-up intervals because he had been incarcerated soon after his surgery. Two other patients could not be contacted 6 months after surgery.

PREOPERATIVE ASSESSMENT

Both groups were similar for age, sex, height, weight, incidence of previous abdominal surgery, duration of symptoms, and medications consumed before surgery. Analysis of the presence or absence of preoperative symptoms (**Table 1**) and the assessment of heartburn using the visual analogue scale (**Table 2**) revealed no significant differences. A significant proportion of patients in each group experienced dysphagia to some extent before surgery, with an incidence of 45% in the anterior repair group and 39% in the posterior repair group when dysphagia was assessed using the 0 to 45 dysphagia score (**Table 3**). While different methods of scoring dysphagia elicited different rates, there was no clinically or statistically significant difference between the study groups before surgery. Preoperative Visick grading was also similar for each group (**Table 4**).

Endoscopic grading of esophagitis before surgery was similar, with 7 (15%) of the anterior repair group and 3 (5%) of the posterior repair group having complicated reflux disease, ie, either Barrett esophagus or stricture formation ($P=.18$). A hiatus hernia was seen preoperatively in 49% of the anterior repair group vs 40% of the posterior repair group ($P=.40$). Barium meal examination was performed preoperatively in 32 of the patients, and a hiatus hernia was demonstrated in 53% of the examinations performed.

Table 1. Summary of Preoperative and Postoperative Symptoms*

	Preoperative		1 mo Postoperative		3 mo Postoperative		6 mo Postoperative	
	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
Heartburn	85	92	7	8	4	10	11	8
Epigastric pain	51	61	30	25	24	14	22	21
Regurgitation	87	86	9	21	9	14	7	11
Odynophagia	13	14	18	15	11	6	13	6
Early satiety	38	55	55	62	52	38	67	30
Epigastric bloat	49	59	30	35	48	26	48	32
Anorexia	9	6	23	13	11	8	9	9
Nausea	36	33	23	17	17	16	2	9
Vomiting	38	29	11	12	9	6	2	6
Nocturnal cough	49	43	5	6	7	8	20	8
Nocturnal wheeze	19	20	2	4	0	4	7	9
Can relieve bloat	86	80	59	71	52	63	48	62
Unable to belch	0	0	36	25	46	38	37	25
Eats normal diet	77	73	36	40	86	72	87	87

*Data are given as percentage of patients. No significant differences were demonstrated between trial groups (ie, $P>.05$ at all follow-up intervals), except epigastric bloat 3 months after surgery ($P=.03$, Fisher exact test), and early satiety 6 months after surgery ($P<.001$).

Table 2. Assessment of Heartburn by Visual Analog Scale

	Mean (95% Confidence Interval)		
	Anterior Repair	Posterior Repair	*P*
Preoperative	4.8 (4.0-5.7)	4.9 (4.0-5.7)	.98
Postoperative			
1 mo	0.1 (–0.003-0.2)	0.5 (–0.03-1.1)	.78
3 mo	0.1 (–0.1-0.3)	0.1 (–0.1-0.4)	>.99
6 mo	0.4 (0.0-0.7)	0.2 (–0.1-0.5)	.79

Preoperative esophageal manometry outcomes were similar. No significant differences were seen between the groups (**Table 5**). Twenty-four–hour ambulatory pH monitoring was performed in 20 of the patients who underwent anterior hiatal repair and 28 of those undergoing posterior repair. The mean percentage exposure time to an acid pH of less than 4 was 10.0% (6.8%-13.2%) for the anterior repair group and 8.7% (6.5%-10.8%) for the posterior repair group.

SURGERY

Surgery was performed by or under the direct supervision of 1 of 4 consultant surgeons (D.I.W., G.G.J., P.G.D., P.A.G.). Of the patients randomized to undergo anterior hiatal repair, 1 had the hiatus repaired posteriorly, as an adequate repair of the hiatal defect could not be achieved by the placement of anterior sutures alone. All patients randomized to posterior hiatal repair underwent this procedure. One patient in each group underwent an anterior 180° partial fundoplication rather than a Nissen fundoplication due to difficulty achieving a satisfactorily loose total fundoplication. In each instance, the surgeon elected to perform a partial fundoplication procedure rather than divide the short gastric vessels. All patients remained in their originally allocated groups for data analysis. In the anterior hiatal repair group, 1 suture was used to narrow the hiatus in 31 patients, 2 sutures in 14, and 4 sutures in 2 patients. In the posterior repair group, 1 suture was used in 38 patients, 2 sutures in 14, 3 sutures in 2, and 4 sutures in 1 patient.

Only 1 procedure was converted to an open operation. This patient was randomized to undergo anterior hiatal repair. The patient's stomach was distended with air at the commencement of the procedure, and a concurrent hiatus hernia made placement of a nasogastric tube for decompression difficult, and it was, therefore, not possible to empty the stomach adequately to enable the planned laparoscopic procedure to proceed. Hence, the procedure was converted to an open operation.

Operating time varied from 20 to 120 minutes (mean [CI], 48.6 [42.6-54.6] minutes) when the hiatus was repaired anteriorly vs 25 to 110 minutes (mean [CI], 52.2 [46.7-57.6] minutes; $P=.40$) when the hiatus was repaired posteriorly. Operating surgeons were asked to rate the difficulty of the operative procedure using a scale from 1 to 10. The perceived difficulty was not influenced by the technique used (mean score, 4.5 for each group).

EARLY HOSPITAL OUTCOMES

The period between surgery and the commencement of oral intake of fluids and solids, as well as the length of hospital stay after surgery was not altered by the repair technique (mean, 0.9, 1.8, and 2.8 days, respectively). The incidence of postoperative complications within 30 days of surgery was also unaffected by the operative technique (11% in each group). In the anterior repair group, 3 patients underwent early endoscopic dilation for dysphagia, 1 experienced transient pulmonary edema (cause unknown), and 1 developed a left pneumothorax, which required no specific treatment. In the posterior repair group, 2 patients underwent early endoscopic dilatation for dysphagia and 4 patients underwent early reoperation (see below).

Table 3. Dysphagia Assessment*

	Preoperative		1 mo Postoperative		3 mo Postoperative		6 mo Postoperative	
	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
Dysphagia for								
Lumpy solids	21	27	45	58	30	42	28	34
Soft solids	2	4	2	2	0	0	0	0
Liquids	2	8	16	10	4	8	4	4
Visual analog scale								
Solids	1.9 (1.1-2.7)	1.5 (0.9-2.1)	4.0 (3.0-5.0)	3.9 (3.0-4.8)	2.5 (1.7-3.4)	3.0 (2.1-4.0)	2.4 (1.5-3.2)	2.4 (1.5-3.2)
Liquids	0.9 (0.4-1.3)	0.6 (0.1-1.1)	1.3 (0.5-2.1)	1.0 (0.3-1.7)	0.8 (0.2-1.4)	0.8 (0.2-1.5)	0.9 (0.2-1.5)	0.4 (0.0-0.8)
Dysphagia score								
Overall result	7.4 (4.0-10.7)	5.5 (3.0-8.1)	11.0 (7.8-14.2)	8.5 (5.7-11.4)	7.8 (5.2-10.4)	8.5 (5.7-11.4)	5.1 (3.3-6.9)	6.7 (4.0-9.4)
Scored 0 only	55	61	30	29	37	33	40	45

*Data are given as percentage of total or mean (95% confidence interval). No tests for significance between groups at comparable follow-up intervals were significant (ie, $P>.05$ at all follow-up intervals).

Table 4. Outcome, Satisfaction, and Visick Grading*

	Preoperative		1 mo Postoperative		3 mo Postoperative		6 mo Postoperative	
	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
Outcome								
Excellent	NA	NA	18	12	33	20	46	47
Good	NA	NA	66	65	56	64	50	41
Fair	NA	NA	14	15	11	10	2	6
Poor	NA	NA	2	8	0	6	2	6
Visick grade								
1	0	0	18	10	30	20	37	42
2	0	0	50	54	59	58	52	40
3	51	43	25	15	7	10	9	8
4	49	57	7	15	4	10	2	8
5	0	0	0	6	0	2	0	2
Satisfaction score, mean (95% CI)	NA	NA	8.4 (7.9-8.9)	8.0 (7.3-8.7)	8.8 (8.4-9.2)	8.3 (7.7-9.0)	9.0 (8.6-9.4)	8.3 (7.6-9.0)

*Data are given as percentages, unless otherwise indicated. NA indicates not applicable; CI, confidence interval. No tests for significance between groups at comparable follow-up intervals were significant (ie, $P>.05$ at all follow-up intervals).

While reoperation within 6 months of surgery was not required for any patient randomized to undergo anterior hiatal repair, 8 (15%) patients randomized to undergo posterior repair underwent 9 further surgical procedures, 4 within 1 week of surgery, and 5 between 1 and 6 months following surgery. The decision to reintervene was made by the surgeon responsible for each patient's clinical care. The early operations were for removal of hiatal repair sutures because of a tight hiatus (2 patients), repair of an acute paraesophageal hiatus hernia (1 patient), and conversion of the total to an anterior partial fundoplication because of significant dysphagia in the presence of a demonstrably loose hiatal repair (1 patient). The 3 procedures for dysphagia were carried out because the patients had significant dysphagia for liquids (2 had aphagia), whereas the later reoperations for dysphagia (see below) were carried out if patients found their level of dysphagia was intolerable.

Four of the late reoperative procedures were to widen a tight esophageal hiatus on days 35, 35, 105, and 180. The last of these patients had previously undergone removal of all hiatal repair sutures on the seventh day after surgery, and despite this developed a tight narrowing of the hiatus due to excessive scarring. While the other patients all had dense fibrosis of the hiatal ring, it is not possible to determine the exact cause of the narrowing, and it is possible that suture narrowing of the hiatal rim may have contributed, at least in part, to this problem. The fifth patient presented on day 100 following excessive consumption of carbonated liquids, resulting in acute distension of the stomach that caused the stomach to rupture. This required open repair of the perforation and reconstruction of the fundoplication. Full details have been reported elsewhere.[14] Overall, there was a higher rate of revision for dysphagia in the group undergoing posterior hiatal repair (anterior hiatal repair group vs posterior hiatial repair group: 0 of 47 vs 6 of 55 patients; $P=.03$).

POSTOPERATIVE SYMPTOM ASSESSMENT AT 1 TO 6 MONTHS

A detailed analysis of the outcome of the blinded standardized clinical assessment is summarized in Tables 1 through 4. No differences between the incidence of assessed symptoms in each group, or overall outcome, were seen at any stage of the initial 6-month follow-up period, with the exception of a higher incidence of epigastric bloating 3 months following surgery and early sati-

Table 5. Esophageal Manometry Results*

Results	Anterior Repair	Posterior Repair	*P*
Preoperative			
Successful swallows	91 (85-97)	91 (86-97)	.67
Patients with normal peristalsis	83	86	.78
LES resting pressure, mm Hg	11.0 (7.8-14.1)	9.9 (7.3-12.5)	.60
LES nadir pressure, mm Hg	2.1 (1.0-3.1)	1.3 (0.6-2.0)	.73
Resting LES pressure <10 mm Hg	60	62	.83
Postoperative			
Successful swallows	81 (66-95)	74 (58-90)	.90
Patients with normal peristalsis	74	59	.51
LES resting pressure, mm Hg	25.0 (20.7-29.3)	21.5 (17.6-25.4)	.15
LES nadir pressure, mm Hg	11.4 (8.0-14.9)	11.8 (9.2-14.4)	.61
Resting LES pressure <10 mm Hg	0	0	. . .

*Data are given as percentage of total or mean (95% confidence interval). Swallowing was assessed from 10 wet swallows. LES indicates lower esophageal sphincter.

ety 6 months after surgery in patients whose hiatus was repaired anterior to the esophagus (Table 1). There was no difference between the 2 study groups with respect to the incidence or severity of dysphagia determined by the symptom scores at each follow-up interval. Of the 6 patients who underwent reoperation for dysphagia, 3 were highly satisfied with their overall outcome at all follow-up intervals, whereas 3 regarded their overall experience to be poor. The latter 3 had all undergone a delayed revision procedure.

OBJECTIVE POSTOPERATIVE INVESTIGATIONS

Fifty-one patients (50%) underwent a postoperative esophageal emptying study, 46 (45%) an endoscopy examination, 43 (42%) esophageal manometry, and 32 (31%) a postoperative 24-hour pH monitoring. The clinical outcomes in patients who underwent postoperative investigation were similar to the outcomes in patients who declined investigation.

Endoscopic examination revealed a small asymptomatic paraesophageal hernia in 1 patient who had undergone anterior hiatal repair. This patient has not required further intervention for this problem, and he has so far had an excellent clinical outcome. No other abnormalities were identified by endoscopic examination. There were no patients with ulcerative esophagitis at postoperative examination, although all patients who had Barrett esophagus diagnosed before surgery had persistence of this condition postoperatively. All fundoplications appeared to be correctly constructed. Esophageal manometry outcomes following surgery are summarized in Table 5. Esophageal body motility parameters were similar. Twenty-four–hour pH monitoring demonstrated normalization of acid exposure times in all studies, including patients who had postoperative "heartburn" symptoms. The mean (CI) esophageal emptying time measured by the radionuclide method was 157 (123-192) seconds in patients who underwent anterior hiatal repair, compared with 146 (117-176; $P=.57$) seconds in those who underwent posterior repair. Fifty-one percent of patients undergoing anterior repair and 49% of patients who underwent posterior hiatal repair had a normal emptying time ($P=.57$).

COMMENT

Laparoscopic surgery for the correction of gastroesophageal reflux has become common throughout the Western world,[15] partly because of better patient acceptance due to a perception that surgical procedures are now less invasive and also because of an apparently increasing incidence of reflux presenting as a clinical problem. The Nissen (total) fundoplication in its various forms remains the most commonly performed procedure, and its long-term efficacy was well established in the era of open surgery.[5,16] Furthermore, this is the procedure against which all other antireflux operations should be compared. Unfortunately, however, it is not a perfect operation, as it can be followed by a variety of adverse effects, and a few patients will require further surgery following their original procedure, either for recurrent reflux or to correct a postoperative problem.

Dysphagia is perhaps the adverse outcome that attracts most attention following Nissen fundoplication. To some extent this is unfair, as many patients, including more than 40% of those entering the trial, have dysphagia to some extent before they even undergo surgery, and in many of the patients with preoperative dysphagia, this problem improves following surgery.[6,9] However, a few patients will develop new dysphagia following laparoscopic Nissen fundoplication, and it is this adverse outcome in these patients that draws attention to the issue of troublesome dysphagia following surgery. Postoperative dysphagia can be due to the technical error of constructing a tight fundoplication. This is probably not related to the issue of whether short gastric vessels are divided or not,[9,10] although this is not accepted by all surgeons. Dysphagia can also be caused by a tight diaphragmatic esophageal hiatus. This problem can be due to either overtightening of the hiatal opening at the time of surgery or excessive fibrosis of the hiatus after surgery, which can occur even when sutures have not been placed to reduce the hiatus.[11] In our overall experience with dysphagia after laparoscopic antireflux surgery, reoperation for hiatal problems has been more prevalent (2%) than problems with the fundoplication (<1%).[17]

While it is possible that posterior hiatal repair could be responsible for some specific instances of dysphagia requiring revision, we believe that hiatal repair is an important step in a laparoscopic fundoplication. We, and others,[7,8] have shown previously that failure to routinely repair the hiatus, even in patients without a hiatus hernia, can lead to a higher incidence of postoperative paraesophageal hiatus herniation. However, it is possible that posterior hiatal repair, by lifting the esophagus forward and changing the axis of the distal esophagus could contribute to dysphagia following Nissen fundoplication. Anterior hiatal repair was not associated with any instances of hiatal herniation during the early follow-up period, and it was not associated with any in-

stances of reoperation for hiatal narrowing. The dysphagia symptom scores at 6 months were similar in the 2 groups, and hence the overall results do not support our original hypothesis. However, this was only achieved by operating again on 5 of the patients who underwent posterior repair and in whom hiatal sutures needed to be removed (2 patients) or the hiatus was tight due to excessive fibrosis (3 patients). It is not surprising that the dysphagia scores at each time point were similar, as the patients with more severe dysphagia usually underwent reintervention before the relevant clinical assessments were performed by the scientific officer.

One interpretation of our study is that anterior hiatal repair is better than posterior repair. However, another interpretation needs to be discussed. The 9% incidence of reoperation for hiatal narrowing in the posterior repair group is much larger than the incidence we have found outside this trial, and in fact, in our most closely observed patients, those involved in 2 other prospective randomized trials,[6,9] the incidence of reoperation for hiatal narrowing following posterior hiatal repair in 209 patients was only 1%. Thus, we may be making a type II statistical error, and we would need to enter a much larger number of patients to be more confident about our findings. We have no explanation for the increase in reoperation rate. It is true that ours is a teaching institution and many of these operations are undertaken by residents—but usually under the supervision of consultant staff. The patients having reoperations were evenly distributed between resident and consultant staff.

It should also be recognized that our management protocol for laparoscopic antireflux surgery encourages a low threshold for early laparoscopic reexploration should a patient's initial postoperative progress be unsatisfactory. The rationale for this, which has been reported previously,[18] recognizes that early laparoscopic readjustment of the original procedure within the first postoperative week is easy, and results in little morbidity. In comparison, later operative reintervention can be difficult, and it is more likely to require an open approach. We are aware that other surgeons will choose not to reoperate if confronted with some of the clinical scenarios encountered in this trial. However, reoperation within the first week of surgery does not lead to patient dissatisfaction, if the possibility is discussed with the patient before performing the original procedure.

Nevertheless, we can draw some conclusions from the outcome of this trial. First, a priori, we had thought that an anterior repair was a less satisfactory repair than a posterior repair, since it somehow seems less "anatomical," it involves suturing under greater tension to oppose the margins of the hiatus, and it tends to make the hiatus a "slit" rather than a "hole." This study at least allows confidence that an anterior repair can be undertaken with, at least, equal efficacy to a posterior repair, in the short term. It provides an adequate barrier to hiatal herniation, and it does not appear to be responsible for new dysphagia following laparoscopic Nissen fundoplication. Second, the trial demonstrates that dysphagia following antireflux surgery is often due to hiatal problems alone. This has implications for surgical strategies when reoperating for the correction of postfundoplication dysphagia. In these circumstances, the hiatus and the fundoplication should be carefully assessed at surgical reexploration, and if the fundoplication is demonstrably loose and the hiatus is tight, then the hiatus alone should be widened, and the fundoplication can be left intact.[18] In our experience this has been a successful strategy for this problem.

We acknowledge Nicky Ascott, Christine Bates-Brownsword, and Carolyn Lally for their invaluable organizational and logistical support.

Corresponding author: David I. Watson, MD, FRACS, University Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia (e-mail: david.watson@adelaide.edu.au).

REFERENCES

1. Trus TL, Laycock WS, Branum G, Waring JP, Mauren S, Hunter JG. Intermediate follow-up of laparoscopic antireflux surgery. *Am J Surg.* 1996;171:32-35.
2. Dallemagne B, Weerts JM, Jeahes C, Markiewicz S. Results of laparoscopic Nissen fundoplication. *Hepatogastroenterology.* 1998;45:1338-1343.
3. Hinder RA, Filipi CJ, Wetscher G, Neary P, DeMeester TR, Perdikis G. Laparoscopic Nissen fundoplication is an effective treatment for gastroesophageal reflux disease. *Ann Surg.* 1994;220:472-483.
4. Watson DI, Jamieson GG, Baigrie RJ, Mathew G, Devitt PG, Game PA. Laparoscopic surgery for gastro-oesophageal reflux: beyond the learning curve. *Br J Surg.* 1996;83:1284-1287.
5. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease: evaluation of primary repair in 100 consecutive patients. *Ann Surg.* 1986;204:9-20.
6. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. A prospective randomised double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg.* 1999;86:123-130.
7. Watson DI, Jamieson GG, Devitt PG, Mitchell PC, Game PA. Paraesophageal hiatus hernia: an important complication for laparaoscopic Nissen fundoplication. *Br J Surg.* 1995;82:521-523.
8. Seelig MH, Hinder RA, Klingler PJ, Floch NR, Branton SA, Smith SL. Paraesophageal herniation as a complication following laparoscopic antireflux surgery. *J Gastrointest Surg.* 1999;3:95-99.
9. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double blind randomised trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg.* 1997;226:642-652.
10. Luostarinen ME, Isolauri JO. Randomized trial to study the effect of fundic mobilization on long-term results of Nissen fundoplication. *Br J Surg.* 1999;86:614-618.
11. Watson DI, Jamieson GG, Mitchell PC, Devitt PG, Britten-Jones R. Stenosis of the esophageal hiatus following laparoscopic fundoplication. *Arch Surg.* 1995; 130:1014-1016.
12. Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. *Ann Surg.* 1994;220:137-145.
13. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol.* 1992;14:99-100.
14. Ackroyd R, Watson DI, Game PA. Fizzy drinks following laparascopic Nissen fundoplication: a cautionary tale of explosive consequences. *Aust N Z J Surg.* 1999; 69:887-888.
15. Watson DI, Jamieson GG. Antireflux surgery in the laparoscopic era [review]. *Br J Surg.* 1998;85:1173-1184.
16. Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. *World J Surg.* 1977;1:439-444.
17. Kennedy JA, Watson DI, Devitt PG, Jamieson GG. Hiatal closure in laparoscopic Nissen fundoplication [abstract]. *Surg Endosc.* 2000;14:S116.
18. Yau P, Watson DI, Devitt PG, Game PA, Jamieson GG. Early reoperation following laparoscopic antireflux surgery. *Am J Surg.* 2000;179:172-176.

The American Journal of Surgery 195 (2008) 61–65
Clinical surgery–International

Laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair: long-term results of a randomized trial

Bas P. L. Wijnhoven, M.D., Ph.D.[a], David I. Watson, M.D., F.R.A.C.S.[a,*], Peter G. Devitt, M.S., F.R.A.C.S.[b], Philip A. Game, M.B.B.S., F.R.A.C.S.[b], Glyn G. Jamieson, M.S., F.R.A.C.S.[b]

[a]*Department of Surgery, Flinders University, Flinders Medical Centre, South Australia, Australia*
[b]*Discipline of Surgery, University of Adelaide, Royal Adelaide Hospital, Adelaide, South Australia, Australia*

Manuscript received November 23, 2006; revised manuscript December 31, 2006

Abstract

Background: Postoperative dysphagia in patients after Nissen fundoplication might be related to the technique used for the closure of the esophageal hiatus.
Methods: A total of 102 patients with gastroesophageal reflux were randomized to undergo laparoscopic Nissen fundoplication with either anterior (47 patients) or posterior (55 patients) repair of the diaphragmatic hiatus.
Results: Clinical data at 5 years after surgery were available for 96% of patients enrolled in the trial. There was no significant difference between the 2 techniques for symptoms of dysphagia at the 5-year follow-up evaluation, although more patients who underwent posterior hiatal repair underwent further surgery for dysphagia-related symptoms (8 vs 2). Better control of heartburn was achieved in patients in the anterior hiatal repair group. Patients from both groups were equally satisfied with the overall outcome after surgery.
Conclusions: At the 5-year follow-up evaluation, there was no significant difference in dysphagia between anterior closure and posterior hiatal repair.

Keywords: Laparoscopy; Nissen; Fundoplication; Hiatal repair; Dysphagia; Randomized trial

After the publication by Rudolph Nissen [1] in 1956 of the so-called *gastroplication* surgery in 2 patients suffering from gastroesophageal reflux, Nissen's fundoplication gradually was adopted worldwide, and it is now the most popular antireflux surgery undertaken. Subsequently, however, Nissen's original surgery was modified by Nissen himself, as well as by other surgeons [2–5]. Currently, the laparoscopic version of this procedure is considered to be the treatment of choice for patients suffering from refractory gastroesophageal reflux disease, and the long-term outcome in patients undergoing such surgery is good, with relief of reflux symptoms reported in 80% to 90% of the patients at longer term follow-up evaluation [6,7]. However, it also is true that dysphagia is a common side effect after laparoscopic Nissen fundoplication [8]. Some dysphagia is reported initially by many patients after surgery [9], although it usually is mild, and it usually improves within the first postoperative months. However, 5% to 10% of patients are affected by troublesome and persistent dysphagia, and 1% to 3% of patients undergoing a Nissen fundoplication require surgical revision for this problem [9].

Numerous factors have been proposed as causes of postoperative dysphagia, and technical modifications to reduce its incidence have been described [2,9–11]. Anatomic problems resulting in dysphagia include paraesophageal hiatus hernia, hiatal fibrosis, slipped fundoplication, and rotational deformity of the esophagus. Interestingly, only up to one third of these anatomic complications result in dysphagia, and many patients are asymptomatic [12–14]. Manometric abnormalities, including high lower esophageal sphincter basal and nadir pressures also have been described in patients with dysphagia after fundoplication [10,15]. Despite all these possible explanations, the underlying pathophysiologic mechanism remains incompletely understood, and there currently are no tests that can reliably predict the onset or severity of postoperative dysphagia after fundoplication.

Closure of the hiatus is now recognized to be an essential part of all antireflux procedures, primarily to avoid postoperative hiatus hernia [13,16]. However, excessive narrowing

* Corresponding author. Tel.: +61-8-8204-6086; fax: +61-8-8204-6130.
E-mail address: david.watson@flinders.edu.au

0002-9610/08/$ – see front matter
doi:10.1016/j.amjsurg.2006.12.046

of the hiatus also can cause dysphagia. Traditionally, the hiatus is closed posteriorly with interrupted sutures, although it also is possible to repair the hiatus in front of the esophagus. In 2001 we published the short-term (6 months) outcome of a randomized trial that compared anterior versus posterior hiatal closure in patients who underwent laparoscopic Nissen fundoplication [17]. It was hypothesized that the anterior repair might be associated with less postoperative dysphagia. We have now followed up the patients in this study for a minimum of 5 years, and in this article we report the long-term outcome of this randomized trial.

Methods

Study design and participants

The detailed study protocol was published previously [17]. Briefly, between July 1997 and October 1999, 102 patients who underwent a laparoscopic Nissen fundoplication for gastroesophageal reflux disease were entered into a randomized controlled trial to undergo either anterior (n = 47) or posterior repair (n = 55) of the diaphragmatic esophageal hiatus. Patients were excluded if they had a significant esophageal motility disorder, if they required a concurrent abdominal procedure, if they had undergone previous antireflux surgery, or if they had a large hiatus hernia that was thought to preclude anterior hiatal repair. In Fig. 1, the enrolment of patients into the trial and their follow-up evaluation is described. No patients were withdrawn from the study after randomization.

Surgical procedures

A laparoscopic Nissen fundoplication was performed as described previously [18]. When patients were randomized to undergo a posterior repair of the hiatus, it was repaired using interrupted sutures before constructing the fundoplication. When assigned to the anterior repair, the hiatus was repaired in front of the esophagus after the fundoplication had been constructed. The surgical technique for anterior and posterior hiatal repair also was described in detail previously [17].

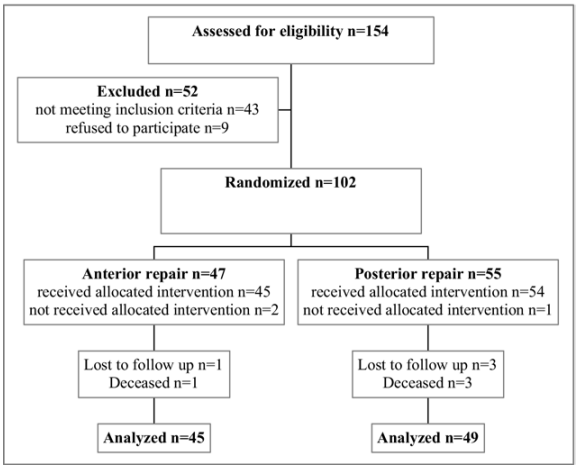


Fig. 1. Flow diagram of the trial. Three patients did not receive the allocated treatment. In the anterior repair arm, 1 patient underwent posterior repair of the hiatal defect because an adequate repair could not be achieved by the placement of anterior sutures alone. In each group, 1 patient underwent a partial anterior 180° fundoplication owing to difficulty achieving a sufficiently loose fundoplication.

Follow-up evaluation

The symptomatic outcome was determined using a structured questionnaire that was mailed to all participating patients yearly. If a questionnaire was not returned, it was sent a second time. If the second follow-up attempt failed, patients were contacted by telephone by a research assistant who was unaware of the actual surgical procedure at the time of the telephone interview. The same structured questionnaire then was used for the telephone interview. Patients were asked whether heartburn or dysphagia were present or absent. Also, symptoms of dysphagia for solids and liquids were assessed using a 0 to 10 visual analog scale (0 = no symptoms, 10 = severe symptoms). In addition, a previously validated and described dysphagia score also was used (0 = no dysphagia; 45 = severe dysphagia) [19]. This scoring system generated a composite score based on the patient's ability to swallow 9 index liquid and solid foods.

The sensation of bloating or distension after eating, the ability to relieve bloating, ability to belch, and whether a normal diet was consumed also were assessed. Overall satisfaction with the outcome of the procedure also was determined using a 0 to 10 visual analog scale (0 = totally dissatisfied; 10 = totally satisfied). Patients also were asked whether or not they thought they had originally made the correct decision to have surgery.

Esophageal manometry, 24-hour pH monitoring, endoscopy, and radionucleotide esophageal emptying studies were performed as part of the study protocol 3 to 4 months after the original surgery. The results of these investigations have been reported previously [17]. During later follow-up evaluation, objective studies were performed only in patients if clinically indicated. Details about adverse outcomes, hospital re-admissions, and re-operations also were recorded. For this article, the clinical outcome at 5 years after surgery was analyzed.

Statistical analysis

Postoperative outcome data were stored in a computerized database (Filemaker Pro, Version 8; FileMaker, Inc, Santa Clara, CA). These data then were analyzed using SPSS (SPSS version 11.0.4. for Mac Os X; SPSS Inc, Chicago, IL) on an intention-to-treat basis. The Fisher exact test was used to determine the significance of 2 × 2 contingency tables. The 2-tailed Mann-Whitney *U* test was used to assess differences in dysphagia, heartburn, and satisfaction scores between both study arms. Statistical significance was set at a *P* value of less than .05. Data are presented as percentages or mean ± SEM.

The Royal Adelaide Hospital Human Research Ethics Committee approved the protocol for this study.

Results

Follow-up evaluation

Of the 102 patients who originally were randomized to anterior or posterior hiatal repair, clinical follow-up data

Table 1
Re-operations performed in patients after Nissen fundoplication with anterior or posterior hiatal hernia repair

Study arm and patient number	Indication	Procedure performed	Time after initial randomization
Anterior repair			
14	Dysphagia	Reconstruction of posterior partial fundoplication and widening hiatus	28 mo
47	Paraesophageal hernia	Reposition herniated stomach and hiatal repair	53 mo
Posterior repair			
10	Dysphagia	Release posterior hiatal suture	3 d
53	Dysphagia	Tight hiatus: removal hiatal stitches	7 d
	Dysphagia	Tight hiatus: further widening hiatus	4 mo
	Dysphagia	reconstruction of a posterior fundoplication	27 mo
22	Dysphagia	Tight wrap: conversion to a partial wrap	2 d
86	Paraesophageal hernia	Reposition and closure hiatus with stitches posteriorly	3 d
43	Dysphagia	Tight hiatus: division of hiatus anterior	1 mo
44	Dysphagia	Tight hiatus: widening hiatus	1 mo
	Dysphagia	Reconstruction of 90º anterior fundoplication	38 mo
78	Dysphagia	Tight hiatus: widening hiatus	6 mo
88	Dysphagia	Tight hiatus: widening hiatus	9 mo

were available for 94 patients at 5 or more years after surgery (Fig. 1). Four patients died during the follow-up period (myocardial infarction, respiratory failure, metastatic colon carcinoma, and mixed drugs-alcohol intoxication). Four patients were lost to follow-up evaluation. Hence, the outcome was known for 98 (96%) patients. The median follow-up period was 5 years (range, 5–7 y) in both study groups.

Reinterventions

After enrollment in the trial, 5 patients have undergone additional surgical procedures that were not related directly to the original antireflux procedure (appendicectomy, 1; repair of umbilical hernia, 2; gastric bypass for morbid obesity, 1; and repair of a gastric perforation, 1 [20]).

Thirteen re-operations for dysphagia or paraesophageal herniation were undertaken in 10 patients (9.8%): 2 of 47 (4.3%) of these patients were in the anterior hiatal repair group, and 8 of 55 (14.5%) were in the posterior hiatal repair group ($P = .094$). There was, however, a significant difference in the actual number of re-operations between the groups: 2 after anterior hiatal repair versus 11 after posterior hiatal repair ($P = .011$). Four re-operations were performed within the first postoperative week, these were all in the posterior repair group. Another 4 re-operations were undertaken between the first postoperative week and 6 months (all were in the posterior repair group), and 5 re-operations were performed between 9 and 53 months after surgery (Table 1). No patient underwent re-operation for recurrent gastroesophageal reflux.

Subjective follow-up evaluation

Tables 2 and 3 summarize postoperative symptoms, as reported by the patients at 5 to 7 years of follow-up evaluation. There were no significant differences between the groups for the percentage of patients with dysphagia, the degree of dysphagia as rated on the visual analog scale, or the composite dysphagia score. Fewer patients in the anterior repair group experienced symptoms of heartburn after the surgery and the mean heartburn score was significantly lower in the anterior repair group. The prevalence of other symptoms was not different between both groups.

Objective tests

At the 6-month follow-up evaluation there was no difference in the outcome of the objective tests that were performed as part of the original study protocol. This was reported previously [17]. Between the 6-month and 5-year follow-up evaluations, esophageal manometry, 24-hour pH study, or an upper-gastrointestinal endoscopy were performed in 16 patients when clinically indicated. The indications for these tests were reflux symptoms, dysphagia, chest pain, or surveillance of Barrett's esophagus. Four asymptomatic patients with Barrett's esophagus underwent all 3 investigations as part of their participation in another study protocol. Normal esophageal motility was found in 10 patients, and abnormal lower esophageal sphincter pressures in 4 patients without further consequences. Upper-gastrointestinal endoscopy was performed in 10 patients and showed a small paraesophageal hernia in 2 patients (1 in each group); 1 patient also had symptoms of reflux, the other was asymptomatic. In 1 patient from the posterior hiatal repair group, endoscopic esophageal dilation was performed with relief of dysphagia after this intervention. All 24-hour pH studies (11 patients) showed a normal esophageal acid exposure.

Table 2
Dysphagia after Nissen fundoplication with anterior or posterior hiatal closure

	Anterior repair (n = 45)	Posterior repair (n = 49)	*P* value
Number of patients with dysphagia for solids (%)	26 (58)	28 (57)	.950
Dysphagia analog score: solids*	2.04 (.33)	2.20 (.35)	.831
Dysphagia analog score: liquids*	1.13 (.28)	.94 (.29)	.423
Composite dysphagia score*	8.69 (1.36)	11.20 (1.55)	.335

* Values are presented as means with SEM in parentheses.

Table 3
Heartburn and other symptoms in patients after Nissen fundoplication with anterior or posterior hiatal repair

	Anterior repair (n = 45)	Posterior repair (n = 49)	*P* value
No heartburn present (%)	34 (76)	29 (59)	.092
Analog heartburn score*	.71 (.22)	1.73 (.38)	.052
Able to eat normal diet (%)	41 (91)	46 (93)	.528
Bloated/distended after eating (%)	23 (53)	25 (51)	.525
Ability to burp (%)	29 (64)	34 (69)	.506

* Value is presented as the mean with SEM in parentheses.

Patient satisfaction

The mean satisfaction scores on the 0 to 10 analog scale were 8.1 (.41) and 7.8 (.46) for the anterior and posterior repair groups, respectively ($P = .919$). Eighty-four percent of the patients randomized to anterior hiatal repair and 83% of the posterior group indicated that they thought they had made the correct decision to have their original surgery.

Comments

Since the introduction of "Eine eifache operation zur beeinflussung der refluxoesophagitis" in 1956, the Nissen fundoplication has undergone many modifications to minimize the side effects of the procedure. In undertaking the surgery, surgeons have focused mainly on issues concerning the optimal length of the wrap, fixation of the wrap, mobilization of the gastric fundus/division of the short gastric vessels, and use of a bougie intraoperatively. Less attention has been paid to the technique of closure of the esophageal hiatus. In the early 1990s, the esophageal hiatus was not repaired routinely and a high incidence of herniation of the wrap and stomach was reported [21,22]. Therefore, it is now widely believed that routine approximation of the left and right hiatal pillars, even when no hiatal hernia is present, is necessary during a laparoscopic fundoplication. This view could be challenged, however, because no randomized controlled trials have addressed this question [23].

Recently, a study from the Netherlands showed that anatomic failure of the wrap, including complete herniation, is common after Nissen fundoplication, but this does not correlate with subjective symptomatic outcome [12]. Moreover, fibrosis of the hiatus is recognized as one of causes of postoperative dysphagia. Dissection of the hiatus and full mobilization of the distal esophagus with electrocautery can be followed by hiatal fibrosis and stenosis, and this results in dysphagia [24]. Also, prosthetic reinforcement of the hiatus, although reducing the incidence of intrathoracic wrap herniation, has been reported to be associated with increased rates of dysphagia, at least in the short term [25]. Hence, the hiatus and its repair can contribute to post–fundoplication dysphagia.

To investigate the possibility that post–Nissen fundoplication dysphagia might be less common after anterior hiatal repair, we commenced the reported randomized controlled trial in 1997 [17]. Our hypothesis was that after posterior hiatal repair, the esophagus is displaced anteriorly (as observed on barium swallow radiographic films), and this angulation might contribute to postoperative dysphagia. On the contrary, when performing anterior hiatal repair, the esophagus is pushed posteriorly, thus keeping its axis close to the usual anatomic position. Hence, this might lead to less dysphagia after fundoplication.

The current data do not support our initial view because we have not established a difference in dysphagia between the study groups, as measured by several scoring systems. However, the initial re-operation rate for dysphagia was higher in the posterior hiatal repair group, and this was sustained after 5 years. This 14% incidence of surgical revision for dysphagia and/or paraesophageal herniation in the posterior group was much higher than we originally expected, and it is higher than the incidence of 1% to 2% found in other randomized trials reported from our group in which posterior repair of the hiatus was undertaken [26,27]. We do not have a good explanation for this. However, as discussed previously [17], a type 2 statistical error is one possible explanation. The reported rate of re-operation after laparoscopic Nissen fundoplication varies in the literature [28,29], with a recent figure of 13.5% at long-term follow-up evaluation of a randomized trial [6].

Patients randomized to the anterior hiatal repair had a lower analog heartburn score, although this was not statistically significantly different and because the scores were low anyway, the difference does not appear to be clinically important. Preoperative test results, in terms of 24-hour pH profiles and manometry data, were similar between both groups, as were the early postoperative test results, and both groups underwent a 360° Nissen fundoplication. Hence, the technique of hiatal closure was the only difference. Unfortunately, we do not have 24-hour pH data 5 years after surgery in these patients, although none of the pH studies that were performed to investigate heartburn symptoms showed abnormal reflux. However, this is consistent with reports that have established that reflux symptoms after Nissen fundoplication do not correlate with the outcomes of objective tests [30,31]. In fact, only 30% of patients with reflux symptoms after fundoplication have an abnormal pH profile [31,32]. Even anatomic failures of Nissen fundoplication have not been shown to predict postoperative symptoms and many patients with an anatomic failure are asymptomatic [12].

Maybe of more importance is how the patients rate their overall satisfaction after the surgery. With both patient groups scoring a mean value close to 8 on a visual analog scale (0–10), this implies that most patients were satisfied with the overall result. Ultimately, the measure of success after a surgical procedure is determined by the patient's view of the outcome, rather than the surgeon's opinion or the results of various investigations.

With a near-complete (96%) long-term follow-up evaluation on the 102 patients randomized to Nissen fundoplication with anterior versus posterior hiatal repair [33], we can conclude that anterior narrowing of the hiatus is at least as good as the traditional posterior suture repair in terms of postoperative control of reflux symptoms and dysphagia. Although this approach might seem less anatomic, it does appear to provide an adequate barrier to hiatal herniation, and the overall outcome is good. Over the past decade posterior hiatal repair with or without prosthetic reinforce-

ment has become the norm. Based on the data in this trial, it seems that anterior hiatal repairs can be performed with acceptable outcomes.

Acknowledgments

This trial was supported by project grants from the National Health and Medical Research Council of Australia. Supported by a grant from the Professor Michaël van Vloten fund and the European Society of Surgical Oncology (B.P.L.W.).

Mrs. Carolyn Lally is greatly acknowledged for her invaluable assistance in completing the follow-up evaluation of the patients and for accurate management of the trial data.

References

[1] Nissen R. [A simple operation for control of reflux esophagitis.] Schweiz Med Wochenschr 1956;86:590–2.
[2] DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. Ann Surg 1986;204:9–20.
[3] DeMeester TR, Stein HJ. Minimizing the side effects of antireflux surgery. World J Surg 1992;16:335–6.
[4] Nissen R. Reminiscences—reflux esophagitis and hiatal hernia. Rev Surg 1970;27:307–14.
[5] Donahue PE, Samelson S, Nyhus LM, et al. The floppy Nissen fundoplication. Effective long-term control of pathologic reflux. Arch Surg 1985;120:663–8.
[6] Draaisma WA, Rijnhart-de Jong HG, Broeders IA, et al. Five-year subjective and objective results of laparoscopic and conventional Nissen fundoplication: a randomized trial. Ann Surg 2006;244:34–41.
[7] Lafullarde T, Watson DI, Jamieson GG, et al. Laparoscopic Nissen fundoplication: five-year results and beyond. Arch Surg 2001;136:180–4.
[8] Hogan WJ, Shaker R. Life after antireflux surgery. Am J Med 2000;108(Suppl 4a):181S–91S.
[9] Wills VL, Hunt DR. Dysphagia after antireflux surgery. Br J Surg 2001;88:486–99.
[10] Bais JE, Wijnhoven BP, Masclee AA, et al. Analysis and surgical treatment of persistent dysphagia after Nissen fundoplication. Br J Surg 2001;88:569–76.
[11] Luostarinen ME, Isolauri JO. Surgical experience improves the long-term results of Nissen fundoplication. Scand J Gastroenterol 1999;34:117–20.
[12] Donkervoort SC, Bais JE, Rijnhart-de Jong H, et al. Impact of anatomical wrap position on the outcome of Nissen fundoplication. Br J Surg 2003;90:854–9.
[13] Horgan S, Pohl D, Bogetti D, et al. Failed antireflux surgery: what have we learned from reoperations? Arch Surg 1999;134:809–17.
[14] Patti MG, Arcerito M, Feo CV, et al. An analysis of operations for gastroesophageal reflux disease: identifying the important technical elements. Arch Surg 1998;133:600–7.
[15] Anvari M, Allen C. Esophageal and lower esophageal sphincter pressure profiles 6 and 24 months after laparoscopic fundoplication and their association with postoperative dysphagia. Surg Endosc 1998;12:421–6.
[16] Hunter JG, Smith CD, Branum GD, et al. Laparoscopic fundoplication failures: patterns of failure and response to fundoplication revision. Ann Surg 1999;230:595–606.
[17] Watson DI, Jamieson GG, Devitt PG, et al. A prospective randomized trial of laparoscopic Nissen fundoplication with anterior vs posterior hiatal repair. Arch Surg 2001;136:745–51.
[18] Jamieson GG, Watson DI, Britten-Jones R, et al. Laparoscopic Nissen fundoplication. Ann Surg 1994;220:137–45.
[19] Dakkak M, Bennett JR. A new dysphagia score with objective validation. J Clin Gastroenterol 1992;14:99–100.
[20] Ackroyd R, Watson DI, Game PA. Fizzy drinks following laparoscopic Nissen fundoplication: a cautionary tale of explosive consequences. Aust N Z J Surg 1999;69:887–8.
[21] Seelig MH, Hinder RA, Klingler PJ, et al. Paraesophageal herniation as a complication following laparoscopic antireflux surgery. J Gastrointest Surg 1999;3:95–9.
[22] Watson DI, Jamieson GG, Devitt PG, et al. Paraoesophageal hiatus hernia: an important complication of laparoscopic Nissen fundoplication. Br J Surg 1995;82:521–3.
[23] Catarci M, Gentileschi P, Papi C, et al. Evidence-based appraisal of antireflux fundoplication. Ann Surg 2004;239:325–37.
[24] Watson DI, Jamieson GG, Mitchell PC, et al. Stenosis of the esophageal hiatus following laparoscopic fundoplication. Arch Surg 1995;130:1014–6.
[25] Granderath FA, Schweiger UM, Kamolz T, et al. Laparoscopic Nissen fundoplication with prosthetic hiatal closure reduces postoperative intrathoracic wrap herniation: preliminary results of a prospective randomized functional and clinical study. Arch Surg 2005;140:40–8.
[26] Ludemann R, Watson DI, Jamieson GG, et al. Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180 degrees fundoplication. Br J Surg 2005;92:240–3.
[27] Watson DI, Jamieson GG, Pike GK, et al. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 1999;86:123–30.
[28] Dutta S, Bamehriz F, Boghossian TG, et al. Outcome of laparoscopic redo fundoplication. Surg Endosc 2004;18:440–3.
[29] Dallemagne B, Weerts JM, Jehaes C, et al. Causes of failures of laparoscopic antireflux operations. Surg Endosc 1996;10:305–10.
[30] Galvani C, Fisichella PM, Gorodner MV, et al. Symptoms are a poor indicator of reflux status after fundoplication for gastroesophageal reflux disease: role of esophageal functions tests. Arch Surg 2003;138:514–9.
[31] Khajanchee YS, O'Rourke RW, Lockhart B, et al. Postoperative symptoms and failure after antireflux surgery. Arch Surg 2002;137:1008–14.
[32] Lord RV, Kaminski A, Oberg S, et al. Absence of gastroesophageal reflux disease in a majority of patients taking acid suppression medications after Nissen fundoplication. J Gastrointest Surg 2002;6:3–10.
[33] Ludemann R, Watson DI, Jamieson GG. Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication. Am J Surg 2003;186:143–7.

World J Surg (2011) 35:2038–2044
DOI 10.1007/s00268-011-1172-x

World Journal of Surgery

Prospective Randomized Trial of Laparoscopic Nissen Fundoplication With Anterior Versus Posterior Hiatal Repair: Late Outcomes

Carolyn R. Chew · Glyn G. Jamieson · Peter G. Devitt · David I. Watson

Published online: 29 June 2011

Abstract
Background The technique used for hiatal closure in laparoscopic Nissen fundoplication might have an impact on the risk of postfundoplication dysphagia and hiatal herniation. In 1997, we commenced a randomized trial to evaluate the impact of anterior versus posterior hiatal repair techniques on these outcomes. In the present study, we evaluated the 10-year outcomes from this trial.
Methods A total of 102 patients were randomized to undergo laparoscopic Nissen fundoplication with either anterior (47 patients) or posterior (55 patients) repair of the diaphragmatic hiatus. Outcomes were assessed using standardized clinical assessment scores that evaluated reflux symptoms, dysphagia, and satisfaction with the outcome following surgery.
Results Clinical outcomes 10 years after surgery were available for 93% of patients, and outcome scores were obtained for 43 patients in each group. Patients undergoing anterior hiatal repair were less likely to report dysphagia for lumpy solid foods (14.0% vs. 39.5%, $p = 0.01$), although there were no significant differences in dysphagia outcomes for six other dysphagia assessment scores. There were no differences between the two groups for reflux symptoms, medication use, and overall satisfaction with the outcome of surgery.
Conclusions At the 10-year follow-up, the outcomes for the two groups were similar. Anterior hiatal repair is an acceptable technique for hiatal closure during laparoscopic Nissen fundoplication.

C. R. Chew · D. I. Watson (✉)
Flinders University Department of Surgery, Flinders Medical Centre, Room 3D211, Bedford Park, SA 5042, Australia
e-mail: david.watson@flinders.edu.au

G. G. Jamieson · P. G. Devitt
Discipline of Surgery, University of Adelaide, Adelaide, SA, Australia

Introduction

Laparoscopic Nissen fundoplication with posterior hiatal repair is the commonest surgical procedure used for the treatment of symptomatic gastroesophageal reflux. Long-term outcome studies have established that it provides satisfactory clinical outcomes and good control of reflux symptoms in most patients [1–3]. However, postoperative dysphagia remains a cause of troublesome morbidity at late follow-up in a subset of patients [4, 5]. The literature proposes many possible explanations for postfundoplication dysphagia, although the causal link between these potential mechanisms and outcomes is still unclear [5].

Although useful for screening for esophageal motility disorders, the utility of preoperative studies such as esophageal manometry has not been shown to predict postoperative dysphagia reliably [5]. What has been shown, however, is a relation between anatomic factors and postoperative dysphagia. Factors such as peptic strictures, paraesophageal hiatus hernia, hiatal stenosis, and rotational deformities of the esophagus are all associated with dysphagia [3, 5, 6]. Interestingly, however, only one-third of patients with these anatomic problems report dysphagia, with most remaining asymptomatic [7]. Nevertheless, correction of these anatomic defects in symptomatic patients results in reversal of dysphagia in most cases [8].

Since first reported in 1991, the operative technique of laparoscopic Nissen fundoplication has evolved in an attempt to improve outcomes and decrease the incidence of postoperative complications [3–5, 9]. Two aspects of surgical technique have been shown unequivocally to have an

impact on postoperative dysphagia: the technique used to construct the fundoplication and the method of hiatal closure. Most studies have focused on construction of the fundoplication, and there is consensus that the creation of a short, loose wrap decreases the incidence of postoperative dysphagia [10, 11]. Closure of the esophageal hiatus is also an important component of antireflux surgery as it prevents postoperative hiatal herniation [8, 12, 13]. However, if excessively narrowed, the hiatal repair can also cause dysphagia. Traditionally, closure has been achieved using posteriorly placed sutures. It is also possible to reduce the hiatal size using an anterior hiatal repair technique, and it has been hypothesized that anterior repair may achieve a more "anatomic" end result due to less anterior displacement of the esophagus. This might result in less postoperative dysphagia.

In 1997, we commenced a randomized study to investigate the hiatal repair technique used during laparoscopic Nissen fundoplication and its influence on dysphagia [14]. We hypothesized that the technique used for repair of the esophageal hiatus would influence the likelihood of postoperative dysphagia. Early (6 months) and intermediate (5 years) follow-up data have been reported previously [14, 15]. In this article, we report the long-term (minimum 10 years) outcomes from this trial.

Methods

Patients undergoing laparoscopic Nissen fundoplication for gastroesophageal reflux disease at the Royal Adelaide Hospital and associated private hospitals in Adelaide, South Australia, were recruited to this study. Patients were excluded from the study if they had an esophageal motility disorder, required a concurrent abdominal procedure at the time of the fundoplication, had previously undergone antireflux surgery, or had a large hiatus hernia (i.e., >50% of the stomach or >10 cm in length). The full details of the trial and earlier outcomes have been reported elsewhere [14, 15].

All patients underwent preoperative investigation with esophageal manometry and endoscopy. Twenty-four hour pH monitoring was undertaken in patients who did not have ulcerative esophagitis at endoscopy, or in those with atypical reflux symptoms. After obtaining informed consent, patients were randomized to undergo either anterior or posterior repair of the esophageal diaphragmatic hiatus. Randomization occurred in the operating room after the commencement of anesthesia and initial laparoscopy. No patients were withdrawn from the study after randomization.

All patients underwent a laparoscopic Nissen fundoplication procedure. Full details of the operative technique have been described elsewhere [14, 16]. In brief, surgery entailed mobilization of the distal esophagus, dissection of the hiatal pillars, and routine preservation of the hepatic branch of the vagus nerve. In most patients, the short gastric vessels were not divided, although they were divided in five patients when a sufficiently loose wrap could not be fashioned.

Closure of the hiatus was performed according to the randomization allocation. Before creation of the fundoplication, posterior hiatal repair was performed using interrupted 2-0 monofilament nonabsorbable sutures, whereas anterior repair of the hiatus was also performed using interrupted 2-0 monofilament nonabsorbable sutures after first constructing the fundoplication. In both instances, the hiatus was closed such that the closure was adequate but not tight. No mesh or pledgets were used to reinforce the sutures. The degree of hiatal closure was initially assessed with a 52F bougie sitting within the esophageal lumen and then further by placing a closed laparoscopic grasping instrument between the hiatal rim and the esophagus to ensure that the repair was not too tight.

For the fundoplication, the anterior wall of the fundus was used to create a 1.5- to 2.0-cm loose total fundoplication. The bougie was also used to ensure the wrap was not fashioned too tight. If the procedure was converted to an open procedure, the randomization was still followed, and the patient remained in the trial. All operations were performed or directly supervised by one of four consultant surgeons, and the technique was standardized by mutual agreement before commencing the trial.

Patients were not informed which type of hiatal repair procedure they underwent, and their randomization group was concealed from them for the duration of the follow-up. The operating surgeon was aware of the procedure performed, but the staff conducting the follow-up were blinded to the randomization of each patient. Clinical follow-up data were collected yearly using mailed questionnaires. If not returned, the questionnaire was mailed a second time. At the 10-year postoperative mark (this study), active steps were taken to track any patients who were lost to follow-up, and patients who did not return questionnaires were phoned and the missing questionnaires were completed verbally.

The presence or absence of each of the following symptoms was sought: heartburn; epigastric pain; regurgitation; dysphagia for lumpy solid food, soft solid food, and liquids; odynophagia; early satiety; inability to belch; epigastric bloating; anorexia, nausea; vomiting; nocturnal coughing and wheezing; increased passage of flatus; diarrhea. Additionally, heartburn was scored using a visual analog score (VAS) (scored 0–10). Dysphagia was further evaluated by several methods, including a VAS (0, no dysphagia; 10, total dysphagia) for both solids and liquids, as well as a previously validated dysphagia score (scored

0–45) [17]. Overall outcome was determined using three scales: a modified Visick grading [18], a visual analog satisfaction score (0, dissatisfied; 10, satisfied), and ranking of the outcome of the surgery as excellent, good, fair, or poor (descriptors described elsewhere [14, 18]). Objective investigations were undertaken at early follow-up (3–4 months after surgery) but were not repeated at the late follow-up.

The primary clinical outcome that this trial was designed to evaluate was postoperative dysphagia. Before the trial commenced, it was determined that 84 patients (42 in each group) would be needed to demonstrate a 20% difference in these outcome measures. To ensure that this was achieved, it was intended that 100 patients would be recruited. Follow-up data were stored in a computerized database (Filemaker Pro; Filemaker, Santa Clara, CA, USA). Statistical analysis was completed using a commercially available statistics program (InStat, Version 3; GraphPad Software, San Diego, CA, USA). The significance of 2×2 contingency tables was assessed using Fisher's exact test. The significance of continuous data sets was determined using a two-tailed Mann-Whitney *U*-test. Results with a $p < 0.05$ were accepted as statistically significant. The Royal Adelaide Hospital Human Research Ethics Committee approved the protocol for this study.

Results

Between July 1997 and October 1999, a total of 102 patients were recruited into this study and randomized to either anterior ($n = 47$) or posterior ($n = 55$) repair of the esophageal hiatus. Full details of the recruitment and exclusions have been reported elsewhere [14]. No patients were withdrawn following randomization. The two trial groups were similar regarding age, sex, height, weight, incidence of previous abdominal surgery, duration, type and severity of symptoms, and medications consumed before surgery. Full preoperative details have been reported previously [14]. All but one procedure was completed laparoscopically (patient in the anterior hiatal repair group), and all patients underwent their intended procedure following randomization.

An outcome was known for 95 (93.1%) of patients at the 10-year follow-up, with minimum 10 years of clinical follow-up data obtained for 86 of 102 patients—their late follow-up data formed the basis of the results reported here. Eight patients died during the 10-year follow-up period, seven (6.9%) were lost to follow-up, and one underwent conversion to gastric bypass.

In the anterior hiatal repair group, data were available for 43 patients, 2 were lost to follow-up and 2 died within 10 years of surgery. Of the two patients lost to follow-up, one reported a satisfaction score of 10/10 at 5 years, whereas the other underwent reversal of the fundoplication at 7 years for recurrent chest pain. In the posterior hiatal repair group, follow-up data were available for 43 patients, 5 were lost to follow-up, 6 died within 10 years, and 1 underwent conversion to gastric bypass for morbid obesity 8 years after the original fundoplication. Of the five lost to follow-up, four patients were satisfied with their surgery at their last follow-up (1, 2, 8, and 9 years, respectively), and one was dissatisfied with the outcome due to persistent "heartburn" symptoms.

Symptoms associated with gastroesophgaeal reflux (heartburn, regurgitation, epigastric pain) and the heartburn scores are summarized in Table 1. There were no significant differences between the two groups for these outcomes. At 10 years, nine patients in the anterior hiatal repair group were using a proton pump inhibitor (PPI), two were using regular antacids, and one was using an H_2-receptor antagonist. In the posterior hiatal repair group, 11 were using PPIs, and 1 was using regular antacids.

Postoperative dysphagia at late follow-up is summarized in Table 2. There were no significant differences between the two groups for the analog dysphagia scores, the composite dysphagia scores, or the yes/no questions that addressed dysphagia for liquids or soft solids. However, more patients in the posterior hiatal repair group reported dysphagia for lumpy solids ($p = 0.01$). The prevalence of other symptoms is summarized in Table 3. There was no significant difference between the two groups for any of these symptoms. Overall satisfaction with the outcome of

Table 1 Heartburn and reflux related symptoms at the 10-year follow-up

Symptom	Anterior hiatal repair ($n = 43$)	Posterior hiatal repair ($n = 43$)	p
Heartburn	3 (7.0%)	6 (14.0%)	0.48
Epigastric pain	7 (16.3%)	10 (23.3%)	0.59
Regurgitation	2 (4.7%)	7	0.16
Analog Heartburn Score: mean and 95% CI	0.70 (0.16, 1.23)	1.02 (0.49, 1.56)	0.37

All figures reported as the number or the mean (95% CI)

CI confidence interval

Table 2 Dysphagia symptoms at the 10-year follow-up

Symptom	Anterior hiatal repair ($n = 43$)	Posterior hiatal repair ($n = 43$)	p
Dysphagia for lumpy solids	6 (14.0%)	17 (39.5%)	0.01
Dysphagia for soft solids	3 (7.0%)	3 (7.0%)	1.0
Dysphagia for liquids	2 (4.7%)	3 (7.0%)	1.0
Odynophagia	3 (7.0%)	3 (14.0%)	1.0
Dysphagia Analog Score			
Solids	1.98 (1.28, 2.68)	2.42 (1.66, 3.17)	0.39
Liquids	0.97 (0.47, 1.48)	1.14 (0.48, 1.80)	0.852
0–45 Dysphagia Score	8.95 (6.15, 11.76)	11.21 (7.57, 14.85)	0.55
No. of patients scoring 0	14 (32.6%)	12 (28%)	0.81

Data are reported as the number or the mean (95% CI)

Table 3 Other symptoms reported at the 10-year follow-up

Symptom	Anterior hiatal repair ($n = 43$)	Posterior hiatal repair ($n = 43$)	p
Early satiety	15 (34.9%)	10 (23.3%)	0.34
Unable to belch	13 (30.2%)	13 (30.2%)	1.00
Bloating	21 (48.8%)	17 (39.5%)	0.52
Anorexia	2 (4.7%)	0	0.49
Nausea	4 (9.3%)	7 (16.3%)	0.52
Vomiting	1 (2.3%)	2 (4.7%)	1.00
Cough	5 (11.6%)	6 (14.0%)	1.00
Wheeze	1 (2.3%)	5 (11.6%)	0.20
Increased flatus	22 (51.2%)	19 (44.2%)	0.67
Diarrhea	12 (27.9%)	5 (11.6%)	0.10
Chest pain	3 (7.0%)	5 (11.6%)	0.71

surgery is summarized in Table 4. All measures of overall satisfaction were similar for the two groups.

During the 10-year follow-up period, 12 patients underwent further surgery, with 19 operations undertaken in these patients. Three (6.4%) patients were in the anterior repair group, and nine (16.4%) were in the posterior repair group ($p = 0.14$). Eight patients (one in the anterior repair group, seven in the posterior repair group) underwent reoperation for dysphagia, two for paraesophageal hiatus hernia (one in each group), one for troublesome bloating (anterior repair group), and one for gastric rupture at 3 months (posterior repair group). Details of the reinterventions during the first 5 years of follow up have been reported elsewhere [14, 15]. Only one patient underwent revisional surgery beyond the first 5-year follow-up. This patient was in the anterior hiatal repair group, and he underwent reversal of the fundoplication at 7 years follow-up for problematic bloating. In addition to these revision procedures, one patient in the posterior hiatal repair group underwent a gastric bypass procedure for morbid obesity at 5 years of follow-up, and by necessity her fundoplication was reversed as part of this procedure. No patient underwent reoperation for recurrent gastroesophageal reflux.

Two patients underwent multiple revision procedures, and both were in the posterior hiatal repair group. One initially underwent revision of the hiatus for dysphagia at day 35 and then had the fundoplication reversed for persistent dysphagia at 3 years of follow-up. The other patient underwent five reoperations including two early revision operations for dysphagia (1 week and 4 months, respectively) and then further revision procedures at 2, 2, and 9 years for dysphagia, abdominal pain and odynophagia/dysphagia, respectively.

Discussion

Previous studies have shown that not all dysphagia following Nissen fundoplication is due to the construction of the fundoplication but that it can also develop following overly tight hiatal repair or postfundoplication scarring at the esophageal hiatus (hiatal stenosis) [9], whereas other studies have emphasized the importance of hiatal repair to prevent the development of a hiatus hernia during postoperative follow-up [19, 20]. Almost all surgeons now routinely repair the hiatus during laparoscopic fundoplication procedures. Hence, it is important to understand how best to repair the hiatus in such a way that the risk of recurrent hernia is minimized and new dysphagia does not develop following surgery.

In 1997, we commenced our current trial to investigate this issue further [14]. Anterior hiatal repair does not lift the esophagus forward, whereas posterior repair can angulate the esophagus at the level of the hiatus. Hence, we hypothesized that there might be less dysphagia after anterior hiatal repair. On the other hand, the anterior hiatal repair could be associated with a less stable hiatal repair and might be associated with a higher risk of recurrent

Table 4 Summary of outcomes and patient satisfaction at the 10-year follow-up

Parameter	Anterior hiatal repair ($n = 43$)	Posterior hiatal repair ($n = 43$)	p
Satisfaction score	8.67 (8.02, 9.33)	8.07 (7.21, 8.93)	0.43
Correct decision to undergo surgery	39/43 (91%)	37/43 (86%)	0.74
Operation outcome			
Excellent	19	18	
Good	17	15	
Fair	6	8	
Poor	1	2	
Excellent or good outcome	36/43 (84%)	33/43 (77%)	0.59
Visick score			
1	17	15	
2	20	19	
3	4	4	
4	1	3	
5	1	2	
Visick 1 or 2	37/43 (86%)	34/43 (79%)	0.57

Data are reported as the number or the mean (95% CI)

hiatus hernia, poorer reflux control, and even more dysphagia when compared with posterior hiatal repair.

We have previously reported 6-month and 5-year outcomes from our randomized trial of anterior versus posterior hiatal repair during Nissen fundoplication and showed equivalent clinical outcomes for dysphagia and reflux control but a higher rate of revision surgery following posterior hiatal repair, particularly for troublesome dysphagia [14, 15]. The results for late follow-up reported in this article also confirm that anterior hiatal repair is at least as good as posterior hiatal repair in patients undergoing laparoscopic Nissen fundoplication for gastroesophageal reflux, and anterior hiatal repair is a suitable alternative to posterior repair during Nissen fundoplication. Our trial has demonstrated equivalence for all outcomes, although the symptom of dysphagia for lumpy solid foods appeared to be less prevalent in the anterior hiatal repair group. There was also a trend toward less reoperative surgery for dysphagia in the anterior hiatal repair group (one versus seven procedures; $p = 0.067$). However, the other dysphagia symptom scores used for follow-up were not different for the two groups. It should be noted that we found only one statistically significant outcome difference ($p = 0.01$) but tested for 23 clinical parameters. Hence, it is possible that the single significant result could have arisen by chance. Further, if a Bonferroni correction is applied to our data analysis, the level of statistical significance becomes $p = 0.002$. The p value for dysphagia for lumpy solid foods was 0.01 (i.e., not significant after applying this correction). Our trial also showed equivalent outcomes for measures of reflux and patient satisfaction. In both groups, there was only one reoperation for hiatus hernia, and no reoperations were required for recurrent reflux during the 10-year follow-up period. These outcomes support the contention that both approaches to hiatal repair are associated with stable anatomy at late follow-up.

There are only a few other studies with high rates of late follow-up following laparoscopic Nissen fundoplication, and our current article adds to a growing body of evidence that laparoscopic Nissen fundoplication is a durable, effective procedure for treatment of reflux. The incidence of patients reporting a good surgical outcome was similar for the two study groups, with 84% of the anterior repair group and 77% of the posterior repair group reporting either a good or excellent outcome. This is consistent with previously published 10-year outcomes at >80% by Kelly et al. [1]. The use of antisecretory medications at late follow-up was also consistent with other reports. Altogether, 23% of patients in our trial were using PPI medication at the 10-year follow-up. This is similar to other post-surgical studies, which generally have reported that approximately 20% of patients use PPIs 10 years after Nissen fundoplication [1, 21].

In our current study, we only evaluated patient reported subjective symptom scores at late follow-up, not objective outcomes such as endoscopy, pH monitoring, or manometric parameters. Objective investigations were evaluated at early follow-up and have been reported elsewhere [14]. However, beyond the initial 6-month follow-up period, compliance with routine objective follow-up tests is difficult to achieve, and objective testing was undertaken only when clinically indicated. A good clinical outcome, as perceived by each individual patient, is what antireflux surgery aims to achieve, and for this reason the symptom scores are still an appropriate method for determining surgical success. The clinical outcomes at 10 years in our

trial suggest that both procedures achieved effective long-term reflux control in most patients. Furthermore, some other studies have shown that the outcomes of objective tests and patient satisfaction with the outcome of surgery do not always correlate strongly [22].

Although the results of our trial suggest equivalent outcomes for the two hiatal repair techniques, further randomized studies enrolling larger patient cohorts are probably needed to demonstrate equivalence adequately for the symptom of dysphagia. As discussed above, our study suggested a difference in only one of the dysphagia scores. All other dysphagia scores were lower in the anterior hiatal repair group, although these differences were not statistically significant, and there was a trend toward less revisional surgery for dysphagia in the anterior hiatal repair group. At this stage, the only firm conclusion that should be drawn from our study is that anterior hiatal repair during laparoscopic Nissen fundoplication is an appropriate technique. At this time, we usually repair the hiatus with posterior sutures, although we do not hesitate to add anterior hiatal repair sutures or repair only with anterior sutures if a posterior repair is technically difficult.

Anterior hiatal repair has been advocated during other procedures that entail surgery at the gastroesophageal junction. In particular, it has been suggested that if a "dimple" is seen in the anterior hiatus at laparoscopic placement of a gastric band for obesity, the anterior hiatus should be opened and then repaired with anterior sutures [23]. Our trial is the only randomized trial to evaluate anterior versus posterior hiatal repair, but its results should not be extrapolated beyond the context of laparoscopic Nissen fundoplication for gastroesophageal reflux. Any application in other surgical procedures such as laparoscopic gastric banding, repair of a very large hiatus hernia, and partial fundoplication procedures requires further evaluation in new randomized trials.

Conclusions

The long-term results of our trial of anterior versus posterior hiatal repair during laparoscopic Nissen fundoplication for gastroesophageal reflux have shown equivalent outcomes after 10 years of follow-up, with a trend toward a better outcome in patients undergoing anterior hiatal repair. Although further studies are warranted to evaluate the issue of dysphagia following these two techniques, surgeons undertaking laparoscopic Nissen fundoplication can expect a good long-term outcome in most patients who undergo either anterior or posterior hiatal repair.

References

1. Kelly J, Watson DI, Chin K et al (2007) Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. J Am Coll Surg 205:570–575
2. Dallemagne B, Weerts J, Markiewicz S et al (2006) Clinical results of laparoscopic fundoplication at ten years after surgery. Surg Endosc 20:159–165
3. DeMeester TR, Bonavina L, Albertucci M (1986) Nissen fundoplication for gastroesophageal reflux disease: evaluation of primary repair in 100 consecutive patients. Ann Surg 204:9–20
4. Watson DI, Jamieson GG, Pike GK et al (1999) Prospective randomized double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 86: 123–130
5. Wills VL, Hunt DR (2001) Dysphagia after antireflux surgery. Br J Surg 88:486–499
6. Bais JE, Wijnhoven BP, Masclee AA et al (2001) Analysis and surgical treatment of persistent dysphagia after Nissen fundoplication. Br J Surg 88:569–576
7. Patti MG, Arcerito M, Feo CV et al (1998) An analysis of operations for gastroesophageal reflux disease: identifying the important technical elements. Arch Surg 133:600–606
8. Hunter JG, Smith CD, Branum GD et al (1999) Laparoscopic fundoplication failures: patterns of failure and response to fundoplication revision. Ann Surg 230:595–604
9. Hunter JG, Swanstrom L, Waring JP (1996) Dysphagia after laparoscopic antireflux surgery: the impact of operative technique. Ann Surg 224:51–57
10. Watson DI, Jamieson GG (1998) Antireflux surgery in the laparoscopic era. Br J Surg 85:1173–1184
11. DeMeester TR, Stein HJ (1992) Minimizing the side effects of antireflux surgery. World J Surg 16:335–336. doi:10.1007/BF02071542
12. Seelig MH, Hinder RA, Klingler PJ et al (1999) Paraesophageal herniation as a complication following laparoscopic antireflux surgery. J Gastrointest Surg 3:95–99
13. Horgan S, Pohl D, Bogetti D et al (1999) Failed antireflux surgery: what have we learned from reoperations? Arch Surg 134: 809–815
14. Watson DI, Jamieson GG, Devitt PG et al (2001) A prospective randomized trial of laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair. Arch Surg 136:745–751
15. Wijnhoven BPL, Watson DI, Devitt PG et al (2008) Laparoscopic Nissen fundoplication with anterior vs. posterior hiatal repair: long-term results of a randomized trial. Am J Surg 195:61–65
16. Jamieson GG, Watson DI, Britten-Jones R et al (1994) Laparoscopic Nissen fundoplication. Ann Surg 220:137–145
17. Dakkak M, Bennett JR (1992) A new dysphagia score with objective validation. J Clin Gastroenterol 14:99–100
18. Watson DI, Pike GK, Baigrie RJ et al (1997) Prospective double blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. Ann Surg 226:642–652
19. Watson DI, Jamieson GG, Mitchell PC et al (1995) Stenosis of the esophageal hiatus following laparoscopic fundoplication. Arch Surg 130:1014–1016
20. Edye M, Salky B, Posner A et al (1998) Sac excision is essential to adequate laparoscopic repair of paraesophageal hernia. Surg Endosc 12:1259–1263
21. Wijnhoven BPL, Lally CJ, Kelly JJ et al (2008) Use of anti-reflux medication after anti-reflux surgery. J Gastrointest Surg 12: 510–517

22. Yang H, Watson DI, Kelly J et al (2007) Esophageal manometry and clinical outcome after laparoscopic Nissen fundoplication. J Gastrointest Surg 11:1126–1133

23. Gulkarov I, Wetterau M, Ren CJ et al (2008) Hiatal hernia repair at the initial laparoscopic adjustable gastric band operation reduces the need for reoperation. Surg Endosc 22:1035–1041

2.4 Anterior 180 degree partial fundoplication vs. Nissen fundoplication

---

Gatenby PAC, Bright T, Watson DI. Anterior 180 Degree Partial Fundoplication – How I do it. *J Gastrointest Surg* (2012) **16**:2297-2303.

This paper described in detail the surgical technique for laparoscopic anterior 180 degree partial fundoplication.

Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M & Devitt PG. Prospective randomized double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg* (1999) **86**:123-130.

This paper reported the clinical and objective outcomes at 6 months (short term) follow-up from a randomized trial comparing laparoscopic anterior 180 degree partial vs. Nissen fundoplication.

Ludemann R, Watson DI, Game PA, Devitt PG & Jamieson GG. Laparoscopic total versus anterior 180^0 fundoplication - five year follow-up of a prospective randomized trial. *Br J Surg* (2005) **92**:240-243.

This paper reported the 5 year (longer term) clinical outcomes from the same trial.

Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180^0 partial fundoplication. *Br J Surg* (2008) **95**;1501-1505.

This paper reported the 10 year (long term) clinical outcomes from the same trial.

Broeders, JA, Broeders EA, Watson DI, Devitt PG, Holloway RH, Jamieson GG. Objective Outcomes 14 Years after Laparoscopic Anterior 180˚ Partial versus Nissen Fundoplication - Results from a Randomized Trial. *Ann Surg* (2013) **258**:233-239.

This paper reported long term (14 years follow-up) objective outcomes from a subset of patients within the trial of laparoscopic anterior 180 degree partial vs. Nissen fundoplication.

Broeders JA, Roks DJ, Jamieson GG, Devitt PG, Baigrie RJ, Watson DI. Five year outcome after laparoscopic anterior partial versus Nissen fundoplication - Four randomized trials. *Ann Surg* (2012) **255**:637-642.

This paper reported analysis of clinical outcomes at 5 years follow-up from a combined data set which included the patients enrolled in this trial, a cohort from Cape Town, South Africa who were enrolled in a trial using a similar protocol, and data sets from 2 trials of anterior 90 degree partial vs. Nissen fundoplication (described in section 2.5).

J Gastrointest Surg (2012) 16:2297–2303
DOI 10.1007/s11605-012-1954-y

HOW I DO IT

Anterior 180° Partial Fundoplication—How I Do It

Piers A. C. Gatenby · Tim Bright · David I. Watson

Received: 10 May 2012 / Accepted: 24 June 2012 / Published online: 6 July 2012

Abstract Laparoscopic Nissen fundoplication is the standard operation for the surgical control of gastro-oesophageal reflux in many centres. However, in some patients, it can be followed by troublesome side effects, and to minimise the risk of these, partial fundoplications have been recommended. One approach is to construct an anterior 180° partial fundoplication. Randomised trials and a large outcome study have confirmed that in most patients, this approach achieves effective reflux control, as well as a reduced incidence of side effects. In this paper, we describe our approach to this procedure. The procedure entails full dissection of the oesophageal hiatus, hiatal repair with posteriorly placed sutures and then construction of an anterior 180° partial fundoplication using three sutures to attach the anterior gastric fundus to the oesophagus and right hiatal pillar, and two further sutures between the fundus and the apex of the hiatus.

Keywords Gastroesophageal reflux · Fundoplication · Laparoscopy

Introduction

Gastro-oesophageal reflux is common in Western countries, with 10 % of these populations reporting daily reflux symptoms and up to 50 % experiencing at least some symptoms every few months.[1, 2] Treatment of reflux aims for symptom control, as well as minimal treatment-related side effects and complications. Whilst most patients are treated with acid-suppressing medications, surgery continues to have an important role in the treatment of patients in whom reflux symptoms are not well controlled by medication. The standard approach to surgery in many parts of the world is the Nissen fundoplication procedure. However, the outcome following this procedure is less than satisfactory in some individuals, with risks of recurrent reflux and side effects impacting on longer-term success. At 5–10 years follow-up, success rates of 85–90 % are generally reported.[3, 4] However, this means that a poorer outcome is reported by the remaining 10–15 %. In particular, some individuals report problems with troublesome dysphagia and wind-related side effects such as abdominal bloating, inability to belch and flatulence, and in some of these, side effects offset the benefits of reflux control.[3, 4]

Side effects are usually associated with the over-competent lower oesophageal sphincter which follows a Nissen fundoplication. This can result in impairment of the passage of food boluses across the gastro-oesophageal junction and inability to belch gas from the stomach.[5] The use of a partial fundoplication has been advocated as a strategy to reduce the risk of these side effects. Meta-analysis of randomised trials of Nissen vs. partial fundoplication confirms a reduced side effect profile following partial fundoplication techniques.[6]

One approach to constructing a partial fundoplication is an anterior 180° partial fundoplication. This approach was originally proposed by Dor et al.[7] and was initially used to prevent reflux following cardiomyotomy for achalasia. Dor's original technique entailed suturing the anterior wall of the gastric fundus to the cut edges of the myotomy, along the left and then right sides of the oesophagus. We have modified and simplified this approach for use as an

P. A. C. Gatenby · T. Bright · D. I. Watson (✉)
Flinders University Department of Surgery,
Flinders Medical Centre,
Bedford Park,
Adelaide, South Australia 5042, Australia
e-mail: david.watson@flinders.edu.au

antireflux procedure, and the modified procedure applied to the treatment of gastro-oesophageal reflux is described in the current paper. Published data from randomised trials have verified that anterior 180° partial fundoplication controls reflux, with reduced side effects, at up to 10 years follow-up.[8] Hence, the anterior 180° partial fundoplication procedure has now become our preferred approach to surgery for gastro-oesophageal reflux. In this paper, we detail our approach to this procedure.

Pre-operative Workup

Pre-operative workup entails a full history, focussing specifically on upper alimentary symptoms including reflux, regurgitation, dysphagia and post-prandial chest pain. Patients also undergo routine upper alimentary endoscopy to delineate relevant anatomy, assess for evidence of reflux oesophagitis and exclude other pathologies. Twenty four-hour ambulatory pH monitoring is used to confirm gastro-oesophageal reflux disease and oesophageal manometry to evaluate oesophageal motility.

Case Selection

In 1995, when we first performed anterior 180° partial fundoplication for the treatment of reflux, we were selective in our approach, initially applying this operation only in patients with significant oesophageal dysmotility. However, with increasing experience and the reassurance of satisfactory longer-term outcomes, we have become progressively less selective and now offer this procedure to all patients undergoing surgery for gastro-oesophageal reflux, irrespective of any perceived risk factors such as a large hiatus hernia, Barrett's oesophagus or more severe grades of oesophagitis. We also add this procedure in all patients undergoing cardiomyotomy for achalasia. At present, we construct a Nissen fundoplication in less than 20 % of patients presenting for antireflux surgery.

Anaesthetic Considerations/Technique

Patients are given a single dose of intravenous antibiotics on induction of anaesthesia. Opioid analgesia is avoided, and intraoperative ondansetron or tropisetron is given to minimise the risk of post-operative nausea and vomiting.

Theatre Set-Up

The patient is positioned supine, in the lithotomy position, with legs extended in the stirrups and knees level with the hips (Fig. 1). The head of the bed is then elevated so that the patient is in 20–30° reverse Trendelenburg. The operating surgeon stands between the patient's legs with the assistant on the patient's left side and scrub nurse on the patient's right side. The video monitor is placed in line with the patient's head, level with the surgeon's eyes or adjacent to the patient's right shoulder. Four operating ports (two 11 mm and two 5 mm) and a Nathanson liver retractor (Cook Medical Technology, Eight Mile Plains, Queensland, Australia) are used. An “iron intern” is used to fix the liver retractor to the operating table. Instrumentation consists of two plain grasping instruments, a diathermy hook and a single needle holder for the surgeon, and one atraumatic grasper, laparoscopic scissors and a 30° 10-mm laparoscope with camera for the assistant.

Fig. 1 Patient positioning for fundoplication. The legs are extended in stirrups, with minimal hip flexion; the patient is positioned 20–30° head up, and the surgeon operates from between the legs

Surgical Technique

Hiatal Exposure and Oesophageal Mobilisation

Using an open insertion technique, an 11-mm port is inserted immediately supra-umbilically, and a pneumoperitoneum is obtained (Fig. 2). This port is used for the laparoscope. In some obese individuals or individuals with a pendulous abdomen, this site can be too low, and an additional 11-mm port can be inserted in the midline, halfway between the umbilicus and the xiphoid to improve access. The Nathanson liver retractor is next introduced through a 5-mm stab wound sited high in the epigastrium, immediately to the left side of the xiphoid process, and the left lobe of the liver is elevated to expose the upper stomach and the oesophageal hiatus. A further 11-mm and two 5-mm ports are sited next. Five-millimetre ports are placed in the right midclavicular line immediately below the costal margin for the surgeon's left-hand instruments and in the left anterior axillary line 3–4 cm below the costal margin for the

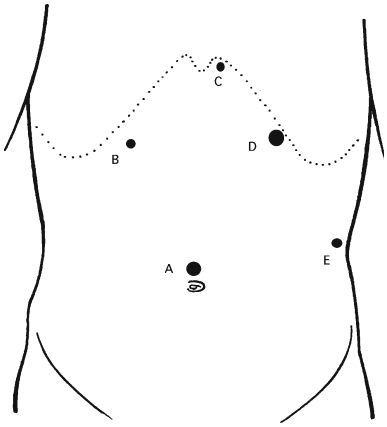


Fig. 2 Port placement for fundoplication: **a** camera port, **b** and **d** surgeon's operating ports, **c** liver retractor insertion site, **e** port for assistant's retractor (Figure reproduced from Wijnhoven and Watson[16])

assistant's instruments. An 11-mm port is placed in the left midclavicular line immediately below the costal margin for the surgeon's right-hand instruments.

Initial dissection entails dissection of the oesophageal hiatus and mobilisation of the oesophagus. The assistant uses an atraumatic grasper on the fat pad overlying the gastric cardia to retract the gastro-oesophageal junction downwards and away from the area dissected. Initially, retraction is to the left, as the first step is to open the pars flacida and lesser omentum on the right side of the oesophageal hiatus, above and below the hepatic branch of the anterior vagus nerve. This nerve is preserved as it provides parasympathetic innervation to the gall bladder and the pylorus, and in addition, when the fundoplication is placed above the preserved nerve, the nerve ensures that the wrap is correctly placed adjacent to the distal oesophagus. Opening the lesser omentum first allows the right hiatal pillar to be demonstrated within the lesser sac, before the phreno-oesophageal ligament is opened and divided. Usually some fat overlies the area of dissection on the right side of the oesophagus, and this should be dissected away to expose the insertion of the phreno-oesophageal ligament onto the right side of the gastro-oesophageal junction. Similarly, peritoneal and fatty attachments between the upper stomach near the angle of His and the left hemidiaphragm should be bluntly dissected to expose the insertion of the phreno-oesophageal ligament onto the left side of the gastro-oesophageal junction.

The oesophageal hiatus is opened, initially by dividing the phreno-oesophageal ligament inside the anterior edge of the right hiatal pillar, near where it inserts onto the oesophagus. As the correct dissection plane is avascular, this can be undertaken using a blunt dissection technique. Dissection continues anteriorly towards the apex of the oesophageal hiatus, separating the diaphragm from the oesophagus and the cardia. It continues across to the left side and then downwards between the left hiatal pillar and the left side of the oesophagus. Dissection continues as far posteriorly as possible to facilitate posterior oesophageal dissection.

The oesophagus should now be virtually fully mobilised, and further minimal posterior dissection behind the oesophagus from the right side allows the passage of the grasper in the surgeon's left hand behind the oesophagus. The oesophagus is then slung with a nylon tape, introduced from the 11-mm left upper abdominal port, transferred to the surgeon's left hand grasper and then passed behind the oesophagus and withdrawn via the same 11-mm port. The port is then removed, and the ends of the tape are retracted and tethered with an artery clip extracorporeally, before reinserting the port so that the tape now lies outside the port. This allows extracorporeal retraction of the oesophagus anteriorly and caudally to fully expose the left and right hiatal pillars, which should then be dissected to their confluence (Fig. 3). The posterior vagus nerve is also dissected away from the oesophagus so that it lies away from the oesophagus, close to the confluence of the hiatal pillars, and ultimately behind the hiatal repair sutures. If any further hiatal surgery is then required, the posterior vagus nerve will be separated from the oesophagus and at less risk of injury during revision.

Hiatal Repair

Non-absorbable monofilament sutures are used. The posterior aspects of the hiatal pillars are approximated with interrupted sutures, spaced approximately 5 mm apart, commencing posteriorly and working anteriorly. Substantial "bites" of the pillars are incorporated with each suture to ensure a stable repair, and care should be taken to ensure that the pillars are opposed but not strangulated by each suture. An intra-oesophageal bougie is not required to calibrate the diaphragmatic closure; rather, the closure is

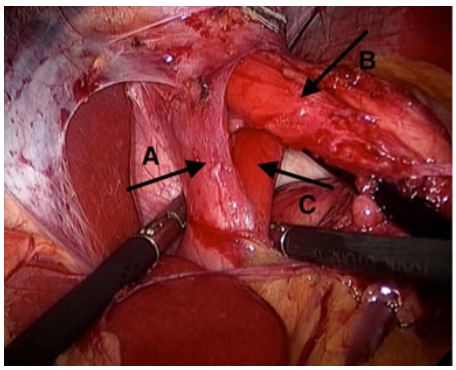


Fig. 3 The hiatus is dissected fully to expose the junction of the hiatal pillars. *A* right hiatal pillar, *B* intra-abdominal oesophagus, *C* left hiatal pillar

tailored to leave approximately 5–7 mm of space posteriorly between the posterior oesophagus and uppermost hiatal repair suture, when the oesophagus is lifted anteriorly (Fig. 4). This usually entails reducing the hiatus to approximately 25–30 mm diameter. One or two sutures are usually placed in patients with either no hiatal hernia or a very small hernia. Additional sutures are required for patients with larger hiatal defects. Currently, we are only using mesh to reinforce the hiatal repair within the context of a randomised trial.

Construction of the Fundoplication

The next step is the construction of the anterior 180° partial fundoplication. The first step is selection of the correct piece of the gastric fundus for the wrap. Whilst the assistant retracts the cardia and oesophagus caudally towards the pelvis, the anterior wall of the fundus, immediately adjacent and lateral to the cardia, is grasped and drawn medially across the front of the oesophagus. If this can be loosely placed across the gastro-oesophageal junction and reach the anterior hiatal repair suture, the adjacent more superior area of the anterior fundus can usually be lifted to reach the apex of the hiatus. It is important to ensure that the fundus can be positioned loosely across the anterior oesophageal wall, so that it reaches the right hiatal pillar without tension (Fig. 5). If any tension is evident, the fundus can always be incrementally adjusted until it lies loosely across the hiatus. Division of the short gastric vessels is never required.

The proposed site for the placement of the first (lowest) fundoplication suture is then temporarily marked on the gastric wall by squeezing the gastric wall between the jaws of the surgeon's grasping instrument. The fundoplication is then constructed. Deep “bites” of all structures—stomach, oesophagus and hiatal rim—are required to ensure the long-term stability of the wrap. Small tentative sutures should be avoided as they are likely to pull out and lead to unravelling of the fundoplication.

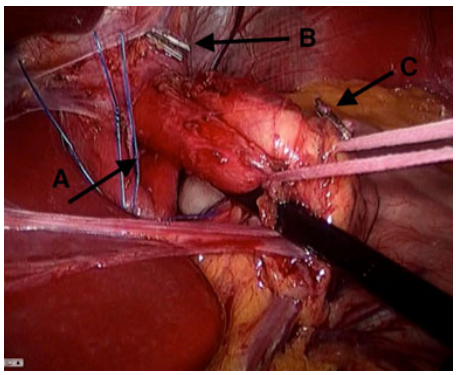


Fig. 4 After hiatal repair, there is still some space (marked *A*) between the oesophagus and the uppermost suture. Note: in this procedure, an aberrant left inferior phrenic artery has been clipped (*B* and *C*) and divided to allow adequate hiatal dissection

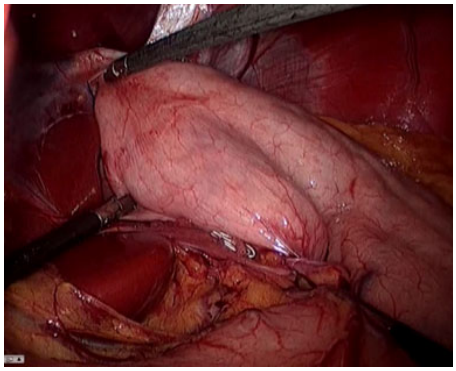


Fig. 5 The anterior wall of the fundus is manipulated until it sits loosely across the front of the oesophagus

Accurate placement of the first suture is critical as it sets up the other fundoplication sutures. This is placed first through the previously “marked” gastric wall, then deeply through the wall of the right postero-lateral oesophagus (7–8 o'clock position) at least 15–20 mm above the gastro-oesophageal junction and then finally through the right hiatal pillar at the level of the highest previously placed hiatal repair suture. This suture is then secured to oppose all three structures (Fig. 6). Once secured, the stomach forms a ridge or edge overlying the oesophagus and the anterior hiatus. It is then quite easy to identify the correct position for suture placement for all subsequent sutures.

The second suture is placed above the first suture and incorporates the fundus 5–7 mm along the ridge of the anterior fundus, then the right antero-lateral wall of the oesophagus 5 mm cranial to the first suture and the right hiatal pillar 5 mm above the first suture. A third suture is placed a further 5–7 mm above the second suture, incorporating the ridge of the anterior fundus, the oesophagus and the right hiatal pillar. Hence, three sutures approximate the anterior fundus, the intra-abdominal oesophagus and the right hiatal pillar. This stabilises 3–4 cm of intra-abdominal oesophagus and fashions a flap valve which prevents reflux (Fig. 7). Attachment of the

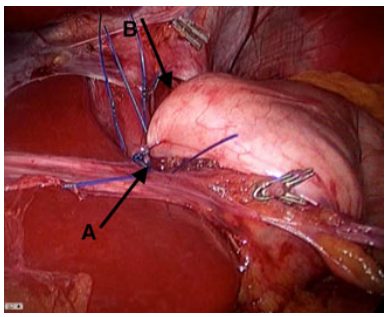


Fig. 6 Placement of the first fundoplication suture anchors the fundus, oesophagus and right hiatal pillar (*A*). Subsequent sutures are placed through the ridge of the stomach which forms across the front of the oesophagus (*B*)

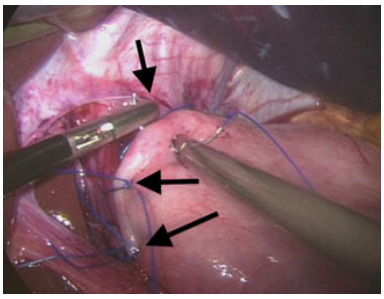


Fig. 7 Three sutures (marked with *arrows*) are placed between the anterior wall of the fundus, the oesophageal wall and the right hiatal pillar

fundoplication to the right hiatal pillar stabilises the wrap and prevents any risk of torsion or rotation of the oesophagus.

Finally, two "crown" sutures are placed to complete the fundoplication (Fig. 8). The first attaches the apex of the fundoplication to the hiatal rim at the 11 o'clock position, and the second attaches the stomach to the hiatal rim or adjacent diaphragm at the 1–2 o'clock position. These sutures do not incorporate the oesophageal wall.

As well as for the surgical treatment of gastro-oesophageal reflux, we often use an anterior 180° partial fundoplication during repair of a very large hiatal hernia. We have never undertaken an oesophageal lengthening procedure during primary antireflux surgery or hiatus hernia repair and are unable to report any experience with combining an anterior 180° partial fundoplication with a Collis procedure in patients perceived to have a shortened oesophagus.

Intraoperative Complications

Bleeding from the liver occasionally occurs because of local trauma from the liver retractor or direct surgical trauma, but is usually minor and ceases without specific intervention. Bleeding from the short gastric vessels should not occur as these vessels are not divided. Damage to the oesophagus or stomach may rarely occur during dissection, and care should be taken to pass the laparoscopic grasper behind the oesophagus under direct vision. Risks are minimised by always dissecting in natural tissue planes and using blunt instruments to separate tissues. Ultrasonic shears are never required, although electrocautery is occasionally used if tissues are particularly tough.

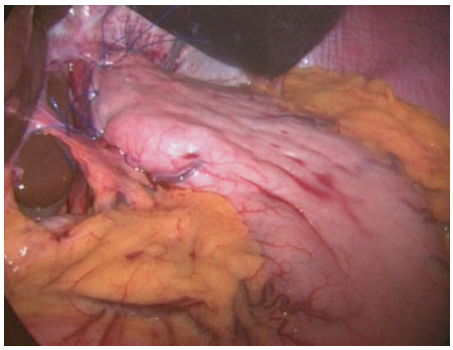


Fig. 8 Completed anterior 180° partial fundoplication, after placement of two apical sutures

Post-operative Care

Following surgery, patients return to a general ward and commence oral fluids on the same day. Opiate analgesia is avoided to minimise the possibility of post-operative vomiting. Local anaesthesia is infiltrated into the surgical wounds peri-operatively, and oral or intravenous paracetamol, supplemented by non-steroidal anti-inflammatory agents, are used for analgesia. Antireflux medication is ceased. On the first post-operative day, a pureed diet is commenced, and a barium swallow X-ray is routinely undertaken to check the post-operative anatomy (Fig. 9).[9] The patient is discharged on the first or second post-operative day, and the pureed diet is continued until follow-up 4 weeks later, after which the diet is graded back to normal over the ensuing 4–8 weeks.

Clinical Outcomes

Ten-year outcomes from a randomised controlled trial of anterior 180° partial vs. Nissen fundoplication have been reported previously.[8] These demonstrated effective reflux control and a low side effect profile, although some trade-offs were evident between a higher risk of recurrent reflux vs. a lower risk of side effects following anterior 180° partial

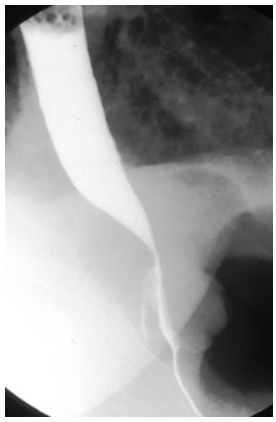


Fig. 9 Post-operative Barium swallow X-ray (lateral view) after anterior 180° partial fundoplication. The oesophagus lies in a relatively straight (anatomical) position and is not lifted forward by placing the fundus behind the oesophagus

fundoplication. Overall, the data from this randomised trial confirmed that anterior 180° partial fundoplication provides a good outcome in more than 90 % of patients at 10 years follow-up. Similarly, a recent meta-analysis of 5-year outcome data from four randomised trials of anterior vs. Nissen fundoplication also identified similar reflux control but less side effects following anterior 180° partial fundoplication.[10] In addition, objective outcomes at early follow-up in the randomised controlled trial of anterior 180° partial vs. Nissen fundoplication confirm effective reflux control, with normalisation of 24-h pH profiles and healing of oesophagitis.[11]

Poorer outcomes following anterior partial fundoplication have been reported by Engstrom et al., with worse control of reflux compared to posterior partial fundoplication.[12] This is probably due to the application of a different surgical technique for anterior partial fundoplication. They constructed a lesser 120° partial fundoplication and did not anchor the wrap to the right hiatal pillar. This lack of anchorage might lead to unravelling of the wrap and a higher risk of recurrent reflux. Others have suggested that posterior partial fundoplication procedures might be relatively less effective in patients with more severe grades of gastro-oesophageal reflux.[13, 14] However, there is no high-level evidence supporting this proposition, and these earlier studies provided low-level evidence from uncontrolled cases series.

More recently, we reported follow-up of 548 patients who underwent an anterior 180° partial fundoplication.[15] This study included patients with all grades of oesophagitis, Barrett's oesophagus and very large hiatal hernia. In this larger series, the median operating time was 60 min, and the conversion rate to open surgery was 2.6 %. Fourteen patients (2.6 %) underwent early re-operation within 1 week of the original procedure (ten for acute hiatus hernia, two for dysphagia and two for intra-abdominal sepsis). Seventeen (3.1 %) patients underwent a later re-operation—13 for recurrent reflux and 3 for recurrent hiatal hernia. There was one (0.2 %) peri-operative death secondary to myocardial infarction, occurring 13 days after surgery in an 83-year-old man who underwent surgery for a very large hiatal hernia with intermittent gastric volvulus. Clinical follow-up with analogue scores which assessed outcomes for heartburn, dysphagia and overall satisfaction revealed considerable improvement in heartburn and dysphagia following surgery and stable outcomes for dysphagia and overall satisfaction at up to 10 years follow-up. However, there was an increase in heartburn scores at 5 and 10 years, compared to follow-up at 3 months and 1 year, suggesting some deterioration in reflux control at extended follow-up. However, recurrent reflux also occurs after other types of fundoplication, and the overall results following anterior 180° partial fundoplication were good. In addition, at late follow-up, 89.0 % of patients could belch effectively, and 88.3 % were eating a normal diet. Of the patients, 11.7 % avoided some food types because of either food intolerance or dysphagia. Of the patients followed for 10 years or more, 91.0 % considered their decision to originally undergo surgery to have been correct. The results from this study, as well as the 10-year outcomes from the randomised trial of anterior 180° vs. Nissen fundoplication,[8] confirm the durability of this approach, demonstrating equivalent reflux control but less side effects, compared to Nissen fundoplication.

Based on these outcomes, we are now happy to offer an anterior 180° partial fundoplication to all patients presenting for surgery for gastro-oesophageal reflux. For those deemed to be at a higher risk of side effects following Nissen fundoplication, we would always recommend an anterior 180° partial fundoplication, whereas for younger patients and those assessed to be at a lower risk of side effects, we offer a choice between anterior 180° vs. Nissen fundoplication, with approximately two thirds of these choosing to undergo a partial fundoplication.

References

1. Locke G, Talley N, Fett S, Zinsmeister A, Melton L. Prevalence and Clinical Spectrum of Gastroesophageal Reflux: A Population-Based Study in Olmsted County Minnesota. Gastroenterology 1997;112:1448-1456.
2. Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut 2005;54:710-717.
3. Gatenby P, Bann S. Antireflux surgery. Minerva Chir 2009;64:169-181.
4. Kelly JJ, Watson DI, Chin KF, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. J Am Coll Surg 2007;205:570-575.
5. Broeders JA, Bredenoord AJ, Hazebroek EJ, Broeders IA, Gooszen HG, Smout AJ. Reflux and belching after 270 degree versus 360 degree laparoscopic posterior fundoplication. Ann Surg. 2012;255:59-65.
6. Broeders JA, Mauritz FA, Ahmed Ali U, Draaisma WA, Ruurda JP, Gooszen HG, Smout AJ, Broeders IA, Hazebroek EJ. Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. Br J Surg. 2010;97:1318-30.
7. Dor J, Humbert P, Dor V et al. L'interet de la technique de Nissen modifiee dans la prevention du reflux apres cardiomyotomie extra-muqueuse de Heller. Mem Acad Chir (Paris) 1962;3:877-883.
8. Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180 degrees partial fundoplication. Br J Surg 2008; 95:1501-1505.
9. Tsunoda S, Jamieson GG, Devitt PG, Watson DI, Thompson SK. Early reoperation after laparoscopic fundoplication: the importance of routine postoperative contrast studies. World J Surg. 2010;34:79-84.
10. Broeders JA, Roks DJ, Jamieson GG, Devitt PG, Baigrie RJ, Watson DI. Five-year outcome after laparoscopic anterior partial versus nissen fundoplication: four randomized trials. Ann Surg 2012; 255:637-642.
11. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M & Devitt PG. Prospective randomized double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 1999; 86;123-130.

12. Engstrom C, Lonroth H, Mardani J, Lundell L. An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. World J Surg 2007; 31:1221-1225.
13. Horvath KD, Jobe BA, Herron DM, Swanstrom LL. Laparoscopic Toupet fundoplication is an inadequate procedure for patients with severe reflux disease. J Gastrointest Surg 1999; 3:583-91.
14. Bell RC, Hanna P, Mills MR, Bowrey D. Patterns of success and failure with laparoscopic Toupet fundoplication. Surg Endosc 1999;13:1189-94.
15. Chen Z, Thompson SK, Jamieson GG, Devitt PG, Game PA, Watson DI. Anterior 180-degree partial fundoplication: a 16-year experience with 548 patients. J Am Coll Surg 2011;212:827-834.
16. Wijnhoven BP, Watson DI. Laparoscopic repair of a giant hiatus hernia-how I do it. J Gastrointest Surg 2008;12:1459–64.

Original article

Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication

D. I. Watson, G. G. Jamieson, G. K. Pike, N. Davies, M. Richardson and P. G. Devitt

The Royal Adelaide Centre for Endoscopic Surgery and University Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia

Correspondence to: Mr D. I. Watson, University Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia

Background: **In the operative management of gastro-oesophageal reflux, a balance must be achieved between adequate control of reflux and excessive dysphagia. The ideal technique is not known. A randomized study was performed to determine whether laparoscopic anterior fundoplication is associated with a lower incidence of postoperative dysphagia than laparoscopic Nissen fundoplication, while achieving equivalent control of reflux.**

Methods: **Patients presenting for laparoscopic antireflux surgery were randomized to undergo either a Nissen fundoplication ($n = 53$) or an anterior 180° hemifundoplication ($n = 54$). Patients were blinded to which procedure had been performed, and follow-up was obtained by a blinded independent investigator. Standardized clinical grading systems were used to assess dysphagia, heartburn and patient satisfaction 1, 3 and 6 months after operation. Objective measurement of lower oesophageal sphincter pressure, oesophageal emptying time, distal oesophageal acid exposure and endoscopic healing of oesophagitis was also performed.**

Results: **Operating time was similar for the two procedures (58 min for the Nissen procedure *versus* 60 min for anterior fundoplication). Resting and residual lower oesophageal sphincter pressures were lower following anterior fundoplication (29 *versus* 18 mmHg, and 13 *versus* 6 mmHg), and oesophageal emptying times were faster (92 *versus* 116 s). Acid exposure times and ability to heal oesophagitis were similar. At 3 months' follow-up clinical outcomes were similar for the two procedures. At 6 months, however, patients who had undergone anterior fundoplication experienced significantly less dysphagia for solid food and were more likely to be satisfied with the clinical outcome.**

Conclusion: **Laparoscopic anterior fundoplication achieved equivalent control of reflux, more physiological postoperative manometry parameters, and an improved clinical outcome at 6 months. Continued follow-up remains necessary to confirm the long-term efficacy of the partial fundoplication procedure.**

Paper accepted 20 July 1998

British Journal of Surgery 1999, **86**, 123–130

Introduction

Since Dallemagne *et al.*[1] first described the technique of laparoscopic Nissen fundoplication in 1991, extensive experience with laparoscopic antireflux surgery has been reported from many centres[2–4]. The outcome of these initial studies has confirmed similar outcomes to those reported for conventional open techniques[5,6]. It is generally accepted that the laparoscopic Nissen procedure is associated with a small but significant incidence of persistent troublesome postoperative dysphagia[6,7]. A number of strategies have been recommended to minimize or prevent the occurrence of this problem, and also to prevent other adverse sequelae such as the gas bloat syndrome. Full mobilization of the gastric fundus by dividing the short gastric vessels is one such strategy[6]. However, the outcome of two recently reported prospective randomized trials has not demonstrated any improvement in postoperative outcome or reduction in the dysphagia rate in patients undergoing Nissen fundoplication with division of short gastric vessels during either laparoscopic[8] or open[9] surgery when compared with fundoplication without division of the short gastric vessels.

Other surgeons have recommended a partial fundoplication procedure. The outcomes of three prospective randomized trials which compared posterior partial fundoplication with Nissen fundoplication in the open surgical era[7,10,11] and a further study in the laparoscopic era[12] have failed to demonstrate a significant reduction in postoperative dysphagia rates following posterior partial fundoplication. Interpretation of additional outcomes from these studies has been controversial, with no clear evidence supporting the routine application of posterior partial fundoplication[13].

Still other surgeons have recommended an anterior partial fundoplication technique[14,15]. Although this technique has been less widely applied than the posterior variant, the outcomes of uncontrolled prospective assessment have suggested advantages. To determine whether the routine performance of a laparoscopic anterior partial fundoplication can reduce the incidence of postoperative dysphagia or other adverse outcomes following laparoscopic Nissen fundoplication, a prospective double-blind randomized trial was performed. The initial outcomes of this study are presented in this paper.

Patients and methods

The protocol used for this study was similar to that applied in another recently reported randomized trial from the authors' department[8].

Participant assignment

Patients undergoing laparoscopic surgery for gastro-oesophageal reflux disease (GORD) were randomized to undergo either Nissen or anterior partial fundoplication using laparoscopic techniques. Informed consent was obtained from all participants, and randomization occurred in the operating theatre by opening one of 120 previously sealed opaque envelopes, after the commencement of anaesthesia.

Patient selection and preoperative investigation

All patients with proven GORD, presenting for primary antireflux surgery by the laparoscopic technique, were considered for entry into the trial. Patients were excluded only if they had a severe oesophageal motility disorder (adynamic oesophagus or achalasia), required a concurrent abdominal procedure at the same time as fundoplication (e.g. cholecystectomy) or had undergone previous antireflux surgery. All patients underwent preoperative investigation with oesophageal manometry and endoscopy. Twenty-four-hour pH monitoring was performed for patients who did not have unequivocal reflux disease demonstrated by endoscopic and manometric studies.

Operating technique and postoperative care

Laparoscopic Nissen fundoplication was performed using a technique described previously[4]. The procedure comprised blunt dissection of the oesophageal hiatus with minimal diathermy, preservation of the hepatic branch of the vagus nerve, routine posterior hiatal repair and the performance of a short, loose Nissen fundoplication around a 52-Fr bougie. The wrap was secured with non-absorbable 2/0 monofilament interrupted sutures, and the short gastric vessels were not divided.

The initial steps for the laparoscopic anterior fundoplication were similar to those for the Nissen procedure, commencing with hiatal dissection with preservation of the hepatic branch of the vagus nerve, and oesophageal mobilization followed by posterior hiatal repair. An 180° anterior partial fundoplication was fashioned by fixing the anterior wall of the fundus to the front of the oesophagus and the diaphragmatic hiatus. This was achieved by suturing the fundus to the right lateral wall of the abdominal oesophagus and to the right hiatal pillar and the posterior hiatal repair, and the left lateral wall of the oesophagus to the left hiatal pillar using five or six non-absorbable 2/0 monofilament sutures. Short gastric vessels were left intact. The anterior partial fundoplication accentuated the angle of His, repaired the hiatus, anchored a 3–5-cm length of oesophagus within the abdomen and fashioned a partial fundoplication which was sutured to the oesophagus and the hiatal ring.

If the laparoscopic procedure was converted to an open procedure because of intraoperative difficulties, the randomization schedule was still followed and the patient remained in the trial for subsequent analysis. Nasogastric tubes were not used, and patients were allowed oral fluids after operation on the evening of surgery and soft solid food the next day. Discharge from hospital was encouraged after the second postoperative day.

Masking

The extent of fundoplication performed laparoscopically was concealed from all patients, and all remained unaware of the exact procedure for the duration of follow-up. All follow-up was obtained by a scientific officer who was 'blinded' to the randomization of each patient, and data were entered into a computerized database by another research assistant who was not otherwise involved in patient follow-up. Final data analysis was

performed independently by two of the authors (G.K.P. and D.I.W.).

Clinical follow-up

Patients were interviewed before operation and then 1, 3 and 6 months after operation by means of a structured questionnaire. Longer-term follow-up will be obtained in the future. The presence or absence of the following symptoms was sought: heartburn, epigastric pain, regurgitation, dysphagia for lumpy solids, soft solids and liquids, odynophagia, early satiety, inability to belch, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing and wheezing. The ability to relieve bloating and whether a normal diet was being consumed were also determined. Heartburn was scored by means of a visual analogue scale (0, no heartburn; 10, severe heartburn).

Dysphagia was scored by several methods. Visual analogue scales (0, no dysphagia; 10, total dysphagia) were independently applied for solids and liquids, as well as a previously validated dysphagia score[8,16] (0, no dysphagia; 45, severe dysphagia) which combines information about difficulty in swallowing nine types of liquids and solids. Overall outcome was determined using three further scales which have been described elsewhere[8]. Patients ranked the outcome of surgery using a modified Visick grading (score 1–5) and were asked to score the outcome as excellent, good, fair or poor. An overall assessment of satisfaction with the operative outcome was also scored by a further visual analogue scale (0, dissatisfied; 10, satisfied).

Objective follow-up

Objective investigation with oesophageal manometry, 24-h pH monitoring, upper gastrointestinal endoscopy and a radionuclide oesophageal emptying study was performed 3–4 months after operation. Investigation sought to assess lower oesophageal sphincter function, control of reflux, postsurgical anatomy, healing of oesophagitis and the presence of any oesophageal obstruction. Details of these tests have been described previously[8].

Statistical analysis

The primary clinical outcomes which the trial was designed to evaluate were postoperative dysphagia and control of reflux symptoms. Before commencing the study it was determined that 84 patients (42 in each group) would be needed to demonstrate a 20 per cent difference in these outcome measures at a significance level of $P < 0.05$, and power of 90 per cent. To ensure that this was achieved, it was intended that at least 100 patients would be recruited, allowing for an estimated 20 per cent of all patients refusing the objective postoperative investigations. All analyses were performed on an intention to treat basis, with all patients remaining in their initially allocated group for this analysis.

Before commencing the trial, it was intended to report initial outcome once patients had been followed for 6 months. This time period is thought to allow for the adequate assessment of any differences in the incidence of postoperative dysphagia between the two trial groups. Longer-term outcomes will be reported when follow-up has matured.

Fisher's exact test was used to determine the significance of 2×2 contingency tables. A two-tailed Mann–Whitney U test was used to assess the significance of non-parametric data sets, and an unpaired Student's t test was employed to determine the significance of data sets where it was reasonable to assume a parametric distribution (height and weight). Unless otherwise stated all data are reported as the percentage of the total patients in each group, or as the mean (95 per cent confidence interval (c.i.)).

Ethical approval

The protocol for this study was approved by the Royal Adelaide Hospital Human Research Ethics Committee.

Results

From December 1995 to April 1997, 107 patients undergoing laparoscopic antireflux surgery were entered into the trial. Fifty-three patients were randomized to undergo Nissen fundoplication and 54 to anterior fundoplication. During the same period 70 further patients underwent a laparoscopic fundoplication performed by surgeons contributing patients to this study. Of the 107 patients entered, 106 (99 per cent) were available for follow-up 1 month after surgery, 104 (97 per cent) at 3 months and 106 (99 per cent) at 6 months. No patient elected to withdraw from the study. Missing data were due to an inability to contact patients at specific follow-up intervals.

Preoperative assessment

Both groups were similar for age, sex, height, weight, cigarette and alcohol consumption, incidence of previous abdominal surgery, duration of symptoms and medications consumed before surgery. Analysis of the presence or absence of preoperative symptoms (*Table 1*), assessment of heartburn (*Table 2*) and dysphagia scores (*Table 3*) revealed no differences between the groups.

Table 1 Number of patients with various preoperative and postoperative symptoms

	Preoperative		6 months after operation	
operation	Anterior	Nissen	Anterior	Nissen
Heartburn	51 (94)	50 (94)	5 (9)	5 (9)
Epigastric pain	37 (69)	36 (68)	9 (17)	17 (32)
Regurgitation	44 (81)	41 (77)	3 (6)	1 (2)
Odynophagia	14 (26)	6 (11)	1 (2)	1 (2)
Early satiety	19 (35)	17 (32)	10 (19)	9 (17)
Epigastric bloat	28 (52)	26 (49)	10 (19)	15 (28)
Anorexia	10 (19)	5 (9)	1 (2)	1 (2)
Nausea	17 (31)	17 (32)	3 (6)	1 (2)
Vomiting	12 (22)	12 (23)	1 (2)	1 (2)
Nocturnal cough	20 (37)	21 (40)	7 (13)	3 (6)
Nocturnal wheeze	9 (17)	9 (17)	7 (13)	2 (4)
Can relieve bloat	43 (80)	43 (82)	44 (83)	36 (68)
Unable to belch	0 (0)	0 (0)	9 (17)	19 (36)*
Eats normal diet	34 (63)	36 (68)	50 (94)	46 (87)
Increased flatus	—	—	15 (28)	26 (49)*
Diarrhoea	—	—	5 (9)	3 (6)
Total	54	53	53	53

*P = 0·046 (Nissen *versus* anterior fundoplication at 6 months, Fisher's exact test)

Table 2 Assessment of heartburn by visual analogue scale before and at intervals after operation

	Anterior	Nissen
Preoperative	4·3 (3·4–5·1)	4·1 (3·1–5·0)
1 month	0·5 (0·03–1·0)	0·1 (– 0·1 to 0·3)
3 months	0·2 (– 0·2 to 0·6)	0·3 (– 0·1 to 0·7)
6 months	0·4 (– 0·04 to 0·8)	0·2 (– 0·04 to 0·3)

Values are mean (95 per cent confidence interval)

Endoscopic grading of oesophagitis before operation was similar, with 24 per cent of patients in the Nissen group and 21 per cent of those in the anterior fundoplication group having either Barrett's oesophagus or stricture formation; a hiatus hernia was seen before operation in 43 per cent of patients having the Nissen procedure and in 50 per cent of those undergoing anterior fundoplication. Preoperative oesophageal manometry results (*Table 4*) were similar. Twenty-four-hour ambulatory pH monitoring was performed in 34 patients undergoing Nissen fundoplication and in 35 having anterior fundoplication. The mean percentage exposure to an acid pH of less than 4 was 12·6 and 12·2 per cent respectively.

Operation

Operation was performed by one of seven surgeons. Two patients randomized to anterior fundoplication underwent a Nissen procedure, and one patient randomized to Nissen fundoplication eventually had an anterior fundoplication at reoperation for dysphagia 23 days later by an open surgical approach. The oesophagus in one patient randomized to anterior fundoplication was perforated posteriorly during initial laparoscopic dissection because of difficulty defining the correct dissection plane. This procedure was converted to an open procedure, the tear repaired, and the procedure completed as a Nissen fundoplication. The other patient in the anterior fundoplication group developed an acute paraoesophageal hiatus hernia requiring laparoscopic reoperation on the third postoperative day. At this procedure the fundoplication was reconstructed as a Nissen procedure.

The laparoscopic procedure in one of the patients in the Nissen group was converted to open surgery during the stage of oesophageal dissection. This was because of difficulty in dissecting the oesophagus within a very large hiatal hernia. Four of the anterior fundoplications were converted to open procedures for the following problems: large hiatus hernia, obesity, oesophageal perforation (discussed above) and bleeding from the liver. Operating time varied from 32 to 184 (median 58) min for Nissen fundoplication, compared with 35–144 (median 60) min for anterior fundoplication ($P = 0{\cdot}10$).

Early hospital outcome

The time intervals between operation and the commencement of oral fluids (median 1 day) and solids (median 2 days), and the length of postoperative hospital stay (median 3 days), were unaltered by the type of fundoplication performed. The incidence of postoperative complications

Table 3 Dysphagia assessment

	Before operation		6 months after operation	
	Anterior (n = 54)	Nissen (n = 53)	Anterior (n = 53)	Nissen (n = 53)
Dysphagia for*				
Lumpy solids	10 (19)	18 (34)	8 (15)	21 (40)‡
Soft solids	2 (4)	6 (11)	1 (2)	1 (2)
Liquids	2 (4)	6 (11)	0 (0)	2 (4)
Visual analogue scale*				
Solids	1·5 (0·8–2·5)	1·4 (0·7–2·1)	0·6 (0·1–1·0)	1·1 (0·6–1·6)¶
Liquids	0·5 (0·1–0·9)	0·7 (0·2–1·1)	0·0 (0·0–0·0)	0·2 (0·05–0·51)
Dysphagia score				
Overall result†	6·7 (3·6–9·7)	5·6 (2·9–8·2)	2·1 (0·3–3·8)	4·2 (2·4–5·9)§
Scored 0 only*	36 (67)	34 (64)	45 (85)	32 (60)‡

*Values in parentheses are percentages; †values are mean (95 per cent confidence intervals). ‡P = 0·008, §P = 0·04, ¶P = 0·051 (Nissen *versus* anterior fundoplication at 6 months, Mann–Whitney U test)

Table 4 Oesophageal manometry results. Swallowing was assessed from ten wet swallows

	Anterior	Nissen
Preoperative	(n = 54)	(n = 53)
No. of propagated swallows*	8·9 (8·4–9·5)	8·6 (8·0–9·2)
No. with normal peristalsis†	43 (83)	42 (82)
LOS resting pressure (mmHg)*	6·4 (4·8–8·1)	8·6 (6·1–11·1)
LOS nadir pressure (mmHg)*	0·7 (0·2–1·2)	1·4 (0·6–2·2)
No. with LOS resting pressure < 10 (mmHg)†	24 (75)	20 (67)
Postoperative	(n = 32)	(n = 30)
No. of propagated swallows*	8·2 (7·2–9·2)	8·7 (7·7–9·6)
No. with normal peristalsis†	24 (75)	27 (90)
LOS resting pressure (mmHg)*	18·3 (14·2–22·4)	28·9 (23·3–34·5)§
LOS nadir pressure (mmHg)*	5·6 (3·4–7·8)	12·8 (9·9–15·7)‡
No. with LOS resting pressure < 10 (mmHg)†	8 (25)	1 (3)¶

*Values are mean (95 per cent confidence interval); †values in parentheses are percentages. LOS, lower oesophageal sphincter. ‡P = 0·0002, §P = 0·004, ¶P = 0·03 *versus* anterior fundoplication (Mann–Whitney U test)

was slightly higher in the anterior fundoplication group (11 *versus* 4 per cent), although most complications were minor (urinary retention, respiratory atelectasis and pneumothorax). However, two patients who underwent anterior fundoplication required laparoscopic revision on the third postoperative day, one for acute postoperative paraoesophageal herniation (discussed above) and the other for severe postoperative dysphagia. In the latter patient, the fundoplication, which appeared to be constructed satisfactorily, was undone and the hiatus was inspected. Although this did not appear to be tight, the highest hiatal repair suture was removed and the anterior fundoplication was refashioned, relieving the severe dysphagia.

One patient (discussed above) underwent open revision of a Nissen fundoplication to an anterior partial fundoplication because of significant early postoperative dysphagia. A further patient who underwent Nissen fundoplication developed a left subphrenic collection on the third postoperative day. This was drained under computed tomographic guidance, and a barium contrast study demonstrated no communication with the gut lumen.

Clinical outcome at 1–6 months after operation

A detailed analysis of the outcome of the clinical assessment at 6 months is summarized in *Tables 1–3* and *5*. At the 1- and 3-month follow-up intervals, no differences were seen between the two groups for any symptoms, including dysphagia. At the 3-month follow-up, however, patients undergoing anterior fundoplication were more likely to report an excellent outcome (52 *versus* 25 per cent) and Visick grade 1 (40 *versus* 23 per cent) than those having a Nissen fundoplication.

At 6 months a number of significant differences became apparent, with the overall outcome favouring anterior partial fundoplication. The incidence of dysphagia for lumpy solid food as well as the 0–45 dysphagia score were

Table 5 Outcome, satisfaction and Visick grading at 6 months after operation

	Anterior (n = 53)	Nissen (n = 53)
Outcome*		
Excellent	28 (53)	14 (26)
Good	19 (36)	31 (59)
Fair	5 (9)	7 (13)
Poor	1 (2)	1 (2)
Visick grade*		
1	28 (54)	14 (26)
2	15 (29)	25 (47)
3	5 (9)	10 (19)
4	3 (6)	3 (6)
5	1 (2)	1 (2)
Mean satisfaction score†	8·8 (8·3–9·3)	8·0 (7·3–8·6)

Values in parentheses are *percentages or †95 per cent confidence intervals. Outcome: P = 0·02 (excellent *versus* good *versus* fair and poor, χ^2 test); Visick grading: P = 0·02 (1 *versus* 2 *versus* 3, 4 and 5, χ^2 test)

significantly lower following anterior fundoplication, and a greater proportion of patients having this operation continued to report an excellent outcome after operation (*Table 5*). Patients were also more likely to be able belch following anterior partial fundoplication and were less likely to complain of increased passage of flatus (*Table 1*). Trends to improved outcome in the anterior fundoplication group were also seen for the solid food visual analogue score (mean 0·6 (95 per cent c.i. 0·1–1·0) *versus* 1·1 (0·6–1·6), $P = 0{\cdot}051$) and satisfaction score (8·8 (8·3–9·3) *versus* 8·0 (7·3–8·6), $P = 0{\cdot}08$). There were no significant differences in the willingness to undergo the procedure again (94 *versus* 83 per cent, $P = 0{\cdot}12$) should similar preoperative circumstances arise.

Overall, both fundoplication variants controlled reflux equally effectively (*Tables 1* and *2*). However, 2 months after an initially successful anterior fundoplication, one patient developed objectively proven recurrent reflux disease. This patient had not undergone further surgery by the 6-month follow-up interval. Although three further patients described recurrent reflux symptoms, two following Nissen and one anterior fundoplication, none had any demonstrable endoscopic or 24-h pH monitoring abnormality.

Objective postoperative investigations

Some 79 (74 per cent) patients underwent a postoperative oesophageal emptying study, 47 (44 per cent) had an upper gastrointestinal endoscopy examination, 62 (58 per cent) had oesophageal manometry and 48 (45 per cent) underwent postoperative 24-h pH monitoring.

Upper gastrointestinal endoscopy examination revealed a small asymptomatic sliding hiatus hernia in two patients following the Nissen procedure and in one after anterior fundoplication. Nineteen of 26 patients having anterior fundoplication had no endoscopic evidence of oesophagitis at follow-up endoscopy, three had persistent Barrett's oesophagus, one had a stricture requiring endoscopic dilatation (also present before operation) and three had evidence of mild oesophagitis (Savary–Miller grade 1). Of 21 patients in the Nissen fundoplication group, 19 had no evidence of oesophagitis, one had persistent Barrett's oesophagus and one had evidence of mild oesophagitis (Savary–Miller grade 1). All fundoplications appeared to be correctly constructed using gastric fundus, irrespective of operative technique.

Oesophageal manometry findings after operation are summarized in *Table 4*. Mean lower oesophageal sphincter resting and nadir pressures were significantly higher in patients who underwent laparoscopic Nissen fundoplication. Twenty-four-hour pH monitoring demonstrated normalization of acid exposure times in all but six of the 48 patients (three in the Nissen group and three in the anterior fundoplication group).

The mean oesophageal emptying time was 92 (95 per cent c.i. 71–113) s in patients in the anterior fundoplication group, compared with 116 (89–143) s for the Nissen group ($P = 0{\cdot}23$). Of patients undergoing anterior fundoplication, 69 per cent had a normal emptying time (less than 93 s), compared with 54 per cent of those who had a Nissen fundoplication ($P = 0{\cdot}25$).

Discussion

The question of which fundoplication technique offers the best outcome for patients undergoing surgery for GORD is controversial[6,14,17]. Whilst uncontrolled studies have reported good results following laparoscopic or open surgery for Nissen, anterior or posterior fundoplication[14,15,18–23], they have done little to resolve this controversy. Studies that have compared the outcome of partial fundoplication with historical experience suggest advantages for partial fundoplication variants[18,21], with a low incidence of postoperative dysphagia and at least four series claiming that dysphagia does not occur beyond the early postoperative period following a laparoscopic partial fundoplication procedure[20,22–24]. Further advantages are reported to be a lower incidence of gas bloat syndrome, improved ability to belch and a reduction in the incidence of other adverse outcomes[20,22,23]. However, the results reported may be subject to significant assessment bias, if experience is compared to that of other surgeons or to historical controls. Only the outcome of prospective randomized trials, if available, should be considered when

determining the advantages of the various partial fundoplication techniques.

The three randomized trials of Nissen *versus* posterior partial fundoplication from the open era[7,10,11], as well as a recent laparoscopic study[12], have all failed to demonstrate a significant reduction in the incidence of dysphagia using a posterior partial fundoplication technique. A study reported by Thor and Silander[11] did suggest that there may be some advantages for the posterior technique. However, a statistically inadequate number of patients (31) was enrolled, thereby not providing any reasonable opportunity to demonstrate advantages for either technique. Furthermore, the Nissen wrap was 4 cm in length and calibrated over a 40-Fr bougie, the hiatus was not repaired and the hepatic branch of the vagus was routinely divided, all factors that might adversely affect outcome following Nissen fundoplication. The study by Walker *et al.*[10] can also be subjected to the same statistical criticisms, as only 52 patients were enrolled. In this study, persistent late dysphagia was more common following posterior partial fundoplication (four patients) than Nissen fundoplication (two). The incidence of early and late gas bloat syndromes was identical, as was the rate of postoperative complications.

Perhaps the only trial to enrol a sufficient number of patients was that performed by Lundell and co-workers. This study was reported in two separate publications[7,25]. The first described 6-month postoperative outcomes in 71 patients[25]. No differences were seen for any clinical outcome, except for dysphagia at 3 months. At 6 months the incidence of dysphagia was identical. The latter report described outcomes after 3–5 years follow-up in 137 patients[7]. Dysphagia at 5 years was equally common following partial and Nissen fundoplication (16 *versus* 10 per cent, P not significant), although in all instances the symptom was reported to be mild. Flatulence was more common after Nissen fundoplication at 2 and 3 years but not at earlier or later time intervals, and both procedures achieved effective long-term reflux control. Interestingly, reoperation was more common following Nissen than posterior partial fundoplication, although this was not statistically significant (five of 65 *versus* one of 71; $P = 0{\cdot}10$, Fisher's exact test). All reoperations in the Nissen group were for postoperative paraoesophageal hiatus herniation, and only one of these five patients underwent hiatal repair at the first operation.

Laws *et al.*[12] recently reported the early outcome from a small randomized trial of laparoscopic Nissen fundoplication *versus* posterior partial fundoplication. Thirty-nine patients were enrolled and no advantages were demonstrated for either procedure. Hence the overall results of the reported randomized trials of posterior *versus* Nissen fundoplication have not provided convincing evidence to support the routine performance of the posterior technique.

An anterior partial fundoplication was chosen for comparison with the Nissen procedure in the present study because it had not been previously tested within a prospective randomized trial, and reported experience with a similar technique suggested that it may have important advantages over the Nissen procedure. Case series[14,15] suggest that the anterior partial fundoplication is associated with less postoperative dysphagia, improved ability to belch and less risk of gas bloat symptoms.

The present randomized study has revealed no important advantages for either of the two procedures at the 1- and 3-month follow-up intervals. However, at 6 months, patients undergoing laparoscopic anterior partial fundoplication were significantly less likely to experience dysphagia for solid food or to be troubled by excessive passage of flatus, and they were more likely to be able to belch normally. This demonstrates for the first time in a prospective randomized trial advantages for a partial fundoplication technique. The way the anterior fundoplication is constructed is different from the posterior fundoplication variants, as the fundus sits in front rather than behind the oesophagus. This may account for the advantages demonstrated for this procedure, and the lack of advantages seen in previous trials of Nissen *versus* posterior partial fundoplication.

Whilst most endoscopies revealed complete healing of oesophagitis, slightly more patients had persistent Savary–Miller grade 1 oesophagitis following partial fundoplication; the mean acid exposure time at pH monitoring was slightly higher, and one patient developed objectively proven recurrent reflux. This suggests that anterior partial fundoplication may not be as effective for the prevention of reflux as Nissen fundoplication. On the other hand, it can be argued that the Nissen technique creates an overcompetent valve whilst anterior fundoplication in this study restored the gastro-oesophageal junction to a more physiological state[26].

Despite the encouraging outcome at 6 months after anterior partial fundoplication, this trial has not resolved which procedure is the most appropriate in the long term. If the durability of the anterior fundoplication proves to be as good as that of the Nissen fundoplication, the results of this study will provide strong evidence for its routine application in patients with GORD requiring surgery. However, it is also possible that the long-term incidence of recurrent reflux following anterior fundoplication may be higher than that seen following Nissen fundoplication, in which case the risk of recurrent reflux will need to be

balanced against the risk of other adverse outcomes for each individual. Long-term follow-up will clarify this issue.

Acknowledgements

The authors thank Mrs L. Mackness, Mrs N. Hanna, Ms T. Ellis and Mrs C Bates-Brownsword for invaluable organizational and logistical support, and Mr P. Game and Mr R. Britten-Jones who contributed patients to the study. The authors also acknowledge financial support from grants received from the Royal Australasian College of Surgeons Research Foundation and the University of Adelaide's Faculty of Medicine Research Committee.

References

1 Dallemagne B, Weerts JM, Jehaes C, Markiewicz S, Lombard R. Laparoscopic Nissen fundoplication: preliminary report. *Surg Laparosc Endosc* 1991; **1:** 138–43.
2 Gotley DC, Smithers BM, Rhodes M, Menzies B, Branicki FJ, Nathanson L. Laparoscopic Nissen fundoplication – 200 consecutive cases. *Gut* 1996; **38:** 487–91.
3 Trus TL, Laycock WS, Branum G, Waring JP, Mauren S, Hunter JG. Intermediate follow-up of laparoscopic antireflux surgery. *Am J Surg* 1996; **171:** 32–5.
4 Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. *Ann Surg* 1994; **220:** 137–45.
5 Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. *World J Surg* 1977; **1:** 439–43.
6 DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. *Ann Surg* 1986; **204:** 9–20.
7 Lundell L, Abrahamsson H, Ruth M, Rydberg L, Lonroth H, Olbe L. Long-term results of a prospective randomized comparison of total fundic wrap (Nissen–Rossetti) or semi-fundoplication (Toupet) for gastro-oesophageal reflux. *Br J Surg* 1996; **83:** 830–5.
8 Watson DI, Pike GK, Baigrie RJ, Mathew G, Devitt PG, Britten-Jones R *et al.* Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg* 1997; **226:** 642–52.
9 Luostarinen M, Koskinen M, Reinikainen P, Karvonen J, Isolauri J. Two antireflux operations: floppy *versus* standard Nissen fundoplication. *Ann Med* 1995; **27:** 199–205.
10 Walker SJ, Holt S, Sanderson CJ, Stoddard CJ. Comparison of Nissen total and Lind partial transabdominal fundoplication in the treatment of gastro-oesophageal reflux. *Br J Surg* 1992; **79:** 410–14.
11 Thor KBA, Silander T. A long-term randomized prospective trial of the Nissen procedure *versus* a modified Toupet technique. *Ann Surg* 1989; **210:** 719–24.
12 Laws HL, Clements RH, Swillie CM. A randomized, prospective comparison of the Nissen fundoplication *versus* the Toupet fundoplication for gastroesophageal reflux disease. *Ann Surg* 1997; **225:** 647–54.
13 Crookes PF, DeMeester TR. Does Toupet fundoplication out-perform the Nissen procedure as the operation of choice for gastro-esophageal reflux disease? *Dis Esoph* 1994; **7:** 265–7.
14 Watson A, Jenkinson LR, Ball CS, Barlow AP, Norris TL. A more physiological alternative to total fundoplication for the surgical correction of resistant gastro-oesophageal reflux. *Br J Surg* 1991; **78:** 1088–94.
15 Watson A, Spychal RT, Brown MG, Peck N, Callender N. Laparoscopic 'physiological' antireflux procedure: preliminary results of a prospective symptomatic and objective study. *Br J Surg* 1995; **82:** 651–6.
16 Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroentrol* 1992; **14:** 99–100.
17 Hill LD. An effective operation for hiatal hernia: an eight year appraisal. *Ann Surg* 1967; **166:** 681–92.
18 Patti MG, De Bellis M, De Pinto M, Bhoyrul S, Tong J, Arcerito M *et al.* Partial fundoplication for gastroesophageal reflux. *Surg Endosc* 1997; **11:** 445–8.
19 Bell RCW, Hanna P, Powers B, Sabel J, Hruza D. Clinical and manometric results of laparoscopic partial (Toupet) and complete (Rosetti–Nissen) fundoplication. *Surg Endosc* 1996; **10:** 724–8.
20 O'Reilly MJ, Mullins SG, Saye WB, Pinto SE, Falkner PT. Laparoscopic posterior partial fundoplication: analysis of 100 consecutive cases. *J Laparoendosc Surg* 1996; **6:** 141–50.
21 McKernan JB. Laparoscopic repair of gastroeophageal reflux disease. Toupet partial fundoplication *versus* Nissen fundoplication. *Surg Endosc* 1994; **8:** 851–6.
22 Mosnier H, Leport J, Aubert A, Kianmanesh R, Sbai Idrissi MS, Guivarc'h M. A 270 degree laparoscopic posterior fundoplasty in the treatment of gastroesophageal reflux. *J Am Coll Surg* 1995; **181:** 220–4.
23 Kraemer SJM, Aye R, Kozarek RA, Hill LD. Laparoscopic Hill repair. *Gastrointest Endosc* 1994; **40:** 155–9.
24 McKernan JB, Champion JK. Laparoscopic antireflux surgery. *Am Surg* 1995; **61:** 530–6.
25 Lundell L, Abrahamsson H, Ruth M, Sandberg N, Olbe LC. Lower esophageal sphincter characteristics and esophageal acid exposure following partial or 360 degrees fundoplication: results of a prospective, randomized, clinical study. *World J Surg* 1991; **15:** 115–21.
26 Anderson JA, Myers JC, Watson DI, Gabb M, Mathew G, Jamieson GG. Concurrent fluoroscopy and manometry reveal differences in laparoscopic Nissen and anterior fundoplication. *Dig Dis Sci* 1998; **43:** 847–53.

Original article

Five-year follow-up of a randomized clinical trial of laparoscopic total *versus* anterior 180° fundoplication

R. Ludemann, D. I. Watson, G. G. Jamieson, P. A. Game and P. G. Devitt

University of Adelaide Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia
Correspondence to: Professor D. I. Watson, Flinders University Department of Surgery, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia (e-mail: david.watson@flinders.edu.au)

Background: **Total fundoplication for gastro-oesophageal reflux disease may be followed by unwanted side-effects. A randomized trial demonstrated that an anterior 180° partial fundoplication achieved effective reflux control and was associated with fewer side-effects in the short term than total fundoplication. This paper reports longer-term (5 year) outcomes from that trial.**
Methods: **Between December 1995 and June 1997, 107 patients were randomized to undergo either laparoscopic total fundoplication or a laparoscopic anterior 180° fundoplication. After 5 years, 101 of 103 eligible patients (51 total, 50 anterior) were available for follow-up. Each patient was interviewed by a single blinded investigator and a standardized questionnaire was completed. The questionnaire focused on symptoms and overall satisfaction with the results of fundoplication.**
Results: **There were no significant differences between the two groups with regard to control of heartburn or patient satisfaction with the overall outcome. Dysphagia, measured by a visual analogue score for solid food and a composite dysphagia score, was worse at 5 years after total fundoplication. Symptoms of bloating, inability to belch and flatulence were also more common after total fundoplication. Reoperation was required for dysphagia in three patients after total fundoplication and for recurrent reflux in three patients after anterior fundoplication.**
Conclusion: **Anterior 180° partial fundoplication was as effective as total fundoplication for managing the symptoms of gastro-oesophageal reflux in the longer term. It was associated with a lower incidence of side-effects, although this was offset by a slightly higher risk of recurrent reflux symptoms.**

Paper accepted 21 May 2004
Published online 17 December 2004 in Wiley InterScience (www.bjs.co.uk). **DOI:** 10.1002/bjs.4762

Introduction

The most widely used surgical treatment of gastro-oesophageal reflux disease is total fundoplication, based on the repair originally described by Nissen. The laparoscopic approach has largely replaced traditional open surgery for reflux, with the benefit of a more rapid recovery. Approximately 90 per cent of patients have a good or excellent outcome at 5–8 years after total fundoplication[1–3], but some are troubled by unwanted side-effects, in particular long-term dysphagia, gas bloat and other gas-related problems[4].

Division of the short gastric blood vessels to mobilize the gastric fundus fully has been suggested as a factor that might improve outcome, but randomized trials have demonstrated that vessel division confers no benefit[4–6]. An alternative approach is the use of partial fundoplication. The authors have described a technique for laparoscopic anterior 180° fundoplication[7] and showed in a randomized trial that it controlled reflux effectively in the short term (6 months) and was associated with less dysphagia than total fundoplication[8]. Before this procedure can be considered for routine application, its long-term efficacy must be demonstrated. It is now more than 5 years since the final patient was entered into the original randomized trial and longer-term outcomes for the original cohort are presented in this paper.

Patients and methods

The complete protocol for this study has been detailed previously[8]. Patients were followed up yearly using a structured interview. At a minimum of 5 years after entry

into the trial, a single investigator attempted to contact each enrolled patient, with a view to conducting a telephone interview and applying a standardized questionnaire. At the time of interview, this investigator was not aware which procedure each patient had undergone. The standardized questionnaire investigated the specific symptoms of heartburn and dysphagia. Patients were asked whether heartburn was present or absent, and whether dysphagia for either liquid and solids was present or not (answer yes or no). In addition, patients were asked to grade symptoms of heartburn, dysphagia for liquids and dysphagia for solids using separate visual analogue scales ranging from zero (symptom absent) to ten (severe symptoms). A previously described dysphagia score[9] was also used. This scoring system generated a composite score based on a scale of zero to five regarding the patient's ability to swallow nine index liquid or solid foods (0, no dysphagia; 45, total dysphagia). Additional questions were asked about symptoms of upper abdominal bloating, ability to belch normally and increased flatulence (answer yes or no). Overall satisfaction with the outcome of surgery was determined using a visual analogue scale from zero to ten (0, highly unsatisfied; 10, highly satisfied) and a modified Visick scale (range 1–5; good outcome 1 or 2). Patients were also asked whether they would elect to undergo the same procedure again under similar preoperative circumstances.

Data analysis was performed on an intention-to-treat basis. Fisher's exact test was used to determine the significance of 2 × 2 contingency tables, and a two-tailed Mann–Whitney *U* test was used to assess differences between sets of non-parametric data.

Results

Of the 107 patients who were enrolled in the trial between December 1995 and June 1997, 103 were potentially available for interview 5 years after surgery. Four patients died during follow-up from causes unrelated to the original antireflux surgery (colonic cancer, lung cancer, hepatocellular cancer and myocardial infarction). Of the remaining 103 patients, 101 (98·1 per cent) were interviewed 5 years after surgery. One patient refused interview and another could not be contacted; both of these patients had had total fundoplication. Of the patients interviewed, 51 had undergone a total fundoplication and 50 an anterior 180° partial fundoplication. These groups were well matched at the time of enrolment. The majority of patients were men (67·3 per cent overall; 35 in the total fundoplication group and 33 in the anterior fundoplication group). The men were younger than the women (mean 50 *versus* 57 years in total group and 44 *versus* 58 years in anterior group).

Clinical outcomes 5 years after surgery are shown in *Table 1*. There were no significant differences in heartburn or the use of proton-pump inhibitors. Total fundoplication was associated with significantly more dysphagia for solids, as assessed by the analogue score and the composite dysphagia score. Patients in the total fundoplication group were more likely to report symptoms of bloating and flatulence, and less likely to be able to belch effectively. The ability to relieve bloating did not differ significantly between groups.

The overall clinical outcome for the two groups was similar. Analogue scores of satisfaction were not significantly different ($P = 0{\cdot}114$) (*Table 2*). Seventy-eight per cent of patients reported a global outcome assessment as either excellent or good after total fundoplication, compared with 86 per cent after anterior fundoplication ($P = 0{\cdot}437$). Eighty-six per cent of patients in the total fundoplication group and 94 per cent in the anterior fundoplication group said they would undergo the operation again for the same problem ($P = 0{\cdot}318$). Five years after surgery the majority of patients reported minimal or no symptoms. Twelve per cent of patients had symptoms that interfered with their quality of life (Visick grade 4 or 5) after total fundoplication,

Table 1 Clinical outcomes at 5 years for heartburn, dysphagia and other side-effects

	Total fundoplication ($n = 51$)	Anterior fundoplication ($n = 50$)	*P*
Reflux symptoms			
Heartburn	5 (10)	10 (20)	0·172*
Mean heartburn analogue score	1·8	1·9	0·757†
Consuming PPI medication	6 (12)	2 (4)	0·269*
Dysphagia assessment			
Dysphagia for solids	14 (27)	9 (18)	0·344*
Mean dysphagia analogue score			
Liquids	1·0	0·6	0·084†
Solids	2·6	1·5	0·013†
Composite dysphagia score	11·4	6·5	0·008†
Other side-effects			
Abdominal bloating	38 (75)	22 (44)	0·002*
Able to relieve bloating	29 (57)	37 (74)	0·095*
Able to belch normally	29 (57)	40 (80)	0·018*
Increased flatulence	41 (80)	31 (62)	0·050*
Diarrhoea	14 (27)	12 (24)	0·821*

Values in parentheses are percentages. PPI, proton-pump inhibitor. *Fisher's exact test; †Mann–Whitney *U* test.

Table 2 Assessment of overall outcome at 5 years

	Total fundoplication ($n = 51$)	Anterior fundoplication ($n = 50$)	P^*
Mean analogue score of satisfaction	8·0	8·7	0·114
Global outcome assessment			
Excellent or good	40 (78)	43 (86)	0·437
Fair or poor	11 (22)	7 (14)	
Visick grade			
1 (no symptoms)	14 (27)	15 (30)	
2 (mild symptoms)	25 (49)	27 (54)	
3 (moderate symptoms)	6 (12)	7 (14)	
4 (symptoms interfering with quality of life)	4 (8)	1 (2)	0·112
5 (worse after surgery)	2 (4)	0 (0)	
Would undergo operation again	44 (86)	47 (94)	0·318

Values in parentheses are percentages. *Fisher's exact test.

compared with 2 per cent after anterior fundoplication ($P = 0{\cdot}112$).

Six patients required reoperation between 6 months and 5 years after fundoplication. Three patients who originally underwent total fundoplication had further surgery because of persistent dysphagia. The procedures performed were laparoscopic conversion of the fundoplication to a posterior partial fundoplication and widening of the oesophageal hiatus (24 months after original operation), laparoscopic widening of the oesophageal hiatus alone (28 months) and open conversion to an anterior partial fundoplication and widening of the oesophageal hiatus (9 months). Three patients in the anterior fundoplication group had laparoscopic conversion to a total fundoplication at 8, 44 and 54 months, all for recurrent reflux disease.

Discussion

The small but significant incidence of troublesome dysphagia and gas-related side-effects associated with total fundoplication has led to the development and evaluation of alternative strategies for the treatment of gastro-oesophageal reflux disease, such as posterior or anterior partial fundoplication. Several randomized comparisons of total and posterior partial fundoplication have failed to demonstrate any reduction in dysphagia[10–12], although Zornig *et al.*[13] recently demonstrated less early dysphagia at 4 months after posterior fundoplication in a randomized trial involving 200 patients. Uncontrolled case series also suggested that anterior partial fundoplication might be a better option[14]. Early results from the present trial demonstrated that anterior 180° partial fundoplication achieved effective reflux control, with less dysphagia and fewer gas-related side-effects than total fundoplication[8]. These clinical outcomes were confirmed by objective manometric and pH monitoring criteria.

Both operations achieved satisfactory control of reflux symptoms, measured by an analogue heartburn scale, although there was a trend towards more patients experiencing heartburn after anterior fundoplication. This symptom was considered to be present if any heartburn had been experienced in the previous month and it did not necessarily equate with recurrent gastro-oesophageal reflux disease. On the other hand, three patients underwent revisional surgery for recurrent reflux, suggesting that anterior 180° partial fundoplication may not be as durable as total fundoplication. Offsetting this, fewer patients consumed antireflux medication at 5 years after anterior fundoplication. It is important to consider the problem of recurrent reflux within the context of the overall outcome, including other side-effects.

Dysphagia, abdominal bloating and inability to belch were less common at 5 years after anterior fundoplication. Such side-effects may detract from an otherwise successful operation and, for this reason, the overall outcome from the patient's perspective is arguably the most important determinant of postoperative outcome. Patient satisfaction scores were high in both groups at 5 years, and were nearly identical to the scores recorded at 6-month follow-up[8]. The other measures of overall outcome tended to favour anterior partial fundoplication. The reduction in side-effects may therefore be offset against any trend towards more reflux at 5 years after anterior partial fundoplication.

More patients from the total fundoplication group rated their overall outcome as poor, although this was not statistically significant. Although only a minority reported a poor outcome, side-effects were nevertheless a problem in these patients. The side-effects of fundoplication are often difficult to treat and further management usually entails surgical revision[15]. On the other hand, recurrent reflux after partial fundoplication can often be managed by medication alone, which is probably a more acceptable adverse outcome.

A strength of the present study is that all but two of the surviving patients were available for interview. Such a high level of late follow-up is important and minimizes bias. Patients who are dissatisfied with their clinical outcome may refuse follow-up, which may lead to inaccurate reporting of outcomes. A recent study that evaluated differences between telephone interview and postal questionnaires, as well as the situation of incomplete and complete follow-up, confirmed the problems associated with incomplete follow-up[16].

Another issue to consider is whether 5-year follow-up gives sufficient information on the long-term efficacy of anterior fundoplication. Few studies have reported outcomes beyond 5 years after total fundoplication[1,2], and few have achieved complete follow-up. Based on the present data, anterior fundoplication seems to be a durable procedure, although further data are required in the longer term and the intention is to continue follow-up of this cohort. In the meantime, the present data support the routine use of anterior partial fundoplication as a treatment for gastro-oesophageal reflux.

Acknowledgements

This trial was supported by a project grant from the National Health and Medical Research Council of Australia.

References

1 Lafullarde T, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG. Laparoscopic Nissen fundoplication: five-year results and beyond. *Arch Surg* 2001; **136**: 180–184.
2 Bammer T, Hinder RA, Klaus A, Klingler PJ. Five- to eight-year outcome of the first laparoscopic Nissen fundoplications. *J Gastrointest Surg* 2001; **5**: 42–48.
3 Liu JY, Woloshin S, Laycock WS, Schwartz LM. Late outcomes after laparoscopic surgery for gastroesophageal reflux. *Arch Surg* 2002; **137**: 397–401.
4 O'Boyle CJ, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication: a prospective double-blind randomized trial with 5-year follow-up. *Ann Surg* 2002; **235**: 165–170.
5 Luostarinen ME, Isolauri JO. Randomized trial to study the effect of fundic mobilization on long-term results of Nissen fundoplication. *Br J Surg* 1999; **86**: 614–618.
6 Blomqvist A, Dalenback J, Hagedorn C, Lonroth H, Hyltander A, Lundell L. Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication. *J Gastrointest Surg* 2000; **4**: 493–500.
7 Watson DI, Liu JF, Devitt PG, Game PA, Jamieson GG. Outcome of laparoscopic anterior 180° partial fundoplication for gastroesophageal reflux disease. *J Gastrointest Surg* 2000; **4**: 486–492.
8 Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg* 1999; **86**: 123–130.
9 Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol* 1992; **14**: 99–100.
10 Walker SJ, Holt S, Sanderson CJ, Stoddard CJ. Comparison of Nissen total and Lind partial transabdominal fundoplication in the treatment of gastro-oesophageal reflux. *Br J Surg* 1992; **79**: 410–414.
11 Laws HL, Clements RH, Swillie CM. A randomized, prospective comparison of the Nissen fundoplication *versus* the Toupet fundoplication for gastroesophageal reflux disease. *Ann Surg* 1997; **225**: 647–654.
12 Lundell L, Abrahamsson H, Ruth M, Rydberg L, Lonroth H, Olbe L. Long-term results of a prospective randomized comparison of total fundic wrap (Nissen–Rossetti) or semifundoplication (Toupet) for gastro-oesophageal reflux. *Br J Surg* 1996; **83**: 830–835.
13 Zornig C, Strate U, Fibbe C, Emmermann A, Layer P. Nissen *vs* Toupet laparoscopic fundoplication. *Surg Endosc* 2002; **16**: 758–766.
14 Watson A, Jenkinson LR, Ball CS, Norris TL. A more physiological alternative to total fundoplication for the surgical correction of resistant gastro-oesophageal reflux. *Br J Surg* 1991; **78**: 1088–1094.
15 Hunter JG, Smith CD, Branum GD, Waring JP, Trus TL, Cornwall M *et al*. Laparoscopic fundoplication failures: patterns of failure and response to fundoplication revision. *Ann Surg* 1999; **230**: 595–604.
16 Ludemann R, Watson DI, Jamieson GG. Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication. *Am J Surg* 2003; **186**: 143–147.

Original article

Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen *versus* anterior 180° partial fundoplication

W. Cai[1], D. I. Watson[1], C. J. Lally[1,2], P. G. Devitt[2], P. A. Game[2] and G. G. Jamieson[2]

[1]Flinders University Department of Surgery, Flinders Medical Centre, Bedford Park and [2]University of Adelaide Discipline of Surgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia

Correspondence to: Professor D. I. Watson, Flinders University Department of Surgery, Room 3D211, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia (e-mail: david.watson@flinders.edu.au)

Background: **A randomized trial of laparoscopic Nissen fundoplication and anterior 180° partial fundoplication was undertaken to determine whether the anterior procedure might reduce the incidence of dysphagia and other adverse outcomes following surgery for gastro-oesophageal reflux disease. This study evaluated clinical outcomes after 10 years.**

Methods: **Some 107 patients were randomized to undergo laparoscopic Nissen or anterior 180° partial fundoplication. Ten-year data were not available for 18 patients. Information was obtained from 89 patients (48 Nissen, 41 anterior fundoplication) using a standard clinical questionnaire that focused on symptoms of reflux, potential postoperative side-effects and overall satisfaction with the outcome of surgery.**

Results: **There were no significant differences between the two groups with regard to reflux symptoms, dysphagia, abdominal bloating, ability to belch and overall satisfaction. Between 5 and 10 years after surgery, revisional surgery was required for reflux in two patients after anterior fundoplication. Two patients had revision after Nissen fundoplication, for reflux and recurrent hiatus hernia.**

Conclusion: **Both laparoscopic anterior 180° partial and Nissen fundoplication are safe, effective and durable at 10 years' follow-up. Most patients are satisfied with the clinical outcome.**

Paper accepted 14 May 2008

Published online 21 October 2008 in Wiley InterScience (www.bjs.co.uk). **DOI:** 10.1002/bjs.6318

Introduction

Fundoplication is an effective treatment for gastro-oesophageal reflux disease (GORD). Results of laparoscopic Nissen fundoplication are equivalent to the open procedure in both the short- and the long-term[1–4]. In some patients this procedure can be followed by unwanted persistent side-effects, including dysphagia, inability to belch and vomit, abdominal bloating and other gas-related problems, which may affect the patient's quality of life[5,6].

To minimize the risk of these problems, the Nissen procedure has been modified in a variety of ways[7–10]. Routine division of the short gastric blood vessels, for example, is based on the assumption that this might facilitate the fashioning of a looser 'floppy' wrap, which might reduce the incidence of postoperative side-effects. Short-term (6 months) and longer-term (5 years) findings in prospective randomized trials, however, have not supported this[7,11]. An alternative approach is to construct a partial fundoplication. Both posterior and anterior partial fundoplication have been recommended, with early outcomes suggesting similar control of reflux to that found with Nissen fundoplication, but a lower incidence of side-effects[8–10,12,13].

To determine whether laparoscopic anterior 180° partial fundoplication can reduce the risk of postoperative dysphagia or other adverse side-effects, patients were enrolled in a prospective randomized double-blind trial to compare the anterior procedure with laparoscopic Nissen fundoplication. Short-term (6 months) and mid-term (5 years) results have been reported previously[9,14]: the anterior procedure achieved good control of reflux and good overall satisfaction but with less dysphagia, bloating and flatulence than the Nissen operation.

It is now more than 10 years since the last patient had surgery in this randomized trial. This article reports the 10-year clinical follow-up data.

Methods

Between December 1995 and June 1997, 107 patients undergoing laparoscopic surgery for gastro-oesophageal reflux were entered into a randomized trial of anterior 180° partial *versus* Nissen fundoplication. Fifty-four patients were randomized to the Nissen arm and 53 to the anterior fundoplication arm. Full details of the trial protocol have been described previously[9]. Patients were excluded if they had a severe oesophageal motility disorder (adynamic oesophagus or achalasia), required a concurrent abdominal procedure such as cholecystectomy, or had undergone previous antireflux surgery.

In brief, the technique for laparoscopic Nissen fundoplication comprised blunt dissection of the oesophageal hiatus with minimal diathermy, preservation of the hepatic branch of the vagus nerve, routine posterior hiatal repair and the performance of a short, loose Nissen fundoplication around a 52-Fr bougie. The wrap was secured with three non-absorbable 2/0 monofilament interrupted sutures. Laparoscopic anterior 180° partial fundoplication also involved hiatal dissection with preservation of the hepatic branch of the vagus nerve, and oesophageal mobilization followed by posterior hiatal repair. An anterior fundoplication was fashioned by fixing the anterior wall of the fundus to the front of the oesophagus and the diaphragmatic hiatus. This was achieved by suturing the fundus to the right lateral wall of the abdominal oesophagus and to the right hiatal pillar, and the left lateral wall of the oesophagus to the left hiatal pillar using five or six non-absorbable 2/0 monofilament sutures. The procedure accentuated the angle of His, and anchored a 3–5-cm length of oesophagus below the diaphragm. If conversion to an open procedure was necessary, the randomization schedule was still followed and the patient remained in the originally allocated trial group.

This study analysed the 10-year clinical outcomes. Any adverse event or reintervention in the first 10 years of follow-up was also included in the data analysis. A single investigator, who was unaware of which procedure patients had undergone, attempted to contact each patient and applied a standard clinical questionnaire by telephone interview. The presence or absence of the following symptoms was sought: heartburn, dysphagia for solids and liquids, inability to belch, epigastric bloating and ability to relieve bloating. Patients were asked to grade symptoms of heartburn, dysphagia for liquids and dysphagia for solids using separate visual analogue scales (0, symptom absent; 10, severe symptoms). In addition, a previously validated dysphagia score (0, no dysphagia; 45, severe dysphagia) was used, which combined information about difficulty in swallowing nine types of liquid or solid[15]. Further questions were asked about symptoms of upper abdominal bloating, ability to relieve bloating, ability to belch normally and ability to eat a normal diet (answer 'yes' or 'no'). An overall assessment of satisfaction with the operative outcome was also scored by a further visual analogue scale (0, dissatisfied; 10, satisfied). In addition to the analogue scores, heartburn, dysphagia for solid food, and satisfaction with the overall outcome were assessed by asking questions requiring 'yes' or 'no' answers. Patients were also asked whether they would choose to undergo the same procedure again under similar preoperative circumstances.

Statistical analysis

Analysis was performed on an intention-to-treat basis, with all patients remaining in their initially allocated group. Data were entered into a dedicated computer database (FileMaker Pro® version 8.0; Filemaker, Santa Clara, California, USA) and analysed using statistical software (Instat version 3.05; Graphpad Software, San Diego, California, USA). Fisher's exact test was used to determine the significance of 2×2 contingency tables. A two-tailed Mann–Whiney U test was employed to assess the differences between non-parametric data sets.

Results

Between December 1995 and June 1997, 107 patients were enrolled in the trial (*Fig. 1*). Of 18 patients not included in the follow-up cohort, one refused interview, three could not be located, three were unable to complete the interview owing to dementia and 11 had died. There were no causes of death linked to antireflux surgery (*Fig. 1*).

Of the 89 patients available for interview 10 years after the original operation, 48 had undergone a total Nissen fundoplication (Nissen group) and 41 an anterior 180° partial fundoplication (anterior group). Most patients were men (70 per cent overall), 34 in the Nissen and 28 in the anterior group, and the mean age was 58·4 and 52·9 years respectively.

Clinical outcomes after a minimum of 10 years are summarized in *Tables 1–4*. There were no significant differences in mean heartburn scores, number of patients reporting heartburn or consumption of proton-pump inhibitors (PPIs). Symptoms of gastro-oesophageal reflux were well controlled in most patients. There were no

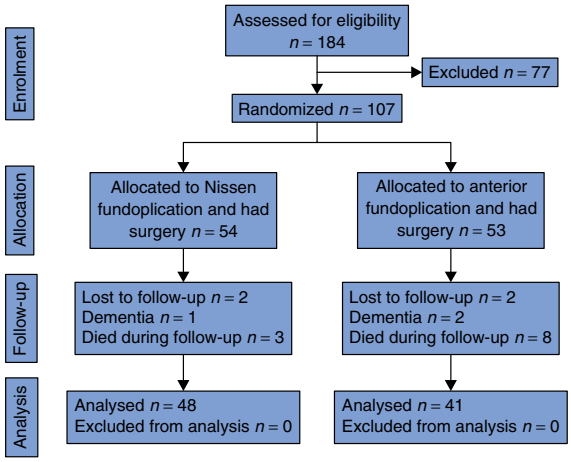


Fig. 1 CONSORT diagram for the randomized trial

Table 1 Outcomes at 10 years for heartburn

	Total fundoplication ($n = 48$)	Anterior fundoplication ($n = 41$)	*P*
Heartburn (yes/no question)	7 (15)	8 (20)	0·580*
Heartburn analogue score			
Mean	1·7	2·3	0·111†
0	28 (58)	16 (39)	
1–3	14 (29)	13 (32)	
4–6	2 (4)	9 (22)	
7–10	4 (8)	3 (7)	
Taking proton-pump inhibitors	9 (19)	11 (27)	0·448*

Values in parentheses are percentages. *Fisher's exact test; †Mann–Whitney *U* test.

significant differences between the groups for the analogue scores for heartburn (*Table 1*) or for dysphagia to liquids or to solids at 10 years' follow-up (*Table 2*). Nor were there significant differences in the symptom of bloating, or the ability to relieve bloating and belch (*Table 3*).

The overall clinical outcome for the two groups was similar. Forty-five of 48 patients in the Nissen group and 38 of 41 patients in the anterior group were satisfied with the outcome of surgery. The mean analogue scores for satisfaction were high in both groups, and not significantly different (*Table 4*). Forty of 41 patients in the anterior group indicated that they would undergo the operation again if the circumstances were similar, compared with 43 of 48 in Nissen group ($P = 0·212$).

Four patients required revisional operations between 5 and 10 years after the initial surgery. Three had a revision fundoplication for recurrent reflux symptoms; two entailed conversion of an anterior partial fundoplication to a total fundoplication at 7 and 10 years, and in the third patient a total fundoplication was refashioned at 6 years.

Table 2 Outcomes at 10 years for dysphagia

	Total fundoplication ($n = 48$)	Anterior fundoplication ($n = 41$)	*P*
Dysphagia for solids (yes/no question)	25 (52)	14 (34)	0·133*
Dysphagia analogue score for liquids			
Mean	1·4	1·0	0·285†
0	28 (58)	30 (73)	
1–3	12 (25)	5 (12)	
4–6	6 (13)	4 (10)	
7–10	2 (4)	2 (5)	
Dysphagia analogue score for solids			
Mean	2·4	1·7	0·229†
0	20 (42)	22 (54)	
1–3	13 (27)	10 (24)	
4–6	12 (25)	8 (20)	
7–10	3 (6)	1 (2)	
Composite dysphagia score (mean)	12·0	7·8	0·121†

Values in parentheses are percentages. *Fisher's exact test; †Mann–Whitney *U* test.

Table 3 Outcomes at 10 years for side-effects other than heartburn or dysphagia

	Total fundoplication ($n = 48$)	Anterior fundoplication ($n = 41$)	*P*
Eats normal diet	45 (94)	38 (93)	1·000*
Side-effects			
Abdominal bloating	14 (29)	19 (46)	0·124*
Able to relieve bloating	17 (35)	12 (29)	0·651*
Able to belch normally	24 (50)	27 (66)	0·141*

Values in parentheses are percentages. *Fisher's exact test.

Table 4 Assessment of overall outcome at 10 years

	Total fundoplication ($n = 48$)	Anterior fundoplication ($n = 41$)	*P*
Satisfied with outcome (yes/no question)	45 (94)	38 (93)	1·000*
Mean analogue score of satisfaction	8·2	8·3	0·707†
Would choose operation again	43 (90)	40 (98)	0·212*

Values in parentheses are percentages. *Fisher's exact test; †Mann–Whitney *U* test.

The fourth patient had laparoscopic repair of a hiatus hernia 8 years after the original Nissen procedure; the fundoplication had remained intact and was not revised. The authors have reported previously[14] that six patients underwent reoperation between 6 months and 5 years after surgery, three for persistent dysphagia after a total Nissen fundoplication and three for recurrent reflux after an anterior procedure. Hence, ten patients (five in each group; 9·3 per cent of 107) underwent a revisional procedure between 6 months and 10 years after fundoplication.

Discussion

Both laparoscopic anterior and Nissen fundoplication achieved satisfactory control of reflux symptoms at 10 years, with no significant differences in heartburn symptoms or PPI usage between the two groups, confirming the efficacy of the anterior approach at late follow-up. In addition, there were no significant differences in the incidence of side-effects such as dysphagia, abdominal bloating or inability to belch at 10 years, although the trend towards fewer side-effects following anterior partial fundoplication was offset by a trend towards more heartburn. Nevertheless, patients rated the overall clinical outcome highly for both procedures, and all but one of the 41 patients in the anterior group stated that they would choose the operation again in similar preoperative circumstances.

Few studies have compared long-term outcomes after Nissen and partial fundoplication. One showed similar overall outcomes but an increased prevalence of heartburn after laparoscopic posterior fundoplication[8], although only 61 per cent of patients were available for follow-up. The only other trial to report longer-term data compared open Nissen with posterior partial fundoplication at a median of 11·5 years' follow-up[16]. Both procedures achieved equivalent control of reflux and had a similar incidence of late dysphagia, but posterior fundoplication was associated with significantly less postprandial fullness and flatulence at late follow-up. One study evaluated the 6–44-month outcome of laparoscopic anterior partial fundoplication[17]. The results also suggested that the incidence of dysphagia was less than that after Nissen fundoplication.

Engström and colleagues[10] recently reported median follow-up of 65 months for a randomized trial of anterior *versus* posterior partial fundoplication. In that study, posterior partial fundoplication achieved better control of gastro-oesophageal reflux, although at the expense of more side-effects, than the anterior partial fundoplication procedure. The anterior partial fundoplication in that trial was different to the procedure performed in the present study. The degree to which the fundus was wrapped over the anterior oesophagus was less, and, unlike in the anterior 180° partial fundoplication constructed in this centre, the wrap was not anchored to the right hiatal pillar. This could account for a poorer outcome for the anterior fundoplication in the trial by Engström and co-workers[10].

The consumption of PPIs after 10 years in the present study was comparable to that reported elsewhere[2]. In a larger non-randomized study of 844 patients, it was found that many patients who took PPIs did not have reflux[18]. It is likely that many patients in the present trial who used PPIs at late follow-up did not have recurrent reflux either, although questions were asked specifically to address this. A slightly higher proportion of patients were taking PPIs 10 years after anterior partial fundoplication (11 of 41) than after the Nissen procedure (nine of 48).

A strength of the present study is the completeness of the 10-year follow-up data, reducing the potential for bias associated with incomplete follow-up[19]. Only four patients refused or were lost to follow-up. The outcome was known for 99 per cent of patients at 6 months[9], 98·1 per cent at 5 years[14] and 96·3 per cent at 10 years. The high rate of follow-up also maximized the collection of data regarding adverse outcomes such as surgical revision. This is important, because the authors have previously shown that incomplete follow-up may indicate an apparently better outcome, and that individuals lost to follow-up are more likely to have had an adverse outcome, or to be less satisfied with the outcome[19].

It might appear that there was excessive mortality during follow-up in the present trial, as was also reported by Spechler and colleagues[20] for patients in the surgery arm of a randomized controlled trial of surgery *versus* medication in a veterans population in the USA. The present authors have examined this issue previously, and found a similar mortality rate during a 10-year follow-up of 250 patients after laparoscopic Nissen fundoplication[2]; Australian Bureau of Statistics data confirmed that this mortality rate was identical to that predicted for matched non-surgical patients.

The present study evaluated only clinical outcome at 10 years. Objective evaluation with oesophageal manometry, pH monitoring or endoscopy was not performed. Previous experience has shown that a significant proportion of patients do not consent to follow-up using invasive investigations[9,19], and for this reason objective follow-up is always less complete than careful clinical assessment. Furthermore, the patient perspective of successful surgery is determined by symptoms rather than the results of investigations.

The present study has confirmed that laparoscopic anterior 180° partial fundoplication is as safe, effective and durable as laparoscopic Nissen fundoplication after 10 years. This procedure is appropriate for the surgical treatment of patients with GORD.

Acknowledgements

This study was supported by a project grant from the National Health and Medical Research Council of Australia.

The authors are grateful for the assistance of Tanya Ellis (database management) and Nicola Ascott (finding 'lost' patients). Their contributions ensured that near-complete clinical follow-up was available for analysis.

References

1 Salminen PT, Hiekkanen HI, Rantala AP, Ovaska JT. Comparison of long-term outcome of laparoscopic and conventional Nissen fundoplication: a prospective randomized study with an 11-year follow-up. *Ann Surg* 2007; **246**: 201–206.

2 Kelly JJ, Watson DI, Chin KF, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. *J Am Coll Surg* 2007; **205**: 570–575.

3 Dallemagne B, Weerts J, Markiewicz S, Dewandre JM, Wahlen C, Monami B *et al*. Clinical results of laparoscopic fundoplication at ten years after surgery. *Surg Endosc* 2006; **20**: 159–165.

4 Cowgill SM, Gillman R, Kraemer E, Al-Saadi S, Villadolid D, Rosemurgy A. Ten-year follow up after laparoscopic Nissen fundoplication for gastroesophageal reflux disease. *Am Surg* 2007; **73**: 748–752.

5 Lundell L, Abrahamsson H, Ruth M, Rydberg L, Lönroth H, Olbe L. Long-term results of a prospective randomized comparison of total fundic wrap (Nissen–Rossetti) or semifundoplication (Toupet) for gastro-oesophageal reflux. *Br J Surg* 1996; **83**: 830–835.

6 Karim SS, Panton ON, Finley RJ, Graham AJ, Dong S, Storseth C *et al*. Comparison of fundoplication in the management of gastroesophageal reflux disease. *Am J Surg* 1997; **172**: 375–378.

7 Watson DI, Pike GK, Baigrie RJ, Mathew G, Devitt PG, Britten-Jones R *et al*. Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg* 1997; **226**: 642–652.

8 Sgromo B, Irvine LA, Cuschieri A, Shimi SM. Long-term comparative outcome between laparoscopic total Nissen and Toupet fundoplication: symptomatic relief, patient satisfaction and quality of life. *Surg Endosc* 2007; **22**: 1048–1053.

9 Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg* 1999; **86**: 123–130.

10 Engström C, Lönroth H, Mardani J, Lundell L. An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. *World J Surg* 2007; **31**: 1221–1225.

11 O'Boyle CJ, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication: a prospective double-blind randomized trial with 5-year follow-up. *Ann Surg* 2002; **235**: 165–170.

12 Stewart GD, Watson AJ, Lamb PJ, Lee AJ, Krukowski ZH, Griffin SM *et al*. Comparison of three different procedures for antireflux surgery. *Br J Surg* 2004; **91**: 724–729.

13 Guérin E, Bétroune K, Closset J, Mehdi A, Lefèbvre JC, Houben JJ *et al*. Nissen *versus* Toupet fundoplication: results of a randomized and multicenter trial. *Surg Endosc* 2007; **21**: 1985–1990.

14 Ludemann R, Watson DI, Jamieson GG, Game PA, Devitt PG. Five-year follow-up of a randomized clinical trial of laparoscopic total *versus* anterior 180° fundoplication. *Br J Surg* 2005; **92**: 240–243.

15 Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol* 1992; **14**: 99–100.

16 Hagedorn C, Lönroth H, Rydberg L, Ruth M, Lundell L. Long-term efficacy of total (Nissen–Rossetti) and posterior partial (Toupet) fundoplication: results of a randomized clinical trial. *J Gastrointest Surg* 2002; **6**: 540–545.

17 Kneist W, Heintz A, Trinh TT, Junginger T. Anterior partial fundoplication for gastroesophageal reflux disease. *Langenbecks Arch Surg* 2003; **388**: 174–180.

18 Wijnhoven BPL, Lally CJ, Kelly JJ, Myers JC, Watson DI. Use of anti-reflux medication after anti-reflux surgery. *J Gastrointest Surg* 2008; **12**: 510–517.

19 Ludemann R, Watson DI, Jamieson GG. Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication. *Am J Surg* 2003; **186**: 143–147.

20 Spechler SJ, Lee E, Ahnen D, Goyal RK, Hirano I, Ramirez F *et al*. Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial. *JAMA* 2001; **285**: 2331–2338.

RANDOMIZED CONTROLLED TRIAL

Objective Outcomes 14 Years After Laparoscopic Anterior 180-Degree Partial Versus Nissen Fundoplication

Results From a Randomized Trial

Joris A. Broeders, MD, PhD, Emily A. Broeders, MD,* David I. Watson, MBBS, MD, FRACS,† Peter G. Devitt, MBBS, MS, FRCS, FRACS,* Richard H. Holloway, MBBS, MD, FRACP,‡§ and Glyn G. Jamieson, MBBS, MS, FRACS**

Objective: To investigate late objective outcomes 14 years after laparoscopic anterior 180-degree partial versus Nissen fundoplication.

Background: Clinical outcomes from randomized clinical trials suggest good outcomes for anterior 180-degree partial fundoplication, with similar control of reflux symptoms and less side effects, compared with Nissen fundoplication. However, objective outcomes at late follow-up have not been reported.

Methods: A subset of participants from a randomized trial of anterior 180-degree versus Nissen fundoplication underwent stationary esophageal high-resolution manometry and ambulatory 24-hour impedance-pH monitoring at 14 years' follow-up. The subset and other patients in the trial also completed a standardized clinical questionnaire to ensure that they were representative of the overall trial.

Results: Eighteen patients (8 anterior, 10 Nissen) underwent objective testing and had a symptom profile similar to those who did not (n = 59) have testing. Total esophageal acid exposure time and the total number of acid and weakly acidic reflux episodes per 24 hours were higher after anterior fundoplication than after Nissen fundoplication. Proximal, midesophageal and distal reflux were proportionately increased after anterior 180-degree fundoplication. The number of liquid and mixed reflux episodes was also higher after anterior fundoplication, which was accompanied by higher clinical heartburn scores. There were no differences in gas reflux, gastric belches, and supragastric belches, which is in line with the observation that gas-related symptoms were similar for both groups. Mean LES resting and relaxation nadir pressure were lower after anterior fundoplication, which was reflected by lower dysphagia scores. Patient satisfaction was similar after both procedures.

Conclusions: At 14 years after randomization, this study demonstrated that acid, weakly acidic, liquid and mixed reflux episodes are more common after anterior 180-degree fundoplication than after Nissen fundoplication. On the contrary, gas reflux and gastric belching and patient satisfaction are similar for both procedures. Mean LES resting and relaxation nadir pressure are lower after anterior fundoplication. Overall, these findings suggest less effective reflux control after anterior 180-degree partial fundoplication, offset by less dysphagia, leading to a clinical outcome that is equivalent to Nissen fundoplication at late follow-up.

Keywords: anterior fundoplication, gastroesophageal reflux disease, high-resolution manometry, impedance monitoring, laparoscopic antireflux surgery, Nissen fundoplication, objective outcome, pH monitoring, randomized clinical trial

(*Ann Surg* 2013;258: 233–239)

Laparoscopic fundoplication is commonly used for the surgical treatment of gastroesophageal reflux, with Nissen fundoplication being the most frequently performed operation. However, the Nissen procedure is often followed by troublesome dysphagia and gas-related side effects.[1–3] To reduce the risk of these problems, partial fundoplications have been developed, and these modifications have been tested in randomized clinical trials.[1,4–6] In the absence of late objective outcomes, some have questioned the durability of partial fundoplications,[7–10] although longer term clinical outcomes from the trials actually support the application of anterior 180-degree and posterior 270-degree partial fundoplication techniques.[4,5,11,12] However, no randomized trial of partial versus Nissen fundoplication has reported objective outcome data at late follow-up.

Previous work has demonstrated the utility of objective monitoring of acid reflux, in addition to subjective outcomes, for the assessment of the efficacy of antireflux surgery.[13] In addition, intraluminal impedance monitoring enables quantification of both acid and weakly acidic reflux and proximal reflux events.[14]

In this study, we used high-resolution esophageal manometry combined with pH and impedance monitoring to evaluate late (14-year) objective outcomes in a subset of patients enrolled in a prospective randomized trial of anterior 180-degree partial versus Nissen fundoplication. To ensure that this subset was representative of the overall trial cohort, we assessed clinical outcomes for the whole trial cohort and compared these with the clinical outcomes in the subset who underwent objective assessment.

METHODS

From December 1995 to April 1997, 103 patients with objectively proven gastroesophageal reflux disease were enrolled in a randomized trial of laparoscopic anterior 180-degree partial versus Nissen fundoplication.[6] For this study, all patients enrolled in this trial, who had not undergone a revision operation during follow-up, were invited to complete an objective study protocol to evaluate reflux and belching after fundoplication. All patients were also asked to complete a standardized clinical questionnaire to assess reflux symptoms and postfundoplication side effects. The subset that agreed to undergo the objective tests formed the focus of this study. The outcomes for the clinical questionnaire and the objective tests were compared within this subset. To determine whether the clinical outcome in the patients who underwent the objective tests was similar to clinical

From the *Discipline of Surgery, University of Adelaide, Royal Adelaide Hospital, Adelaide, South Australia; †Flinders University Department of Surgery, Flinders Medical Centre, Bedford Park, South Australia; ‡Department of Gastroenterology and Hepatology, Royal Adelaide Hospital, Adelaide, South Australia; and §Discipline of Medicine, University of Adelaide, Adelaide, South Australia.

The randomized trial is registered with the Australia and New Zealand Clinical Trials Registry ACTRN12607000303448. The authors declare no conflicts of interest.

Disclosure: This study was supported by a University Medical Center Utrecht Alexandre Suerman MD/PhD grant (to J.A.B.). Support for the randomized clinical trial from which the patient cohort was obtained has been provided by Research Project grants from the National Health and Medical Research Council (NHMRC) of Australia (grant numbers—157986 and 375111).

Reprints: Joris A.J.L. Broeders, MD, PhD, Department of Surgery, Royal Adelaide Hospital, Level 5, Eleanor Harrald Bldg, Adelaide, South Australia 5000, Australia. E-mail: joris.broeders@adelaide.edu.au.

ISSN: 0003-4932/13/25802-0233
DOI: 10.1097/SLA.0b013e318278960e

outcomes in those who did not undergo the tests, the outcomes for the clinical questionnaire were compared for patients undergoing versus not undergoing the objective tests.

The full details of the randomized trial protocol and surgical procedures have been reported previously.[6] Six-month,[6] 5-year,[4,5] and 10-year[11] clinical outcome data have been reported elsewhere. The protocol for the original trial and this study were approved by the Royal Adelaide Hospital Human Research Ethics Committee.

Objective Study Protocol

All patients who had not undergone a revision operation during follow-up were invited to complete the objective study and the clinical symptom assessment. The objective assessment protocol was similar to the protocol described elsewhere by Bredenoord et al.[15] It was comprised of the assessment of reflux and belching using high-resolution manometry and concurrent combined esophageal impedance-pH monitoring initially after a meal and then after provocation by intragastric air inflation, followed by ambulatory assessment using 24-hour impedance monitoring.[15]

Acid-suppressing medication and medication that potentially affects gastrointestinal motility were discontinued 7 days before objective assessment. A manometry catheter was introduced transnasally and a combined impedance-pH monitoring catheter was also positioned transnasally on the basis of the manometric findings (see later). With each subject in the supine position, the manometric response to 10 standardized wet swallows (5 mL water bolus) was studied. Thereafter, subjects were positioned upright and were asked to minimize head movements to avoid axial displacement of the catheters. The subjects then consumed a standardized meal within 30 minutes that was comprised of a 274-g hamburger ("Burger King Whopper" consisting of a bun, beef, tomato, lettuce, mayonnaise, ketchup, pickle, and onion), 116 g of french fries, and 400 mL of orange juice (total 1131 kcal). After the meal, pressure and impedance-pH were recorded for 90 minutes, and at the end of this time a syringe was used to manually infuse 600 mL of air into the stomach through the manometry catheter over a 5-minute period. After air infusion, recording was continued for another 20 minutes. Next, the manometry catheter was removed and 24-hour ambulatory impedance-pH measurement commenced. To minimize the effect of the previously infused air, the first 2 hours of the 24-hour recording were discarded.[15]

Stationary High-Resolution Manometry

High-resolution manometry and impedance-pH monitoring were performed by a single investigator (J.A.B.). A water-perfused system (Medical Measurements Systems; Enschede, The Netherlands) with a multiple-lumen 21-channel catheter was used (Dentsleeve International; Mississuaga, Ontario, Canada). This catheter had 1 gastric channel (0 cm), 12 distal channels (3–14 cm), 4 midesophageal channels (18, 22, 26, and 30 cm), and 4 proximal channels (37, 39, 41, and 43 cm). The catheter was positioned in such a way that its distal 12 side holes, spaced at 1-cm intervals, straddled the esophagogastric junction and the most distal side hole was positioned intragastrically. The gastric baseline pressure was registered and served as the zero reference point.

Combined Esophageal Impedance-pH Monitoring

Combined esophageal impedance-pH monitoring was performed in an identical manner to the methodology described in 2 previous studies.[14,16]

Clinical Assessment Protocol

All clinical data were collected prospectively by a research nurse using a previously described standardized questionnaire that was completed either by telephone interview or by mail.[4]

Analysis of Objective Outcome Data

The classification of belches and reflux characteristics was undertaken in an identical manner to the categorization described in previous studies.[14–16] The 24-hour impedance-pH tracings were manually analyzed using a dedicated software program (Medical Measurements Systems; Enschede, The Netherlands). To minimize observer bias, the investigator (J.A.B.) analyzing these studies was blinded to the patient characteristics and outcomes.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation unless stated otherwise. Differences in age and body mass index between groups were analyzed using an independent *t* test. All other comparisons of continuous parameters between groups were performed using the Mann-Whitney *U* test. Ordinal variables were expressed as percentages and differences between groups were analyzed using the χ^2 test. $P < 0.05$ was considered statistically significant. The statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL).

RESULTS

Subjects

The randomized trial originally enrolled 107 patients. During follow-up, 14 patients died of causes unrelated to their original antireflux surgery and 2 were unable to complete an interview due to dementia (Fig. 1). A further 10 patients underwent revision surgery (5 in each arm of the trial). The clinical outcome was available for these patients, but they were excluded from participating in this study. Hence, 81 patients met the eligibility criteria for this study. Of these, a clinical outcome could be determined for 81 patients, and 77 patients (95.1%) completed the clinical assessment protocol. Two patients were lost to follow up and 2 refused participation in this study. More patients underwent surgical reintervention for recurrent reflux in the anterior 180-degree fundoplication group and more for dysphagia

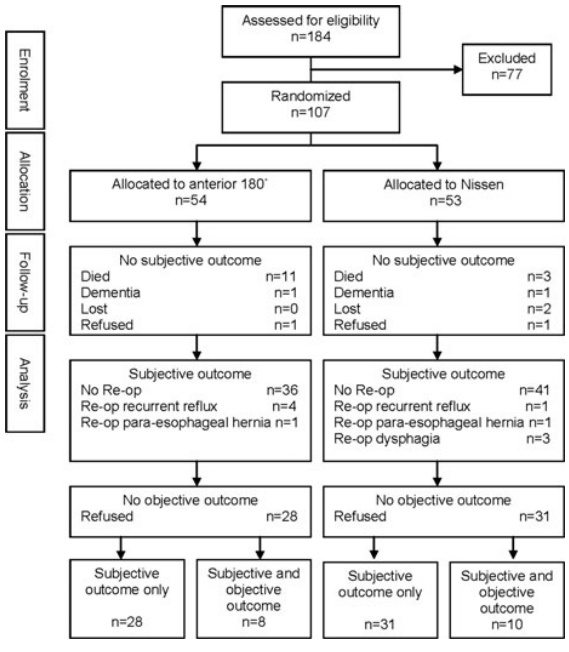


FIGURE 1. Study profile: CONSORT analysis 14-year follow-up.

in the Nissen fundoplication group (Fig. 1). Eighteen patients completed the objective study protocol and the symptom assessment, and 59 patients completed the symptom assessment only.

Clinical Outcome

Baseline characteristics (Table 1) were comparable for patients in the anterior 180-degree partial fundoplication (n = 36) and Nissen fundoplication groups (n = 41). Eight patients in the anterior 180-degree partial fundoplication group and 10 in the Nissen fundoplication group agreed to participate in the objective studies. There were no differences in reflux symptoms, dysphagia scores, gas-related symptoms, and patient satisfaction (Table 2) between participants who completed the objective study protocol (n = 18) and those who did not (n = 59).

Stationary High-Resolution Manometry and Ambulatory 24-Hour Impedance pH Study

The 18 patients completed the full research protocol. The results of these studies are summarized in Tables 3 and 4. Total esophageal acid exposure time was higher after anterior 180-degree fundoplication than after Nissen fundoplication. One out of the 8 patients in the anterior group and 7 out of the 10 patients in the Nissen group had nil esophageal acid exposure. In the patients with acid reflux, individual total esophageal acid exposure times were 5.9%, 6.5%, 7.1%, 7.5%, 16.5%, 20.2%, and 24.3% in the anterior group and 0.9%, 8.7%, and 18.1% in the Nissen group. The total number of acid and weakly acidic reflux episodes was higher after anterior 180-degree partial fundoplication than after Nissen fundoplication. Both liquid and mixed reflux episodes were more frequent in the anterior 180-degree partial fundoplication group (Table 3). The number of proximal, midesophageal, and distal reflux episodes was proportionately increased after anterior 180-degree fundoplication. Mean proximal reflux extent was not different (Table 4). The differences in the number of reflux episodes were reflected by significantly higher heartburn scores in the anterior 180-degree fundoplication group (Table 5), a difference which was also identified in the subgroup analysis of patients who completed the objective tests (Table 6).

In contrast, there were no differences in gas reflux between the 2 groups. In addition, gastric belches and belches experienced by the patient were comparable (Table 3). In line with these observations, there were no differences in gas-related symptoms between the groups for both the whole trial cohort (Table 5) and the subgroup analysis (Table 6). Supragastric belching only occurred in specific patients; it was observed in 4 patients in the anterior 180-degree fundoplication group and 6 patients in the Nissen fundoplication group. The total number of supragastric belches and the number of supragastric belches with and without reflux were similar in both groups (Table 3).

LES resting pressure [16.5 (7.6) mm Hg vs 19.2 (7.3) mm Hg; $P = 0.274$] and LES relaxation nadir pressure [8.3 (7.7) mm Hg vs 10.1 (6.3) mm Hg; $P = 0.460$) were lower after anterior 180-degree partial fundoplication than after Nissen fundoplication, but these differences did not reach statistical significance. The lower LES resting and LES relaxation nadir pressure were accompanied by a lower analog score for dysphagia for solids and the mean 0 to 45 dysphagia score after anterior fundoplication (Table 5). There were no significant differences in these scores in the subgroup that completed the objective study protocol (Table 6).

Postprandial Study

The results of the 90-minute postprandial measurement period were in line with the findings of the ambulatory study.

Intragastric Air Infusion Study

The 20-minute measurement period after intragastric air infusion yielded similar results as those obtained from the ambulatory and postprandial study.

DISCUSSION

Laparoscopic Nissen fundoplication is the most frequently performed operation for reflux disease[13,17] but is often followed by dysphagia and gas-related symptoms. A recent meta-analysis and the pooled results of 2 trials have demonstrated that posterior 270-degree partial[1] and anterior 180-degree partial fundoplication[4] reduce these symptoms and still achieve similar control of reflux symptoms at up to 5 years of follow-up. The first author recently demonstrated that gas reflux and gastric belches are reduced less after posterior partial fundoplication than after Nissen fundoplication, with similar reduction of acid and weakly acidic reflux at 6 months.[16] Cohort studies have raised concerns about the durability of the control of reflux symptoms beyond 5 years after partial fundoplication,[7–10] and such studies might have impeded wider application of these procedures. This study evaluated differences in objective outcomes at very late follow-up, 14 years after randomization, for laparoscopic anterior 180-degree partial versus Nissen fundoplication.

In this study, we have shown that acid, weakly acidic, liquid and mixed reflux episodes are more common after anterior 180-degree fundoplication than after Nissen fundoplication, and that proximal, midesophageal, and distal reflux are proportionately increased after anterior 180-degree fundoplication compared with Nissen fundoplication. These data are consistent with higher clinical heartburn scores occurring after anterior 180-degree fundoplication. In contrast, we observed no differences in gas reflux, gastric belches, and supragastric belches, which is in line with the observation that gas-related symptoms are similar for both groups. On the contrary, mean LES resting and relaxation nadir pressure are lower after anterior 180-degree fundoplication, and this is consistent with lower dysphagia scores after anterior 180-degree partial fundoplication.

Our study demonstrates that the total number of acid and weakly acidic reflux episodes at 14 years (15.0) is similar to results previously reported[16] at 6 months after Nissen fundoplication (7.4). In contrast, the total number of reflux episodes at 14 years is higher after anterior 180-degree fundoplication (40.4), with more liquid and mixed reflux episodes than after Nissen fundoplication. In addition, total esophageal acid exposure time was higher after anterior 180-degree fundoplication than after Nissen fundoplication.

However, differences in the effectiveness of antireflux surgery are determined not only by any reduction in the number of reflux episodes but also by the proximal reflux extent.[18] There were more reflux episodes after anterior 180-degree fundoplication, but mean proximal reflux extent is not higher than after Nissen fundoplication. There were no differences in objective reflux control at 6 months[6] and reflux symptoms at 5 years[4,5] and 10 years[11] between both arms of this trial. However, extension of follow-up to 14 years identified a significantly higher rate of acid and weakly acidic reflux and heartburn after anterior 180-degree fundoplication. In retrospect, mean heartburn scores did not increase from 5-year (1.8)[4,5] to 10-year (1.7)[11] to 14-year follow-up (1.4) after Nissen fundoplication. In contrast, in the anterior 180-degree arm, we observed some increase in mean heartburn scores from 5-year (1.9)[4,5] to 10-year (2.3)[11] to 14-year follow-up (2.7).

Patients with an objective reduction of gastric belches after fundoplication have higher symptom scores for inability to belch and gas bloating than patients who do not have an objective reduction of gastric belches.[19] It has recently been demonstrated that gas reflux and gastric belches are reduced less after posterior 270-degree partial

TABLE 1. Baseline Characteristics for Patients in the Anterior 180-Degree Partial Versus Nissen Fundoplication Group

	Anterior 180 Degrees (n = 36)	Nissen (n = 41)	*P*
Age (range), yr	42.3 (22–74)	46.4 (21–68)	0.169
Male/female sex	25/11	31/10	0.544
Body mass index (kg/m^2)*	27.7 (4.2)	28.7 (4.0)	0.417
Total esophageal acid exposure (%)*	13.4 (11.1)	13.0 (11.8)	0.972
Follow-up interval (yr)*	14.2 (1.0)	14.0 (1.2)	0.432

*Values are given as mean (standard deviation).

TABLE 2. Heartburn Score, Dysphagia, Gas-Related Symptoms, and Patient Satisfaction of Participants Who Completed Both the Objective and Subjective Study Protocols Versus Those Who Participated in the Subjective Study Only

	Objective and Subjective Outcomes (n = 18)	Subjective Outcome Only (n = 59)	*P*
Reflux			
Analog score for heartburn*	2.2 (2.5)	1.9 (2.7)	0.475
Dysphagia			
Analog score for dysphagia for liquids*	0.9 (1.7)	1.4 (2.5)	0.856
Analog score for dysphagia for solids*	2.0 (2.1)	2.5 (2.9)	0.911
0–45 dysphagia score*	9.6 (8.3)	8.2 (9.7)	0.358
Gas-related symptoms			
Inability to belch	2/18 (11.1%)	14/57 (24.6%)	0.225
Gas bloating	11/18 (61.1%)	26/57 (45.6%)	0.252
Inability to relieve bloating	3/18 (16.7%)	13/57 (22.8%)	0.579
Patient satisfaction			
Analog score for satisfaction*	8.4 (2.3)	7.8 (2.6)	0.240
Visick score			0.530
No symptoms	5 (27.8%)	12 (20.7%)	
Mild symptoms	10 (55.6%)	35 (60.3%)	
Moderate symptoms	1 (5.6%)	6 (10.3%)	
Symptoms interfering with life	0	3 (5.2%)	
Symptoms not improved	2 (11.1%)	2 (3.4%)	

*Values are given as mean (standard deviation).

TABLE 3. Total Esophageal Acid Exposure Time, Number of Liquid-Containing Reflux Episodes, Gas Reflux, and Belches per 24 Hours After Anterior 180-Degree Partial Versus Nissen Fundoplication

	Anterior 180 Degrees (n = 8)	Nissen (n = 10)	*P*
Total esophageal acid exposure time (%)	11.0 (8.3)	2.8 (6.0)	0.027
Total reflux episodes	40.4 (38)	15.0 (19)	0.043
Liquid reflux	24.0 (24)	11.4 (17)	0.146
Mixed reflux	16.4 (15)	3.6 (3.2)	0.043
Gas reflux	37.8 (15)	55.8 (50)	0.829
Gastric belches	51.4 (26)	57.0 (50)	0.999
Belches experienced by the patient	4.1 (4.1)	4.0 (4.5)	0.897
Supragastric belches (Anterior, n = 4; Nissen, n = 6)	21.3 (21)	30.3 (25)	0.762
With reflux	5.0 (3.5)	4.3 (9.7)	0.114
Without reflux	16.3 (21)	26.0 (24)	0.476

fundoplication, resulting in fewer gas-related symptoms than after Nissen fundoplication at 6 months.[16]

The long-term results evaluated in our current study were different. The number of gas reflux episodes at 14 years after anterior 180-degree (37.8) and Nissen fundoplication (55.8) was similar to the preoperative numbers described[16] for Nissen fundoplication (36.3). At 14 years, the number of gastric belches after anterior 180-degree (51.4) and Nissen fundoplication (57.0) was also comparable with the preoperative numbers reported[16] for Nissen fundoplication (67.8). These results indicate that short-term differences in gas reflux and gastric belches disappear over time, because gas reflux and belches have increased to preoperative values in both groups at 14 years. This would suggest that with time fundoplications become more compliant to the passage of air. The fact that fundoplication controls reflux

TABLE 4. Extent of Liquid-Containing Reflux Events per 24 Hours and Mean Proximal Reflux Extent After Anterior 180-Degree Partial Versus Nissen Fundoplication

	Anterior 180 Degrees (n = 8)	Nissen (n = 10)	*P*
Proximal reflux	9.4 (10)	2.8 (5.2)	0.021
Midesophageal reflux	25.0 (26)	8.7 (8.5)	0.055
Distal reflux	6.0 (4.1)	3.5 (6.0)	0.068
Mean proximal reflux extent (cm)	8.5 (3.5)	8.7 (1.6)	0.460

TABLE 5. Heartburn Score, Dysphagia, Gas-Related Symptoms, and Patient Satisfaction After Anterior 180-Degree Partial Versus Nissen Fundoplication

	Anterior 180 Degrees (n = 36)	Nissen (n = 41)	*P*
Analog score for heartburn*	2.5 (2.6)	1.5 (2.6)	0.018
Dysphagia			
Analog score for dysphagia for liquids*	1.2 (2.2)	1.3 (2.4)	0.754
Analog score for dysphagia for solids*	1.8 (2.5)	2.9 (2.8)	0.028
0–45 dysphagia score*	5.4 (7.0)	11.3 (10)	0.006
Gas-related symptoms			
Inability to belch	6/35 (17.1%)	10/40 (25.0%)	0.407
Gas bloating	15/35 (42.9%)	22/40 (55.0%)	0.294
Inability to relieve bloating	5/35 (14.3%)	11/40 (27.5%)	0.163
Analog score for satisfaction*	8.3 (2.1)	7.6 (2.8)	0.324
Visick score			0.645
No symptoms	8 (22.2%)	9 (22.5%)	
Mild symptoms	22 (61.1%)	23 (57.5%)	
Moderate symptoms	2 (5.6%)	5 (12.5%)	
Symptoms interfering with life	1 (2.8%)	2 (5.0%)	
Symptoms not improved	3 (8.3%)	1 (2.5%)	

*Values are given as mean (standard deviation).

TABLE 6. Heartburn Score, Dysphagia, Gas-Related Symptoms, and Patient Satisfaction of Participants Who Completed Both the Objective and the Subjective Study Protocols After Anterior 180-Degree Partial Versus Nissen Fundoplication

	Anterior 180 Degrees (n = 8)	Nissen (n = 10)	*P*
Reflux			
Analog score for heartburn*	4.1 (2.4)	0.6 (1.1)	0.001
Dysphagia			
Analog score for dysphagia for liquids*	1.0 (1.9)	0.9 (1.6)	0.762
Analog score for dysphagia for solids*	2.8 (2.4)	1.4 (1.6)	0.203
0–45 dysphagia score*	11.8 (9.0)	7.9 (7.7)	0.360
Gas-related symptoms			
Inability to belch	1/8 (12.5%)	1/10 (10.0%)	0.867
Gas bloating	6/8 (75.0%)	5/10 (50.0%)	0.280
Inability to relieve bloating	1/8 (12.5%)	2/10 (20.0%)	0.671
Patient satisfaction			
Analog score for satisfaction*	7.3 (2.8)	9.4 (1.1)	0.034
Visick score			0.201
No symptoms	1 (12.5%)	4 (40.0%)	
Mild symptoms	5 (62.5%)	5 (50.0%)	
Moderate symptoms	0	1 (10.0%)	
Symptoms interfering with life	0	0	
Symptoms not improved	2 (25.0%)	0	

*Values are given as mean (standard deviation).

without impairing venting of air from the stomach at 14 years can be explained by the observation that the low viscosity of air facilitates passage through a competent esophagogastric junction compared with liquids.[20] In earlier reports of clinical outcomes from our randomized trial, we reported significantly more inability to belch, gas bloating, and inability to relieve bloating at 6 months[6] and 5 years[4,5] after Nissen fundoplication. Our current study demonstrated no differences in these gas-related symptoms at 14 years. Moreover, the rate of gas bloating (42.9% vs 55.0%) and inability to relieve bloating (14.3% vs 27.5%) were similar compared with preoperative rates of gas bloating (51.9% vs 49.0%) and inability to relieve bloating (20.4% vs 18.9%) reported[6] for the anterior 180-degree fundoplication versus Nissen

fundoplication. The finding that gas reflux and gastric belches have returned to preoperative values at 14 years explains why gas-related symptoms return to preoperative rates in both groups. In sharp contrast to gastric belches, supragastric belches are esophageal belches that do not allow air venting from the stomach.[21] Fundoplications alter the belching pattern by reducing gastric belching and increasing supragastric belching at 6 months.[16] Supragastric belches at 14 years after anterior 180-degree (21.3) and Nissen fundoplication (30.3) were similar to the preoperative quantities recorded[16] for Nissen fundoplication (34.2) elsewhere.

A recent meta-analysis found that at 1 year, lower esophageal sphincter relaxation is more likely to be incomplete after posterior than anterior partial fundoplication.[22] This study demonstrates that at 14 years, both lower esophageal sphincter resting and relaxation nadir pressure are reduced after anterior 180-degree fundoplication compared with Nissen fundoplication. It has previously been demonstrated that esophageal sphincter relaxation nadir pressure is the only standard manometry parameter correlated with postfundoplication dysphagia.[23,24] In this study, the reduced esophageal sphincter relaxation pressure after anterior 180-degree fundoplication was also reflected by lower dysphagia scores than after Nissen fundoplication. Overall, patient satisfaction was stable throughout follow-up and similar in the anterior 180-degree and Nissen groups: at 5 years, 8.7 versus 8.0[4,5]; at 10 years, 8.3 versus 8.2[11]; and at 14 years, 8.3 versus 7.6. We can only speculate as to why this might be, given the poorer outcome in terms of reflux control with anterior fundoplication. Perhaps the lower rate of dysphagia complaints, or control of preoperative volume reflux, or ability to control reflux symptoms with less medications than before surgery may all play a role. We did not explore these latter possibilities, however.

A limitation of this study is that most of the patients who completed subjective follow-up would not undergo the extensive objective study protocol. This could lead to selection bias. However, the risk of selection bias was minimized by demonstrating equivalent clinical outcome scores in patients who underwent objective studies versus those who did not. The sample size of the objective study protocol, however, was small, but large differences between both groups were expected after 14 years and, indeed, statistically significant differences were found. We acknowledge that the possibility of both types of statistical error is real in the subgroup of patients who underwent objective testing. However, the differences in objective outcome observed in this subset were confirmed by corresponding differences in subjective outcome recorded for the whole group.

In conclusion, this study demonstrates that at 14 years after randomization, acid, weakly acidic, liquid and mixed reflux episodes are more common after anterior 180-degree fundoplication than after Nissen fundoplication. Proximal, midesophageal, and distal reflux are proportionately increased after anterior 180-degree fundoplication, which is accompanied by higher clinical heartburn scores than that after Nissen fundoplication. In contrast, there were no differences in gas reflux, gastric belches, and supragastric belches, which is in line with the observation that gas-related symptoms were similar for both groups. On the contrary, mean LES resting and relaxation nadir pressure are lower after anterior 180-degree fundoplication, which is reflected by lower dysphagia scores. Patient satisfaction is similar after both procedures. Overall, these findings suggest less effective reflux control after anterior 180-degree partial fundoplication, offset by less dysphagia, leading to a clinical outcome which is equivalent to Nissen fundoplication at late follow-up. No doubt, some may take these findings as strongly supporting the role of a total fundoplication for all patients having antireflux surgery. We take the view that these long-term results support tailoring of fundoplication according to age, performing a total fundoplication in younger patients to ensure durable reflux control and an anterior 180-degree partial fundoplication in older patients to minimize dysphagia. Nevertheless, the similarity in patient satisfaction scores and the small numbers involved in the objectively tested groups mean that we cannot make definitive statements about the best antireflux operation.

ACKNOWLEDGMENTS

The authors thank Marcus Tippett, for assisting the stationary high-resolution esophageal manometries and 24-hour impedance-pH monitoring studies, and Lorelle Smith, Janet Sullivan, and Nicky Carney, for maintaining the prospective database.

REFERENCES

1. Broeders JA, Mauritz FA, Ahmed AU, et al. Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. *Br J Surg*. 2010;97:1318–1330.
2. Catarci M, Gentileschi P, Papi C, et al. Evidence-based appraisal of antireflux fundoplication. *Ann Surg*. 2004;239:325–337.
3. Varin O, Velstra B, De SS, et al. Total vs partial fundoplication in the treatment of gastroesophageal reflux disease: a meta-analysis. *Arch Surg*. 2009;144:273–278.
4. Broeders JA, Roks DJ, Jamieson GG, et al. Five-year outcome after laparoscopic anterior partial versus Nissen fundoplication: four randomized trials. *Ann Surg*. 2012;255:637–642.
5. Ludemann R, Watson DI, Jamieson GG, et al. Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180 degrees fundoplication. *Br J Surg*. 2005;92:240–243.
6. Watson DI, Jamieson GG, Pike GK, et al. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg*. 1999;86:123–130.
7. Dallemagne B, Weerts J, Markiewicz S, et al. Clinical results of laparoscopic fundoplication at ten years after surgery. *Surg Endosc*. 2006;20:159–165.
8. Fein M, Bueter M, Thalheimer A, et al. Ten-year outcome of laparoscopic antireflux surgery. *J Gastrointest Surg*. 2008;12:1893–1899.
9. Horvath KD, Jobe BA, Herron DM, et al. Laparoscopic Toupet fundoplication is an inadequate procedure for patients with severe reflux disease. *J Gastrointest Surg*. 1999;3:583–591.
10. Patti MG, Robinson T, Galvani C, et al. Total fundoplication is superior to partial fundoplication even when esophageal peristalsis is weak. *J Am Coll Surg*. 2004;198:863–869.
11. Cai W, Watson DI, Lally CJ, et al. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180 (degrees) partial fundoplication. *Br J Surg*. 2008;95:1501–1505.
12. Mardani J, Lundell L, Engstrom C. Total or posterior partial fundoplication in the treatment of GERD results of a randomized trial after 2 decades of follow-up. *Ann Surg*. 2011;253:875–878.
13. Draaisma WA, Rijnhart-de Jong HG, Broeders IA, et al. Five-year subjective and objective results of laparoscopic and conventional Nissen fundoplication: a randomized trial. *Ann Surg*. 2006;244:34–41.
14. Broeders JA, Bredenoord AJ, Hazebroek EJ, et al. Effects of anti-reflux surgery on weakly acidic reflux and belching. *Gut*. 2011;60:435–441.
15. Bredenoord AJ, Draaisma WA, Weusten BL, et al. Mechanisms of acid, weakly acidic and gas reflux after anti-reflux surgery. *Gut*. 2008;57:161–166.
16. Broeders JA, Bredenoord AJ, Hazebroek EJ, et al. Reflux and belching after 270 degree versus 360 degree laparoscopic posterior fundoplication. *Ann Surg*. 2012;255:59–65.
17. Broeders JA, Rijnhart-de Jong HG, Draaisma WA, et al. Ten-year outcome of laparoscopic and conventional Nissen fundoplication: randomized clinical trial. *Ann Surg*. 2009;250:698–706.
18. Bredenoord AJ, Weusten BL, Curvers WL, et al. Determinants of perception of heartburn and regurgitation. *Gut*. 2006;55:313–318.
19. Straathof JW, Ringers J, Lamers CB, et al. Provocation of transient lower esophageal sphincter relaxations by gastric distension with air. *Am J Gastroenterol*. 2001;96:2317–2323.
20. Pandolfino JE, Shi G, Trueworthy B, Kahrilas PJ. Esophagogastric junction opening during relaxation distinguishes nonhernia reflux patients, hernia patients, and normal subjects. *Gastroenterology*. 2003;125:1018–1024.

21. Bredenoord AJ, Weusten BL, Sifrim D, et al. Aerophagia, gastric, and supragastric belching: a study using intraluminal electrical impedance monitoring. *Gut.* 2004;53:1561–1565.
22. Broeders JA, Roks DJ, Ali UA, et al. Laparoscopic anterior versus posterior fundoplication for gastroesophageal reflux disease systematic review and meta-analysis of randomized clinical trials. *Ann Surg*. 2011;254:39–47.
23. Mathew G, Watson DI, Myers JC, et al. Oesophageal motility before and after laparoscopic Nissen fundoplication. *Br J Surg*. 1997;84: 1465–1469.
24. Scheffer RC, Samsom M, Frakking TG, et al. Long-term effect of fundoplication on motility of the oesophagus and oesophagogastric junction. *Br J Surg*. 2004;91:1466–1472.

RANDOMIZED CLINICAL TRIAL

Five-Year Outcome After Laparoscopic Anterior Partial Versus Nissen Fundoplication

Four Randomized Trials

Joris A. Broeders, MD, PhD, David J. Roks, MD,* Glyn G. Jamieson, MBBS, MS, FRACS,* Peter G. Devitt, MBBS, MS, FRCS, FRACS,* Robert J. Baigrie, MBBS, MD, FRCS,† and David I. Watson, MBBS, MD, FRACS‡*

Objective: To compare longer term (5-year) outcomes for reflux control and postsurgery side effects after laparoscopic anterior (90° and 180°) partial versus Nissen fundoplication for gastroesophageal reflux.

Background: Laparoscopic Nissen fundoplication is the most frequently performed surgical procedure for gastroesophageal reflux. It achieves excellent control of reflux, but in some patients it is followed by troublesome side effects. To reduce the risk of side effects laparoscopic anterior partial fundoplication variants have been advocated, although some studies suggest poorer reflux control.

Methods: From 1995 to 2003, 461 patients with gastroesophageal reflux were enrolled in 4 randomized controlled trials comparing anterior partial versus Nissen fundoplication. Two trials evaluated anterior 180° and 2 anterior 90° partial fundoplication. The original trial data were combined, and a reanalysis from original data was undertaken to determine outcomes at 5 years follow-up. Reflux symptom control and side effects were evaluated in a blinded fashion using standardized questionnaires, including 0 to 10 analog scores (0 = no symptoms, 10 = severe symptoms).

Results: At 5 years, patients who underwent an anterior 90° or 180° partial fundoplication had less side effects than those who underwent Nissen fundoplication and were equally satisfied with the overall outcome. Reflux control, measured by heartburn scores and antisecretory medication use, was similar for anterior 180° partial versus Nissen fundoplication, but inferior after anterior 90° partial versus Nissen fundoplication.

Conclusions: Anterior 180° partial fundoplication achieves durable control of reflux symptoms and fewer side effects compared with Nissen fundoplication. Reflux control after anterior 90° partial fundoplication appears less effective than after Nissen fundoplication. This data supports the use of anterior 180° partial fundoplication for the surgical treatment of gastroesophageal reflux.

(*Ann Surg* 2012;255:637–642)

Laparoscopic fundoplication is the surgical approach of choice for the treatment of gastroesophageal reflux disease. It achieves similar long-term reflux control, with less short and long-term problems, compared with open fundoplication.[1] Laparoscopic Nissen fundoplication is the most frequently performed antireflux operation and alters the anatomy of the gastroesophageal junction. The gastroesophageal junction serves 3 functions. The first is to allow swallowed solids and liquids to pass from esophagus to the stomach. The second is to allow venting of gas from the stomach to the mouth (ie, belching), and the third function is to prevent the backward flow of gastric contents into the esophagus (ie, gastroesophageal reflux). Nissen fundoplication restores the third function and provides excellent reflux control.[1–3] However, it delivers a supracompetent valve, which can impair the first 2 functions. Three meta-analyses have demonstrated that Nissen fundoplication is followed by a significant incidence of troublesome postfundoplication side effects, including troublesome postoperative dysphagia and gas-related problems.[4–6]

Laparoscopic partial fundoplication procedures have been proposed as alternatives and aim to reduce the incidence of postfundoplication side effects. Recently published American guidelines for antireflux surgery state that partial fundoplication provides similar 5-year reflux control, but with less postoperative dysphagia and fewer reoperations than Nissen fundoplication.[7] The guidelines suggested that laparoscopic anterior partial fundoplication may be less effective in the long-term. However, there may be important differences between different anterior partial fundoplication variants (eg, 90° vs 120° vs 180°), and therefore generalizing all anterior partial fundoplication procedures into a single category might not be appropriate. Furthermore, specific differences between different anterior partial fundoplication variants are not well understood. A recent meta-analysis also pooled anterior 90°, 120°, and 180° partial fundoplications, and compared this group to pooled results of posterior 180°, 200°, and Nissen fundoplication.[8] This analysis also suggested that reflux control for the pooled anterior fundoplication types was inferior to the pooled results of the posterior and Nissen fundoplication procedures.[8] However, this analysis failed to recognize and consider important differences between the fundoplication subtypes, and that technical differences might be important for achieving good clinical outcomes. Furthermore, this meta-analysis did not access raw data from the original trials. Hence, it is not appropriate to extrapolate its conclusions to specific fundoplication procedures.

To overcome the problems inherent in previous studies, we combined raw data sets from 4 randomized controlled trials of laparoscopic anterior partial versus laparoscopic Nissen fundoplication, and used the original data to determine the clinical outcomes at 5 years follow-up. Two of the trials compared anterior 90° partial with Nissen fundoplication,[9,10] and 2 compared anterior 180° with Nissen fundoplication.[11,12] These combined data sets allowed randomized comparisons of both anterior partial fundoplication variants with Nissen fundoplication.

METHODS

Study Design and Participants

Data sets from 4 previously reported randomized controlled trials of anterior 180°[11,12] or anterior 90°[9,10] partial fundoplication versus Nissen fundoplication were combined and reanalyzed (Fig. 1).

From the *Discipline of Surgery, University of Adelaide, Royal Adelaide Hospital, Adelaide, South Australia; †Gastrointestinal Surgical Unit, Kingsbury Hospital, University of Cape Town, Cape Town, South Africa; and ‡Flinders University Department of Surgery, Flinders Medical Centre, Bedford Park, South Australia.

Disclosure: The authors declare no conflict of interest.

Reprints: Joris A.J.L. Broeders, MD, PhD, Department of Surgery, Royal Adelaide Hospital, Level 5, Eleanor Harrald Building, Adelaide, South Australia 5000, Australia. E-mail: joris.broeders@adelaide.edu.au.

ISSN: 0003-4932/12/25504-0637
DOI: 10.1097/SLA.0b013e31824b31ad

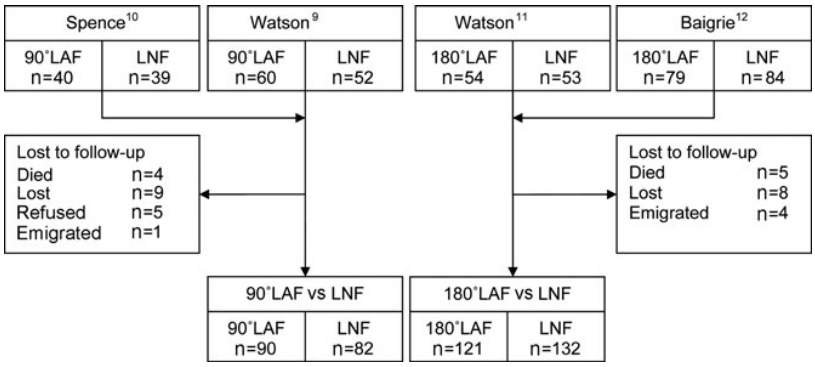


FIGURE 1. Study profile: CONSORT analysis 5-year follow-up for the anterior 90° partial (90° LAF), anterior 180° partial (180° LAF), and Nissen fundoplication (LNF) groups.

Patients presenting for primary antireflux surgery from 1995 to 2003 were recruited into these trials. Two trials compared anterior 90° partial versus Nissen fundoplication[9,10] and 2 compared anterior 180° partial versus Nissen fundoplication.[11,12] Five-year outcome data for 2 of the trials has been reported previously.[13,14]

All trials used a common methodology. Procedures were standardized across all centers, follow-up was undertaken in a blinded fashion, and common standardized symptom and outcome scores were used in all studies. All enrolled patients had objective evidence of gastroesophageal reflux disease at either 24-hour pH monitoring (pH < 4 for more than 7% of time) or upper endoscopy (ulcerative esophagitis).[9–12] Three hundred ninety-three patients underwent laparoscopic fundoplication in either Adelaide, South Australia,[9–11] or in Cape Town, South Africa.[12] Sixty-eight patients underwent surgery elsewhere in Australia or New Zealand within a multicentre trial of anterior 90° versus Nissen fundoplication, which was coordinated from Adelaide.[9] The lead clinician in the South African study worked in Adelaide in 1995 and participated in the development of the first anterior 180° partial versus Nissen fundoplication trial undertaken in Adelaide.[11] He applied the same surgical techniques, clinical outcome scores, and follow-up methodology in the South African trial.

Exclusion criteria were age less than 18 years or more than 75 years, esophageal motility disorders that precluded Nissen fundoplication, contemporaneous abdominal procedures, and previous gastric or esophagogastric junction surgery. Data for preoperative work-up, perioperative care and follow-up was collected prospectively and entered into computerized databases. Follow-up was undertaken yearly by "blinded" research nurses. The human research ethics committees of the hospitals in which surgery was undertaken approved the protocols of all trials.

Surgical Procedures

In each trial, patients were randomized 1:1 to undergo either anterior (90° or 180°) partial or Nissen fundoplication. All procedures were commenced laparoscopically. The surgical techniques have been described in detail elsewhere.[9–12] The initial steps for all 3 types of fundoplication were identical: hiatal dissection with minimal use of diathermy, preservation of the hepatic branch of the vagus nerve, mobilization of the distal esophagus and routine posterior hiatal repair. Short gastric blood vessels were not routinely divided, except in patients undergoing Nissen fundoplication in one of the 4 trials.[9]

Laparoscopic anterior 90° partial fundoplication was fashioned by first stabilizing the intra-abdominal esophagus with a posterior esophagopexy suture. The angle of His was then accentuated by placing 2 sutures between the left side of the esophagus and the adjacent gastric fundus—the upper suture also incorporating the hiatal rim. Next, the gastric fundus was sutured loosely over the left side and the front of the esophagus using an apical suture that anchored the fundus to the anterior esophagus and the apex of the hiatal rim in the midline. The inferior edge of the fundal fold was also sutured to the anterior esophagus in the midline.[9,10] Laparoscopic anterior 180° partial fundoplication was constructed by suturing the anterior fundal wall to the right and left hiatal pillars and the apex of the hiatal rim using 5 to 6 sutures.[11,12] The key difference between the 2 anterior partial fundoplication techniques was that the fundus was anchored to the right hiatal pillar during anterior 180° fundoplication, but not during anterior 90° fundoplication. Laparoscopic Nissen fundoplication entailed construction of a loose 1- and 2-cm long 360° fundoplication with a 52 to 60 Fr intraesophageal bougie present to help ensure a tension-free wrap.[9–12,15] Three sutures were used to secure the wrap.[9–12,15]

Clinical Outcomes

Preoperative, perioperative, and follow-up data were collected prospectively. Follow-up entailed the application of a standardized set of questions, administered each year by either postal questionnaire or telephone interview, 5-year follow-up data was analyzed. Other events during the follow-up period, such as endoscopic dilatation for dysphagia or surgical reoperation, were also identified prospectively and recorded. Visual analog scores were used to assess symptoms. Heartburn was evaluated using an analog score (0 = no heartburn; 10 = severe heartburn) and by determining the use of antisecretory medications. The presence of dysphagia (yes/no question) and analog scores for solids and liquids (0 = no dysphagia; 10 = severe dysphagia) were recorded. A validated 0 to 45 dysphagia score[16] was used to quantify the ability to swallow 9 types of liquids and solids (0 = no dysphagia; 45 = severe dysphagia).[17] Patients were also asked whether they were able to eat a normal diet. Gas-related symptoms were assessed by yes/no questions, which determined the ability to belch, presence of abdominal bloating symptoms, ability to relieve bloating by belching, and increased flatulence. Patient satisfaction was scored using an analog score (0 = dissatisfied; 10 = satisfied) and a Visick score (1 = no symptoms; 2 = mild symptoms; 3 = moderate symptoms; 4 = moderate symptoms interfering with life; 5 = symptoms as bad or worse after surgery).[17] Patients were also asked whether they still regarded their initial decision to undergo surgery to be correct.

Statistical Analysis

Statistical analysis was performed using SPSS version 17.0 (SPSS inc, Chicago, IL). Data were analyzed according to the intention-to-treat principle. Continuous variables were expressed as mean ± standard deviation [SD], and groups were compared using the Mann-Whitney *U* test. Ordinal variables were expressed as percentages, and differences between groups were analyzed using the χ^2 test. Differences in the number of patients undergoing endoscopic

dilatation for dysphagia or reoperation were determined using Kaplan-Meier survival curves with log-rank tests.

RESULTS

A total of 461 patients were enrolled in the 4 randomized controlled trials and underwent either laparoscopic anterior partial fundoplication (n = 233) or laparoscopic Nissen fundoplication (n = 228) for gastroesophageal reflux. A 5-year outcome was available for 434 (94.1%). Nine (2.0%) patients died during follow-up, and clinical outcome scores were available for 425 (92.2%) patients 5 years after surgery—anterior partial (n = 211), Nissen fundoplication (n = 214). Full details of patient follow-up are summarized in Figure 1. Data were available from a subset of 172 patients for comparison of anterior 90° partial (n = 90) versus Nissen fundoplication (n = 82), and from 253 patients for comparison of anterior 180° partial (n = 121) versus Nissen fundoplication (n = 132). Baseline patient characteristics were similar for the anterior partial and fundoplication Nissen groups (Table 1).

Anterior 90° Partial Versus Nissen Fundoplication

Outcomes at 5 years for anterior 90° partial versus Nissen fundoplication are summarized in Table 2. Heartburn scores were higher after anterior 90° partial fundoplication, and the use of antisecretory medication was more common. However, dysphagia was less common, more patients were able to eat a normal diet, the mean analog score for dysphagia for solid food was lower, and the mean 0 to 45 dysphagia score was lower after anterior 90° partial fundoplication. Gas-related symptoms were less common after anterior 90° partial fundoplication, with better preserved ability to belch, and less flatulence. All measures of overall satisfaction with the outcome of surgery were similar for the 2 procedures.

There were no significant differences in the number of endoscopic dilatations performed for dysphagia (2.0% vs 6.0%; $P = 0.202$) or the overall number of reoperations (10.0% vs 4.9%; $P = 0.212$) undertaken within the 5-year follow-up period (Fig. 2). In the group that underwent anterior 90° partial fundoplication, most reoperations were performed for recurrent reflux (6.7%), whereas in the Nissen fundoplication group, most reoperations were for dysphagia (3.7%).

TABLE 1. Baseline Characteristics of Patients According to Treatment Group

	Anterior 90° vs Nissen Fundoplication		Anterior 180° vs Nissen Fundoplication	
	Anterior 90°	**Nissen**	**Anterior 180°**	**Nissen**
Patients (n)	90	82	121	132
Age (yr)	46.5 (22–76)	47.7 (22–72)	44.9 (20–74)	44.7 (16–71)
Male/female sex	52/38	48/34	72/49	82/50
Body mass index (kg/m^2)*	29.5 [5.1]	30.0 [5.7]	27.7 [4.3]	30.0 [6.6]
Follow-up interval (mo)*	64.7 [9.6]	63.2 [8.2]	67.7 [10.1]	67.4 [9.6]

*Values are given as mean [SD].

TABLE 2. Symptomatic Outcome at 5 Years After Anterior 90° and Nissen Fundoplication

	Anterior 90°	**Nissen**	***P*-value**
Reflux symptoms			
Analog heartburn score*	2.2 [2.5] (n = 78)	1.6 [2.5] (n = 73)	0.043
Use of antisecretory drugs	29/84 [34.5%]	9/76 [11.8%]	0.001
Dysphagia			
Dysphagia	26/84 [30.9%]	38/76 [50.0%]	0.014
Analog score for dysphagia for liquids*	0.7 [1.6] (n = 90)	1.2 [2.5] (n = 82)	0.399
Analog score for dysphagia for solids*	1.6 [2.4] (n = 89)	2.9 [3.0] (n = 81)	0.001
0–45 Dysphagia score*	6.4 [8.3] (n = 90)	10.8 [11.0] (n = 82)	0.007
Normal diet	83/87 [95.4%]	68/82 [82.9%]	0.009
Dilatation for dysphagia	2/90 [2.2%]	5/82 [6.1%]	0.202
Gas-related symptoms			
Inability to belch	3/87 [3.4%]	29/82 [35.4%]	<0.001
Gas bloating	48/89 [53.9%]	47/82 [57.3%]	0.656
Inability to relieve bloating	32/64 [50.0%]	26/61 [42.6%]	0.408
Increased flatulence	36/88 [40.9%]	55/82 [67.1%]	0.001
Patient satisfaction			
Analog score for satisfaction*	7.3 [3.3] (n = 90)	7.5 [3.0] (n = 82)	0.975
Correct decision for surgery?	72/87 [82.8%]	68/81 [84.0%]	0.836
Visick score			0.404
1 (no symptoms)	24 [27.6%]	17 [20.7%]	
2 (mild symptoms)	36 [41.4%]	37 [45.1%]	
3 (moderate symptoms)	7 [8.0%]	7 [8.5%]	
4 (symptoms interfering with life)	8 [9.2%]	14 [17.1%]	
5 (symptoms not improved)	12 [13.8%]	7 [8.5%]	
Visick 1 and 2 (no or mild symptoms)	60/87 [69.0%]	54/82 [65.9%]	0.666

*Values are gives as mean [SD].

Anterior 180° Partial Versus Nissen Fundoplication

The outcomes at 5 years for anterior 180° partial versus Nissen fundoplication are summarized in Table 3. Heartburn scores and the use of antisecretory medication were similar for the 2 procedures. Dysphagia was less common after anterior 180° partial fundoplication, the mean analog scores for dysphagia for solids and liquids was lower, and the mean 0 to 45 dysphagia score was lower after anterior 180° partial fundoplication. Gas-related symptoms were also less common after anterior 180° partial fundoplication, belching ability and the ability to relieve bloating were better preserved, and flatulence was less troublesome. All measures of overall satisfaction with the outcome of surgery were similar for the 2 procedures.

There were no significant differences in the number of endoscopic dilatations performed for dysphagia (2.0% vs 5.0%; $P = 0.191$) or the overall number of reoperations (9.9% vs 6.1%; $P = 0.256$) undertaken (Fig. 2). In the group that underwent anterior 180° partial fundoplication most reoperations were performed for recurrent reflux (7.4%), whereas in the Nissen fundoplication group most reoperations were for dysphagia (6.1%).

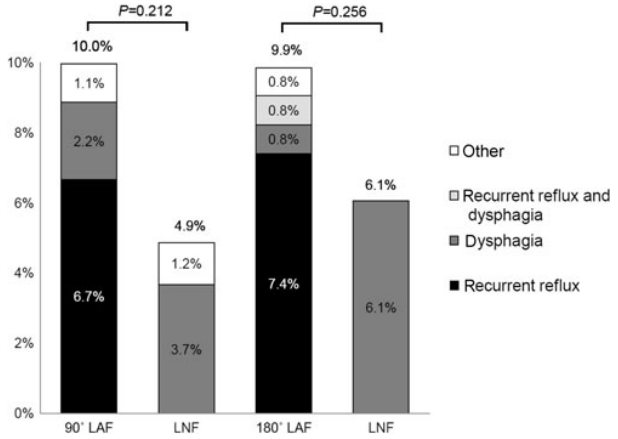


FIGURE 2. Reoperation rate and indications for reoperation at 5 years after anterior 90° partial (90° LAF) versus Nissen fundoplication (LNF), and anterior 180° partial (180° LAF) versus Nissen fundoplication (LNF).

DISCUSSION

Antireflux surgery aims to provide durable reflux control with minimal postfundoplication side effects. In general, for most patients this is achieved, although some are troubled by side effects. To minimize the risk of side effects, routine use of a partial fundoplication has been proposed. However, the perception that there is a paucity of long-term follow-up data for antireflux surgery has recently led to published American guidelines for the surgical treatment of reflux recommending "controlled studies with long-term follow-up" to determine the surgical therapy of choice.[7] Long-term follow-up data is available in many relevant randomized controlled trials,[13,14,18,19] and excellent outcomes have been demonstrated for anterior partial fundoplication variants in randomized controlled trials at 5 and 10 years follow-up.[13,14,18] In contrast, the 5-year outcomes of another trial has suggested inferior reflux control after anterior partial fundoplication.[19] In our current study, we provide further analysis of long-term outcome data from 4 randomized controlled trials, and by combining the 5-year outcome data sets for further analysis of the original data we have accessed the largest randomized controlled data set, which evaluates anterior partial versus Nissen fundoplication. The American guidelines for antireflux surgery correctly conclude that differences in outcome between anterior 90° and 180° partial fundoplication have not been investigated.[7] To identify potential differences in outcome between the anterior fundoplication subtypes,

TABLE 3. Symptomatic Outcome at 5 Years After Anterior 180° and Nissen Fundoplication

	Anterior 180°	Nissen	*P*
Reflux symptoms			
Analog heartburn score*	1.8 [2.7] (n = 120)	1.6 [2.7] (n = 132)	0.316
Use of antisecretory drugs	2/51 [3.9%]	4/52 [7.7%]	0.414
Dysphagia			
Dysphagia	8/38 [21.1%]	19/33 [57.6%]	0.002
Analog score for dysphagia for liquids*	0.5 [1.4] (n = 121)	1.2 [1.8] (n = 132)	<0.001
Analog score for dysphagia for solids*	1.3 [2.1] (n = 121)	2.5 [2.8] (n = 131)	<0.001
0–45 Dysphagia score*	5.3 [7.3] (n = 120)	8.8 [9.5] (n = 132)	0.003
Normal diet	106/119 [89.1%]	114/131 [87.0%]	0.618
Dilatation for dysphagia	2/121 [1.7%]	6/132 [4.5%]	0.191
Gas-related symptoms			
Inability to belch	19/120 [15.8%]	46/132 [34.8%]	0.001
Gas bloating	63/120 [52.5%]	77/132 [58.3%]	0.352
Inability to relieve bloating	30/100 [30.0%]	55/123 [44.7%]	0.024
Increased flatulence	57/110 [51.8%]	79/119 [66.4%]	0.025
Patient satisfaction			
Analog score for satisfaction*	8.5 [2.2] (n = 119)	8.2 [2.8] (n = 130)	0.643
Correct decision for surgery?	107/116 [92.2%]	111/124 [89.5%]	0.465
Visick score			0.254
1 (no symptoms)	55 [47.4%]	51 [39.5%]	
2 (mild symptoms)	41 [35.3%]	54 [41.9%]	
3 (moderate symptoms)	13 [11.2%]	10 [7.8%]	
4 (symptoms interfering with life)	5 [4.3%]	6 [4.7%]	
5 (symptoms not improved)	2 [1.7%]	8 [6.2%]	
Visick 1 and 2 (no or mild symptoms)	96/116 [82.8%]	105/129 [81.4%]	0.781

*Values are gives as mean [SD].

we stratified and compared these subtypes separately with Nissen fundoplication in a randomized fashion.

At 5 years follow-up, control of heartburn symptoms were similar for anterior 180° partial versus Nissen fundoplication, but inferior for anterior 90° fundoplication versus Nissen fundoplication. The use of antisecretory medication after anterior 180° partial fundoplication was similar to Nissen fundoplication, but more common after anterior 90° partial fundoplication versus Nissen fundoplication. This supports the contention that anterior 90° partial fundoplication creates a less effective antireflux barrier than the Nissen fundoplication. It should be noted, however, that use of antisecretory medication does not imply that all patients using these medications have recurrent reflux. Earlier studies have demonstrated that only a small proportion of these patients have abnormal esophageal acid exposure on pH monitoring[1,2,20] or endoscopic evidence of fundoplication disruption.[3] Others have demonstrated that approximately two thirds of patients who take these medications after fundoplication, use them for atypical symptoms, unrelated to the original symptoms, or use medication in combination with nonsteroidal anti-inflammatory agents for gastric mucosal protection.[1,20] The use of antisecretory medications should therefore only be interpreted as a "relative" indicator of recurrent reflux.[1,20] Both anterior 90° and 180° partial fundoplications were associated with less dysphagia and gas-related symptoms compared with Nissen fundoplication, and the extent of the reduction in this problem was similar for both anterior partial fundoplication procedures. Consistent with these outcomes was a higher incidence of reoperation for recurrent reflux after anterior partial fundoplication, a higher incidence of reoperation for dysphagia after Nissen fundoplication, even though the overall number of operative revision procedures were not significantly different for all procedures. Measures of overall patient satisfaction were not significantly different for both types of anterior partial fundoplication and Nissen fundoplication. Overall, this suggests that the best clinical outcome at 5 years follow-up was achieved after anterior 180° partial fundoplication.

The long-term differences in postfundoplication symptoms between anterior and Nissen fundoplication are supported by studies that have evaluated physiological effects of fundoplication. Impaired lower esophageal sphincter relaxation correlates with postfundoplication dysphagia.[21,22] A recent meta-analysis suggested that lower esophageal sphincter relaxation is more likely to be incomplete after posterior than anterior partial fundoplication.[8] This is probably a consequence of placement of the stomach behind the intra-abdominal esophagus, and this mechanism probably contributes to the higher incidence of dysphagia after Nissen fundoplication. Furthermore, it is commonly assumed that impairment of the ventilation of swallowed air from the stomach (ie, inability to belch) causes gas bloating and flatulence after fundoplication.[23] A recent study by our group suggests that air venting from the stomach is easier after partial than Nissen fundoplication, and this could explain a reduced risk of gas bloat and flatulence.[28]

A previous randomized controlled trial reported by Hagedorn et al demonstrated poorer reflux control 5 years after an anterior 120° partial fundoplication, compared with posterior partial fundoplication.[19,24] Might different types of anterior partial fundoplication have different outcomes? The key difference between the anterior 180° and the 90° and 120° variants is extent of anchorage of the fundoplication to the hiatal rim on the right side of the esophagus. In the anterior 180° partial fundoplication, the gastric fundus is sutured securely to the right hiatal pillar and to the esophageal wall with 3 to 4 sutures, whereas the stomach is not sutured to the right hiatal pillar in the 90° and 120° variants. When undertaking revision surgery for recurrent reflux, we have noted that an anterior 180° fundoplication always remains securely attached to the right hiatal pillar, whereas with the lesser anterior 90° and 120° partial fundoplications, lack of anchorage on the right side can allow the fundoplication to unravel to some extent in some patients. This might account for differences in the rates of recurrent reflux. In general, posterior partial fundoplications are also anchored to the hiatal rim, and the Nissen fundoplication is constructed in a manner that does not allow it to "unwind." Variation in construction probably accounts for different clinical outcomes between different wrap types at late follow-up, and we now believe that secure anchorage of a partial fundoplication to a rigid structure such as the hiatal rim during construction is a key step for achieving effective long-term control of reflux.

Strengths of our current study are the randomized design, common protocols across all trials, the large sample size (n = 461), and the use of raw data sets for our current data analysis. Surgical techniques for construction of the fundoplication were identical, except that in one trial short gastric vessels were routinely divided in the Nissen fundoplication arm.[9] However, multiple randomized controlled trials have shown that division of the short gastric blood vessels during Nissen fundoplication provides no advantage.[5] Bias associated with incomplete follow-up[25] was limited by the high level of complete follow-up at 5 years across our combined data set (94.1%).

A potential limitation of our study is that 3 of the 4 trials were performed in Australia,[9–11] and 1 in South Africa.[12] However, the principal investigator of the South African trial worked with the Australian research group during the first trial, and then applied identical surgical techniques and questionnaires in the South African patient population.[12] The only difference in data collection was that the use of antisecretory medication was not assessed in the South African trial.[12] Another limitation is that we relied on clinical follow-up using validated questionnaires and we did not repeat pH monitoring, esophageal manometry, or endoscopy at 5 years. Objective studies were undertaken at early follow-up in each trial, and the results have been reported previously.[9–11] At early follow-up, there were no differences in endoscopic findings or normalization of acid exposure times between the different types of fundoplication.[9–11] Our previous experience with trying to obtain compliance with objective follow-up in otherwise well patients has shown that a high rate of compliance with studies such as manometry and pH monitoring at multiple points during clinical trials is not feasible in our communities.[11,25] Despite this, the clinical outcomes we have reported are still informative, and these clinical outcomes are arguably more relevant to day-to-day clinical practice, in which patients determine the success of antireflux surgery by the resolution of clinical symptoms, rather than the results of objective investigations.

Even though our data has demonstrated equivalence for reflux control, and less side effects for anterior 180° partial versus Nissen fundoplication, it remains possible that subgroups of patients might have different outcomes. For example, equivalence of reflux control might not be true for individuals with more severe gastroesophageal reflux, and a tailored approach to fundoplication might have some merit. Unfortunately, however, it is difficult to undertake meaningful subgroup analyses on smaller groups of patients without compromising the statistical validity of our current data analysis. Further appropriately designed studies are needed to specifically explore whether some clinical subgroups might do better after one or other type of fundoplication.

Recently published meta-analyses comparing posterior partial (Toupet) with Nissen fundoplication have also concluded that posterior partial fundoplication offers similar reflux control, but with fewer troublesome postfundoplication side effects compared with the Nissen procedure.[4,26] Our study demonstrates that anterior 180° partial fundoplication has the same advantages over Nissen fundoplication. Two randomized controlled trials of an anterior versus posterior partial fundoplication have been reported, and both suggest better reflux

control after posterior fundoplication, less side effects after anterior partial fundoplication, and equivalent overall satisfaction with the outcome of surgery.[19,27] However, as discussed above, Hagedorn et al evaluated an anterior 120° not a 180° partial fundoplication.[19,24] The trial reported by Khan et al did evaluate an anterior 180° partial fundoplication, but only reported 12 months follow-up, and this follow-up was incomplete, being available for only 57% of the enrolled patients at this early time point.[27] Hence, more trials are needed to address the relative advantages, if any, of anterior 180° versus posterior partial fundoplication for the surgical treatment for gastroesophageal reflux.

In conclusion, in this comparison of anterior 90° and anterior 180° versus Nissen fundoplication at 5 years follow-up, anterior 180° partial fundoplication achieved the best overall outcome, with equivalent reflux symptom control but less side effects compared with Nissen fundoplication. Reflux control after anterior 90° partial fundoplication appears less effective than after Nissen fundoplication, and overall this suggests that an anterior 180° partial fundoplication is an appropriate operation for the treatment of uncomplicated gastroesophageal reflux disease, and in our centers this is now the most commonly performed antireflux procedure.

ACKNOWLEDGMENTS

The authors acknowledge the support of Dr Stephen Archer, Dr Justin Bessell, Dr Michael Booth, Dr Richard Cade, Dr Graham Cullingford, Professor David Fletcher, Dr James Hurley, Dr George Kiroff, Professor Christopher Martin, Dr Ian Martin, Professor Lesley Nathanson, and Professor John Windsor who contributed patients to a multicenter trial of anterior 90° partial versus Nissen fundoplication.[10] Dr Philip Game and Dr Robert Britten-Jones contributed patients to the trial of anterior 180° partial versus Nissen fundoplication undertaken in Adelaide, South Australia.[11]

J.A.B. was supported by a University Medical Center Utrecht Alexandre Suerman MD/PhD grant. The randomized controlled trials conducted in Australia were supported by research project grants from the National Health and Medical Research Council (NHMRC) of Australia (grant Nos 157986 & 480401). These trials were registered with the Australasian Clinical Trials Register (ACTRN12607000298415, ACTRN12607000303448 & ACTRN12607000304437).

REFERENCES

1. Broeders JA, Rijnhart-de Jong HG, Draaisma WA, et al. Ten-year outcome of laparoscopic and conventional Nissen fundoplication: randomized clinical trial. *Ann Surg*. 2009;250:698–706.
2. Draaisma WA, Rijnhart-de Jong HG, Broeders IA, et al. Five-year subjective and objective results of laparoscopic and conventional Nissen fundoplication: a randomized trial. *Ann Surg*. 2006;244:34–41.
3. Salminen PT, Hiekkanen HI, Rantala AP, et al. Comparison of long-term outcome of laparoscopic and conventional Nissen fundoplication: a prospective randomized study with an 11-year follow-up. *Ann Surg*. 2007;246:201–206.
4. Broeders JA, Mauritz FA, Ahmed AU, et al. Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. *Br J Surg*. 2010;97:1318–1330.
5. Catarci M, Gentileschi P, Papi C, et al. Evidence-based appraisal of antireflux fundoplication. *Ann Surg*. 2004;239:325–337.
6. Varin O, Velstra B, De SS, et al. Total vs partial fundoplication in the treatment of gastroesophageal reflux disease: a meta-analysis. *Arch Surg*. 2009;144:273–278.
7. Stefanidis D, Hope WW, Kohn GP, et al. Guidelines for surgical treatment of gastroesophageal reflux disease. *Surg Endosc*. 2010;24:2647–2669.
8. Broeders JA, Roks DJ, Ali UA, et al. Laparoscopic anterior versus posterior fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. *Ann Surg.* 2011;254:39–47.
9. Watson DI, Jamieson GG, Lally C, et al. Multicenter, prospective, double-blind, randomized trial of laparoscopic nissen vs anterior 90 degrees partial fundoplication. *Arch Surg*. 2004;139:1160–1167.
10. Spence GM, Watson DI, Jamiesion GG, et al. Single center prospective randomized trial of laparoscopic Nissen versus anterior 90 degrees fundoplication. *J Gastrointest Surg*. 2006;10:698–705.
11. Watson DI, Jamieson GG, Pike GK, et al. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg*. 1999;86:123–130.
12. Baigrie RJ, Cullis SN, Ndhluni AJ, et al. Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. *Br J Surg*. 2005;92:819–823.
13. Ludemann R, Watson DI, Jamieson GG, et al. Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180 degrees fundoplication. *Br J Surg*. 2005;92:240–243.
14. Nijjar R, Watson D, Jamieson G, et al. Five-year follow-up of a multicenter, double-blind randomized clinical trial of laparoscopic Nissen vs anterior 90 degrees partial fundoplication. *Arch Surg*. 2010;145:552–557.
15. Jamieson GG, Watson DI, Britten-Jones R, et al. Laparoscopic Nissen fundoplication. *Ann Surg*. 1994;220:137–145.
16. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol*. 1992;14:99–100.
17. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg*. 1997;226:642–652.
18. Cai W, Watson DI, Lally CJ, et al. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180(degrees) partial fundoplication. *Br J Surg*. 2008;95:1501–1505.
19. Engström C, Lönroth H, Mardani J, et al. An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. *World J Surg*. 2007;31:1221–1225.
20. Wijnhoven BP, Lally CJ, Kelly JJ, et al. Use of antireflux medication after antireflux surgery. *J Gastrointest Surg*. 2008;12:510–517.
21. Scheffer RC, Samsom M, Frakking TG, et al. Long-term effect of fundoplication on motility of the oesophagus and oesophagogastric junction. *Br J Surg*. 2004;91:1466–1472.
22. Mathew G, Watson DI, Myers JC, et al. Oesophageal motility before and after laparoscopic Nissen fundoplication. *Br J Surg*. 1997;84:1465–1469.
23. Woodward ER, Thomas HF, McAlhany JC. Comparison of crural repair and Nissen fundoplication in the treatment of esophageal hiatus hernia with peptic esophagitis. *Ann Surg*. 1971;173:782–792.
24. Hagedorn C, Jonson C, Lonroth H, et al. Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial. *Ann Surg*. 2003;238:189–196.
25. Ludemann R, Watson DI, Jamieson GG. Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication. *Am J Surg*. 2003;186:143–147.
26. Shan CX, Zhang W, Zheng XM, et al. Evidence-based appraisal in laparoscopic Nissen and Toupet fundoplications for gastroesophageal reflux disease. *World J Gastroenterol*. 2010;16:3063–3071.
27. Khan M, Smythe A, Globe J, et al. Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease. *ANZ J Surg*. 2010;80:500–505.
28. Broeders JA, Bredenoord AJ, Hazebroek EJ, Broeders IA, Gooszen HG, Smout AJ. Reflux and belching after 270 degree versus 360 degree laparoscopic posterior fundoplication. *Ann Surg*. 2012;255:59–65.

2.5 Anterior 90 degree partial fundoplication vs. Nissen fundoplication with division of the short gastric blood vessels

---

Krysztopik RJ, Jamieson, GG, Devitt PG & Watson DI. A further modification of the Nissen fundoplication – 90^0 anterior fundoplication. *Surg Endosc* (2002) **16**:1446-1451.

This paper described in detail the surgical technique for laparoscopic anterior 90 degree partial fundoplication.

Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin C, Martin IJG, Nathanson LK, Windsor J. Multicentre prospective double blind randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. *Arch Surg* (2004) **139**:1160-1167.

This paper reported the clinical and objective outcomes at 6 months (short term) follow-up from a multi-centre randomized trial comparing laparoscopic anterior 90 degree partial vs. Nissen fundoplication with division of the short gastric blood vessels.

Woodcock SA, Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin CJ, Martin IJG, Nathanson LK, Windsor JA. Quality of life following laparoscopic anterior 90^0 versus Nissen fundoplication - results from a multicentre randomized trial. *World J Surg* (2006) **30**:1856-1863.

This paper reported quality of life outcomes at up to 2 years follow-up from the same trial.

Nijjar RS, Watson DI, Jamieson GG, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin IJG, Nathanson LK, Windsor J. Five year follow-up of a multicentre double blind randomized clinical trial of laparoscopic Nissen vs. anterior 90^0 partial fundoplication. *Arch Surg* (2010) **145**:552-557.

This paper reported the 5 year (longer term) clinical outcomes from the same trial.

Surg Endosc (2002) 16: 1446–1451
DOI: 10.1007/s00464-002-8801-2

SURGICAL ENDOSCOPY
and Other Interventional Techniques

A further modification of fundoplication

90° anterior fundoplication

R. J. Krysztopik, G. G. Jamieson, P. G. Devitt, D. I. Watson

University of Adelaide Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia

Received: 9 January 2002/Accepted in final form: 9 April 2002/Online publication: 27 June 2002

Abstract
Background: Laparoscopic Nissen fundoplication is the most widely applied procedure for the surgical treatment of gastroesophageal reflux. However, it can be followed by adverse outcomes, including dysphagia and "wind-related" problems. To reduce the likelihood of side effects, we have progressively modified this procedure to an anterior 90° partial fundoplication.
Methods: The procedure entails posterior hiatal repair, posterior esophagopexy, accentuation of the angle of His, and construction of a 90° anterior partial fundoplication. Clinical follow-up was performed prospectively using a standardized questionnaire.
Results: From February 1999 to June 2001, 83 patients underwent 90° anterior fundoplication for gastroesophageal reflux disease. In 45 the procedure was chosen because of specific patient or surgeon preference, and in 38 it was performed within the context of an ongoing randomized trial. Operating time ranged from 20 to 140 minutes (median, 52 min), and all but one of the procedures were completed laparoscopically. One patient experienced a major postoperative complication—small bowel injury from Veress needle. Follow-up extends up to 2 years (median, 1 year). Two patients have undergone further surgery, both for recurrent reflux. Control of reflux has been acceptable, with a reduction in heartburn symptom scores and high overall satisfaction. Postoperative dysphagia measured using a visual analog scale was less following surgery compared with preoperative scores. Eighty-two percent of patients could belch normally 3 and 12 months after surgery.
Conclusions: Ninety-degree anterior fundoplication achieves good control of reflux and a low incidence of side effects. To further evaluate its potential, we are currently undertaking a prospective randomized trial.

Key words: Fundoplication — 90° antireflux procedure

Despite its efficacy, laparoscopic Nissen fundoplication is associated with a small but significant incidence of troublesome side effects. These side effects are typically those of dysphagia, gas bloat, and inability to belch [4, 10]. A number of technical modifications have been tried [10] in an attempt to reduce postfundoplication problems by reducing the "tightness" of the esophagogastric junction. Although there is a reduction in so-called postfundoplication side effects in these series, there remains a small number of patients who believe that the side effects outweigh the benefits of fundoplication. This led us to explore further modifications of an anterior fundoplication, leading to the development of a 90° anterior fundoplication. In a porcine experimental model, this wrap proved effective in increasing the lower esophageal sphincter (LOS) pressure and restoring LOS competence [13]. The procedure is now being used as a treatment for reflux in our department, and its efficacy is being investigated in an ongoing randomized controlled trial. This article describes the technical details of 90° anterior fundoplication and reports early clinical outcomes.

Materials and methods

Between February 1999 and June 2001, 83 patients underwent a 90° antireflux procedure primarily for the treatment of gastroesophageal reflux disease. This comprised all of the patients undergoing this procedure in our department. During the same time period, a total of 286 patients underwent laparoscopic fundoplication in our department. Patients were chosen for the 90° wrap as part of a randomized trial (38 patients) or because they were hopeful that the procedure would be associated with less "wind" and dysphagia problems (45 patients).

Data concerning the outcome for all patients undergoing 90° anterior fundoplication were collected prospectively. Operations were performed by or under the supervision of one of three surgeons (GGJ,

Presented at the 8th World Congress of Endoscopic Surgery, New York, New York, USA, March 2002
Correspondence to: D. I. Watson

DIW, and PGD). A scientist, using a standardized data form and clinical questionnaire, collected preoperative, operative, and postoperative data. Patients were interviewed before operation and then 3, l2, and 24 months after surgery. The presence of the following symptoms were sought: heartburn, dysphagia for solids and liquids, inability to belch, epigastric bloating, ability to relieve bloating, and increased passage of flatus. Heartburn was scored using a visual analog scale (0, no heartburn; 10, severe heartburn). Dysphagia to liquids and solids was scored using a visual analog scale (0, no dysphagia; 10, total dysphagia) as well as a previously validated dysphagia score [2], (0, no dysphagia; 45, severe dysphagia). Patients were also asked to indicate a level of satisfaction with their result, again using a visual analog scale (0, dissatisfied; 10, satisfied). Patients who were part of a randomized clinical trial were investigated with postoperative manometry 3 or 4 months after surgery.

Operative technique

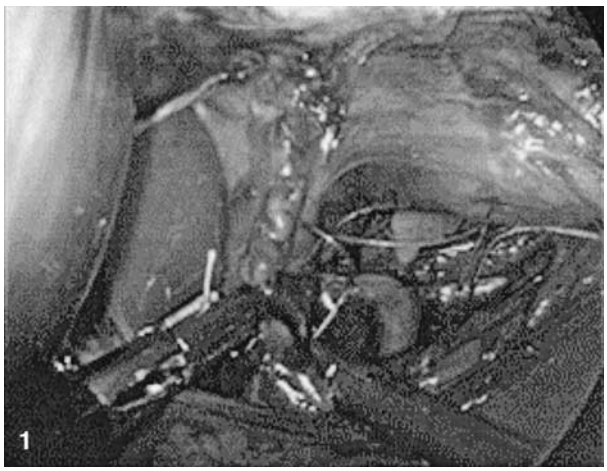
Initial patient positioning and port placement are identical to those described for laparoscopic Nissen [5]. The patient is placed in the Lloyd Davies position, with the table tilted head up. The operating surgeon stands between the patient's legs, and an assistant stands on the patient's left. Four ports are placed: an 11-mm port in the midline above the umbilicus to receive the laparoscope and a second 11-mm port in the left midclavicular line 1–3 cm below the costal margin for suturing and dissecting instruments. Two 5-mm ports are placed: one in the right midclavicular line, just below the costal margin, for the operating surgeons grasping forceps and a second in the left flank for the use of instruments by the assistant. A Nathanson liver retractor (Cook Medical Technology, Eight Mile Plains, Queensland, Australia) is passed through a 5-mm stab wound in the epigastrium just below the xiphisternum.

Hiatal dissection is achieved by blunt dissection with minimal use of diathermy or scissors. The lesser omentum, first below and then above the hepatic branch of the vagus, is opened while preserving this nerve. This facilitates identification of the right hiatal pillar. Next, the plane between the right pillar and esophagus is opened by blunt separation. This maneuver is usually bloodless if the correct dissection plane is identified. The phrenicoesophageal ligament across the front of the hiatus is divided, usually by blunt separation, and the dissection is continued along the anterior edge of the left hiatal pillar, dissecting the pillar inferiorly as far as possible.

A grasping forceps is then passed behind the esophagus, from right to left, in front of the left pillar and a nylon tape is then pulled back through this space to facilitate anterior and lateral retraction of the esophagus, enabling complete dissection of the posterior hiatus and exposure of both hiatal pillars under the esophagus from the right side. Next, the hiatus is repaired posteriorly using interrupted nonabsorbable 2–0 monofilament sutures. This suture material is used throughout the repair.

The 90° anterior fundoplication begins with an "esophagopexy" suture between the posterolateral aspect of the right side of the esophagus at or just above the esophagogastric junction and posteriorly to the right pillar or, more commonly, both pillars where they have been sutured together, thus securing an intraabdominal length of esophagus (Fig. 1). Next, a suture is placed at the angle of His. The fat pad lying over the cardia is grasped and downward traction applied to emphasize the angle of His and facilitate placement of a suture at the angle between the esophagogastric junction and the gastric fundus (Fig. 2). A second suture is then placed more cranially to further close the angle of His and bring the left side of the intraabdominal esophagus and adjacent gastric fundus into apposition at the level of the left hiatal pillar (Fig. 3). Occasionally, it seems appropriate to include the left pillar with this suture to further secure a length of intraabdominal esophagus.

The gastric fundus is then manipulated in such a way that it sits loosely over the front of the esophagus, reaching the midline. An apical suture is placed that anchors the fundus to the anterior esophagus as it emerges through the hiatus, the phrenicoesophageal ligament, and to the apex of the hiatus (Fig. 4). This suture is at the "12 o'clock" position and creates the top extent of the 90° fundoplication. Finally, the inferior edge of the fundal fold is stitched to the anterior esophagus at the esophagogastric junction in the midline (i.e., again at the 12 o'clock position on the esophagus) (Fig. 5). This produces a loose wrap, which covers approximately 90° of the circumference of the intraabdominal esophagus, from the apex of the angle of His to the anterior midline. The short gastric vessels are left intact and an intraesophageal bougie is not required.



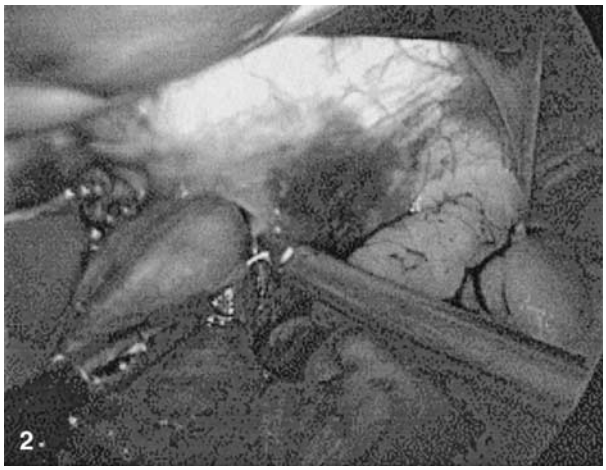


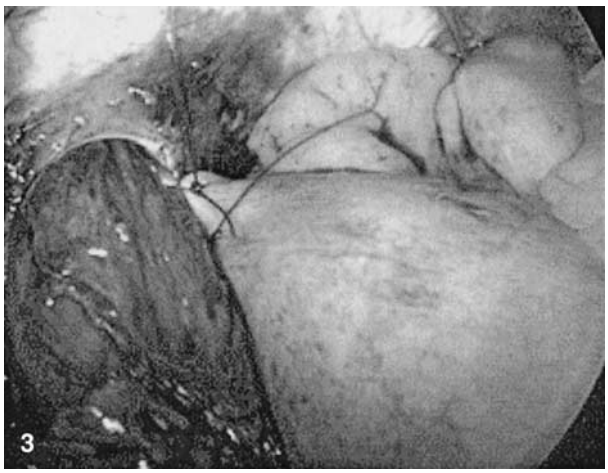
Fig. 1. "Esophagopexy" created by suturing the posterolateral aspect of the right side of the distal esophagus to the hiatal pillars posteriorly. The figure shows the suture needle being passed through the hiatal pillars. The suture material has already been passed through the esophagus above this.
Fig. 2. The fat pad overlying the cardia is pulled down to reconstitute the angle of His and a suture is placed between the left lateral esophagus and the adjacent gastric fundus.

Postoperative care

After recovery from anaesthesia, patients return to a surgical ward. Nasogastric tube drainage is not used. Patients are allowed oral fluids on the day of surgery and start a soft diet the next day. Discharge from the hospital is usually on postoperative day 2.

Results

The study included 44 men and 39 women, with a median age of 49 years (range, 19–81 years). Follow-up was available for 78 (94%) patients at 3 months after surgery, 44 (53%) at 1 year, and 10 (13%) at 2 years. No patients were lost to follow-up. Endoscopy and esoph-



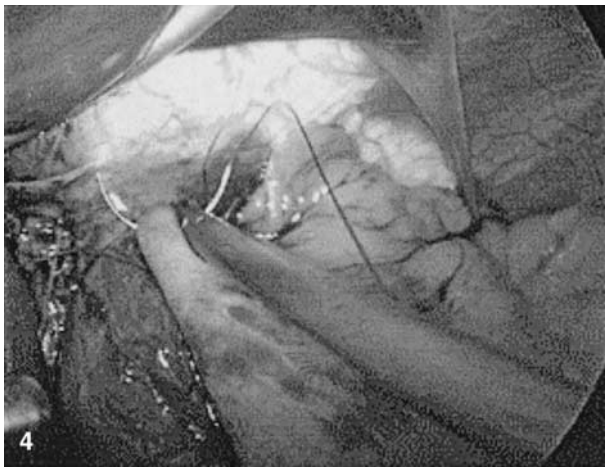


Fig. 3. The first row of sutures has been placed, closing the angle of His and bringing the left side of the esophagus and the adjacent gastric fundus into apposition.
Fig. 4. Suturing the gastric fundus over the front of the esophagus to the apex of the hiatus to create the top extent of the fundoplication.

ageal manometry were carried out preoperatively in all patients. Endoscopy showed some degree of ulcerative esophagitis in 69 (83%) patients, with the remainder having an abnormal 24-hour pH study. At preoperative endoscopy, 16% had Barrett's esophagus and 6% a peptic esophageal stricture. Manometry was successful in 74 (89%) patients. Of these, 21 (25% of total) had distal esophageal hypomotility (less than 70% primary propagation on wet swallow and/or distal peristaltic amplitude of less than 25 mmHg).

Operating time ranged from 20 to 140 minutes (median, 52 min). One patient had a 90° anterior fundoplication completed by open surgery because of dense adhesions. Median postoperative stay was 2 days (range, 1–12 days). There was one major complication: a Veress needle induced small bowel injury, which required laparotomy and repair 3 days after fundoplication. There was no mortality.

Clinical outcome at 12 weeks was available for 78 patients. Table 1 shows the clinical assessment of these patients using the visual analog scales. Seventy-one percent of patients had complete absence of heartburn

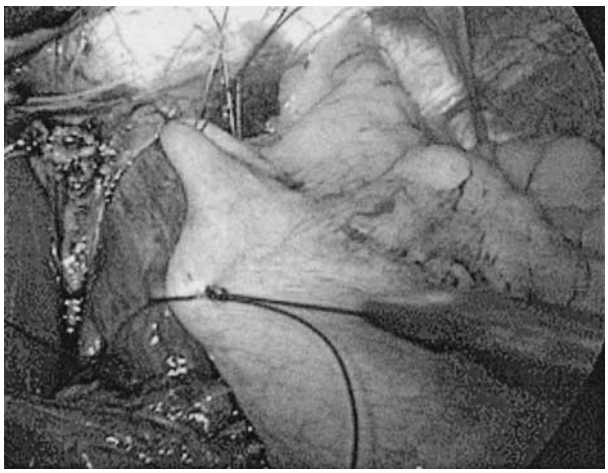


Fig. 5. Placement of the final suture between the inferior edge of the fundal fold and the anterior esophagus in the midline. This completes the 90° fundoplication.

symptoms. Preoperative dysphagia for solids was present in 51% patients. Tables 2 and 3 show the effects of fundoplication on the severity of preexisting dysphagia after 3 and 12 months, respectively. Table 4 shows the results in regard to new-onset dysphagia. Reoperation for recurrent reflux was undertaken in two patients, one at 5 months and the second at 7 months after surgery. Both patients had developed widening of the hiatus with slippage of the wrap into the lower chest. Both cases were laparoscopically converted to a Nissen fundoplication. The operating times for these re-do cases were 80 and 90 minutes, respectively. Both operations were considered to be technically straightforward.

Recurrent reflux symptoms have occurred in a further 7 patients at this stage. Of these, 2 patients described return of their reflux symptoms after an episode of straining (lifting in one case and vomiting in the second); the remainder described no clear precipitating event prior to return of reflux symptoms. Epigastric bloating was a common postoperative symptom (56% at 3 months and 48% at 12 months). An ability to relieve bloating was reported by 68% at both 3 and 12 months. Inability to belch was reported by 18% at both 3 and 12 months. Increased passage of flatus was reported by 67% of patients at 3 months. Patient satisfaction, as assessed by a visual analog score, was 8.5 [confidence interval (CI) 8.0–8.9] at 3 months and 8.1 (CI 7.3–8.8) at 12 months. Table 5 shows the results of 14 patients who have undergone postoperative manometry to date.

Discussion

The restoration of hiatal anatomy and the antireflux mechanism is not a new concept. In 1951, Allison described the "anatomical" repair of hiatus hernia. This operation involved a transthoracic approach to reduce the hiatus hernia, narrow the esophageal hiatus, and accentuate the angle of His. Short-term relief of symp-

Table 1. Pre- and postoperative heartburn and dysphagia outcomes using visual analog scales and dysphagia score[a]

	Preoperative	3 months postoperative	12 months postoperative
Heartburn	6.7 (5.9–7.5)	0.9 (0.5–1.3)*	1.9 (1.1–2.7)*
Dysphagia for liquids	1.7 (1.0–2.4)	0.8 (0.4–1.2)*	0.7 (0.1–1.3)*
Dysphagia for solids	2.9 (2.1–3.8)	1.9 (1.3–2.5)*	1.7 (0.9–2.4)*
Dysphagia score		9.9 (6.8–11.9)	7.4 (4.3–10.4)

[a] Data are expressed as mean (95% confidence intervals). Student's *t*-test was used to compare preoperative and postoperative scores
* $p < 0.05$

Table 2. The effect of fundoplication after 3 months on the severity of dysphagia for solids in patients with pre-existing dysphagia[a]

	Visual analog scale			
	0 (None)	1–3 (Mild)	4–6 (Moderate)	7–10 (Severe)
Preoperative (%)		26	31	43
Postoperative (%)	43	29	20	6

[a] Dysphagia was present in 35 of 69 patients with dysphagia scores at 3 months

Table 3. The effect of fundoplication after 12 months on the severity of dysphagia for solids in patients with preexisting dysphagia[a]

	Visual analog scale			
	0 (None)	1–3 (Mild)	4–6 (Moderate)	7–10 (Severe)
Preoperative (%)		26	37	37
Postoperative (%)	53	31	5	10

[a] Dysphagia was present in 21 of 39 patients with dysphagia scores at 12 months

Table 4. The incidence of new-onset dysphagia 3 and 12 months after fundoplication[a]

	No change	Mild	Moderate	Severe
3 months	19 (56%)	7 (20%)	3 (9%)	6 (15%)
12 months	14 (70%)	2 (5%)	5 (25%)	0 (0%)

[a] Preexisting dysphagia to solids was absent in 34 of 69 patients at 3 months and 20 of 39 patients at 12 months

Table 5. Manometric changes before and after 90° fundoplication[a]

	Preoperative	Postoperative 3 months
Lower esophageal sphincter resting pressure	11.5 (5.1–18.0)	18.9 (10.1–27.6)
Lower esophageal sphincter residual relaxation pressure	1.6 (0.1–3.1)	3.4 (0.7–6.0)
% patients propagating < 70% wet swallows	75	71
% patients with distal esophageal peristaltic amplitudes > 40 mmHg	71	71

[a] Data are expressed as mean (95% confidence intervals)

toms was excellent in 91% of patients; however, when reassessed at 20 years the percentage decreased to 66% [1]. The only report of 20-year outcome following open Nissen fundoplication described a 76% success rate [9]. Although this is 10% better than the rate quoted by Allison, it is noteworthy that Allison achieved more than 90% complete follow-up of his 153 patients, whereas Luostarinen et al. [9] achieved only 54% of his 46 patients.

Despite its ability to correct reflux, laparoscopic Nissen fundoplication can still be associated with the problems of dysphagia, bloating, and inability to belch [4, 10]. The question of whether the wrap type has any effect on these symptoms has been extensively investigated. Randomized trials of posterior partial versus Nissen fundoplication have not provided convincing evidence of a reduction in postoperative side effects [7, 8]. However, a more anatomical reconstruction of the antireflux mechanism by anterior 180° partial fundoplication has been shown to have a lower incidence of dysphagia and other side effects, such as flatulence, than Nissen fundoplication [11]. This approach has been further adapted in the development of the 90° anterior fundoplication described here.

A possible explanation for the reduced incidence of dysphagia following anterior fundoplication may be the more ''physiological'' manometric profile of the lower esophagus seen after anterior fundoplication. Anterior fundoplication reduces the resistance to bolus transport seen after Nissen fundoplication. Manometric studies show that the increase in LOS resting pressure, and particularly LOS nadir pressure, is not as pronounced as that seen after Nissen fundoplication [11]. In our current series using the 90° anterior fundoplication, our findings were similar.

Bloating and epigastric fullness are somewhat subjective symptoms and notoriously difficult to measure objectively. Their incidence is often unchanged by surgery. Inability to belch is perhaps a little more objective and is probably linked to the antireflux properties of an operation. In this series only 18% of patients reported an inability to belch, which is lower than the 60% to 80% reported after anterior or Nissen fundoplication [11]. The incidence of increased flatus of 67% at 3 months appears high. However, this symptom often improves with longer follow-up, and as time progresses it is anticipated that this will be less frequent. Furthermore, most patients reporting this symptom were not troubled by it.

The problem of postfundoplication dysphagia is also difficult to assess. Not only is postoperative dysphagia often measured in an unspecified way, with different systems of measurement producing a wide range of incidences [12], but also preoperative dysphagia is frequently unreported. Preoperative dysphagia in some form is present in 30% to 50% of patients undergoing laparoscopic fundoplication [3, 6]. The apparent incidence is influenced by which preoperative questions are asked (if any) and what scoring system is used. Furthermore, it does not correlate with manometrically measured dysmotility. Improvement in dysphagia was seen in 17% of patients at 6 months in de Beaux et al.'s [3] report, whereas in our series a much more impressive 41% and 42% at 3 and 12 months respectively, was seen. Generally, the severity of dysphagia is reduced by fundoplication, with a significant reduction in patients experiencing severe dysphagia [6]. The early outcome of the 90° fundoplication suggests that the reduction is even more pronounced than that seen after Nissen or 180° fundoplication. Although severe dysphagia is less common after surgery, many patients still have some dysphagia, but it is not usually troublesome and does not lead to dietary modification.

These initial results suggest that recurrence of reflux symptoms (l1% in this series) is potentially higher than after a Nissen fundoplication, and it is possible that some would regard this rate at such an early stage as unacceptably high. It is therefore worth noting that reoperations may prove much simpler in these patients. Although ease of reoperation can hardly be used as a factor in advocacy of a primary operation, if there are other benefits of such an operation, we believe ease of reoperation is not an inconsequential circumstance. Furthermore, it is important to establish scientifically whether recurrent reflux is more likely after 90° fundoplication, and we have instituted a randomized trial against Nissen fundoplication to try to answer these questions. Recurrence of reflux was due to proximal migration of the gastroesophageal junction beneath an intact fundoplication in the two patients who underwent surgical revision for reflux. It is possible that the same mechanism was acting in the other patients who developed further reflux type symptoms during follow-up.

It should be noted that follow-up in this study is predominantly clinical; thus, some patients complaining of ''reflux''-type symptoms may not actually have reflux if subjected to pH monitoring. Also, there may be patients who have no symptoms who still have reflux esophagitis, at least to some degree. Objective follow-up with pH studies would give a better understanding of distal esophageal acid exposure, although ultimately patient satisfaction with outcome perhaps best reflects the potential satisfaction with outcome for future patients.

We think it is unlikely that the 90° fundoplication will replace Nissen fundoplication in the majority of patients requiring antireflux surgery. However, there are some patients for whom a 90° procedure might be preferable: patients with an adynamic esophagus, patients with a giant paraesophageal hernia or intrathoracic stomach, where there is no certain disorder of the antireflux mechanism, and patients (typically women) for whom the avoidance of excessive flatus is important.

The data in this report are very preliminary, with our aim being to report the technical details of the 90° fundoplication, the fact that in the majority of patients it is an effective antireflux operation, and that it has a low incidence of postfundoplication side effects. The long-term efficacy of the procedure will be assessed in due course, and as mentioned previously, we have commenced a randomized trial comparing this procedure with the Nissen fundoplication, and we expect this will help clarify the effectiveness of this procedure.

References

1. Allison PR (1973) Hiatus hernia: a 20-year retrospective survey. Ann Surg 178: 273–276
2. de Beaux AC, Watson DI, O'Boyle C, Jamieson GG (2001) Role of fundoplication in patient symptomatology after laparoscopic antireflux surgery. Br J Surg 88: 1117–1121
3. Dakkak M, Bennett JR (1992) A new dysphagia score with objective validation. J Clin Gastroenterol 14: 99–100
4. DeMeester TR, Bonavina L, Albertucci M (1986) Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. Ann Surg 204: 9–20
5. Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M (1994) Laparoscopic Nissen fundoplication. Ann Surg 220: 137–145
6. Lafullarde T, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG (2001) Laparoscopic Nissen fundoplication: five-year results and beyond. Arch Surg 136: 180–184
7. Laws HL, Clements RH, Swillies CM (1997) A randomized, prospective comparison of the Nissen fundoplication versus the Toupet fundoplication for gastroesophageal reflux disease. Ann Surg 225: 647–653
8. Lundell L, Abrahamsson H, Ruth M, Rydberg L, Lonroth H, Olbe L (1996) Long-term results of a prospective randomized comparison of total fundic wrap (Nissen–Rossetti) or semifun-

doplication (Toupet) for gastro-oesophageal reflux. Br J Surg 83: 830–835
9. Luostarinen M, Isolauri J, Laitinen J, Koskinen M, Keyrilainen O, Markkula H, Lehtinen E, Uusitalo A (1993) Fate of Nissen fundoplication after 20 years. A clinical, endoscopical, and functional analysis. Gut 34: 1015–1020
10. Watson DI, Jamieson GG (1998) Antireflux surgery in the laparoscopic era. Br J Surg 85: 1173–1184
11. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG (1999) Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 86: 123–130
12. Watson DI, Pike GK, Baigrie RJ, Mathew G, Devitt PG, Britten-Jones R, Jamieson GG (1997) Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. Ann Surg 226: 642–652
13. Yau P, Watson DI, Ascott N, Lafullarde T, Jamieson GG (2000) Efficacy of a 90 degree anterior fundoplication vs a total fundoplication in an experimental model. Surg Endosc 14: 830–833

ORIGINAL ARTICLE

Multicenter, Prospective, Double-blind, Randomized Trial of Laparoscopic Nissen vs Anterior 90° Partial Fundoplication

David I. Watson, MD; Glyn G. Jamieson, MS; Carolyn Lally, RN; Stephen Archer, PhD; Justin R. Bessell, MD; Michael Booth, MB BS; Richard Cade, MB BS; Graham Cullingford, MB BS; Peter G. Devitt, MS; David R. Fletcher, MD; James Hurley, MB BS; George Kiroff, MS; Christopher J. Martin, MSc; Ian J. G. Martin, MB BS; Leslie K. Nathanson, MB, ChB; John A. Windsor, MD; for the International Society for Diseases of the Esophagus–Australasian Section

Hypothesis: Laparoscopic anterior 90° partial fundoplication for gastroesophageal reflux is associated with a lower incidence of postoperative dysphagia and other adverse effects compared with laparoscopic Nissen fundoplication.

Design: A multicenter, prospective, double-blind, randomized controlled trial.

Setting: Nine university teaching hospitals in 6 major cities in Australia and New Zealand.

Participants: One hundred twelve patients with proven gastroesophageal reflux disease presenting for laparoscopic fundoplication were randomized to undergo either a Nissen (52 patients) or an anterior 90° partial procedure (60 patients). Patients with esophageal motility disorders, patients requiring a concurrent abdominal procedure, and patients who had undergone previous antireflux surgery were excluded from this study.

Interventions: Laparoscopic Nissen fundoplication with division of the short gastric vessels or laparoscopic anterior 90° partial fundoplication.

Main Outcome Measures: Independent assessment of dysphagia, heartburn, and overall satisfaction 1, 3, and 6 months after surgery using multiple clinical grading systems. Objective measurement of esophageal manometric parameters, esophageal acid exposure, and endoscopic assessment.

Results: Postoperative dysphagia, and wind-related adverse effects were less common after a laparoscopic anterior 90° partial fundoplication. Relief of heartburn was better following laparoscopic Nissen fundoplication. Overall satisfaction was better after anterior 90° partial fundoplication. Lower esophageal sphincter pressure, acid exposure, and endoscopy findings were similar for both procedures.

Conclusions: At the 6-month follow-up, laparoscopic anterior 90° partial fundoplication is followed by fewer adverse effects than laparoscopic Nissen fundoplication with full fundal mobilization, and it achieves a higher rate of satisfaction with the overall outcome. However, this is offset to some extent by a greater likelihood of recurrent gastroesophageal reflux symptoms.

Arch Surg. 2004;139:1160-1167

Author Affiliations: Flinders University of South Australia, Adelaide (Drs Watson and Bessell); University of Adelaide, Adelaide, Australia (Messers Jamieson and Devitt and Ms Lally); University of Western Australia, Crawley (Drs Archer and Fletcher); University of Auckland, Auckland, New Zealand (Drs Booth and Windsor); Melbourne University, Melbourne, Australia (Drs Cade and Hurley and Mr Kiroff); University of Sydney, Sydney, Australia (Dr Martin); University of Queensland, Brisbane, Australia (Drs Martin and Nathanson).

ALTHOUGH MEDICATIONS that suppress acid achieve adequate symptom control for most patients with gastroesophageal reflux (GER) disease, some patients with more severe reflux have a poor response to medication. These patients will often benefit from surgery. In addition, fundoplication is also an effective treatment for many younger patients who do not wish to take tablets for the rest of their lives. The 360° fundoplication that was first described by Nissen remains the most commonly performed anti-GER procedure worldwide. It achieves excellent control of acid reflux although this is at the expense of a small, but nevertheless important, incidence of troublesome postoperative adverse effects.[1] To overcome this, technical aspects of this procedure have been progressively modified.

Partial fundoplication has the potential to produce a more physiological gastroesophageal junction and with this fewer adverse effects.[1,2] While variants of posterior fundoplication are arguably the more common approach to partial fundoplication, the alternative anterior partial fundoplication procedure has the potential to reduce even further the risk of adverse effects.[3] In 1999, the early outcomes of a randomized trial of Nissen vs anterior 180° fundoplication were reported by some of us.[3] That study demonstrated the potential for an anterior par-

tial fundoplication to produce adequate GER control and a low rate of postoperative adverse effects. Subsequent longer-term follow-up has confirmed the durability of the anterior 180° fundoplication procedure.[4] Nevertheless, even this procedure is followed by a small incidence of troublesome adverse effects.

This provided impetus for the further refinement of the anterior fundoplication procedure to an anterior 90° partial fundoplication. Previously reported laboratory and clinical studies have confirmed the short-term effectiveness of this approach and its potential to achieve a very low rate of adverse effects.[5,6] Before proceeding to wider clinical application, however, we chose to evaluate the new procedure within a multicenter, prospective, randomized, controlled clinical trial to compare the anterior 90° partial fundoplication procedure with a standard approach to Nissen fundoplication.

METHODS

This multicenter study investigated the hypothesis that laparoscopic anterior 90° partial fundoplication could achieve effective control of GER symptoms, but with fewer adverse effects, compared with laparoscopic Nissen fundoplication. Fifteen surgeons from 9 university teaching hospitals in 6 Australian and New Zealand cities contributed patients to this study, with each surgeon aiming to contribute a quota of 10 patients to the study.

PARTICIPANT ASSIGNMENT

Patients undergoing laparoscopic fundoplication for GER disease were randomly assigned to undergo either a total fundoplication with division of short gastric blood vessels and full mobilization of all fundal attachments or an anterior 90° partial fundoplication. Informed consent was obtained from all participants, and randomization occurred in the operating theater, after commencing general anesthesia. Randomization was performed by opening 1 of 150 previously sealed opaque envelopes. The envelopes were prepared by a research officer (C.L.) before the trial began. Sets of 10 randomly selected envelopes were sent to each participating surgeon, and each surgeon opened an envelope at the time of the operation to determine the specific procedure to be performed. Patients were not stratified according to the operating surgeon or any other criteria.

PATIENT SELECTION AND PREOPERATIVE INVESTIGATION

Patients with proven GER disease who presented for primary antireflux surgery were considered for enrollment in this trial. Exclusion criteria were (1) an esophageal motility disorder that precluded a 360° fundoplication, (2) a planned concurrent abdominal procedure along with fundoplication (eg, cholecystectomy), and (3) previous antireflux surgery. Patients underwent preoperative investigation with esophageal manometry and endoscopy. In general, 24-hour pH monitoring was performed to confirm GER disease in patients who did not have unequivocal GER disease demonstrated by preliminary endoscopic and manometric studies.

OPERATING TECHNIQUE

Laparoscopic Nissen fundoplication was performed according to a common technique that was agreed to by the study participants before the trial commenced. This entailed posterior hiatal repair for all patients and full mobilization of the gastric fundus. The short gastric vessels were divided using ultrasonic shears, starting at the level of the inferior pole of the spleen, and progressing superiorly along the greater curvature of the stomach up to the left pillar of the esophageal hiatus. The uppermost short gastric vessel and all posterior attachments of the fundus were always divided, ensuring a very "floppy" wrap. Care was taken to ensure that the completed total fundoplication was not tight by having a 52F to 60F bougie within the lumen of the abdominal esophagus when constructing the fundoplication. Nonabsorbable sutures were used to secure a fundoplication that was between 1 and 2 cm in length.

A laparoscopic anterior 90° partial fundoplication was also performed according to an agreed on common technique. This has been described in detail in a previous report.[5] The esophageal hiatus was dissected first using an identical technique to that used for total fundoplication, and the hiatus was repaired posteriorly in all patients. The 90° anterior fundoplication commenced with an esophagopexy suture between the posterolateral aspect of the right side of the esophagus at or just above the esophagogastric junction, and the posterior aspect of either the right pillar or both pillars. This stabilized a length of intra-abdominal length of esophagus. Two sutures were then placed between the left side of the esophagus and the adjacent gastric fundus to reconstruct and accentuate the angle of His. Next the gastric fundus was attached loosely over the front of the esophagus, using an apical suture that anchored the fundus to the anterior esophagus as it emerged through the esophageal hiatus, and to the apex of the hiatus in the 12-o'clock position. Finally, the inferior edge of the fundal fold lying in front of the abdominal esophagus was sutured to the anterior esophagus at the esophagogastric junction in the midline. This produced a loose fundoplication, covering the intra-abdominal esophagus from the apex of the angle of His to the anterior aspect of the esophagus in the midline. The short gastric vessels were left intact and an intra-esophageal bougie was not used for this procedure. With either procedure, if the laparoscopic procedure was converted to an open procedure because of intraoperative difficulties, the randomization schedule was still followed and the patient remained in the trial.

Before commencing this trial, we endeavored to standardize the operative techniques across all sites. This was attempted by applying several strategies. First, most of the surgeons participating in this study attended meetings of the Australasian Section of the International Society for Diseases of the Esophagus in December 10-11, 1998, and December 8-9, 2000. The operative techniques were discussed in detail, videotape demonstrations were shown, and the technical aspects of the operative techniques were discussed, refined, and agreed on. In addition, reference videotapes of the standard operative techniques were provided to surgeons participating in this study. Additional informal discussion occurred between the initiators of the trial and contributing surgeons at key time points. Because of limited funding and the large distances between centers, it was in general impossible for surgeons to travel to different centers to see other surgeons operate, or for surgeons from different cities to assist other surgeons with these procedures.

POSTOPERATIVE CARE

Patients were allowed oral fluids postoperatively on the evening of the day of surgery or the next day, and soft solid food soon after. Patients were instructed to maintain a soft diet for the first 3 to 4 weeks after surgery, and then to gradually increase the consistency of their diet.

Table 1. Modified Visick Grading System

Grade	Meaning
1	No symptoms
2	Mild symptoms easily controlled by simple care such as avoiding certain foods or small meals, etc
3	Moderate symptoms not controlled by simple care but not interfering with social or economic life
4	Moderate symptoms interfering with social or economic life
5	Symptoms as bad or worse than preoperatively

Table 2. Outcome Assessment

Rating	Meaning
Excellent	Complete recovery
Good	Major improvement with minor problems
Fair	Major improvement with still significant problems or adverse effects
Poor	Minor or no improvement or deterioration

MASKING

Which procedure had been performed was concealed from patients during this initial period of follow-up. Patients had no direct access to case notes or trial records, and both laparoscopic procedures were performed through identical operative wounds. While operating surgeons were aware of the exact procedure performed, follow-up was obtained by a research assistant (C.L.) who was based at the Royal Adelaide Hospital and masked to the randomization of each patient. The research assistant was not involved in the initial surgery and remained unaware of the allocated group for each patient throughout the follow-up period. Final data analysis was performed by a surgeon investigator (D.I.W.). Raw data were circulated to all surgeons who contributed patients to this study, allowing the analysis to be independently checked by all surgeon participants.

CLINICAL FOLLOW-UP

Preoperative data were collected using a standard form. This was administered by the responsible surgeon before either surgery or before randomization was undertaken. Patients underwent a structured telephone interview that was performed by a research assistant (C.L.) 1, 3, and 6 months after surgery. Longer-term follow-up will be sought in due course. The presence or absence of each of the following symptoms was sought: heartburn; epigastric pain; regurgitation; dysphagia for lumpy solids, soft solids, and liquids; odynophagia; early satiety; inability to belch; epigastric bloating; anorexia; nausea; vomiting; wheezing; nocturnal coughing; increased flatulence; and diarrhea. The ability to relieve bloating and whether a normal diet was being consumed were also determined. Heartburn was also scored using a visual analog scale (0 [no heartburn] to 10 [severe heartburn]).

Dysphagia was scored by several methods. Visual analog scales (0 [no dysphagia] to 10 [total dysphagia]) were applied separately for solids and liquids, as well as a previously validated score (0 [no dysphagia] to 45 [severe dysphagia]) that combines information about difficulty swallowing 9 types of liquids and solids. This scoring system has been described in detail elsewhere.[7] Overall outcome was determined using 3 further scales and a question. Patients were asked whether they thought that their initial decision to have a laparoscopic fundoplication was correct or not. They were also asked to rank the outcome of surgery using a modified Visick grading system (**Table 1**) and were asked to score the outcome as excellent, good, fair, or poor (**Table 2**). An overall assessment of satisfaction with the operative outcome was scored by a further visual analogue scale (0 [dissatisfied] to 10 [satisfied]).

OBJECTIVE FOLLOW-UP

Objective investigation with esophageal manometry, 24-hour pH monitoring, and endoscopy were performed 3 to 4 months after surgery. Investigation sought to assess lower esophageal sphincter function, control of GER, and postsurgical anatomy.

STATISTICAL ANALYSIS

The primary clinical outcomes, which the trial was designed to evaluate, were postoperative dysphagia and control of GER symptoms. Before the trial commenced, it was determined that 120 patients (60 in each group) would be needed to demonstrate a 15% difference in these outcome measures at a statistical significance level of $P<.05$ and power of 80%. All analyses were performed on an intention-to-treat basis, with all patients remaining in their initial allocated group for this analysis. Before commencing this trial, it was intended to publish the initial outcomes and results of postoperative testing once all patients had been followed up for an initial 6-month period (this article). Longer-term outcomes will be reported once the follow-up duration is longer.

All data were entered in a computerized database (Filemaker Pro version 5.0; Filemaker Corp, Santa Clara, Calif) and analyzed using statistical software (InStat version 3; GraphPad Software Inc, San Diego, Calif). The Fisher exact test was used to determine the significance of 2×2 contingency tables. A 2-tailed Mann-Whitney test was used to assess the significance of nonparametric data sets and an unpaired t test to determine the significance of data sets where it was reasonable to assume a parametric distribution (eg, weight). Statistical significance was accepted at $P<.05$. Unless otherwise stated, all data are reported as the percentage of the total patients in each group or as the mean (95% confidence intervals [CIs]).

ETHICAL APPROVAL

The protocol for this study was approved by the human research ethics committee at each participating hospital. The study was conducted in accord with the World Medical Association Declaration of Helsinki (revised 1989) and the National Health and Medical Research Council of Australia's guidelines on human experimentation.

RESULTS

From February 11, 2000, to February 26, 2003, 112 patients undergoing a laparoscopic fundoplication were enrolled in this trial. This fell short of the original target of 120 patients owing to recruitment difficulties in some centers. Fifty-two patients were randomized to undergo a Nissen fundoplication, and 60 to undergo anterior 90° partial fundoplication. Of these patients 96 (86%) were interviewed 1 month after surgery, 99 (88%) at 3 months, and 108 (96%) at 6 months. Missing data at the earlier time points were owing to an inability to contact patients at these specific follow-up time points. Only 4 pa-

tients did not provide clinical data 6 months after surgery. Two of these 4 could not be contacted then. They both had a satisfactory outcome at 3 months' follow-up. Two patients withdrew from the study before 6 months and refused a follow-up interview at 6 months. As far as could be determined, they also had a satisfactory clinical outcome at 6 months and were free of GER symptoms. Only data that were obtained by telephone interview were included in the data analysis below.

PREOPERATIVE ASSESSMENT

Both study groups were well matched for demographic parameters (**Table 3**) and the presence or absence of various preoperative symptoms (**Table 4** and **Table 5**), with the exception of a greater proportion of patients who underwent a laparoscopic Nissen fundoplication having undergone previous upper abdominal surgery. A significant proportion of patients in each group experienced preoperative dysphagia to some extent, with a preoperative incidence of 53% for the 90° partial fundoplication group and 56% for the laparoscopic Nissen group when assessed using the 0 to 45 dysphagia score (×6).

Endoscopic grading of esophagitis before surgery was similar. Ten (17%) of the 52 laparoscopic Nissen group and 3 (6%) of the 60 anterior 90° partial fundoplication group had Barrett esophagus at preoperative endoscopy (P=.08). A hiatus hernia was seen preoperatively in 33 (63%) of the laparoscopic Nissen group vs 35 (58%) of the anterior 90° partial fundoplication group (P=.68).

Preoperative esophageal manometry outcomes (**Table 6**) were similar for most parameters, although basal lower esophageal sphincter pressure and the percentage of normal swallows at manometry were slightly lower in the anterior 90° partial fundoplication group. However, the actual magnitude of these differences was small. Twenty-four–hour ambulatory pH monitoring was performed in 70% of patients. The mean percentage exposure to an acid pH of less than 4 was 11.5% for the anterior 90° partial fundoplication group and 11.2% for the laparoscopic Nissen group (P=.95).

SURGERY

Fifteen surgeons participated in the study. All patients had a fundoplication constructed according to the randomization schedule. Operating time varied from 30 to 195 minutes (mean, 88 minutes; median, 80 minutes; 95% CI, 76-100) for anterior 90° partial fundoplication, vs 25 to 230 minutes (mean, 96 minutes; median, 87 minutes; 95% CI, 83-109; P=.30) for Nissen fundoplication. The corresponding operating room times were 47 to 270 minutes (mean, 121 minutes; median, 110 minutes; 95% CI, 106-137) vs 40 to 400 minutes (mean, 135 minutes; median, 115 minutes; 95% CI, 113-156; P=.40). The laparoscopic procedure was converted to open surgery in 1 patient in the anterior 90° partial fundoplication group because of intra-abdominal adhesions and in 2 patients in the Nissen fundoplication group owing to adhesions in one patient, and intra-abdominal obesity plus bleeding in the other. Operating surgeons were asked to rate the difficulty of the operative procedure using a scale from 1 to 10. Anterior 90° partial fundoplication was thought to be an easier operation; mean score for the anterior 90° partial fundoplication was 4.1 (95% CI, 3.4-4.7) vs 5.3 (95% CI, 4.6-6.0) for Nissen fundoplication (P=.01).

Table 3. Preoperative Parameters in 112 Patients*

Variable	Type of Fundoplication: AP (n = 60)	LN (n = 52)	*P* Value
Age, y	47 (43 to 51)	49 (45 to 52)	.57
Sex, M/F	35/25	33/19	.70
Height, cm	170 (167 to 174)	171 (169 to 174)	.37
Weight, kg	84 (80 to 87)	84 (79 to 89)	.98
Patients who underwent previous abdominal surgery, %	54	43	.31
Patients who underwent previous upper abdominal surgery, %	6	29	.003
Duration of symptoms, y	9.6 (7.2 to 12.0)	10.2 (7.0 to 13.4)	.75

Abbreviations: AP, anterior 90° partial; LN, laparoscopic Nissen.
*Data are given as mean (95% confidence interval) unless otherwise indicated.

Table 4. Assessment of Heartburn by Visual Analog Scale*

Status	Type of Fundoplication: AP (n = 60)	LN (n = 52)	*P* Value
Preoperative	5.2 (4.3 to 6.1)	4.9 (3.9 to 5.8)	.63
Postoperative, mo			
1	0.5 (–.1 to 1.0)	0.8 (0.1 to 1.4)	.73
3	0.9 (0.2 to 1.5)	0.6 (0.1 to 1.0)	.82
6	1.0 (0.4 to 1.5)	0.1 (–0.004 to 0.2)	.15

Abbreviations: AP, anterior 90° partial; LN, laparoscopic Nissen.
*Data are given as mean (95% confidence interval).

EARLY HOSPITAL OUTCOMES

The periods between surgery and the commencement of oral fluids and solids and the length of postoperative hospital stay were not influenced by the type of laparoscopic fundoplication performed (**Table 7**). Patients took a mean of 2.6 weeks to return to normal physical activity following the 90° anterior 90° partial fundoplication and 2.9 weeks following laparoscopic Nissen fundoplication (P=.72). After the anterior 90° partial fundoplication, there was 1 of each of the following 5 complications: intraoperative pneumothorax, wound infection, urinary retention, pulmonary embolism, and small-bowel injury. The small-bowel injury was a complication of the use of a Veress needle for the commencement of insufflation, and it led to a laparotomy for peritonitis on the third postoperative day. Following laparoscopic Nissen fundoplication there was 1 of each of the following 4 complications: intraoperative pneumothorax, urinary retention, respiratory failure, and splenic infarction. The splenic infarct entailed the loss of blood sup-

Table 5. Summary of Preoperative and Postoperative Symptoms*

	Preoperative Status		Postoperative Status					
			At 1 mo		At 3 mo		At 6 mo	
Condition	AP	LN	AP	LN	AP	LN	AP	LN
Heartburn	88	92	12	13	14	10	19†	4†
Epigastric pain	85	75	24	40	22	38	32	37
Regurgitation	80	69	6	11	16	35	10	12
Odynophagia	20	15	16	22	4	4	3	10
Early satiety	58	56	63	58	37‡	67‡	36	46
Epigastric bloat	60	63	47§	27§	43‖	65‖	39	47
Anorexia	10	17	10	11	8	17	5	4
Nausea	43	38	31	29	16	29	22	29
Vomiting	23	33	8	0	8	0	3	4
Coughing	43	54	10	11	10	13	15	12
Wheezing	20	25	2	9	6	10	10	16
Can relieve bloat	64	65	81	54	81¶	50¶	74	53
Unable to belch	0	0	18#	53#	18	29	12**	43**
Eats normal diet	71	64	50	47	92	81	95	86
Increased flatus	NA	NA	65	64	53	69	51†	71†

Abbreviations: AP, anterior 90° partial fundoplication; LN, laparoscopic Nissen fundoplication; NA, not applicable.
*Data are given as percentages. Overall, no statistically significant differences were demonstrated between the 2 trial groups (ie, $P>.05$ at all follow-up intervals), except where indicated.
†$P=.03$.
‡$P=.005$.
§$P=.05$.
‖$P=.04$.
¶$P=.0007$.
#$P=.0005$.
**$P=.0003$.

ply to approximately 75% of the spleen following clipping of a bleeding vessel during division of the short gastric vessels. None of the complications following Nissen fundoplication required further surgical intervention.

1- TO 6-MONTH POSTOPERATIVE CLINICAL OUTCOME

A detailed analysis of the outcome of the masked standardized clinical assessment is summarized in **Tables** 4, 5, **8**, and **9**. At the 1-month follow-up, the ability to belch and symptoms of epigastric bloating were better preserved following anterior 90° partial fundoplication. There were no other statistically significant differences seen for any of the other outcomes assessed. At the 3-month follow-up, the outcome following anterior 90° partial fundoplication was better for the symptoms of early satiety, epigastric bloating, and dysphagia for solid food. At 6 months after surgery, patients who underwent the anterior 90° partial fundoplication were less likely to experience dysphagia or flatulence.

The incidence and severity of heartburn assessed by the yes/no question and the visual analog scale was identical at the 1- and 3-month follow-up points (Table 4). However, at 6 months patients were more likely to report heartburn (assessed by yes/no question) after anterior 90° partial fundoplication. Outcomes were also similar at the 1- and 3-month follow-up intervals for measures of overall outcome, visual analog scale satisfaction score, outcome scale, and modified Visick grading system (Table 9). At 6 months, a greater proportion of the patients who underwent an anterior 90° partial fundoplication (98% vs 88%) indicated that they thought they had made the correct decision to have a laparoscopic fundoplication.

One patient in the anterior 90° partial fundoplication group underwent revision surgery at 5 months after the original fundoplication. This entailed conversion to a posterior partial fundoplication for the treatment of recurrent GER. None of the Nissen fundoplication group underwent further surgery during the 6-month follow-up period.

OBJECTIVE POSTOPERATIVE INVESTIGATIONS

Seventy-three patients (65%) underwent postoperative endoscopy, 62 (55%) esophageal manometry, and 57 (51%) postoperative 24-hour pH monitoring. The clinical outcomes in patients who underwent postoperative investigation were similar to the outcomes in those patients who declined investigation. Endoscopy demonstrated an intact fundoplication in all patients who had undergone anterior 90° partial fundoplication, and in all but 1 patient following Nissen fundoplication. Following Nissen fundoplication 2 patients had ulcerative esophagitis compared with 4 patients after anterior 90° partial fundoplication.

Esophageal manometry outcomes following surgery are summarized in Table 6. Esophageal body motility parameters and lower esophageal sphincter parameters were similar for the 2 procedures, although there was a trend toward more complete sphincter relaxation with swallowing following anterior 90° partial fundoplication.

Table 6. Esophageal Manometry Results*

Variable	Type of Fundoplication		*P* Value
	AP	LN	
Preoperative status			
No. of propagated swallows†	8.9 (8.4 to 9.4)	9.6 (9.3 to 10.0)	.03
No. of normal peristalsis‡	75	85	.31
LES resting pressure	8.1 (5.4 to 10.8)	9.5 (7.7 to 11.4)	.01
LES residual relaxation pressure	0.3 (–0.2 to 0.9)	0.6 (–0.1 to 1.3)	.52
Resting LES pressure <10‡	75	61	.13
Postoperative status			
No. of propagated swallows†	8.0 (6.5 to 9.4)	7.7 (6.3 to 9.1)	.67
No. of normal peristalsis‡	88	84	.99
LES resting pressure	16.4 (12.0 to 20.7)	14.1 (11.6 to 16.6)	.39
LES residual relaxation pressure	2.4 (1.0 to 3.9)	5.0 (2.7 to 7.3)	.06
Resting LES pressure <10	29	31	.99

Abbreviations: AP, anterior 90° partial; LES, lower esophageal sphincter; LN, laparoscopic Nissen.
*Data are given as mean (95% confidence interval). All pressures are expressed in millimeters of mercury.
†Swallowing was assessed from 10 wet swallows.
‡Data are given as the percentage of the total number.

Twenty-four–hour pH monitoring demonstrated normalization of acid exposure times in all but 6 patients (2 in the Nissen group and 4 in the anterior 90° partial fundoplication group). Three of these patients had symptoms of recurrent GER—all following anterior 90° fundoplication, and 3 had no GER symptoms (Nissen fundoplication group, 2 patients; anterior 90° partial fundoplication group, 1 patient). Overall postoperative exposure to acid pH (<4) was similar for the 2 groups—anterior 90° partial fundoplication group, 2.7% (95% CI, 0.6%-4.8%) and Nissen fundoplication group, 1.6% (95% CI, 0.5%-2.7%).

Table 7. Early Hospital Outcomes*

Variable	Type of Fundoplication		*P* Value
	AP	LN	
Postoperative stay, d	2.7 (2.3 to 3.1) [2]	2.5 (2.1 to 3.0) [2]	.52
Days to taking oral fluids	0.9 (0.6 to 1.2) [1]	0.6 (0.5 to 0.8) [1]	.23
Days to taking solid foods	1.8 (1.5 to 2.1) [2]	1.6 (1.4 to 1.8) [1]	.34

*Data are given as mean (95% confidence interval) [median].

COMMENT

While Nissen fundoplication and its various modifications have been in clinical practice for half a century, it continues to be associated with troublesome postoperative adverse effects in a small, but important, proportion of patients who undergo antireflux surgery.[1] Modification to a partial fundoplication has been recommended as a strategy with the potential to yield a better overall outcome. Worldwide, posterior partial fundoplication variants are the more usual surgical approach although anterior partial fundoplication has been gaining support recently.[3,8,9]

The outcomes of 5 prospective randomized trials of Nissen vs posterior partial fundoplication have been reported.[2,10-13] Three of these demonstrated no difference in outcome, although in each instance the number of patients enrolled was small and the studies were insufficiently powered to demonstrate real differences.[10,11,13] Hagedorn et al[2] reported a trial of 137 patients with follow-up extending for more than 10 years. Their study demonstrated a reduction in the gas-related adverse effects following posterior partial fundoplication, although the incidence and severity of dysphagia was not influenced by the surgical technique. In 2002 Zornig et al[12] reported the very early outcomes of a trial of 200 patients that showed a reduction in dysphagia at 4 months after posterior partial fundoplication. However, to our knowledge, longer-term outcomes have not yet been described.

The alternative of anterior partial fundoplication has been described in several articles. An anterior 120° partial fundoplication was reported in 1991 and the initial results of this procedure have been promising.[14] In the laparoscopic era, this procedure was modified by some of us to an anterior 180° partial fundoplication.[3] This included sutures that anchored the fundus of the stomach to the right side of the esophageal hiatal rim, a step which was not included in the anterior 120° partial fundoplication procedure. The 180° approach has been validated in a prospective randomized trial of 107 patients, at 6-month[3] and 5-year follow-ups.[4] This trial demonstrated effective GER control and a reduced incidence of dysphagia and other adverse effects following anterior 180° fundoplication. In 2003 Hagedorn et al[15] reported the 12-month follow-up of a trial in which 95 patients were randomized to undergo either an anterior 120° partial fundoplication or a posterior partial fundoplication. The study results suggested that the anterior fundoplication provided less effective GER control than posterior fundoplication. However, the outcome for GER control for the anterior fundoplication in this trial was much worse than has been reported in other studies.[3,14]

In an attempt to further reduce the adverse effects of antireflux surgery, some of us initiated laboratory[6] and early clinical work[5] to determine whether modification

Table 8. Dysphagia Assessment*

	Preoperative Status		Postoperative Status					
			At 1 mo		At 3 mo		At 6 mo	
Variable	AP	LN	AP	LN	AP	LN	AP	LN
Dysphagia†	35	35	49	40	16‡	35‡	14	22
For lumpy solids	2	2	10	16	6	15	2	10
For soft solids	4	6	6	16	4	10	0§	10§
For liquids								
Visual analog scale‖								
Solids	2.0 (1.3 to 2.7)	2.4 (1.5 to 3.2)	4.3 (3.3 to 5.3)	4.9 (3.8 to 5.9)	1.3 (0.6 to 1.9)§	2.7 (1.8 to 3.6)§	0.9 (0.4 to 1.5)	1.7 (0.9 to 2.6)
Liquids	0.6 (0.1 to 1.0)	1.0 (0.4 to 1.5)	0.9 (0.2 to 1.6)	1.7 (0.7 to 2.7)	0.5 (0.0 to 0.9)	0.7 (0.2 to 1.2)	0.2 (−0.03 to 0.4)	1.0 (0.3 to 1.7)
Dysphagia score‖								
Overall result	7.9 (5.2 to 10.6)	9.0 (6.1 to 12.0)	NA	NA	5.8 (3.2 to 8.3)	10.4 (6.9 to 13.9)	3.2 (1.6 to 4.7)	7.5 (3.9 to 11.0)
Scored 0 only	47	44	NA	NA	57	45	66	55

Abbreviation: AP, anterior 90° partial fundoplication; LN, laparoscopic Nissen fundoplication; NA, not assessable owing to diet restrictions.
*No significant differences demonstrated between trial groups (ie, $P>.05$ at all follow-up intervals), except where indicated.
†Data are given as the percentage of total.
‡$P=.04$.
§$P=.02$.
‖Data are given as the mean (95% confidence interval).

Table 9. Outcome, Satisfaction, and Visick Grading*

	Preoperative		Postoperative Status					
			At 1 mo		At 3 mo		At 6 mo	
Variable	AP	LN	AP	LN	AP	LN	AP	LN
Outcome†								
Excellent	NA	NA	22	10	35	15	37	20
Good	NA	NA	56	62	46	60	46	67
Fair	NA	NA	18	17	10	19	9	10
Poor	NA	NA	4	12	8	6	9	2
Modified Visick grade‡								
1	0	0	12	2	26	15	29	16
2	6	7	53	56	52	56	48	61
3	47	32	20	19	11	17	10	8
4	47	61	12	12	4	8	3	12
5	0	0	4	12	7	4	9	2
Satisfaction score								
Mean score	NA	NA	8.6	8.1	8.4	8.2	8.4	8.6
95% CI	NA	NA	8.0 to 9.3	7.2 to 9.1	7.8 to 9.1	7.4 to 8.9	7.8 to 9.1	7.9 to 9.2
Would have the operation again	NA	NA	94	90	93	87	98§	88§

Abbreviations: AP, anterior 90° partial fundoplication; CI, confidence interval; LN, laparoscopic Nissen fundoplication; NA, not applicable.
*Data are given as percentages unless otherwise indicated. No significant differences were demonstrated between trial groups (ie, $P>.05$ at all follow-up intervals) except where indicated.
†See Table 2 for an explanation of the assessment rating.
‡See Table 1 for an explanation of the modified Visick grading system.
§$P=.05$.

to an anterior 90° partial fundoplication could achieve a durable outcome but with even fewer adverse effects than the previous procedures. Initial testing in a porcine model demonstrated the short-term effectiveness of this approach,[6] and an initial clinical study demonstrated effective GER control and a low rate of adverse effects.[5] This supported further evaluation of this technique within a randomized trial. In addition, all previous randomized studies that compared partial with total fundoplication have been single-center studies, and this has limited the generalizability of the outcomes to community practice. For this reason, we commenced this multicenter study.

The results of our trial have demonstrated that the anterior 90° partial fundoplication procedure is followed by fewer postoperative adverse effects than Nissen fundoplication. In particular, the anterior 90° partial fundoplication procedure was associated with less gas-related adverse effects at all follow-up intervals and less dysphagia. While not all differences in the measures of dysphagia reached statistical significance, some did, and the trends for all other measures of dysphagia were to-

ward less dysphagia following the anterior 90° partial fundoplication.

However, this better adverse effect profile was counterbalanced by a higher likelihood of postoperative GER symptoms. In particular, the responses to the direct yes/no heartburn question suggest a higher incidence of GER at 6 months after undergoing an anterior 90° partial fundoplication. However, this is a blunt tool for detecting further GER. It does not discriminate between mild and more troublesome symptoms, and an affirmative answer is not always associated with objective evidence of GER. Furthermore, effective control of GER was achieved for most patients, and the heartburn visual analog scale confirmed this in most patients in both study groups.

When considering the outcome of an antireflux procedure, it is important to consider the patient's perspective as well as measures of technical success. Measures of overall outcome that balance control of GER against postoperative adverse effects are arguably more important to individual patients. The direct question that asked whether patients believed that they had made the correct decision to have a laparoscopic fundoplication confirmed a high rate of satisfaction 6 months after undergoing anterior 90° partial fundoplication (98%; 59 of 60 patients). This was significantly better than that following Nissen fundoplication. The outcome for the other measure (visual analog satisfaction score) was equally high in both patient groups.

A possible criticism of our trial is that it can be difficult to standardize technical aspects of the surgical procedures across multiple sites. However, this could also be a strength because the multicenter design of this study and the similar number of patients contributed by each surgeon aiming for a quota means that it should be possible to generalize the outcome to community practice with greater confidence. In addition, we endeavored to standardize both operative procedures by discussing techniques at face-to-face meetings and circulating a reference videotape. This ensured that the core aspects of each technique were performed in a similar way. Furthermore, follow-up bias was minimized by performing all follow-up interviews in a masked fashion. For 12 of the 15 surgeons the anterior 90° partial fundoplication was a new operation with the Nissen fundoplication being the operation with which they were most familiar. In other words, if bias exists in this study, it is probably against the anterior 90° partial fundoplication.

The outcome of this trial is similar to the results from the trial of Nissen vs anterior 180° partial fundoplication conducted previously at the Royal Adelaide Hospital,[3] that is, there is a trade-off between the risk of adverse effects and the risk of recurrent GER. This tension between opposing outcomes must be weighed when determining what type of fundoplication to apply in clinical practice. The current trial has demonstrated that laparoscopic anterior 90° partial fundoplication provides effective GER control with a low rate of postoperative adverse effects at the 6-month follow-up, and that this technique is associated with a high rate of patient satisfaction. These early outcomes support the continued evaluation of this technique although longer-term follow-up is needed before this procedure can be recommended for routine clinical application.

Accepted for Publication: March 16, 2004.
Correspondence: David I. Watson, MD, Department of Surgery, Flinders University of South Australia, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia (david.watson@flinders.edu.au).
Funding/Support: This study was supported in part by funds from the National Heath and Medical Research Council of Australia, Canberra, and a grant from Astra Upper Gastrointestinal Research through the Royal Australasian College of Surgeons, Melbourne, Australia.
Acknowledgment: We acknowledge the assistance of Nicola Ascott and Tanya Ellis for their invaluable organizational and logistical support.

REFERENCES

1. Watson DI, Jamieson GG. Antireflux surgery in the laparoscopic era. *Br J Surg.* 1998;85:1173-1184 [review].
2. Hagedorn C, Lonroth H, Rydberg L, Ruth M, Lundell L. Long-term efficacy of total (Nissen-Rossetti) and posterior partial (Toupet) fundoplication: results of a randomized clinical trial. *J Gastrointest Surg.* 2002;6:540-545.
3. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. A prospective randomised double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg.* 1999;86:123-130.
4. Ludemann R, Watson DI, Game PA, Devitt PG, Jamieson GG. Laparoscopic Nissen fundoplication versus anterior 180° fundoplication: five-year follow-up of a prospective randomized trial. *Br J Surg.* In press.
5. Krysztopik RJ, Jamieson GG, Devitt PG, Watson DI. A further modification of the Nissen fundoplication: 90 degree anterior fundoplication. *Surg Endosc.* 2002; 16:1446-1451.
6. Yau P, Watson DI, Ascott N, Lafullarde T, Jamieson GG. Efficacy of a 90 degree anterior fundoplication versus a total fundoplication in an experimental model. *Surg Endosc.* 2000;14:830-833.
7. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol.* 1992;14:99-100.
8. Ross S, Jabbar A, Ramsay CR, Watson AJ, Grant AM, Krukowski ZH. Symptomatic outcome following laparoscopic anterior partial fundoplication: follow-up of a series of 200 patients. *J R Coll Surg Edinb.* 2000;45:363-365.
9. Windsor JA, Yellapu S. Laparoscopic anti-reflux surgery in New Zealand: a trend towards partial fundoplication. *Aust N Z J Surg.* 2000;70:184-187.
10. Walker SJ, Holt S, Sanderson CJ, Stoddard CJ. Comparison of Nissen total and Lind partial transabdominal fundoplication in the treatment of gastro-oesophageal reflux. *Br J Surg.* 1992;79:410-414.
11. Thor KB, Silander T. A long-term randomized prospective trial of the Nissen procedure versus a modified Toupet technique. *Ann Surg.* 1989;210:719-724.
12. Zornig C, Strate U, Fibbe C, Emmermann A, Layer P. Nissen vs Toupet laparoscopic fundoplication. *Surg Endosc.* 2002;16:758-766.
13. Laws HL, Clements RH, Swillies CM. A randomized, prospective comparison of the Nissen versus the Toupet fundoplication for gastroesophageal reflux disease. *Ann Surg.* 1997;225:647-654.
14. Watson A, Jenkinson LR, Ball CS, Norris TL. A more physiological alternative to total fundoplication for the surgical correction of resistant gastro-oesophageal reflux. *Br J Surg.* 1991;78:1088-1094.
15. Hagedorn C, Jonson C, Lonroth H, Ruth M, Thune A, Lundell L. Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial. *Ann Surg.* 2003;238:189-196.

World Journal of Surgery

Published Online: 4 September 2006

World J Surg (2006) 30: 1856–1863
DOI: 10.1007/s00268-005-0623-7

Quality of Life Following Laparoscopic Anterior 90° Versus Nissen Fundoplication: Results from a Multicenter Randomized Trial

Sean A. Woodcock, MS, FRCS,[1] David I. Watson, MD, FRACS,[1] Carolyn Lally, RN,[2] Stephen Archer, PhD, FRACS,[3] Justin R. Bessell, MD, FRACS,[1] Michael Booth, MB, BS, FRACS,[4] Richard Cade, MB, BS, FRACS,[5] Graham L. Cullingford, MB, BS, FRACS,[3] Peter G. Devitt, MS, FRACS,[2] David R. Fletcher, MD, FRACS,[3] James Hurley, MB, BS, FRACS,[5] Glyn G. Jamieson, MS, FRCS, FRACS,[2] George Kiroff, MS FRACS,[5] Christopher J. Martin, MSc, FRACS,[6] Ian J.G. Martin, MB, BS, FRACS,[7] Leslie K. Nathanson, MB, ChB, FRACS,[7] John A. Windsor, MD, FRACS,[4] for the International Society for Diseases of the Esophagus – Australasian Section

[1] *Flinders University of South Australia, Adelaide, SA, Australia*
[2] *University of Adelaide, Adelaide, SA, Australia*
[3] *University of Western Australia, Crawley, WA, Australia*
[4] *University of Auckland, Auckland, New Zealand*
[5] *Melbourne University, Melbourne, VIC, Australia*
[6] *University of Sydney, Sydney, NSW, Australia*
[7] *University of Queensland, Brisbane, QLD, Australia*

Abstract

Background: The short-term clinical outcomes from a multicenter prospective randomized trial of laparoscopic Nissen versus anterior 90° partial fundoplication have been reported previously. These demonstrated a high level of satisfaction with the overall outcome following anterior 90° fundoplication. However, the results of postoperative objective tests and specific clinical symptoms are not always consistent with an individual patient's functional status and general well being following surgery, and quality of life (QOL) is also an important outcome to consider following surgery for reflux. Hence, QOL information was collected in this trial to investigate the hypothesis: improvements in QOL following laparoscopic antireflux surgery are greater after anterior 90° partial fundoplication than after Nissen fundoplication.

Methods: Patients undergoing a laparoscopic fundoplication for gastro-esophageal reflux at one of nine university teaching hospitals in six major cities in Australia and New Zealand were randomized to undergo either laparoscopic Nissen or anterior 90° partial fundoplication. Quality of life before and after surgery was assessed using validated questionnaires – the Short Form 36 general health questionnaire (SF36) and an Illness Behavior Questionnaire (IBQ). Patients were asked to complete these questionnaires preoperatively and at 3, 6, 12 and 24 months postoperatively.

Correspondence to: David I. Watson, MD, FRACS, Department of Surgery, Flinders University of South Australia, Room 3D211, Flinders Medical Centre, Bedford Park, SA, 5042 Australia, e-mail: david.watson@flinders.edu.au

Results: One hundred and twelve patients were randomized to undergo a Nissen fundoplication (52) or a 90° anterior fundoplication (60). Patients who underwent anterior fundoplication reported significant improvements in eight of the nine SF36 scales compared to four of the nine following a Nissen fundoplication. The majority of these improvements occurred early in the postoperative period. With respect to the illness behavior data, there were no significant differences between the two procedures. Both groups had a significant improvement in disease conviction scores at all time points compared to their preoperative scores.
Conclusions: Patients undergoing laparoscopic anterior 90° partial fundoplication reported more QOL improvements in the early postoperative period than patients undergoing a Nissen fundoplication. However, the QOL outcome for both procedures was similar at later follow-up.

The surgical management of gastro-esophageal reflux has evolved over the last 50 years. Most operations are now performed laparoscopically, and excellent reflux control is reported following laparoscopic Nissen fundoplication.[1,2] Unfortunately, however, in some patients Nissen fundoplication is followed by persistent dysphagia, epigastric bloating, inability to belch and flatulence.[3] Partial fundoplication variants have been developed to overcome these problems.[2,4,5] Posterior partial fundoplication has been the usual approach to this, although good reflux control with minimal side effects have also been reported following various types of anterior partial fundoplication.[6–9] Two randomized trials have reported good outcomes following an anterior 180° partial fundoplication at 2- and 5-year follow-ups.[7,10] Despite these variants, however, the anterior partial fundoplication procedures in these trials were still associated with an incidence, albeit low, of side effects.

To investigate the hypothesis that an anterior 90° partial fundoplication is an effective antireflux procedure, and is associated with an even lower risk of side effects, we commenced a multicenter prospective randomized trial of laparoscopic Nissen versus anterior 90° partial fundoplication. The short-term clinical outcomes of this trial have been reported previously.[9] A high level of satisfaction with the overall surgical outcome was demonstrated following anterior 90° fundoplication. However, in this and other randomized trials, the reduction in postoperative side effects following anterior partial fundoplication has been to some extent balanced against an increased risk of recurrent reflux.

When comparing different procedures, most trials focus on clinical symptoms and objective outcome measures, such as esophageal manometry and 24-hour pH monitoring.[7,11] Alternatively, assessments of postoperative anatomy by either endoscopy or contrast X-ray studies are also often undertaken.[12] The results of these objective tests, however, are not always consistent with an individual patient's functional status, general well being or satisfaction following surgery.[13] Despite a technically good procedure, and satisfactory objective postoperative parameters, some patients are not satisfied with the outcome of the surgery. For this reason, quality of life (QOL) is also an important outcome to consider following surgery for reflux.

A range of research instruments have been used to measure QOL; these include such global measures of QOL as the Short Form 36 (SF36) as well as organ-specific measures, such as the Gastrointestinal Quality-of-Life Index. We have also reported that the outcome of fundoplication is determined, in part, by preoperative illness behavior.[14] This observation can also be quantitatively measured. Hence, when we established our randomized trial of Nissen versus anterior 90° partial fundoplication, we included a global QOL assessment and illness behavior assessment in the follow-up protocol. This paper reports the early outcomes from these assessments.

METHODS

In a multicenter randomized study we investigated the hypothesis that a laparoscopic anterior 90° partial fundoplication results in greater improvements in QOL than laparoscopic Nissen fundoplication. Fifteen surgeons from nine teaching hospitals in Australia and New Zealand contributed patients to this study. The full details of the protocol have been reported elsewhere.[9] In this paper we report the use of QOL assessments, with follow-up of up to 2 years.

Patients with objectively proven gastro-esophageal reflux disease (GORD) and who presented for primary antireflux surgery were considered for entry into this trial. These patients were randomly assigned, in the operating theater, after commencing general anesthesia, to undergo either a laparoscopic Nissen fundoplication with division of short gastric blood vessels, or a laparoscopic

anterior 90° partial fundoplication. The full details of the surgical techniques have been reported elsewhere.[8,9] In both procedures, the esophageal hiatus was routinely repaired with posterior sutures. The laparoscopic Nissen fundoplication included full mobilization of the gastric fundus to create a "floppy" short wrap. The laparoscopic anterior 90° was constructed using an 'esophagopexy' suture between the distal esophagus and the posterior aspect of either the right hiatal pillar or both pillars. Two sutures were used to accentuate the angle of His, one suture to anchor the gastric fundus to the anterior esophagus, and to the apex of the esophageal hiatus, and one suture to fix the inferior edge of the fundal fold to the anterior esophagus. This produced a limited fundoplication. Surgical techniques were standardized across all sites before commencing the study. Details of the postoperative care and clinical follow-up have also been described elsewhere.[9]

A measure of QOL (SF36), and a measure of illness behavior (Illness Behavior Questionnaire, IBQ) were used during follow-up. Patients were followed clinically at 1, 3, 6, 12 and 24 months following surgery by means of a telephone interview. Following the interview the questionnaires were mailed out to the patients, who were asked to return the completed questionnaires using a reply-paid envelope. The returned questionnaires were scored, and data entered onto a computerized database (FILEMAKER PRO ver. 5.5; Filemaker Corp, Santa Clara, Calif.).

The SF36 questionnaire comprises 36 questions that were designed to measure nine generic health concepts. These are summarized in Table 1. The SF36 has been validated previously and has been used elsewhere for the assessment of QOL following laparoscopic management of GORD.[15]

The IBQ, designed and validated by Pilowsky and Spence, consists of 62 yes/no items which elicit various dimensions of illness behavior. It was developed as a self-report instrument to record seven aspects of illness behavior, in particular those attitudes that suggest inappropriate or maladaptive modes of responding to one's state of health (Table 2).[16] We have described its use for the assessment of patients undergoing laparoscopic surgery for reflux in a previous paper.[14] Patient responses to the IBQ were used to generate seven first-order factors. For each factor, a score on an ordinal scale was obtained, with higher scores usually representing less desirable psycho-social states or illness behavior.

Data sets were compared for patients within each trial group before versus after surgery. Comparisons were also made between the two trial groups at identical time points. All analyses were performed on an intention-to-treat basis, with all patients remaining in their initial allocated group for data analysis. Data were analyzed using statistical software (INSTAT ver. 3; GraphPad Software, San Diego, Calif.). The Wilcoxon rank test was used to assess the significance of differences between data sets. Statistical significance was accepted at a P value of less than 0.05.

The protocol for this study was approved by the Human Research Ethics Committee at each participating hospi-

Table 1.
Parameters measured by the Short Form 36 (SF36)

Concept	Summary
Physical functioning	Extent to which health limits physical activities
Role functioning – physical	Extent to which physical healthy interferes with work or other daily activities
Bodily pain	Intensity of pain and effect of pain on normal work
General health	Personal evaluation of health
Vitality	Feeling energetic
Social functioning	Extent to which physical health or emotions interfere with social activities
Role functioning – emotional	Extent to which emotional problems interfere with work or daily activities
Mental health	General mental health
Reported health transition	Evaluation of current health compared to 1 year ago

Table 2.
Parameters measured by the Illness Behavior Questionnaire (IBQ)

Aspect of illness behavior	Summary
Illness-related psycho-social factors	
General hypochondriasis	General factor marked by phobic concern about one's state of health
Disease conviction	Affirmation that physical disease exists
Psychological vs. somatic perception of illness	Patient feels responsible for and deserves illness
General factors	
Affective inhibition	Difficulty in expressing personal feelings
Affective disturbance	Feelings of anxiety/sadness
Denial	Tendency to deny life's stresses
Irritability	Presence of angry feelings and interpersonal friction

tal. The study was conducted in accordance with the World Medical Association declaration of Helsinki (revised 1989), and the National Health and Medical Research Council of Australia's guidelines on human experimentation.

RESULTS

From February 2000 to February 2003, 112 patients undergoing a laparoscopic fundoplication were entered into this trial. Fifty two patients were randomized to undergo a Nissen fundoplication, and 60 to undergo an anterior 90° partial fundoplication. Both study groups were well matched for demographic parameters. The full clinical outcome data as well as the results of objective follow-up using esophageal manometry, pH monitoring and endoscopy have been reported elsewhere.[9] In general, the objective outcomes supported the previous clinical findings that anterior 90° partial fundoplication is followed by fewer side effects but with more reflux than Nissen fundoplication. There were also no significant differences between the clinical or objective outcomes achieved in each of the centers which contributed patients to this trial, and all centers performed a similar proportion of anterior 90° and Nissen fundoplications.

Preoperatively, an adequately completed SF36 questionnaire was obtained from 96 (86%) patients. Completion rates following surgery were: 51 (45%) at 1 month after surgery, 73 (65%) at 3 months, 71 (63%) at 6 months, 44 (39%) at 12 months and 52 (46%) at 24 months. Data from completed IBQs were obtained from 91 patients (81%) preoperatively, 51 (45%) at 1 month after surgery, 70 (63%) at 3 months, 68 (61%) at 6 months, 40 (36%) at 12 months and 54 (48%) at 24 months. The completion rates were similar in both groups of patients. Missing data were sometimes due to being unable to contact patients at specific time points, although more commonly it was because some patients chose not to complete and return the questionnaires. In most instances, however, patients who did not complete questionnaires still participated in a telephone interview to elucidate the clinical outcomes which have been reported elsewhere.[9] Only data which were obtained from completed questionnaires have contributed to the data analysis in the current paper.

Short Form 36

There were no differences between the two groups with respect to preoperative data collected for each parameter. The data for each parameter are summarized in Figures 1–6. Unless otherwise stated, there were no statistically significant differences between the patient groups. Overall, there were a range of factors which improved following fundoplication in both trial groups. Patients who underwent anterior fundoplication reported significant improvements in eight of the nine SF36 scales at some stage after surgery, compared to four of the nine following a Nissen fundoplication. The majority of improvements occurred early in the postoperative period, particularly following anterior partial fundoplication. At later follow-up (1 and 2 years) the outcomes for the two study groups were similar.

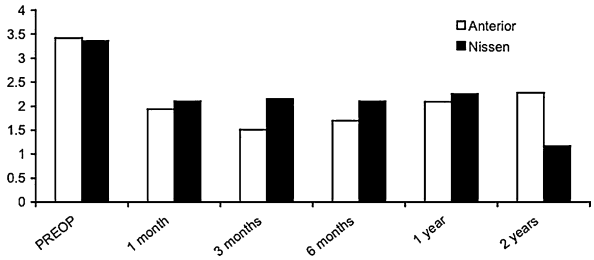


Figure 1. Short Form 36 (SF36) Reported health transition scores.

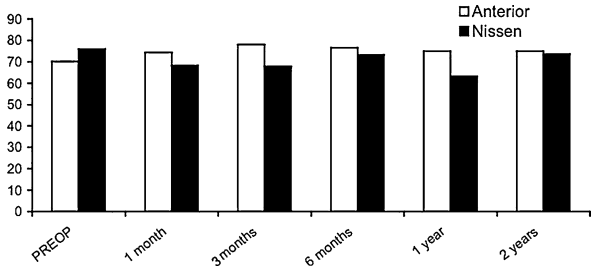


Figure 2. SF36 Physical functioning scores.

Health Transition Scores (Fig. 1). Both procedures were followed by a significant improvement in their Health transition scores at all postoperative time points when compared to preoperative scores. At 3 months following surgery, there was a significant difference in this score in favor of those patients who underwent an anterior partial fundoplication ($P = 0.05$).

Physical Functioning (Fig. 2). Patients who underwent an anterior partial fundoplication reported a significant improvement in their Physical functioning scores at 3 ($P = 0.05$) and 6 months ($P = 0.007$) postoperatively compared to preoperative scores. No improvements were seen following Nissen fundoplication.

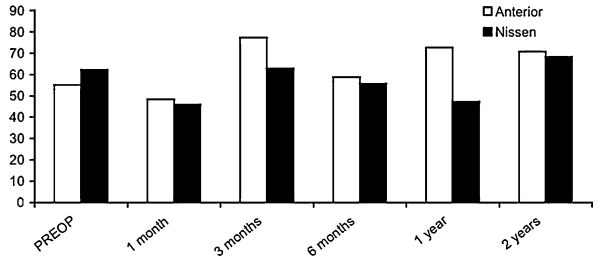


Figure 3. SF36 Role functioning – physical scores.

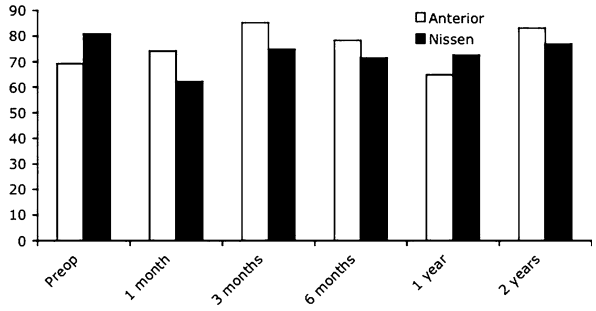


Figure 4. SF36 Social functioning scores.

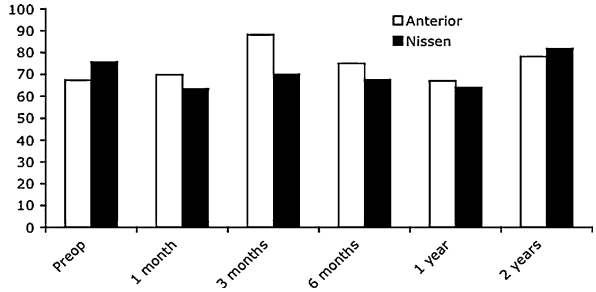


Figure 5. SF36 Role functioning – emotional scores.

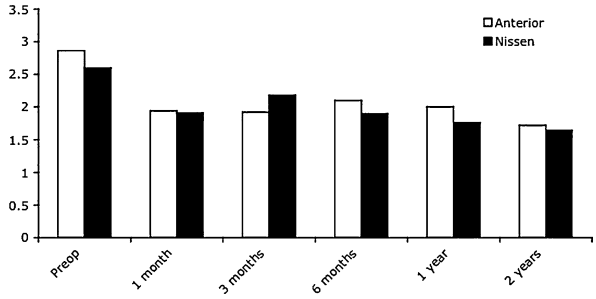


Figure 6. Illness Behavior Questionnaire (IBQ) Disease conviction scores.

Role Functioning – Physical (Fig. 3). Both procedures were associated with a significant improvement in the Role functioning – physical scores at 3 months postoperatively, compared to preoperative scores. At 12 months after surgery, there was a significant difference in favor of those patients who underwent an anterior partial fundoplication compared to Nissen fundoplication ($P = 0.05$).

Bodily Pain. Both procedures were followed by significant improvements in Bodily pain scores at follow-up from 3 to 24 months. However, there were no significant differences seen between the two study groups.

General Health. Patients who underwent an anterior partial fundoplication reported a significant improvement in their General health scores 3 months after surgery. Patients who underwent a Nissen fundoplication had a significant improvement in General Health scores at 1,3,6 and 24 months after surgery. There were no differences between the two groups at any of the follow-up time points.

Vitality. There were no differences for Vitality scores in either group, except at 24 months after surgery. At this time there was a significant improvement in scores in patients who had undergone a Nissen fundoplication, compared to the preoperative score. However, there were no significant differences between the study groups for this parameter at the 24-month follow-up.

Social Functioning (Fig. 4). There was a significant deterioration in Social functioning scores 1 month after surgery in those patient who had undergone a Nissen fundoplication, compared to preoperative scores. Patients who had undergone an anterior partial fundoplication had significant improvements in Social functioning scores at 3, 6 and 24 months postoperatively, compared to preoperative scores.

Role Emotional (Fig. 5). A significant improvement in the Role emotional score was reported at 3 months after surgery in patients who had undergone an anterior partial fundoplication, compared to both preoperative scores and to patients who had undergone a Nissen fundoplication at the same time point.

Mental Health. Patients who underwent an anterior partial fundoplication reported a significant improvement in Mental health scores at 1 and 3 months postoperatively, compared to preoperative scores. No significant improvements were seen for patients who had undergone

a Nissen fundoplication. For this parameter, there were no differences between the study groups at follow-up time point.

Illness Behavior Questionnaires

There were no significant differences between the two study groups with respect to preoperative data or postoperative data for the following parameters: general hypochondriasis, psychological compared to somatic perception of illness, affective inhibition, affective disturbance, denial and irritability. Both procedures were, however, followed by a significant improvement in Disease conviction scores at all follow-up time points, compared to preoperative scores (Fig. 6). There were no other statistically significant changes following surgery in either group.

DISCUSSION

Laparoscopic approaches to antireflux surgery have made surgery more appealing to patients with gastro-esophageal reflux. A range of procedures are now applied, and these include total (Nissen) fundoplication and various types of partial fundoplication. However, opinions continue to differ about which procedure achieves the best outcome. Following concerns about some patients developing troublesome long-term dysphagia and other side effects following Nissen fundoplication, we have investigated the alternative of anterior partial fundoplication for the surgical treatment of reflux. Previous studies, including randomized trials, have shown that most patients have a good outcome following anterior 180° partial fundoplication and that this procedure is followed by an acceptably low rate of recurrent reflux as well as a low risk of side effects.[7,9,17]

We subsequently undertook laboratory-based experiments to determine whether a more anatomical approach to reconstruction of the anatomy at the gastro-esophageal junction would yield an even better outcome. These experiments and early clinical studies have confirmed the efficacy of an anterior 90° partial fundoplication for the treatment of gastro-esophageal reflux.[8,18] This work was followed by this multicenter Australasian randomized trial, which compared the anterior 90° partial fundoplication with a standard Nissen fundoplication. The early clinical and objective outcomes from this trial have been reported elsewhere.[9] At the 6-month follow-up, 90° anterior partial fundoplication achieved effective reflux control, with a low rate of short-term side effects and a higher level of overall satisfaction with the outcome, thereby highlighting the potential for this approach to achieve a more acceptable overall outcome for patients undergoing laparoscopic antireflux surgery. The longer term outcomes from this trial will be reported as the follow-up matures.

The previous report from our trial as well as most other outcome studies on antireflux surgery have focused on standard clinical symptoms of reflux and potential side effects and/or objective outcome parameters – for example, esophageal manometry and 24-hour ambulatory pH monitoring.[7,10,19] Quality of life, however, is another important aspect of the postoperative outcome.[20,21] It measures, in an objective fashion, the overall outcome from the patient's perspective. A range of QOL measures have been described and validated. In general, these can be classified as either general or disease-specific QOL measures. In our trial we used two general QOL measures. The IBQ was selected because we had had previous experience with its use as a tool for evaluating outcome following Nissen fundoplication[14] in which some of the parameters measured by the IBQ were shown to correlate with the outcome of surgery. The SF36 was chosen because it is a good measure of overall QOL. Furthermore, it is readily available, widely used and well validated. Because we have examined clinical symptoms in detail as part of the clinical follow-up of our randomized trial, we did not apply a gastrointestinal disease-specific measure.

The results from our trial demonstrate general improvements in QOL and health status following both laparoscopic anterior 90° partial and Nissen fundoplication. In general, the degree of improvement was greater after anterior 90° partial fundoplication, predominantly during the first 1–6 months of follow-up; at later follow-up, the outcomes were more similar. This result demonstrates that both types of fundoplication improve overall QOL, presumably because they are both effective antireflux procedures. The early advantages of anterior fundoplication, however, appear to disappear as the follow-up lengthens. The difference in early outcome is probably due to the reduced rate of side effects seen in early follow-up following anterior fundoplication, as reported previously. As time progresses following Nissen fundoplication, however, adverse effects, such as dysphagia, bloating and flatulence, tend to improve, and this might account for the similar QOL outcome at the 12-month and 2-year follow-up. Other studies have also confirmed that the QOL measured by SF-36 improves following antireflux surgery.[22,23]

A possible weakness of our current report, however, is that some patients did not complete follow-up SF-36 or

IBQ questionnaires. This has made our data analysis less robust than it would have been if the follow-up was complete. The difference in follow-up rates of 96% in our previously reported clinical study[9] versus 40–65% at different time points in the current study reflects different the follow-up methods. For clinical follow-up in this trial we used a telephone interview, whereas the QOL follow-up was obtained by mailing out two questionnaires. The lower response rate is consistent with the different follow-up methodology. Unfortunately, our resources constrained us from administering the QOL assessment by telephone or personal interview. The results of our current study, however, do add support to the conclusion of our previous report of early clinical follow-up, in which we achieved a 96% rate of follow-up; i.e., at the 6-month follow-up, anterior 90° partial fundoplication achieves effective reflux control, a high rate of satisfaction, and it is followed by fewer side effects.

Similar outcomes to our study have been reported in a non-randomized study which used the Gastrointestinal Quality of Life Index to compare outcomes following laparoscopic Nissen and Toupet fundoplications 5 years after surgery. This study also demonstrated that fundoplication was followed by significant improvements in QOL and that the QOL scores were almost equal for both operations – and comparable to values in healthy controls.[24]

It will be interesting to see the longer term clinical follow-up for patients in our randomized trial. The results of the QOL assessment in our current study suggest that some of the clinical outcome differences and advantages for anterior 90° partial fundoplication might disappear with longer follow-up, particularly if the side effects of Nissen fundoplication improve with time. However, the early and late (5 year) outcomes of a randomized trial of anterior 180° partial versus Nissen fundoplication study suggest that early differences continue into late follow-up and that the advantage of fewer side effects following anterior fundoplication remains.[7] Similar clinical outcomes have also been reported in another randomized trial of Nissen versus anterior partial fundoplication with a 2-year follow-up.[10]

While there were some advantages seen in terms of the QOL outcome following anterior 90° partial fundoplication at the short-term follow-up, the outcomes for both procedures were similar at the later (1–2 years) follow-up. For the present, however, it seems reasonable to conclude that anterior 90° partial fundoplication achieves a good short- to medium-term outcome for patients undergoing surgery for reflux. A longer term follow-up will be required before this procedure can be recommended for routine use.

ACKNOWLEDGMENTS

The authors wish to acknowledge the assistance of Ms. N. Ascott and Ms. T. Ellis for their invaluable organizational and logistical support. The authors also wish to acknowledge financial support for this study from the National Heath and Medical Research Council of Australia and from the Astra Upper Gastrointestinal Research Grant (through Upper Gastrointestinal Section of the Royal Australasian College of Surgeons).

REFERENCES

1. Watson DI, Jamieson GG. Antireflux surgery in the laparoscopic era (Review). Br J Surg 1998;85:1173–1184.
2. Hagedorn C, Lonroth H, Rydberg L, *et al.* Long-term efficacy of total (Nissen-Rossetti) and posterior partial (Toupet) fundoplication: results of a randomized clinical trial. J Gastrointest Surg 2002;6:540–545.
3. de Beaux A, Watson DI, O'Boyle C, *et al.* Role of fundoplication in patient symptomatology after laparoscopic antireflux surgery. Br J Surg 2001;88:11117–11121.
4. Gadenstatter M, Klingler A, Prommegger R, *et al.* Laparoscopic partial posterior fundoplication provides excellent intermediate results in GERD patients with impaired esophageal peristalsis. Surgery 1999;126:548–552.
5. Mir J, Ponce J, Juan M, *et al.* The effect of 180° anterior fundoplication on gastroesophageal reflux. Am J Gastroenterol 1986;81:172–175.
6. Watson DI, Jamieson GG, Pike GK, *et al.* A prospective randomised double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 1999;86:123–130.
7. Ludemann R, Watson DI, Game PA, *et al.* Laparoscopic total versus anterior 180° fundoplication – five year follow-up of a prospective randomized trial. Br J Surg 2005; 92:240–243.
8. Kryzztopik RJ, Jamieson GG, Devitt PG, *et al.* A further modification of the Nissen fundoplication – 90° anterior fundoplication. Surg Endosc 2002;16:1446–1451.
9. Watson DI, Jamieson GG, Lally C, *et al.* Multicenter prospective double blind randomized trial of laparoscopic Nissen versus anterior 90° partial fundoplication. Arch Surg 2004;139:1160–1167.
10. Baigrie RJ, Cullis SN, Ndhluni AJ, *et al.* Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. Br J Surg 2005; 92:819–823.
11. Lundell L, Miettinen P, Myrvold HE, *et al.* Continued (5-year) followup of a randomized clinical study comparing antireflux surgery and omeprazole in gastroesophageal reflux disease. J Am Coll Surg 2001;192:172–181.

12. Frantzides CT, Madan AK, Carlson MA, *et al.* A prospective, randomized trial of laparoscopic polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. Arch Surg 2002;137:649–652.
13. Kamolz T, Pointner R, Velanovich V. The impact of gastroesophageal reflux disease on quality of life. Surg Endosc 2003;17:1193–1199.
14. Watson DI, Chan ASL, Myers JC, *et al.* Illness behavior influences the outcome of laparoscopic antireflux surgery. J Am Coll Surg 1997;184:44–48.
15. Korolija D, Sauerland S, Wood-Dauphinee S, *et al.* Evaluation of quality of life after laparoscopic surgery: evidence-based guidelines of the European Association for Endoscopic Surgery. Surg Endosc 2004;18:879–897.
16. Pilowsky I. The diagnosis of abnormal illness behavior. Aust NZ J Psychol 1971;5:136–138.
17. Watson DI, Liu JF, Devitt PG, *et al.* Outcome of laparoscopic anterior 180° partial fundoplication for gastrooesophageal reflux disease. J Gastrointest Surg 2000; 4:486–492.
18. Yau P, Watson DI, Ascott N, *et al.* Efficacy of a 90° anterior fundoplication versus a total fundoplication in an experimental model. Surg Endosc 2000;14:830–833.
19. Hagedorn C, Jonson C, Lonroth H, *et al.* Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial. Ann Surg 2003;238:189–196.
20. Kamolz T, Wykypiel H, Bammer T, *et al.* Quality of life after laparoscopic antireflux surgery – Nissen fundoplication. Chirug 1998;69:947–950.
21. Fernando HC, Schauer PR, Rosenblatt M, *et al.* Quality of life after antireflux surgery compared with nonoperative management for severe gastroesophageal reflux disease. J Am Coll Surg 2002;194:23–27.
22. Hunter JG, Trus TL, Branum GD, *et al.* A physiologic approach to laparoscopic fundoplication for gastroesophageal reflux disease. Ann Surg 1996;223:673–685.
23. Fernando HC, Luketich JD, Christie NA, *et al.* Outcomes of laparoscopic Toupet compared to laparoscopic Nissen fundoplication. Surg Endosc 2002;16:905–908.
24. Kamolz T, Granderath FA, Bammer T, *et al.* "Floppy" Nissen vs. Toupet laparoscopic fundoplication: quality of life assessment in a 5-year follow-up (part 2). Endoscopy 2002;34:917–922.

ORIGINAL ARTICLE

Five-Year Follow-up of a Multicenter, Double-Blind Randomized Clinical Trial of Laparoscopic Nissen vs Anterior 90° Partial Fundoplication

Rajwinder S. Nijjar, MBChB, MSc, FRCS; David I. Watson, MD, FRACS; Glyn G. Jamieson, MS, FRACS; Stephen Archer, PhD, FRACS; Justin R. Bessell, MD, FRACS; Michael Booth, MBBS, FRACS; Richard Cade, MBBS, FRACS; Graham L. Cullingford, MBBS, FRACS; Peter G. Devitt, MS, FRCS, FRACS; David R. Fletcher, MD, FRACS; James Hurley, MBBS, FRACS; George Kiroff, MS, FRACS; Ian J. G. Martin, MBBS, FRACS; Leslie K. Nathanson, MBChB, FRACS; John A. Windsor, MD, FRACS; for the International Society for the Diseases of the Esophagus–Australasian Section

Hypothesis: Laparoscopic 90° anterior partial fundoplication for gastroesophageal reflux disease achieves equivalent results to laparoscopic Nissen fundoplication.

Design: A multicenter, prospective, double-blind randomized clinical trial with a minimum of 5 years' follow-up.

Setting: Nine university teaching hospitals in 6 major cities throughout Australia and New Zealand.

Participants: One hundred twelve patients undergoing primary antireflux surgery were randomized to undergo either laparoscopic Nissen fundoplication (52 patients) or anterior 90° partial fundoplication (60 patients).

Interventions: Laparoscopic Nissen fundoplication with division of the short gastric vessels or laparoscopic anterior 90° partial fundoplication.

Main Outcome Measures: Blinded assessment at 1 and 5 years' follow-up of clinical outcome for postoperative heartburn, dysphagia, gas-related symptoms, and satisfaction with the surgical outcome. Analog scales ranging from 0 to 10 were used to assess symptom severity.

Results: Ninety-seven patients underwent follow-up at 5 years. Three others died during follow-up, 4 refused follow-up, and 8 were lost to follow-up; 89% remained at 5-years' follow-up. At 5 years' follow-up, mean analog scores for heartburn were 2.2 for anterior fundoplication vs 0.9 for Nissen fundoplication ($P = .003$). There were no significant differences between the groups for dysphagia scores. The mean score for outcome satisfaction was 7.1 after anterior fundoplication vs 8.1 after Nissen fundoplication ($P = .18$). Eighty-eight percent reported a good or excellent outcome following Nissen fundoplication vs 77% following anterior fundoplication.

Conclusions: Laparoscopic Nissen and anterior 90° partial fundoplication achieve similar levels of patient satisfaction at 5 years' follow-up, with similar adverse effect profiles. However, at 5 years' follow-up, laparoscopic Nissen fundoplication achieves superior control of reflux symptoms.

Trial Registration: Australian New Zealand Clinical Trials Register Identifier: ACTRN12607000298415.

Arch Surg. 2010;145(6):552-557

Author Affiliations are listed at the end of this article.
Group Information: The members of the International Society for the Diseases of the Esophagus–Australasian Section are listed at the end of this article.

LAPAROSCOPIC NISSEN FUNDOplication is generally considered to be the surgical procedure of choice for the treatment of gastroesophageal reflux disease. It provides durable control of reflux but at the expense of a small

See Invited Critique at end of article

but significant rate of dysphagia and gas-related adverse effects.[1] To minimize the risk of such adverse effects, partial fundoplications, anterior and posterior, have been adapted from the original Nissen fundoplication. In the recently reported long-term follow-up of a randomized trial comparing laparoscopic Nissen fundoplication with laparoscopic anterior 180° partial fundoplication, it has been shown that both procedures produce equivalent and durable control of reflux at up to 10 years' follow-up, with trends toward less dysphagia and better preservation of belching following anterior 180° partial fundoplication.[2]

CME available online at www.jamaarchivescme.com and questions on page 511

With the aim of developing an effective antireflux procedure, but with minimal adverse effects, we modified the anterior 180° fundoplication further to an anterior 90° partial fundoplication.[3,4] We first piloted this procedure in an experimental animal reflux model, and postfundoplication manometry in the model showed that the resting lower esophageal pressures and reflux were corrected similarly by the anterior 90° fundoplication when compared with a standard Nissen fundoplication.[3] This technique was then evaluated clinically against laparoscopic Nissen fundoplication in a multicenter, double-blind randomized control trial—this study.[5] We have previously reported 6 months' follow-up outcomes from this trial, and these early results suggested that patients were more likely to be able to belch and relieve gas bloat symptoms after anterior 90° partial fundoplication, offset by more heartburn-like symptoms, compared with patients who underwent laparoscopic Nissen fundoplication.[5] Overall satisfaction with the outcome of antireflux surgery was very high (98%) at 6 months following anterior 90° partial fundoplication, and the early data lent support to the hypothesis that anterior 90° fundoplication is an appropriate surgical procedure for the treatment for gastroesophageal reflux disease, although longer-term follow-up was needed to support this early outcome data. Five years have passed since the early outcomes were evaluated, and in this article, we are now able to report longer-term (5 years' follow-up) clinical outcomes from this randomized trial.

METHODS

The trial was undertaken in 9 university teaching hospitals in 6 major cities in Australia and New Zealand. Fifteen surgeons performed the surgical procedures, and all had significant experience with laparoscopic antireflux surgery before the trial commenced. The full details of the trial protocol have been described previously.[5] In brief, symptomatic patients with objective evidence of gastroesophageal reflux at upper gastrointestinal endoscopy or 24-hour pH monitoring were considered for entry. Patients were excluded if they had an esophageal motility disorder that was deemed to preclude performing a Nissen fundoplication or if they were undergoing a concurrent procedure or had undergone previous antireflux surgery.

Randomization was performed by opening a sealed envelope that specified the type of fundoplication to be performed. The envelopes were prepared independently and were only opened after the operation had commenced and it was determined that both operative approaches were feasible. The operative techniques have been described previously.[4,5] Common to both procedures was a laparoscopic approach and routine posterior hiatal repair. A loose 1- to 2-cm Nissen fundoplication was fashioned following division of the short gastric vessels and full mobilization of the gastric fundus. Key steps for the anterior 90° partial fundoplication included a posterior esophagopexy to the right hiatal pillar, fixation of a length of esophagus within the abdomen, recreation of the angle of His, and construction of a fundoplication that covered the left anterolateral intra-abdominal esophagus. A bougie was not used, and short gastric blood vessels were not divided. If a laparoscopic procedure was converted to an open approach, the selected fundoplication was still performed, and patients were still included in the data analysis on an intention-to-treat basis. Operative techniques were standardized by agreement between participating surgeons. Additional quality control was achieved by presentation and distribution of videotape demonstrations at meetings in December 1998 and December 2000.

The type of procedure performed was concealed from the patient as well as the research assistant performing subsequent clinical follow-up. Preoperative information was collected pro forma by the operating surgeon. Postoperatively, a research assistant collected information using a structured telephone interview at 1, 3, and 6 months and then annually thereafter. Details of the interview have been published previously.[5] Patients were asked about the presence or absence of certain symptoms and asked to grade heartburn and dysphagia (separately for liquids and solids) using analog scores from 0 to 10 (0=no symptoms, 10=severe symptoms). Dysphagia was also scored using a previously validated composite dysphagia score graded from 0 to 45.[6] Patients were also asked whether they were able to belch and eat a normal diet.

The overall outcome was graded using an analog score for overall satisfaction (0=unsatisfied, 10=totally satisfied) and a previously described 4-point outcome scale (excellent, good, fair, and poor).[7] Patients were considered to be satisfied if the outcome was rated as good or excellent. A further yes/no question asked whether patients thought they had made the correct decision to undergo antireflux surgery.

Data were analyzed on an intention-to-treat basis, with all patients remaining in their initially allocated groups. Data were stored in a database (Filemaker Pro version 8.5; Filemaker Corp, Santa Clara, California) and statistical analysis was performed with GraphPad Prism version 5a (GraphPad Software Inc, La Jolla, California). The human research ethics committee in each participating hospital approved the study protocol. The study was conducted in accordance with the guidance of the World Medical Association of Helsinki (revised 1989) and the National Health and Medical Research Council of Australia guidelines on human experimentation.

RESULTS

From February 11, 2000, to February 26, 2003, 112 patients were enrolled in this trial, and all underwent surgery. Sixty were randomized to undergo laparoscopic anterior 90° partial fundoplication and 52 to laparoscopic Nissen fundoplication. All patients underwent the specific fundoplication type that was allocated by the randomization process. There was 1 conversion to open operation during anterior 90° partial fundoplication. This was due to intra-abdominal adhesions. There were 2 conversions during Nissen fundoplication due to intra-abdominal obesity and bleeding.

Demographic, preoperative, and early postoperative (first 6 months) data for the 2 groups have been reported earlier.[5] There were no significant differences with respect to any preoperative variable except that a higher proportion of patients in the Nissen fundoplication group had undergone previous upper abdominal surgery.

At 1-year follow-up, data were collected from 105 patients (57 anterior, 48 Nissen; 94% follow-up). Three patients died between 1 and 5 years' follow-up from unrelated causes. At 5 years, follow-up data were not able to be obtained from a further 12 patients. Hence, a clinical outcome was available for 89% at 5 years. In the anterior fundoplication group, 5 patients were lost to follow-up, 1 refused follow-up, and 1 died, whereas in the Nissen fundoplication group, 3 were lost to follow-up, 3

Table 1. Clinical Outcomes at 12 Months for Heartburn, Dysphagia, and Other Adverse Effects

	No. (%)		
	Nissen Fundoplication (n=48)	Anterior Fundoplication (n=57)	*P* Value
Reflux symptoms			
Heartburn	5 (10)	15 (26)	.048[a]
Mean heartburn analog score	0.7	1.5	.04[b]
Consuming PPI medication	6 (12.5)	10 (17)	.59[a]
Dysphagia assessment			
Dysphagia for solids	25 (52)	12 (21)	.001[a]
Mean dysphagia analog score			
Liquids	0.9	0.4	.59[b]
Solids	1.7	1.6	.24[b]
Composite dysphagia score	7.2	3.5	.06[b]
Eats normal diet	41 (85)	55 (96)	.07[a]
Other adverse effects			
Abdominal bloating	18 (37)	25 (44)	.55[a]
Able to relieve bloating	29 (60)	45 (79)	.05[a]
Able to belch normally	30 (63)	52 (91)	.001[a]

Abbreviation: PPI, proton pump inhibitor.
[a]Fisher exact test.
[b]Mann-Whitney *U* test.

Table 2. Clinical Outcomes at 5 Years for Heartburn, Dysphagia, and Other Adverse Effects

	No. (%)		
	Nissen Fundoplication (n=44)	Anterior Fundoplication (n=53)	*P* Value
Reflux symptoms			
Heartburn	12 (27)	21 (44)	.28[a]
Mean heartburn analog score	0.9	2.2	.003[b]
Consuming PPI medication	2 (4.5)	13 (24)	.01[a]
Dysphagia assessment			
Dysphagia for solids	18 (41)	17 (32)	.40[a]
Mean dysphagia analog score			
Liquids	0.5	0.5	.29[b]
Solids	2.1	1.5	.16[b]
Composite dysphagia score	6.7	5.5	.62[b]
Eats normal diet	37 (84)	48 (91)	.37[a]
Other adverse effects			
Abdominal bloating	26 (59)	31 (58)	>.99[a]
Able to relieve bloating	25 (57)	36 (68)	.29[a]
Able to belch normally	28 (68)	50 (94)	.001[a]

Abbreviation: PPI, proton pump inhibitor.
[a]Fisher exact test.
[b]Mann-Whitney *U* test.

refused follow-up, and 2 died. No revision operations were undertaken in either group during the 6 months' to 5 years' postoperative follow-up period.

Clinical follow-up data at 12 months and 5 years are summarized in **Tables 1**, **2**, **3**, and **4**. When patients were asked using a yes/no question whether they had heartburn at 12 months' follow-up, significantly more reported heartburn after anterior 90° partial fundoplication (Table 1), although at 5 years there was no statistically significant difference (Table 2). However, when heartburn was assessed using the 0-10 analog score, patients reported significantly more heartburn after anterior 90° partial fundoplication at both 12 months' and 5 years' follow-up (Table 1 and Table 2).

Table 3. Assessment of Overall Outcome at 12 Months

	No. (%)		
	Total Fundoplication (n=48)	Anterior Fundoplication (n=57)	*P* Value
Satisfied with outcome	44 (92)	45 (79)	.10[a]
Mean analog score of satisfaction	8.4	8.2	.99[b]
Would choose operation again	43 (90)	50 (87)	.77[a]

[a]Fisher exact test.
[b]Mann-Whitney *U* test.

At 12 months after surgery, patients were less likely to report dysphagia for solids following anterior 90° partial fundoplication, although there were no significant differences between the 2 groups for the dysphagia scores for both liquids and solids at 1 year (Table 1), and at 5 years' follow-up, the incidence and severity of dysphagia were not significantly different for the 2 groups for all measures of dysphagia. The ability to belch was better preserved 1 and 5 years after anterior fundoplication (Table 1 and Table 2). At 12 months' and 5 years' follow-up, there were no significant differences for any measures of satisfaction with the overall outcome (Table 3 and Table 4).

COMMENT

Antireflux surgery has an important role in the treatment of patients with refractory gastroesophageal reflux disease and in patients who do not wish to continue taking lifelong antisecretory medication. Traditionally, the Nissen 360° fundoplication has been widely applied, and it provides good control of reflux for most patients, with success rates approaching 90% at 10 years' follow-up.[8,9] However, in some patients, achieving excellent reflux control can be followed by significant long-term adverse effects, most commonly dysphagia, inability to belch, gas bloat, and flatulence. To minimize the risk of adverse effects, many surgeons construct a partial fundoplication.[2,4,10] This strategy is reported to reduce the risk of dysphagia and wind-related adverse effects, although there has been concern that the control of gastroesophageal reflux may not be adequate following a partial fundoplication.[11]

When constructing a partial fundoplication, there are 2 broad approaches to consider: anterior vs posterior. Posterior fundoplications have been more widely performed, particularly in North America and Europe, and studies of case series generally report good outcomes. This type of partial fundoplication has been compared with Nissen fundoplication in randomized controlled trials.[10,12,13] In general, the results from these trials demonstrate similar outcomes for reflux control and dysphagia, but with less wind-related adverse effects following posterior partial fundoplication. To our knowledge, only 1 randomized trial has demonstrated less dysphagia following posterior partial fundoplication, and this was only

at 4 months' follow-up.[13] Hence, we have hypothesized that anterior partial fundoplication may be associated with fewer adverse effects but still achieve adequate reflux control.

Four randomized trials, including our current trial, have compared an anterior partial fundoplication variant with Nissen fundoplication.[2,5,14,15] Two of these evaluated an anterior 180° partial fundoplication.[2,14] Outcomes at 6 months and 5 years from the trial undertaken in Adelaide, Australia, demonstrated similar reflux control, but less dysphagia and other adverse effects, following anterior 180° partial fundoplication.[16,17] However, at the 10-year follow-up, the outcome following anterior 180° partial fundoplication was not significantly different from that of Nissen fundoplication.[2] The second trial from Baigrie et al[14] also demonstrated fewer adverse effects offset by more heartburn symptoms at 2 years' follow-up following anterior 180° partial vs Nissen fundoplication. In both of these trials, high rates of patient-reported satisfaction were observed following anterior 180° partial fundoplication at up to 10 years' follow-up. Anterior 90° partial fundoplication has also been compared with Nissen fundoplication (without division of the short gastric blood vessels) in a further trial from Adelaide.[15] The 6 months' follow-up outcomes were similar to the early outcomes from our current trial, ie, fewer adverse effects following anterior 90° partial fundoplication, good reflux control, and high rates of satisfaction.[15] The only trial to report a poor result following an anterior partial fundoplication variant was reported by Hagedorn et al.[11] They compared anterior 120° partial fundoplication with posterior fundoplication. In their trial, there was a high rate of recurrent reflux following anterior partial fundoplication at early follow-up, and this was confirmed by pH monitoring. However, these outcomes were very different from those reported in the other trials. A possible explanation for this is that the construction of the anterior 120° partial fundoplication applied in the trial reported by Hagedorn et al was different from that tested in other trials, with fewer sutures used to attach the gastric fundus to the right hiatal pillar and therefore less anchorage of the esophagus and fundoplication within the abdomen.

In our current trial, the initial 6-month follow-up outcomes were excellent following anterior 90° partial fundoplication.[5] Reflux control, as measured by symptom scores and pH monitoring, was very good, adverse effects were less frequent, and 98% of patients were highly satisfied with the overall outcome following anterior 90° partial fundoplication. However, when treating reflux surgically, long-term outcomes are very important, and the 5-year follow-up reported in the current article suggests patients were more likely to experience reflux symptoms at later follow-up following anterior 90° partial fundoplication. Furthermore, the previously reported advantages of better satisfaction and fewer adverse effects were not seen at 5 years' follow-up. However, while there were no statistically significant differences between the dysphagia scores for the 2 study groups, there was a trend toward less dysphagia following anterior 90° partial fundoplication, and this trend is consistent with the results of other trials.

Table 4. Assessment of Overall Outcome at 5 Years

	No. (%)		
	Total Fundoplication (n=44)	Anterior Fundoplication (n=53)	*P* Value
Satisfied with outcome	39 (88)	41 (77)	.10[a]
Mean analog score of satisfaction	8.1	7.1	.18[b]
Would choose operation again	40 (91)	45 (84)	.37[a]

[a] Fisher exact test.
[b] Mann-Whitney *U* test.

In considering heartburn and other clinical indicators of recurrent reflux, we use 3 clinical questions. While it is unlikely that any one of these correlates perfectly with reflux, it is likely that they do provide an overall indication of the relative risk of further reflux following each operation. For instance, heartburn was assessed with a yes/no question and an analog score. Affirmative answers to these questions do not always indicate reflux, as other symptoms could be confused with actual reflux. Similarly, not all individuals who consume proton pump inhibitors following fundoplication have reflux.[18] For these reasons, it is unlikely that 27% and 44% of patients had recurrent reflux after Nissen and anterior fundoplication, respectively, particularly because at 5 years' follow-up satisfaction with surgery was approximately 90% following both procedures. Nevertheless, the reported clinical outcomes are likely to be informative, to the extent that they suggest reflux is a greater problem at 5 years' follow-up following anterior 90° partial fundoplication compared with the Nissen procedure.

Unlike other randomized trials that have evaluated antireflux procedures within a single unit, our current trial is a multicenter study from 9 sites spread across Australia and New Zealand. While all the surgeons involved in the trial work in university teaching hospitals, they also work in both teaching hospital and private practice environments, and approximately 50% of the patients in this trial were managed in the private sector. Furthermore, the majority of laparoscopic antireflux surgery in our countries is performed by specialist upper gastrointestinal surgeons who work in these settings, and this reflects the range of patients recruited into the trial. For these reasons, we believe that the results better reflect the outcomes for this type of surgery across Australia and New Zealand than previously reported studies from single centers.

The follow-up rate of approximately 90% at 5 years in our trial was not as high as the 96% to 99% follow-up rates reported in other randomized controlled trials from Adelaide.[2,7,15,17] This was because the multicenter recruitment process increased the difficulties associated with tracking patients across multiple Australian states and New Zealand. Nevertheless, we were still able to obtain a high rate of follow-up, and few other randomized trials have been able to obtain this level of long-term follow-up. The outcomes reported in this trial were clinical symptom scores. Even though at late follow-up we did not un-

dertake further investigation with studies such as pH monitoring, we are confident that the symptom scores reflect the clinical situation and provide reliable information about the surgical outcome. Esophageal manometry, pH monitoring, and endoscopy were undertaken at early follow-up, but in our community, it is not possible to obtain adequate compliance with pH studies and other investigations at multiple points during clinical trials. When patients undergo surgery for gastroesophageal reflux, arguably the most important outcome is a patient who is satisfied with the overall result following surgery. When patients consider this outcome, they balance reflux control against new postsurgical adverse effects. Some patients with excellent postsurgical reflux control are unsatisfied with the results of antireflux surgery because they developed unwanted adverse effects. There were no statistically significant differences between the satisfaction outcomes at 1 or 5 years in this trial.

Given the outcome at 5 years, how have the results of our trial influenced the practice of antireflux surgery in our hospitals? Following completion of the enrolment phase, the majority of participating surgeons reverted to their standard clinical practice. For most surgeons, this meant undertaking a Nissen fundoplication, although some surgeons adopted posterior or anterior 180° partial fundoplication procedures, with 1 surgeon continuing to apply the anterior 90° partial fundoplication for selected patients undergoing surgery for reflux. In general, however, the participants chose to await the longer-term outcomes from the trial before considering routine clinical application of the anterior 90° partial fundoplication procedure.

In conclusion, at 5 years' follow-up, patients who underwent a laparoscopic Nissen fundoplication were less likely to report heartburn-type symptoms compared with those undergoing anterior 90° partial fundoplication. For the other outcomes (adverse effects and satisfaction), the results were not significantly different at 5 years' follow-up. This suggests a better overall outcome at 5 years following laparoscopic Nissen fundoplication compared with anterior 90° partial fundoplication.

Accepted for Publication: June 17, 2009.
Author Affiliations: University of Adelaide (Drs Nijjar, Jamieson, and Devitt) and Flinders University of South Australia (Drs Watson and Bessell), Adelaide, South Australia, Melbourne University, Melbourne (Drs Cade, Hurley, and Kiroff), University of Queensland, Brisbane (Drs Martin and Nathanson), and University of Western Australia, Crawley (Drs Archer, Cullingford, and Fletcher), Australia; and University of Auckland, Auckland, New Zealand (Drs Windsor and Booth).
Correspondence: David I. Watson, MD, FRACS, Flinders University Department of Surgery, Room 3D211, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia (david.watson@flinders.edu.au).
Author Contributions: *Study concept and design:* Watson, Devitt, Fletcher, Martin, and Nathanson. *Acquisition of data:* Nijjar, Watson, Archer, Bessell, Booth, Cade, Cullingford, Fletcher, Hurley, Kiroff, Nathanson, and Windsor. *Analysis and interpretation of data:* Nijjar, Watson, Jamieson, Archer, Cade, Fletcher, and Windsor. *Drafting of the manuscript:* Watson, Devitt, and Nathanson. *Critical revision of the manuscript for important intellectual content:* Archer, Bessell, Booth, Cade, Cullingford, Fletcher, Hurley, Kiroff, Martin, and Windsor. *Statistical analysis:* Nijjar and Watson. *Obtained funding:* Watson. *Administrative, technical, and material support:* Nijjar, Watson, Archer, Booth, Cade, Fletcher, Martin, and Windsor. *Study supervision:* Watson, Jamieson, Bessell, Devitt, Hurley, and Windsor.
International Society for the Diseases of the Esophagus–Australasian Section: Rajwinder S. Nijjar, MBChB, MSc, FRCS; David I. Watson, MD, FRACS; Glyn G. Jamieson, MS, FRACS; Stephen Archer, PhD, FRACS; Justin R. Bessell, MD, FRACS; Michael Booth, MBBS, FRACS; Richard Cade, MBBS, FRACS; Graham L. Cullingford, MBBS, FRACS; Peter G. Devitt, MS, FRCS, FRACS; David R. Fletcher, MD, FRACS; James Hurley, MBBS, FRACS; George Kiroff, MS, FRACS; Ian J. G. Martin, MBBS, FRACS; Leslie K. Nathanson, MBChB, FRACS; John A. Windsor, MD, FRACS.
Financial Disclosure: None reported.
Funding/Support: This trial was supported by project grants from the National Health and Medical Research Council of Australia.
Additional Contributions: Carolyn Lally, RN, RM, Lorelle Smith, BNurs, Janet Pinno, and Nicky Ascott conducted the follow-up in this trial and managed the trial database. The late Christopher Martin, MD, FRACS, Nepean Hospital, Sydney, Australia, supported this trial and contributed patients to the study. We continue to appreciate his contribution and support.

REFERENCES

1. Watson DI, Jamieson GG. Anti-reflux surgery in the laparoscopic era. *Br J Surg.* 1998;85(9):1173-1184.
2. Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180(degrees) partial fundoplication. *Br J Surg.* 2008;95(12):1501-1505.
3. Yau P, Watson DI, Ascott N, Lafullarde T, Jamieson GG. Efficacy of a 90 degree anterior fundoplication vs a total fundoplication in an experimental model. *Surg Endosc.* 2000;14(9):830-833.
4. Krysztopik RJ, Jamieson GG, Devitt PG, Watson DI. A further modification of fundoplication: 90 degrees anterior fundoplication. *Surg Endosc.* 2002;16(10): 1446-1451.
5. Watson DI, Jamieson GG, Lally C, et al; International Society for Diseases of the Esophagus–Australasian Section. Multicenter, prospective, double-blind, randomized trial of laparoscopic Nissen vs anterior 90 degrees partial fundoplication. *Arch Surg.* 2004;139(11):1160-1167.
6. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol.* 1992;14(2):99-100.
7. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg.* 1997;226(5):642-652.
8. Kelly JJ, Watson DI, Chin KF, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. *J Am Coll Surg.* 2007; 205(4):570-575.
9. Cowgill SM, Gillman R, Kraemer E, Al-Saadi S, Villadolid D, Rosemurgy A. Ten-year follow up after laparoscopic Nissen fundoplication for gastroesophageal reflux disease. *Am Surg.* 2007;73(8):748-752.
10. Hagedorn C, Lönroth H, Rydberg L, Ruth M, Lundell L. Long-term efficacy of total (Nissen-Rossetti) and posterior partial (Toupet) fundoplication: results of a randomized clinical trial. *J Gastrointest Surg.* 2002;6(4):540-545.
11. Hagedorn C, Jönson C, Lönroth H, Ruth M, Thune A, Lundell L. Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial. *Ann Surg.* 2003;238(2):189-196.

12. Guérin E, Bétroune K, Closset J, et al. Nissen versus Toupet fundoplication: results of a randomized and multicenter trial. *Surg Endosc*. 2007;21(11):1985-1990.
13. Strate U, Emmermann A, Fibbe C, Layer P, Zornig C. Laparoscopic fundoplication: Nissen versus Toupet two-year outcome of a prospective randomized study of 200 patients regarding preoperative esophageal motility. *Surg Endosc*. 2008; 22(1):21-30.
14. Baigrie RJ, Cullis SNR, Ndhluni AJ, Cariem A. Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. *Br J Surg*. 2005;92(7):819-823.
15. Spence GM, Watson DI, Jamiesion GG, Lally CJ, Devitt PG. Single center prospective randomized trial of laparoscopic Nissen versus anterior 90 degrees fundoplication. *J Gastrointest Surg*. 2006;10(5):698-705.
16. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. Prospective randomized double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg*. 1999;86(1):123-130.
17. Ludemann R, Watson DI, Jamieson GG, Game PA, Devitt PG. Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180 degrees fundoplication. *Br J Surg*. 2005;92(2):240-243.
18. Wijnhoven BPL, Lally CJ, Kelly JJ, Myers JC, Watson DI. Use of anti-reflux medication after anti-reflux surgery. *J Gastrointest Surg*. 2008;12(3):510-517.

INVITED CRITIQUE

Better Is the Enemy of Good

This pearl is usually imparted to a trainee attempting to add perfection to an adequate operation. Trying to create perfection has plagued antireflux surgery more than most operations, ever since Harrington[1] published the first series of diaphragmatic hernia repairs (28 patients) in the *Archives* in 1928. Allison reported his anatomical repair in 1945, then Nissen experimented with several techniques over 25 years, initially favoring Allison's technique, then gastropexy, before settling on fundoplication in the 1960s. Belsey, Hill, Rosetti, and Toupet all tried to make a good operation better, while Angelchik tried to invent a new one. However, the biggest redefinition of outcome resulted from the introduction of laparoscopy.

This group, led by Jamieson and Watson, has unarguably made the greatest contribution to the evidence surrounding laparoscopic fundoplication, publishing a series of well-constructed randomized trials on many aspects, including division vs no division of short gastric vessels and partial vs total fundoplication. The first modification studied by them was the anterior 180° wrap, and their recently published 10-year outcome[2] confirmed their early success with this operation, which sustained good reflux control while reducing adverse effects. This success encouraged their investigation of the minimalist 90° wrap.

This article reports the 5-year outcome of their multicenter trial comparing the 90° wrap with Nissen fundoplication, and the results suggest that there is a limit to minimalism. Recurrent heartburn was reported by 44% of the patients who underwent the 90° procedure and there was no benefit for dysphagia after 1 year. While not quite reaching statistical significance, the trends to both poorer Visick and satisfaction scores in the 90° group are highly suggestive. They correctly conclude that laparoscopic Nissen has a better overall outcome at 5 years compared with the 90° version. Tellingly, they concede that 14 of the 15 participating trial surgeons have abandoned this operation altogether, while 1 uses it selectively.

Nijjar et al are to be congratulated on their honest and conclusive study, which should result in the 90° wrap being bracketed with current endoscopic techniques as a disappointing procedure that has failed to make better an already good (if imperfect) therapy.

Robert John Baigrie, BSc, MBChB, MD, FRCS

Author Affiliations: Department of Gastro-intestinal Surgery, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa.
Correspondence: Dr Baigrie, Harfield House, Wilderness Road, Claremont, 7708, South Africa (robertb @surgcare.co.za).
Financial Disclosure: None reported.

1. Harrington SW. Diaphragmatic hernia. *Arch Surg*. 1928;16(1):386-415.
2. Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180(degrees) partial fundoplication. *Br J Surg*. 2008; 95(12):1501-1505.

2.6 Anterior 90 degree partial fundoplication vs. Nissen fundoplication without division of the short gastric blood vessels

---

Spence GM, Watson DI, Jamieson GG, Lally CJ & Devitt PG. Single centre prospective randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. *J Gastrointest Surg* (2006) **10**:698-705.

This paper reported the 12 month (short term) clinical and objective outcomes from a single centre randomized trial comparing laparoscopic anterior 90 degree partial vs. Nissen fundoplication without division of the short gastric blood vessels.

Watson DI, Devitt PG, Smith L, Jamieson GG. Anterior 90^0 partial vs Nissen fundoplication - 5 year follow-up of a single-centre randomized trial. *J Gastrointest Surg* (2012) **16**:1653-1658.

This paper reported the 5 year (longer term) clinical outcomes from the same trial.

Single Center Prospective Randomized Trial of Laparoscopic Nissen Versus Anterior 90° Fundoplication

Gary M. Spence, M.D., F.R.C.S., David I. Watson, M.D., F.R.C.S., Glyn G. Jamiesion, M.S., F.R.C.S., F.R.A.C.S., Carolyn J. Lally, R.N., R.M., Peter G. Devitt, M.S., F.R.C.S., F.R.A.C.S.

Although Nissen fundoplication is a very effective treatment for gastroesophageal reflux, it is associated with a small incidence of troublesome postoperative side effects. To prevent this, progressive modification of surgical techniques has led to the development of an anterior 90° fundoplication. We undertook a prospective randomized trial to compare this procedure with Nissen fundoplication to determine whether it would achieve a better clinical outcome. Patients presenting to a single center for primary laparoscopic antireflux surgery were randomized to undergo either an anterior 90° fundoplication (n = 40) or a Nissen fundoplication without division of the short gastric vessels (n = 39). Clinical questionnaires were used to assess outcome at 1 month, 3–6 months, and 12 months. Both patients and the clinical interviewer were masked as to which procedure was performed. Follow-up with endoscopy, esophageal manometry, and pH monitoring was also undertaken. Operating time was similar for the two procedures (60 minutes for anterior vs. 55 minutes for Nissen fundoplication). Early postoperative complications were more common after Nissen fundoplication (18% vs. 5%). Two patients underwent laparoscopic reoperation for recurrent reflux after anterior 90° fundoplication, and four underwent laparoscopic reoperation after Nissen fundoplication (dysphagia, 3 patients; acute hiatus hernia, 1 patient). One year after surgery, dysphagia and other wind-related side effects were less common after anterior 90° fundoplication. Control of reflux symptoms and satisfaction with the overall outcome was similar for the two procedures. Anterior 90° fundoplication is followed by fewer side effects than Nissen fundoplication. This advantage is offset by a greater likelihood of reflux recurrence. However, this does not diminish patient satisfaction. (J GASTROINTEST SURG 2006;10:698–705)

KEY WORDS: Anterior partial fundoplication, dysphagia, gastroesophageal reflux, laparoscopy, Nissen fundoplication

Laparoscopic fundoplication has become the operative modality of choice for the surgical treatment of moderate to severe gastroesophageal reflux.[1] The majority of laparoscopic fundoplications currently constructed are 360° fundal wraps, similar to the procedure originally described by Nissen. Despite achieving excellent control of reflux in the majority of patients, however, the 360° fundoplication can be followed by troublesome postoperative side effects. These include dysphagia and wind-related problems such as abdominal bloating, inability to belch, and flatulence.[2]

To overcome this, Nissen's operation has been progressively modified. Undertaking a laparoscopic anterior partial fundoplication instead of a Nissen procedure has the potential to give good reflux control, but with less side effects. In 1999, we reported the early results of the first prospective randomized trial that compared the outcome of a Nissen fundoplication with an anterior 180° partial fundoplication.[3] This study demonstrated that both procedures achieved satisfactory early control of reflux, but with less side effects after anterior 180° fundoplication. Longer term follow-up has since

From the University of Adelaide Department of Surgery, Royal Adelaide Hospital (G.M.S., G.G.J., C.J.L., P.G.D.), Adelaide, South Australia; and Flinders University Department of Surgery, Flinders Medical Centre (D.I.W.), Bedford Park, South Australia, Australia.
Financial support for this study was provided from a project grant (no. 157986) from the National Heath and Medical Research Council of Australia (to D.I.W. and G.G.J.).
Reprint requests: David I. Watson, M.D., F.R.C.S., Head, Flinders University Department of Surgery, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia. e-mail: david.watson@flinders.edu.au

Published by Elsevier Inc.
1091-255X/06/$—see front matter
doi:10.1016/j.gassur.2005.10.003

confirmed the durability of the anterior 180° fundoplication procedure beyond 5 years.[4]

Although side effects are less likely after anterior 180° fundoplication compared with Nissen fundoplication, a small risk of persistent dysphagia and wind-related problems remains. This led us to further refine the anterior fundoplication technique, resulting in the development of an anterior 90° fundoplication. Experimental and initial clinical studies have confirmed that anterior 90° fundoplication achieves good short-term reflux control, with a low risk of side effects.[5,6]

In addition, a multicenter prospective double-blind randomized trial of laparoscopic Nissen fundoplication versus anterior 90° fundoplication has recently been published.[7] This study was coordinated by our unit, and we contributed patients to it. The trial demonstrated that overall satisfaction with surgery was better 6 months after anterior 90° fundoplication, although this was offset to some extent by better reflux control in patients who underwent a Nissen fundoplication.[7] In this recently reported study, the laparoscopic Nissen fundoplication procedures included division of the short gastric blood vessels. Four other randomized trials, including one from our unit, have shown that dividing these vessels is unnecessary during Nissen fundoplication,[8–13] and two of these trials have demonstrated an association between division of the vessels and wind-related side effects.[8,10] For this reason, we initiated another randomized trial of laparoscopic anterior 90° versus Nissen fundoplication, in which the short gastric vessels were not divided during Nissen fundoplication. This new trial is a single center experience with a different cohort of patients, rather than the combined experience of a larger group of surgeons.

PATIENTS AND METHODS

The protocol used for this study was similar to that used in other reported randomized trials undertaken by the authors and reported elsewhere.[3,9]

Participant Assignment

Patients undergoing laparoscopic fundoplication for gastroesophageal reflux were randomly assigned to undergo either a total 360° (Nissen) fundoplication without division of the short gastric blood vessels or an anterior 90° partial fundoplication. Informed consent was obtained from all participants, and randomization was undertaken in the operating theater by opening one of 100 previously sealed opaque envelopes after surgery commenced.

Patient Selection and Preoperative Investigation

All patients with reflux who presented for laparoscopic antireflux surgery were considered for enrollment. Patients were excluded if they had a severe esophageal motility disorder that precluded the performance of a Nissen fundoplication, if they required a contemporaneous abdominal procedure (e.g., cholecystectomy), or had previously undergone any type of gastric surgery. All patients underwent preoperative investigation with esophageal manometry and endoscopy. Twenty-four-hour pH monitoring was performed to confirm reflux in patients who did not have unequivocal reflux disease demonstrated by endoscopy.

Operative Technique and Postoperative Care

Laparoscopic Nissen fundoplication was performed using a technique described previously.[14] This comprised preservation of the hepatic branch of the vagus nerve, routine posterior hiatal repair, and the construction of a short, loose Nissen fundoplication around a 52 Fr intraesophageal bougie. The short gastric vessels were not divided in any patients. The technique for anterior 90° fundoplication has also been described previously.[6] The initial steps are similar to those undertaken for the Nissen procedure—mobilization of the esophagus, preservation of the hepatic branch of the vagus nerve, and posterior hiatal repair. The anterior 90° fundoplication was fashioned by first placing an esophagopexy suture between the posterolateral aspect of the right side of the distal esophagus and the posterior aspect of either the right pillar or both pillars of the esophageal hiatus. Two sutures were next placed between the left side of the esophagus and the adjacent gastric fundus to accentuate the angle of His, and the gastric fundus was then sutured loosely over the left side of the front of the esophagus by using an apical suture that anchored the fundus to the anterior esophagus and the apex of the hiatus. Finally, the inferior edge of the fundal fold lying in front of the esophagus was sutured to the esophagogastric junction in the midline. The short gastric vessels were not divided, and an intraesophageal bougie was not used.

Patients were allowed oral fluids postoperatively on return to the ward, and soft solid food was commenced on the first postoperative day. Patients were instructed to remain on a soft diet for the first 3–4 weeks after surgery and then to gradually increase the consistency of their food intake thereafter.

Masking

The type of fundoplication performed was concealed from the patients during follow-up. Follow-up was undertaken by a research assistant who was masked to the randomization of each patient. Final data analysis for this paper was performed in late 2004 by a surgeon investigator (G.M.S) who was not involved in the original surgery.

Clinical Follow-up

Preoperative and postoperative data were collected using a standard form. Follow-up data at 1 month, 3–6 months, and 1 year after surgery were obtained by telephone interview. Longer-term follow-up will be obtained in due course. The presence or absence of the following symptoms was sought: heartburn, epigastric pain, regurgitation, dysphagia for solids, dysphagia for liquids, odynophagia, early satiety, epigastric bloating, anorexia, nausea, vomiting, wheezing, coughing, and increased flatulence. The ability to relieve bloating and whether a normal diet was being consumed were also determined. Heartburn was also scored using a visual analogue scale (0 = no heartburn, 10 = severe heartburn). Dysphagia was scored by several methods. Visual analogue scales (0 = no dysphagia, 10 = total dysphagia) were applied separately for solids and liquids; a previously validated score (0 = no dysphagia, 45 = severe dysphagia) that combines information about difficulty swallowing nine types of liquids and solids was used as well.[9,15]

Overall outcome was determined using three further scales and a question. Patients were asked to assess the outcome of surgery by using a modified Visick grading (Table 1) and were asked to score the outcome as excellent, good, fair, or poor (Table 2). An overall assessment of satisfaction with the operative outcome was also determined using a further visual analogue scale (0 = dissatisfied, 10 = satisfied). In addition, patients were asked whether they thought that their initial decision to have a laparoscopic fundoplication was correct or not. The occurrence of any complications and the need for further surgery, whether early (within 6 weeks of the initial surgery) or late, was also recorded.

Table 1. Modified Visick grading system

1	No symptoms
2	Mild symptoms easily controlled by simple care such as avoiding certain foods or eating small meals, etc.
3	Moderate symptoms not controlled by simple care but not interfering with social or economic life
4	Moderate symptoms interfering with social or economic life
5	Symptoms as bad worse than preoperatively

Table 2. Outcome assessment

Excellent	Complete recovery
Good	Major improvement with minor problems
Fair	Major improvement with still significant problems or adverse effects
Poor	Minor or no improvement or deterioration

Objective Follow-up

Three to six months after surgery, patients were invited to undergo esophageal manometry, 24-hour-ambulatory pH monitoring, and endoscopy. These investigations sought to obtain an objective assessment of lower esophageal sphincter function, postsurgical anatomy, and the degree to which reflux was controlled.

Statistical Analysis

The primary clinical outcomes that the trial was designed to evaluate were postoperative dysphagia and control of reflux symptoms. It was determined that 80 patients (40 in each group) would be needed to demonstrate a 15% difference in these outcome measures at a statistical significance level of $P < 0.05$ and power of 80%. All analyses and comparisons between the two groups were performed on an intention-to-treat basis.

Data were entered onto a computerized database (Filemaker Pro version 7, Filemaker Corporation, Santa Clara, CA) and analyzed with SPSS version 10 for Windows (SPSS Inc, Chicago, IL). Data are expressed as mean (standard error of the mean; mean [SEM]) or median (interquartile range; median [IQR]). Categorical variables were compared by using the Fisher exact test. Continuous variables that followed a parametric distribution were compared by using the independent samples t test. Nonparametric data were compared using the Mann-Whitney U test. Statistical significance was accepted if $P < 0.05$.

The protocol for this trial was approved by the Human Research Ethics Committee of the Royal Adelaide Hospital.

RESULTS

Seventy-nine patients who underwent a laparoscopic fundoplication between February 1999 and August 2003 at the Royal Adelaide Hospital were

entered into this trial. Thirty-nine patients were randomized to undergo a Nissen fundoplication and 40 patients an anterior 90° partial fundoplication. Follow-up data was available for 71 (90%) patients at the 1-month follow-up point, 72 (91%) patients at 3–6 months follow-up, and 64 (81%) at 1 year follow-up. Missing data were due to the inability to contact patients at these specific follow-up points. Of the 15 patients who were not contacted at 1-year postsurgery, 14 had 3–6 month follow-up data available, and 10 of these 14 patients had a good or excellent outcome at the point of last review. Data was available for 78 (99%) patients in at least one of the last two follow-up points.

Preoperative Assessment

Both study groups were well matched for preoperative parameters (Tables 3 and 4). The degree of heartburn experienced by each group and scored on a visual analogue scale was also comparable between both groups (Table 5), as was dysphagia (Table 6). Likewise, preoperative esophageal manometric parameters and endoscopic findings were similar for the two groups.

Operation

Operations were carried out under the care of three surgeons. Thirty-one procedures (39%) were performed by a consultant, and 48 (61%) were performed by a trainee under supervision. The seniority of the first operator was different for the two groups, there being a higher representation of trainees as the primary surgeon in the Nissen fundoplication group (74% vs. 48%; $P = 0.02$). There was no deliberate bias for this parameter, as randomization was always undertaken after commencing surgery.

One patient who was randomized to undergo a Nissen fundoplication underwent an anterior 90° fundoplication, when the surgeon could not bring the gastric fundus behind the esophagus. This was due to the combined difficulties of excessive adipose tissue in the region of the cardia and a thickened gastric wall. The operating surgeon thought that this problem would not be solved by dividing the short gastric vessels, and hence, a partial fundoplication was performed. All other patients had a fundoplication constructed according to the randomization schedule. Outcomes were analyzed on an intention-to-treat basis.

The laparoscopic procedure was converted to open surgery for one patient in the anterior 90° fundoplication group. This was because of intra-abdominal adhesions. All other procedures were completed laparoscopically. Operating times were similar for the two groups (median 60 minutes; interquartile range 45–75 minutes for anterior 90° fundoplication vs. median 55 minutes; interquartile range 40–65 minutes for Nissen fundoplication; $P = 0.18$). Operating surgeons were asked to rate the degree of difficulty of the operative procedure by using a scale from 1 to 10. There was no difference in difficulty rating between the two groups (4 [3–7] for anterior 90° fundoplication vs. 4 [3–7] for Nissen fundoplication; $P = 0.92$).

Table 3. Preoperative patient characteristics

Variable	Type of fundoplication		
	Anterior (n = 40)	Nissen (n = 39)	*P* value
Age, y	46 (2)	47 (2)	0.62*
Sex, M/F	24/16	19/20	0.37‡
Height, cm	171 (3)	169 (2)	0.51*
Weight, kg	84 (3)	86 (3)	0.59*
Previous upper abdominal surgery	6 (15%)	6 (15%)	0.99†
Duration of symptoms (y)	7 [4–12]	6 [3–20]	0.81‡

Data are given as mean (standard error of mean), or median [interquartile range].
*Student's *t* test.
†Fisher exact test.
‡Mann-Whitney *U* test.

Early Hospital Outcome

The time interval between surgery and the commencement of oral fluids as well as the duration of postoperative hospital stay were not influenced by the type of fundoplication. Time to commencement of solids was longer in the Nissen fundoplication group (Table 7). The incidence of postoperative complications was higher in the Nissen fundoplication group (18% vs. 5%; $P = 0.09$). However, most complications were minor and did not surgically require intervention, or delay discharge from the hospital. After anterior 90° fundoplication, there was one episode of chest infection and one episode of intraoperative cervical subcutaneous emphysema. After Nissen fundoplication, one patient developed urinary retention, one patient developed an umbilical port-site hernia, one patient suffered from excessive retching in the early postoperative period, which settled spontaneously, and three patients developed an intraoperative pneumothorax (none of which required any specific intervention). In addition, one patient in the Nissen group was found to have an acute paraesophageal hernia on a routine barium

Table 4. Assessment of symptoms

	Preoperative		Postoperative					
			1 month		3–6 months		1 year	
Symptom	Anterior %	Nissen %	Anterior %	Nissen %	Anterior %	Nissen %	Anterior %	Nissen %
Heartburn	100	97	11	14	22	3	16	12
Epigastric pain	56	71	49	39	36	33	29	46
Regurgitation	79	89	11*	39*	15	26	3*	27*
Odynophagia	15	24	20	33	18	15	7	18
Early satiety	35	53	60	61	49	59	26*	67*
Epigastric bloating	50	61	37	47	55	56	32	39
Anorexia	9	16	26	31	9	10	3	12
Nausea	29	50	23	19	27	26	7*	30*
Vomiting	35	34	3	17	9	8	7	6
Cough	35	34	20	25	21	13	26	15
Wheeze	24	26	9	11	3	13	0	0
Can relieve bloat	55	53	38	56	50	61	69	50
Eats normal diet	70	70	47	27	89	74	90	83
Increased flatus	NA	NA	54	44	46	67	42*	79*

*$P < 0.05$ (Nissen vs. anterior fundoplication, Fisher exact test).

swallow X-ray carried out on the day after surgery. This was repaired laparoscopically on the second postoperative day, and the patient then made an uneventful recovery.

Clinical Outcome at 1 Month to 1 Year After Operation

A detailed analysis of the clinical outcome at 1 month, 3–6 months, and 1 year are summarized in Tables 4, 5, 6, and 8. At 1 and 3–6 months, there were significant differences between the two groups for the symptoms of regurgitation at 1 month (less after anterior 90° fundoplication) and heartburn at 3–6 months (less after Nissen fundoplication). At 1 year, there were significant differences in the incidence of regurgitation, early satiety, nausea, and flatulence (all less after anterior 90° fundoplication). There was no significant difference between the two groups for the assessment of heartburn by the yes/no question at 1 year (Table 4). With regard to the assessment of heartburn by using the visual analogue scale, the findings were similar to the findings determined by the yes/no question. A statistically significant difference was found in the heartburn scores at 3–6 months (less after Nissen fundoplication), but this was not found at 1 year (Table 5).

Table 5. Assessment of heartburn by visual analogue scale

	Types of fundoplication		
	Anterior	Nissen	*P* value
Preoperative	7 [2.8–9.1]	5 [3–8]	0.31
Postoperative			
1 month	0 [0–0]	0 [0–0]	0.99
3–6 months	0 [0–0.5]	0 [0–0]	0.01*
1 year	0 [0–2]	0 [0–0]	0.08

Data are expressed as median [interquartile range].
*$P < 0.05$ (Nissen vs. anterior fundoplication, Mann Whitney *U* test).

With regard to the clinical assessment of dysphagia, there were significant differences between the two study groups, with less dysphagia experienced after anterior 90° fundoplication (Table 6). At 1 year, the incidence of dysphagia for solid foods, the visual analogue scores for dysphagia (for both liquids and solids), and the 0–45 dysphagia score all concurred.

The satisfaction score, outcome profile, and modified Visick grading all failed to reveal a statistically significant advantage for either type of the fundoplication (Table 8). In both groups, most patients were satisfied with the outcome of their surgery. At both 3–6 months and 1 year postprocedure, more patients in the anterior 90° fundoplication group expressed the view that they had made the correct decision to undergo surgery (86% vs. 77% at 3–6 months, 87% vs. 76% at 1 year). However, these differences were not statistically significant (Table 8).

Postoperative Investigations

Patient compliance with scheduled objective postoperative investigations was low. Twenty-five (32%) patients underwent postoperative upper gastrointestinal endoscopy, 23 (29%) underwent 24-hour-pH

Vol. 10, No. 5
2006

Table 6. Assessment of dysphagia

	Preoperative		Postoperative					
			1 month		3–6 months		1 year	
Symptom	Anterior	Nissen	Anterior	Nissen	Anterior	Nissen	Anterior	Nissen
Dysphagia for:								
Solids, %	32	21	63	69	30	49	13*	49*
Liquids, %	6	8	3	14	0*	21*	0	3
Visual Analogue Scale								
Solids	0 [0–3.3]	0 [0–5]	3 [0–6.8]*	5 [3.3–7.8]*	0 [0–2.5]*	2.5 [0–6.3]*	0 [0–2]*	2 [0–6]*
Liquids	0 [0–0]	0 [0–2.5]	0 [0–0]*	0 [0–4.3]	0 [0–0]	0 [0–1]	0 [0–0]*	0 [0–3]*
Dysphagia score								
Overall result†	1.7 [0–19.5]	8.2 [0–15.9]	16 [0–25.5]*	24 [17.7–29.9]*	0 [0–12]*	9.5 [0–23.5]*	0 [0–8.7]*	12 [3.5–19.5]*
Scored 0 only, %	50	44	27	11	66*	33*	56*	18*

*$P < 0.05$.
†Data are expressed as % or median [interquartile range].

monitoring, and 25 (32%) underwent esophageal manometry. Upper gastrointestinal endoscopy revealed an intact fundoplication and satisfactory repair of hiatus hernia in all patients studied. With regards to Savary-Miller grading of esophagitis, one of eight patients was scored as Savary-Miller grade 1 after anterior 90° fundoplication, and 1 of 16 patients had grade 3 esophagitis after Nissen fundoplication. Esophagitis was not present in any other patient.

Twenty-four-hour pH monitoring demonstrated normalization of acid exposure times in all but one of the 23 patients studied. This patient had undergone a Nissen fundoplication. The percentage time with pH less than 4 over the 24-hour study period was significantly less in the Nissen fundoplication group (0% [0%–0.6%] vs. 0.7% [0.3%–2.5%]; $P = 0.02$). The postoperative lower esophageal sphincter resting pressure measured at esophageal manometry was similar for the two groups (anterior 14 mmHg [10–24] vs.

Table 7. Early hospital outcomes

	Types of fundoplication		
Variable	Anterior	Nissen	*P* value
Postoperative stay (days)	2 [2–3]	2 [2–3]	0.42
Days to taking oral fluids	1 [1–1]	1 [1–1]	0.52
Days to taking solid foods	1.5 [1–2]*	2 [1.5–2]*	0.03

Data expressed as median [interquartile range].
*$P < 0.05$.

Table 8. Postoperative Visick grading, outcome grading, and satisfaction scores

	Postoperative status			
	3–6 months		1 year	
Variable	Anterior	Nissen	Anterior	Nissen
Modified Visick grade α				
1	25%	21%	32%	16%
2	47%	54%	48%	52%
3	6%	3%	8%	13%
4	8%	18%	0	19%
5	14%	5%	12%	0
Outcome				
Excellent	43%	28%	40%	21%
Good	30%	41%	33%	50%
Fair	11%	23%	13%	29%
Poor	16%	8%	13%	0%
Satisfaction score*	9 [7.5–10]	9 [7–10]	9 [6.1–10]	9 [6–10]
"Made correct decision"	86%	77%	87%	76%

*Data are given as %, or median [interquartile range].

Nissen 18 [14–29]; $P = 0.22$). Lower esophageal sphincter residual relaxation pressure was, however, significantly higher after Nissen fundoplication (7 mm Hg [3–13] vs. 3 [0–5]; $P = 0.02$).

Late Reoperation

A reoperative procedure was performed between 4 and 10 months after surgery in five patients—two after anterior 90° fundoplication, and three after Nissen fundoplication. All of these procedures were undertaken and completed laparoscopically. The two reoperations in the anterior 90° fundoplication group were undertaken at 7 and 10 months postoperatively, and entailed conversion to a Nissen fundoplication for recurrent reflux. In the Nissen fundoplication group, all three reoperations were for dysphagia. They were performed at 4, 6, and 9 months after the original procedure. In two of these operations, the hiatus was tight and it was widened. In these patients, the fundoplication was thought to be loose, and therefore it was left intact. In the other operation, the hiatus was widened and the Nissen fundoplication was converted to a posterior partial fundoplication.

DISCUSSION

Controversy remains as to which fundoplication technique offers the best outcome for patients. Although uncontrolled studies have reported good results for Nissen, anterior partial, and posterior partial fundoplication variants,[6,14,16] these studies should not be used to determine which technique is best. In recent years, there has been an increase in the number of prospective randomized trials that compare the short-term[3,17,18] and long-term[4,19] outcomes of various laparoscopic partial fundoplication techniques with the "gold-standard" Nissen 360° fundoplication. Hence, better evidence is becoming available that can help to determine the relative merits of the different types of laparoscopic fundoplication currently undertaken.

We have evaluated progressive modifications to Nissen's original procedure as part of a program to develop a fundoplication technique that achieves effective control of gastroesophageal reflux, but with minimal side effects and excellent patient acceptance. We have reported longer-term outcomes from a previous trial of anterior 180° partial fundoplication, which demonstrates that this approach achieves an excellent outcome compared with the Nissen procedure.[4] Similar results have also been reported by Baigrie et al.[20] Unfortunately, anterior 180° fundoplication is still followed by some side effects, and for this reason we developed the lesser anterior 90° fundoplication. Its antireflux efficacy has been demonstrated in previous laboratory and clinical studies. More recently, we reported the outcome from a larger multicenter randomized trial of Nissen fundoplication versus anterior 90° partial fundoplication[7] and demonstrated the short-term efficacy of this procedure and its potential to significantly reduce the risk of side effects.

We undertook the current prospective randomized trial independently of the recently reported multicenter study to further evaluate the anterior 90° technique in a single center against a Nissen procedure at which the short gastric vessels were not divided. Overall, the results from our new trial broadly concur with the findings from the multicenter study, that is, the anterior 90° technique is followed by fewer postoperative adverse effects.

It could be argued that the increased wind-related problems associated with Nissen fundoplication might be attributable to division of short gastric vessels, and this step was integral to the design of the multicenter study protocol.[8] Short gastric vessel division at Nissen fundoplication has previously been shown by our group, and others, to be associated with an increased risk of long-term wind-related problems without improving any outcome.[8,10] In our current study, division of the short gastric vessels was not undertaken in any patients, suggesting that differences in wind-related symptoms in this trial are a function of the type of fundoplication, and not division of the short gastric vessels.

In addition to any differences inherent in division of the short gastric vessels during Nissen fundoplication, the fact that our current study was undertaken at a single center also differentiates it from the previously reported multicenter study. The restriction of the current trial to a single unit, with all procedures undertaken or supervised by one of three surgeons, guaranteed the standardization of the technical aspects of the surgical procedures. This is particularly important when one is comparing a novel technique with a technique that is already established. It is possible that bias can be introduced in a multicenter setting, because surgeons in some of the centers may not be familiar with the newer of the techniques under scrutiny, leading to it being performed less well relative to the more conventional treatment. The fact that the results for the two trials are similar, however, also suggests that the anterior 90° fundoplication can be reliably performed by a wide range of surgeons.

Our current trial, like all other trials including an anterior fundoplication variant, has demonstrated a lower incidence of postoperative dysphagia. Disparity in dysphagia profiles between the two procedures was evident from assessment at the end of the first postoperative month, continuing through

Vol. 10, No. 5
2006

to assessment at 1 year. Statistical significance was reached for most measures of dysphagia at 1 year. However, it should also be noted that the better adverse effect profile of the anterior 90° fundoplication group is, to some extent, counterbalanced by less effective control of reflux, and this is a similar outcome to the results from the other trial of anterior 90° fundoplication.[7] Hence, there seems to be a trade-off between the risk of adverse effects and risk of recurrent reflux when comparing partial versus total fundoplication procedures. This premise is also strengthened by the indications for reoperation in the two groups in the present study. This outcome is also similar to that of other trials.

A possible criticism of our current study is the asymmetrical distribution of operator level between the two groups, with a higher proportion of trainees undertaking the surgery in the Nissen group. Although this is a potential confounder, we have previously shown that outcome after laparoscopic fundoplication is not affected by the seniority of the principal operator.[21] A further criticism could be the low rate of patients undergoing objective postoperative investigation with upper gastrointestinal endoscopy, 24-hour-pH monitoring, and esophageal manometry. However, overall satisfaction with the clinical outcome was similar after both types of fundoplication.

In summary, our current study confirms that anterior 90° fundoplication is followed by fewer side effects than Nissen fundoplication. There is a trade off between this benefit and a greater likelihood of recurrent or incompletely controlled reflux, although overall satisfaction is at least as good after anterior 90° fundoplication. This outcome is similar to that reported in a previous trial, and it supports continued evaluation of anterior 90° fundoplication. However, longer-term follow-up is needed to determine the durability of this antireflux procedure.

The authors thank Nicky Ascott and Tanya Ellis for assistance with data collection and logistical support.

REFERENCES

1. Watson DI, Jamieson GG. Antireflux surgery in the laparoscopic era (review). Br J Surg 1998;85:1173–1184.
2. Watson DI. Laparoscopic treatment of gastro-oesophageal reflux disease. Best Pract Res Clin Gastroenterol 2004;18: 19–35.
3. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. A prospective randomised double blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 1999;86:123–130.
4. Ludemann R, Watson DI, Game PA, Devitt PG, Jamieson GG. Laparoscopic total versus anterior 180 degree fundoplication - five year follow-up of a prospective randomized trial. Br J Surg 2005;92:240–243.
5. Yau P, Watson DI, Ascott N, Lafullarde T, Jamieson GG. Efficacy of a 90 degree anterior fundoplication versus a total fundoplication in an experimental model. Surg Endosc 2000; 14:830–833.
6. Krysztopik RJ, Jamieson GG, Devitt PG, Watson DI. A further modification of the Nissen fundoplication—90 degree anterior fundoplication. Surg Endosc 2002;16:1446–1451.
7. Watson DI, Jamieson GG, Lally C, et al. Multicentre prospective double blind randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. Arch Surg 2004;139:1160–1167.
8. O'Boyle CJ, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication—A prospective double blind randomized trial with five year follow-up. Ann Surg 2002;235:165–170.
9. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double blind randomised trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. Ann Surg 1997;226:642–652.
10. Luostarinen ME, Isolauri JO. Randomized trial to study the effect of fundic mobilization on long-term results of Nissen fundoplication. Br J Surg 1999;86:614–618.
11. Luostarinen MES, Koskinen MO, Isolauri JO. Effect of fundal mobilisation in Nissen-Rossetti fundoplication on oesophageal transit and dysphagia. Eur J Surg 1996;162: 37–42.
12. Blomqvist A, Dalenback J, Hagedorn C, Lonroth H, Hyltander A, Lundell L. Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication. J Gastrointest Surg 2000;4:493–500.
13. Chrysos E, Tzortzinis A, Tsiaoussis J, Athanasakis E, Vassilakis JS, Xynos E. Prospective randomized trial comparing Nissen to Nissen-Rossetti technique for laparoscopic fundoplication. Am J Surg 2001;182:215–221.
14. Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. Ann Surg 1994;220:137–145.
15. Dakkak M, Bennett JR. A new dysphagia score with objective validation. J Clin Gastroentrol 1992;14:99–100.
16. Richardson WS, Trus TL, Thompson S, Hunter JG. Nissen and Toupet fundoplications effectively inhibit gastroesophageal reflux irrespective of natural anatomy and function. Surg Endosc 1997;11:261–263.
17. Lundell L, Abrahamsson H, Ruth M, Sandberg N, Olbe LC. Lower esophageal sphincter characteristics and esophageal acid exposure after partial or 3600 fundoplication: Results of a prospective, randomized clinical study. World J Surg 1991;15:115–121.
18. Laws HL, Clements RH, Swillies CM. A randomized, prospective comparison of the Nissen versus the Toupet fundoplication for gastroesophageal reflux disease. Ann Surg 1997; 225:647–654.
19. Hagedorn C, Lonroth H, Rydberg L, Ruth M, Lundell L. Long-term efficacy of total (Nissen-Rossetti) and posterior partial (Toupet) fundoplication: Results of a randomized clinical trial. J Gastrointest Surg 2002;6:540–545.
20. Baigrie RJ, Cullis SN, Ndhluni AJ, Cariem A. Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. Br J Surg 2005;92:819–823.
21. O'Boyle CJ, Watson DI, deBeaux AC, Jamieson GG. Preoperative prediction of long-term outcome after laparoscopic fundoplication. ANZ J Surg 2002;72:471–475.

J Gastrointest Surg (2012) 16:1653–1658
DOI 10.1007/s11605-012-1920-8

ORIGINAL ARTICLE

Anterior 90° Partial vs Nissen Fundoplication—5 Year Follow-Up of a Single-Centre Randomised Trial

David Ian Watson · Peter G. Devitt · Lorelle Smith · Glyn G. Jamieson

Received: 25 March 2012 / Accepted: 15 May 2012 / Published online: 26 May 2012

Abstract
Introduction Nissen fundoplication can be followed by side effects, and this has driven modifications, including partial fundoplications. We previously reported early outcomes from a randomised trial of Nissen vs anterior 90° partial fundoplication. This paper reports 5-year follow-up outcomes to determine whether anterior 90° fundoplication achieves a satisfactory longer-term outcome.
Methods From February 1999 to August 2003, 79 patients were randomised to Nissen vs anterior 90° fundoplication. Patients were followed yearly using a standardized clinical questionnaire which included symptom scores to assess heartburn, dysphagia, other post-fundoplication side effects and overall satisfaction with the outcome. Five-year clinical outcomes were analysed.
Results Seventy-four patients were available for follow-up at 5 years. There were no significant differences for heartburn or satisfaction, although more patients used antisecretory medication after anterior 90° fundoplication (29.7 vs 8.1 %). Dysphagia was greater after Nissen fundoplication when measured by an analogue score for solid food and a composite dysphagia score. Symptoms of bloating were more common following Nissen fundoplication (80.0 vs 32.4 %), and less patients could eat a normal diet (78.4 vs 94.6 %). Re-operation was undertaken in four patients after Nissen fundoplication (dysphagia, three; hiatus hernia, one) vs three after anterior 90° fundoplication (recurrent reflux, three).
Conclusions At 5 years, anterior 90° partial fundoplication was associated with less side effects, offset by greater use of antisecretory medication. Reflux symptoms and overall satisfaction were similar to Nissen fundoplication. Laparoscopic anterior 90° partial fundoplication is an effective treatment for gastro-esophageal reflux.

Keywords Gastro-esophageal reflux disease · Nissen fundoplication · Anterior partial fundoplication · Laparoscopy · Randomised controlled trial

Trial registration—This trial is registered with the Australia and New Zealand Clinical Trials Registry ACTRN12607000304437.

D. I. Watson (✉) · L. Smith
Flinders University Department of Surgery,
Flinders Medical Centre,
Room 3D211, Bedford Park,
Adelaide, South Australia 5042, Australia
e-mail: david.watson@flinders.edu.au

P. G. Devitt · L. Smith · G. G. Jamieson
Discipline of Surgery, University of Adelaide,
Royal Adelaide Hospital,
Adelaide, South Australia, Australia

Introduction

Laparoscopic fundoplication is well established for the treatment of gastro-esophageal reflux disease, and good outcomes are obtained for the majority of patients who undergo this surgery. However, Nissen fundoplication, whilst achieving good long-term outcomes in 80–90 % of patients,[1] is followed by troublesome side effects such as dysphagia and gas-related symptoms in some individuals, and in an attempt to improve clinical outcomes, the Nissen fundoplication procedure has been progressively modified. One approach has been to construct a partial fundoplication, and this approach appears to have the greatest potential to minimise side effects. The commonest partial fundoplication technique entails the posterior approach, and randomised trials have consistently shown that this reduces the risk of gas-

related side effects.[2,3] However, the results of trials have been more variable for dysphagia, and a proportion of patients continue to report this problem after posterior partial fundoplication.[2,3]

Anterior partial fundoplication is an alternative approach, and randomised trials have also shown that these techniques also reduce the risk of wind-related side effects, as well as consistently reducing the risk of post-fundoplication dysphagia.[4–7] A range of techniques have been described, including anterior 180°, anterior 120°[7] and anterior 90°.[4,6] Each technique differs with respect to the extent of anchorage of the gastric fundus to the right hiatal pillar. The anterior 180° partial fundoplication entails anchoring the fundus firmly to the right hiatal pillar,[4,5] whereas with the other techniques, the fundus is anchored only to the left side and anterior aspects of the esophagus and the hiatal rim.[6,7] Two randomised trials have shown excellent results at up to 10 years of follow-up for the anterior 180° partial fundoplication approach.[5,8] However, results from randomised trials which have evaluated anterior 120° and anterior 90° partial fundoplication techniques report more mixed results, with the reduced risk of side effects traded off against a greater risk of recurrent reflux during follow-up in some trials.[6,7]

We have previously reported 5-year clinical outcomes from a multicentre Australia and New Zealand trial of Nissen fundoplication with short gastric vessel division vs anterior 90° partial fundoplication.[6] This showed more reflux, less side effects, but equivalent overall satisfaction with the outcome of surgery after anterior 90° partial fundoplication.[6] After completing the enrolment phase of this trial, we commenced a second randomised trial of anterior 90° partial fundoplication vs Nissen fundoplication without short gastric vessel division and undertook this trial in a single centre.[9] The results at up to 12 months of follow-up in this trial have been reported previously, and they demonstrated reduced side effects following anterior 90° fundoplication and equivalent reflux symptom control.[9] This suggested that the early outcome following anterior 90° fundoplication was at least as good as for Nissen fundoplication. However, in the absence of longer-term outcomes, there has been understandable reluctance to consider the anterior 90° partial fundoplication for the treatment of gastro-esophageal reflux outside clinical trials. Hence, we determined and analysed the longer-term (5-year follow-up) outcomes for patients enrolled in this trial, and these results are reported in this paper.

Patients and Methods

The protocol and methods for the randomised controlled trial have been fully described previously.[9] In brief, patients with proven gastro-esophageal reflux disease (ulcerative esophagitis at endoscopy and/or an abnormal 24-h pH study) were considered for entry into the trial. Exclusion criteria included an esophageal motility disorder which precluded a Nissen fundoplication, the need for a concurrent abdominal procedure, previous antireflux surgery or age greater than 75 years. Patients were investigated preoperatively with esophageal manometry and endoscopy, and 24-h pH monitoring was performed selectively for patients who did not have both typical reflux symptoms and ulcerative esophagitis at endoscopy. Informed consent was obtained from all patients.

Patients were randomised to undergo either laparoscopic Nissen or anterior 90° partial fundoplication. Randomization occurred in the operating room after the induction of general anaesthesia, by opening a pre-sealed envelope. Patients were blinded during follow-up to which procedure had been performed. The surgical techniques have been described in detail elsewhere.[10,11] Posterior hiatal repair was performed in all patients. For Nissen fundoplication, the short gastric vessels were not divided, and a 1.5- to 2-cm-long loose 360° total fundoplication was constructed, with a 52-F intra-esophageal bougie in situ. Anterior 90° partial fundoplication entailed suturing the posterior esophagus to the right hiatal pillar, recreation of the angle of His by suturing the fundus to the left side of the esophagus, and construction of a fundoplication which was secured to the anterior hiatal rim, thereby covering only the left anterolateral intra-abdominal esophagus (Fig. 1). A bougie was not used, and short gastric blood vessels were not divided during the partial fundoplication procedures.

Early outcomes at up to the 12-month follow-up have been reported elsewhere.[9] For the current study, 5-year follow-up outcomes were determined and analysed. Patients were followed yearly by a research nurse who used a standardized clinical questionnaire. To maximize the completeness of follow-up, the questionnaire was applied either by telephone interview or mail. The research nurses

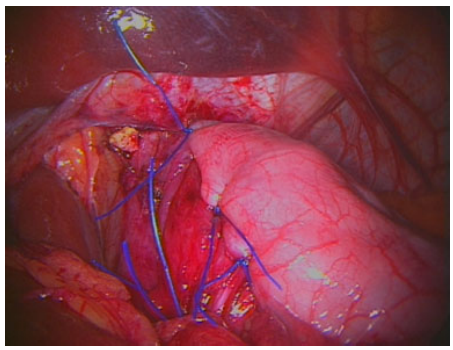


Fig. 1 Completed anterior 90° partial fundoplication. The anterior fundus is sutured halfway across the front of the esophagus, leaving the right anterolateral wall of the esophagus uncovered. The fundus lies adjacent to 25–30 % of the wall of the intra-abdominal esophagus

managing the follow-up were blinded to the type of fundoplication which had been constructed.

The questionnaire investigated the symptoms of heartburn, dysphagia and other post-fundoplication side effects.[9] Questions entailed yes/no questions asking whether "heartburn" or "dysphagia for solids" was present or absent, and the use of antisecretory medications was sought. Antisecretory medications were considered to be in use in any individual who reported either continuous or intermittent use over the previous 4 weeks. Patients were also asked to grade symptoms of heartburn, dysphagia for liquids and dysphagia for solids using separate 0-to-10 analogue scales (0=symptom absent, 10=severe symptoms). A previously described dysphagia score[12] was also used. This scoring system generated a composite score from each patient's ability to swallow nine index liquid or solid foods (0=no dysphagia, 45=total dysphagia). Additional yes/no questions were asked about symptoms of upper abdominal bloating and the ability to belch normally. Overall satisfaction with the outcome of surgery was determined using another 0-to-10 analogue scale (0=highly unsatisfied, 10=highly satisfied). Patients were also asked whether, if faced with similar preoperative circumstances, they still considered their original decision to undergo surgery to be correct.

This trial was designed to identify differences between the two procedures for recurrent reflux and dysphagia. Preliminary power calculations determined that 80 patients (40 in each group) would be needed to demonstrate a 15 % difference in outcomes at a significance level of $p<0.05$ and power of 80 %. Data analysis was undertaken using InStat version 3.1a (GraphPad Software Inc.) and performed on an intention-to-treat basis, with all patients remaining in their initial allocated group for this analysis. Fisher's exact test was used to determine the significance of 2×2 contingency tables, the Chi-squared test for larger contingency tables, and a two-tailed Mann–Whitney test was used to assess differences between sets of non-parametric data. This trial was approved by the Human Research Ethics Committee of the Royal Adelaide Hospital.

Results

From February 1999 to August 2003, 79 patients were enrolled in this trial. Forty were randomised to undergo anterior 90° partial fundoplication vs 39 to undergo Nissen fundoplication. Seventy-four (94 %) patients provided follow-up data at the 5-years follow-up—37 in each group (Fig. 2). In the anterior 90° partial fundoplication group, one patient died from breast cancer 3 years after fundoplication, and one withdrew from the trial. Three further patients were lost to follow-up (Nissen, two; anterior 90°, one). Demographic details for both study groups have been

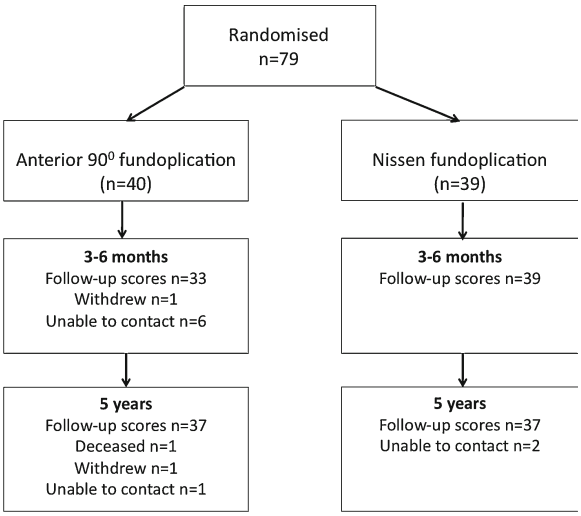


Fig. 2 Consort diagram for randomised trial. Five-year follow-up data are reported in the current paper. Earlier follow-up reported elsewhere[9]

reported previously[9] and are summarized in Table 1. Both groups were well matched at enrolment. Overall, 54.4 % of patients were male.

Table 2 summarizes the outcome for heartburn, dysphagia and other side effects. At the 5-year follow-up, there were no statistically significant differences between the two groups for the symptom of "heartburn" or for the analogue scores for heartburn. However, the use of antisecretory medication was significantly higher in the anterior 90° partial fundoplication group (29.7 vs 8.1 %). Three of the four measures used to assess dysphagia were significantly lower after anterior 90° partial fundoplication at the 5-year follow-up, including the yes/no question (29.7 vs 70.3 %), the composite dysphagia score (mean, 6.4 vs 14.1) and the analogue score for solids (mean, 1.6 vs 3.7). Only the difference for the analogue score for liquids (mean, 0.9 vs 1.9) failed to reach statistical significance. Abdominal bloating was significantly less common (32.4 vs 80.0 %), and more patients could eat a normal diet after anterior 90° partial fundoplication (94.6 vs 78.4 %). There were no significant differences between the groups for the ability to belch and the ability to relieve bloating symptoms.

The overall clinical outcome for the two groups was similar (Table 3). There were no statistically significant differences between the groups for the satisfaction score (mean, 7.6 vs 6.7) or for the yes/no question (83.8 vs 75.7 %) which assessed satisfaction with the original surgical decision making, although the trends were towards higher levels of satisfaction after anterior 90° partial fundoplication.

Seven (8.9 %) patients underwent re-operation during the 5-year follow-up period. All revision operations were

Table 1 Preoperative patient characteristics

	Nissen fundoplication (n=39)	Anterior 90° fundoplication (n=40)	p value
Age (years)	45.7 (42.4, 49.1)	45.8 (42.1, 49.4)	0.775
Gender (M/F)	19 M:20 F	24 M:16 F	0.370
Height (cm)	168 (163, 172)	171 (167, 176)	0.203
Weight (kg)	88.1 (82.5, 93.7)	83.0 (75.2, 90.7)	0.238
Previous upper abdominal surgery	6 (15.3 %)	6 (15.0 %)	0.766

All figures are mean (95 % confidence intervals) or no. (in percent)

undertaken laparoscopically. Four of these patients originally underwent a Nissen fundoplication, and persistent dysphagia was the indication for revision surgery in three of the four patients in this group (undertaken at 4, 6 and 9 months). In two of the operations undertaken for dysphagia, the Nissen fundoplication was converted to a partial fundoplication, and in the other, the diaphragmatic hiatus was widened and the fundoplication left intact. The other revision procedure in the Nissen fundoplication group was for an acute para-esophageal hiatus hernia occurring 2 days after the original surgery. All three revision operations in the anterior 90° partial fundoplication group were undertaken for recurrent reflux, with surgery entailing conversion to a Nissen fundoplication. This was undertaken at 7 months, 9 months and 2 years following the original operation.

Discussion

Whilst most patients report a successful outcome following antireflux surgery, troublesome side effects occur in some patients following Nissen fundoplication, and this has led to technical modifications, such as partial fundoplication techniques, in an attempt to reduce the risk. Unfortunately, the results from randomised trials of posterior partial vs Nissen fundoplication show that some patients are still troubled by side effects such as dysphagia and bloating after posterior partial fundoplication, even though the risks might be less than following the Nissen procedure.[2,3] In an attempt to further minimise the risk of these side effects, we have developed and evaluated techniques for anterior partial fundoplication.

In 1996, we commenced a randomised trial of Nissen vs anterior 180° partial fundoplication, and we have reported 5- and 10-year follow-up from this trial.[5,13] This demonstrated similar levels of reflux control, but significantly less dysphagia and wind-related side effects after anterior 180° partial fundoplication, although a small group of patients still reported side effects. In 2000, we took this concept further and developed a new technique for anterior 90° partial fundoplication.[14] The early laboratory and clinical outcomes confirmed that this created a more "anatomical" repair, rather than an overcompetent valve at the gastro-esophageal junction.[14,15] Two randomised controlled trials

Table 2 Clinical outcomes at 5 years for heartburn, dysphagia and other side effects

	Nissen fundoplication (n=37)	Anterior 90° fundoplication (n=37)	p value
Reflux symptoms			
Heartburn present	14 (37.8 %)	11 (29.7 %)	0.624
Heartburn analogue score	2.00 (1.05, 2.95)	1.703 (0.91, 2.49)	0.921
Using antisecretory medications	3 (8.1 %)	11 (29.7 %)	0.035
Dysphagia assessment			
Dysphagia for solids	26 (70.3 %)	11 (29.7 %)	0.0010
Dysphagia analogue scores			
Liquids	1.92 (0.94, 2.90)	0.92 (0.27, 1.57)	0.107
Solids	3.70 (2.62, 4.79)	1.60 (0.80, 2.39)	0.0019
Composite dysphagia score	14.14 (10.41, 17.86)	6.38 (3.48, 9.28)	0.0010
Other side effects			
Abdominal bloating	27 (80.0 %)	12 (32.4 %)	0.0010
Able to relieve bloating	24 (64.9 %)	21 (56.8 %)	0.482
Ability to belch normally	22 (59.5 %)	29 (78.4 %)	0.131
Able to eat a normal diet	29 (78.4 %)	35 (94.6 %)	0.047

All figures are mean (95 % confidence intervals) or no. (in percent)

Table 3 Overall outcome assessment at 5 years

	Nissen fundoplication (n=37)	Anterior 90° fundoplication (n=37)	p value
Analogue score of "satisfaction"	6.68 (5.58, 7.78)	7.65 (6.56, 8.74)	0.114
Satisfaction score 0–3	7 (18.9 %)	6 (16.2 %)	
Satisfaction score 4–6	6 (16.2 %)	3 (8.1 %)	
Satisfaction score 7–10	24 (64.9 %)	28 (75.7 %)	0.500
"Would choose operation again"	28 (75.7 %)	31 (83.8 %)	0.564

All figures are mean (95 % confidence intervals) or no. (in percent)

of anterior 90° partial vs Nissen fundoplication have been undertaken to evaluate this further. The first entailed a multicentre trial, conducted in six cities in Australia and New Zealand, and the results at the 5-year follow-up demonstrated similar levels of satisfaction with the overall outcome for the two procedures, less side effects after anterior 90° partial fundoplication, but offset by a higher incidence of recurrent reflux.[6,15] The Nissen fundoplication performed in this trial included division of the short gastric vessels.

To compare the outcome for anterior 90° partial fundoplication with a Nissen fundoplication in which the short gastric vessels were not divided, we commenced the current trial.[9] Enrolment was limited to a single centre and commenced after the recruitment phase for the first trial was completed. All surgery was undertaken by or under the direct supervision of three surgeons (DIW, GGJ and PGD). The initial results at 6- to 12-month follow-up were promising, demonstrating less side effects but similar reflux control after anterior 90° partial fundoplication.[9] With longer-term follow-up, our current study has shown acceptable outcomes to 5 years. These results clearly demonstrate less dysphagia and wind-related side effects after anterior 90° fundoplication, and reflux symptoms, as measured by the heartburn score, were similar for the two groups, even though the use of antisecretory medication and the rate of revision surgery for recurrent reflux were both higher following anterior 90° fundoplication. This suggests less effective, but still adequate, control of reflux at the 5-year follow-up. It should be recognized, however, that even though there was an apparent excess of reoperations for recurrent reflux in the anterior 90° fundoplication, this was fully offset by reoperative surgery for dysphagia after Nissen fundoplication, and the overall satisfaction with the clinical outcome at 5 years was at least as good after anterior 90° fundoplication. These results are consistent with results from all other trials of anterior partial vs Nissen fundoplication,[4–8] as well as a recent meta-analysis.[16]

The outcomes for the yes/no questions used in this study might initially seem to show unusually high rates of side effects such as dysphagia or bloating. However, it is important to recognize that the way a question is structured impacts on how it is answered. In our study, patients were only allowed to answer "yes" or "no", and a "yes" was given, even if symptoms occurred only occasionally. Previous trials using this approach have also reported similar high rates of response, both during follow-up and also before surgery.[5,6] It is important, therefore, to focus on the differences between response rates for each question, and it is not appropriate to compare absolute percentages with outcomes from other studies in a non-randomised fashion.

In the current trial, we have shown a significant difference between the two groups for the usage of antisecretory medications. Whilst this is informative about the relative risk of recurrent reflux symptoms for each procedure, we have also shown previously that only one out of three antisecretory medication uses at late follow-up after fundoplication is actually for recurrent reflux, and approximately two out of three patients use antisecretory medications for other reasons.[17] The rate of PPI consumption 5 years after anterior 90° partial fundoplication in our current study was similar to the 33 % PPI use rate reported at mean 5.9 years after Nissen fundoplication in 525 patients enrolled in a medication usage study.[17] The 8.1 % rate of PPI use at 5 years after Nissen fundoplication in our current trial is actually much lower than is usually reported at late follow-up in other studies.[17] Despite this, it is difficult to interpret the difference in medication usage as showing anything but a difference in reflux control. How is this rationalized with other data, such as the similar heartburn symptom scores and satisfaction scores? The heartburn scores assessed the status of symptoms at 5 years, and these might be controlled by surgery alone, medication alone (if reflux has recurred) or by a combination of surgery and reflux. Most patients enrolled in our trial had reflux symptoms which were not controlled by medication at the time of entry into the trial, and for them, a partial failure of reflux control after surgery which requires the use of medication to now achieve full symptom control appears to actually be acceptable to many of these patients, whereas full reflux control offset by ongoing dysphagia is often not acceptable.

The follow-up in our trial was obtained using standardized clinical questionnaires, and we did not measure objective outcomes using pH monitoring, impedance, manometry or endoscopy at late follow-up. Whilst objective data might strengthen the conclusions drawn, repeated objective investigations are not acceptable to most asymptomatic Australian

patients following antireflux surgery. We did undertake pH monitoring, esophageal manometry and endoscopy at 6 months after surgery, and data from these studies were reported elsewhere.[9] The results were consistent with the early clinical outcomes in this trial. Our experience with conducting several trials in this area confirms that the clinical assessment scores are quite informative about outcomes and differences and that the global satisfaction scores probably better assess the actual outcome as perceived by the patient, whereas the results of objective tests are often of less relevance to the clinical outcome as perceived by the individual patient.

The 5-year follow-up outcomes from our randomised trial of anterior 90° partial vs Nissen fundoplication suggest equivalent overall outcomes, with a significantly lower rate of side effects after anterior 90° partial fundoplication, but a greater likelihood of recurrent reflux. Rates of satisfaction and actual reflux symptoms were similar for the two procedures at the 5-years follow-up. In clinical practice, we currently undertake a mix of anterior 90°, anterior 180° and Nissen fundoplication and often tailor the type of fundoplication to the perceived risk of side effects. In particular, we now always prefer an anterior partial fundoplication in individuals who are at a higher risk of post-fundoplication side effects, and as longer-term outcome studies show good reflux control following anterior 180° fundoplication,[5] this has been the commonest procedure performed in our departments over recent years. Whilst awaiting the outcomes from the randomised trials of Nissen vs anterior 90° fundoplication, we have tended to use the anterior 90° partial fundoplication in the more elderly patient group undergoing surgery primarily for very large hiatus hernia, in whom reflux is often less of an issue, but in whom side effect minimization is important. The results of our current trial, however, suggest that anterior 90° partial fundoplication is an effective operation for the surgical treatment of gastro-esophageal reflux disease, and these data support a wider application for this procedure in clinical practice.

Acknowledgments This trial was supported by research project grants from the National Health and Medical Research Council (NHMRC) of Australia (grant numbers 157986 and 375111). We are grateful for the assistance of Ms. J. Sullivan, Ms. N. Carney and Ms. C. Lally who contributed to follow-up data collection.

References

1. Engström C, Jamieson GG, Devitt PG, Watson DI. Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of short gastric vessels during Nissen fundoplication. Br J Surg 2011;98:1063-1067.
2. Lundell L, Abrahamsson H, Ruth M, Rydberg L, Lonroth H & Olbe L. Long-term results of a prospective randomized comparison of total fundic wrap (Nissen-Rossetti) or semifundoplication (Toupet) for gastro-esophageal reflux. Br J Surg 1996;83:830-835.
3. Booth MI, Stratford J, Jones L, Dehn TC. Randomized clinical trial of laparoscopic total (Nissen) versus posterior partial (Toupet) fundoplication for gastro-esophageal reflux disease based on preoperative esophageal manometry. Br J Surg 2008;95:57-63.
4. Ludemann R, Watson DI, Jamieson GG, Game PA, Devitt PG. Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180 degrees fundoplication. Br J Surg 2005;92:240-243.
5. Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180° partial fundoplication. Br J Surg 2008;95:1501-1505.
6. Nijjar R, Watson D, Jamieson G, Archer S. Five-year follow-up of a multicenter, double-blind randomized clinical trial of laparoscopic Nissen vs anterior 90 degrees partial fundoplication. Arch Surg 2010;145:552-557.
7. Engström C, Lönroth H, Mardani J, Lundell L. An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. World J Surg 2007;31:1221-1225.
8. Baigrie RJ, Cullis SN, Ndhluni AJ, Cariem A. Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. Br J Surg 2005;92:819-823.
9. Spence GM, Watson DI, Jamieson GG, Lally CJ, Devitt PG. Single center prospective randomized trial of laparoscopic Nissen versus anterior 90 degrees fundoplication. J Gastrointest Surg 2006;10:698-705.
10. Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. Ann Surg 1994;220:137-145.
11. Krysztopik RJ, Jamieson, GG, Devitt PG & Watson DI. A further modification of the Nissen fundoplication – 90° anterior fundoplication. Surg Endosc 2002;16:1446-1451.
12. Dakkak M & Bennett J. A new dysphagia score with objective validation, J Clin Gastroenterol 1992;14:99-100.
13. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M & Devitt PG. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 1999;86:123-30.
14. Yau P, Watson DI, Ascott N, Lafullarde T & Jamieson GG. Efficacy of a 90° anterior fundoplication versus a total fundoplication in an experimental model. Surg Endosc 2000;14:830-833.
15. Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M et al. Multicenter, prospective, double-blind, randomized trial of laparoscopic Nissen vs anterior 90 degrees partial fundoplication. Arch Surg 2004;139:1160-1167.
16. Broeders JA, Roks DJ, Jamieson GG, Devitt PG, Baigrie RJ, Watson DI. Five year outcome after laparoscopic anterior partial versus Nissen fundoplication - 4 randomized trials. Ann Surg 2012;255:637-642.
17. Wijnhoven BPL, Lally CJ, Kelly JJ, Myers JC, Watson DI. Use of Anti-Reflux Medication After Anti-Reflux Surgery. J Gastrointest Surg 2008;12:510-517.

2.7 Anterior 180 degree partial fundoplication vs. posterior partial fundoplication

---

Daud WMBW, Thompson SK, Jamieson GG, Devitt PG, Martin IJG, Watson DI. Randomized controlled trial of laparoscopic anterior 180° partial vs. posterior 270° partial fundoplication. *ANZ J Surg* (2013) DOI: 10.1111/ans.12476. (published online).

This paper reported the clinical and objective outcomes at 12 months (short term) follow-up from a randomized trial comparing laparoscopic anterior 180 degree vs. posterior 270 degree partial fundoplication.

ORIGINAL ARTICLE

ANZJSurg.com

Randomized controlled trial of laparoscopic anterior 180° partial versus posterior 270° partial fundoplication

Wan Najmi Wan Daud,* Sarah K. Thompson,† Glyn G. Jamieson,† Peter G. Devitt,† Ian J. G. Martin‡ and David I. Watson*

*Department of Surgery, Flinders University, Adelaide, South Australia, Australia
†Discipline of Surgery, University of Adelaide, Adelaide, South Australia, Australia and
‡Department of Surgery, University of Queensland, Brisbane, Queensland, Australia

Key words
fundoplication, gastro-oesophageal reflux disease, laparoscopy, randomized controlled trial.

Correspondence
Professor David I. Watson, Department of Surgery, Flinders University, Room 3D211, Flinders Medical Centre, Bedford Park, Adelaide, SA 5042, Australia.
Email: david.watson@flinders.edu.au

W. N. W. Daud MD, MS; **S. K. Thompson** PhD, FRCSC, FRACS; **G. G. Jamieson** MS, FRACS; **P. G. Devitt** MS, FRCS, FRACS; **I. J. G. Martin** MBBS, FRACS; **D. I. Watson** MD, FRACS.

This trial is registered with the Australia and New Zealand Clinical Trials Registry ACTRN12605000035628.

Accepted for publication 26 October 2013.

doi: 10.1111/ans.12476

Abstract

Background: Previous trials show good outcomes following anterior and posterior partial versus Nissen fundoplication for gastro-oesophageal reflux. However, it is unclear which partial fundoplication performs best. This study compared anterior 180° versus posterior 270° fundoplication.

Methods: At three hospitals, patients were randomized to anterior 180° versus posterior 270° partial fundoplication, and clinical outcomes were determined using a structured questionnaire at 3, 6 and 12 months. Heartburn, dysphagia and satisfaction were assessed using 0–10 analoue scales, and adverse outcomes and side effects were determined. Endoscopy, manometry and pH monitoring were performed 6 months after surgery.

Results: Forty-seven patients were randomized to anterior ($n = 23$) versus posterior ($n = 24$) fundoplication. Clinical outcomes for 93–98% of patients were available at each follow-up point. At 12 months, the mean heartburn score was higher following anterior fundoplication (2.7 versus 0.8, $P = 0.045$), although differences were not significant at earlier follow-up. Conversely, following posterior fundoplication, patients were less able to belch at 3 (56% versus 16%, $P = 0.013$) and 6 months (43% versus 9%, $P = 0.017$). No significant differences were demonstrated for dysphagia. Both groups had high rates of satisfaction with the outcome – 85% versus 86% satisfied at 12 months follow-up.

Conclusion: Both partial fundoplications are effective treatments for gastro-oesophageal reflux. Posterior partial fundoplication is associated with less reflux symptoms offset by more side effects.

Introduction

While medication is effective treatment for gastro-oesophageal reflux disease, some individuals respond poorly and require antireflux surgery. Previous randomized trials have shown good outcomes following both anterior and posterior partial versus Nissen fundoplication for the treatment of reflux.[1–9] However, it is not clear which type of partial fundoplication performs best. Two comparative trials have been reported. A comparison of anterior 120° versus posterior fundoplication showed equivalent satisfaction, but trade-offs between recurrent reflux versus side effects.[10] The other study compared anterior 180° versus posterior fundoplication and found similar outcomes.[11] However, different types of anterior fundoplication were used in these trials, and follow-up in the second study was 58% at 12 months. As the type of partial fundoplication which yields the best outcome remains uncertain, we undertook a prospective randomized trial of anterior 180° versus posterior 270° partial fundoplication to compare the best performing anterior fundoplication variant[1] with a posterior fundoplication.

Methods

Two techniques for laparoscopic partial fundoplication (anterior 180° versus posterior 270°) were compared. Five consultant surgeons from three teaching hospitals participated. The trial was approved by each hospital's research ethics committee, and consent

was obtained from all participants. Initial outcomes at up to 12 months follow-up are reported.

All patients had objective evidence of gastro-oesophageal reflux, and symptoms that were not controlled by medication. Patients were randomized in the operating theatre to either anterior 180° or posterior 270° partial fundoplication by opening a sealed envelope. All patients undergoing laparoscopic fundoplication were considered for entry. Exclusion criteria were previous gastric surgery, large hiatus hernia and a preference for Nissen fundoplication. Patients underwent preoperative investigation with oesophageal manometry and endoscopy. pH monitoring was performed selectively to confirm reflux in those without erosive oesophagitis, or with atypical symptoms.

Operative techniques were standardized. The lower oesophagus was dissected, with preservation of the hepatic branch of the vagus nerve and short gastric blood vessels, followed by posterior hiatal repair. Posterior partial fundoplication entailed placement of the gastric fundus behind the intra-abdominal oesophagus, with anchorage to the oesophagus on the right and left sides at the 10 and 2 o'clock positions, and also to the hiatal rim postero-laterally on the right side, leaving the anterior oesophagus uncovered. Details of the anterior 180° fundoplication have been described elsewhere.[12] The fundoplication was constructed by suturing the anterior wall of the fundus across the front of the oesophagus to attach it to the postero-lateral wall of the oesophagus and the right hiatal pillar, and apical sutures were added to close the anterior hiatus.

Follow-up data was collected by a nurse who was blinded to the randomization, and patients were blinded to the type of partial fundoplication. Clinical follow-up used a standardized questionnaire (described elsewhere[13]). Patients were interviewed preoperatively, 3, 6 and 12 months after surgery by telephone. The presence of various symptoms was sought: heartburn, epigastric pain, regurgitation, dysphagia for lumpy solids, soft solids, fluids, odynophagia, inability to belch, postprandial fullness, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing, wheezing, diarrhoea and increased flatulence, ability to relieve bloating and consumption of a normal diet. The severity of heartburn, dysphagia for solids and dysphagia for liquids was determined using analogue scores (0 = no symptoms, 10 = severe symptoms). A validated dysphagia score (0 = no dysphagia, 45 = severe dysphagia), which integrated dysphagia for various liquids and solids, was also applied.[14]

Overall outcome was determined by asking whether patients thought that their decision to have surgery was correct, and by grading the outcome using a previously described Visick grade,[13] an outcome grade[13] – excellent, good, fair versus poor, and analogue satisfaction score (0 = dissatisfied, 10 = satisfied). Objective investigation was undertaken approximately 6 months after surgery using endoscopy, oesophageal manometry and 24 h pH monitoring.

A power calculation determined that 100 patients would be needed to demonstrate a 20% difference in measures of reflux or dysphagia at $P < 0.05$ and power = 80%. Analyses were performed on intention to treat basis. Data were analysed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Fisher's exact test was used to assess contingency tables, and the Mann–Whitney test to assess continuous data sets. Significance was accepted at $P < 0.05$.

Results

Forty-seven patients (12 men, 35 women) underwent surgery from September 2005 to February 2012. Twenty-three were randomized to anterior and 24 to posterior fundoplication. Groups were well matched (Tables 1–5). Twenty-four-hour pH monitoring was performed before surgery in 85%, with mean % pH < 4 in 13.8% in the anterior group versus 11.2% in the posterior group ($P = 0.081$).

All but one patient had a fundoplication constructed as randomized. In one, an attempt was made to perform a posterior fundoplication, but as a satisfactory posterior fundoplication could not be fashioned an anterior fundoplication was constructed. Operating time ranged from 30 to 147 min (mean 87.2) in the anterior group versus 32–146 (mean 90.4; $P = 0.767$) in the posterior group.

Both groups recommenced oral intake at a similar time (0.7 versus 0.8 days), and the hospital stay was also similar (1.8 versus 1.7 days). Two complications occurred in each group: anterior group – umbilical wound infection and severe shoulder pain; posterior group – cardiac arrhythmia requiring anticoagulation, and unsuccessful re-exploration 2 days after surgery for a lost suture needle.

Table 2 Assessment of heartburn using 0–10 visual analogue scale

Status	Type of fundoplication		*P*-value
	Anterior (*n* = 23)	Posterior (*n* = 24)	
Preoperative	5.35 (4.11 to 6.59)	6.58 (5.77 to 7.40)	0.124
Post-operative			
3 months	2.3 (0.8 to 3.8)	1.4 (0.2 to 2.7)	0.285
6 months	2.1 (0.9 to 3.4)	0.5 (0 to 1.0)	0.200
12 months	2.7 (1.1 to 4.2)	0.8 (0.1 to 1.4)	0.045

All data are expressed as mean (95% CIs) or *n* (%).

Table 1 Preoperative parameters

Variable	Type of fundoplication		*P*-value
	Anterior (*n* = 23)	Posterior (*n* = 24)	
Age (years)	57.8 (53.8 to 61.8)	57.3 (52.5 to 62.0)	0.860
Gender (M : F)	6:17	6:18	0.932
Height (cm)	1.64 (1.6 to 1.70)	1.65 (1.6 to 1.7)	0.824
Weight (kg)	79.3 (72.8 to 85.9)	81.2 (75.8 to 86.5)	0.656
BMI	29.3 (27.8 to 30.8)	29.9 (28.0 to 31.8)	0.607
Duration of symptoms (years)	14.5 (8.2 to 20.8)	9.9 (6.1 to 13.6)	0.109

All data are expressed as mean (95% CIs) or *n* (%). BMI, body mass index.

Table 3 Preoperative and post-operative symptoms assessed using yes versus no questions

Symptom	Preoperative		Post-operative					
			At 3 months		At 6 months		At 12 months	
	AP (n = 23)	PP (n = 24)	AP (n = 22)	PP (n = 23)	AP (n = 21)	PP (n = 23)	AP (n = 22)	PP (n = 22)
Heartburn	95%	100%	23%	9%	24%	4%	19%	10%
Epigastric pain	78%	79%	59%	39%	43%	35%	43%	30%
Regurgitation	74%	88%	4%	0%	9%	13%	2%	15%
Odynophagia	22%	29%	9%	17%	9%	9%	19%	10%
Postprandial fullness	52%	54%	82%	69%	62%	65%	67%	75%
Epigastric bloat	69%	88%	63%	56%	52%	61%	71%	60%
Anorexia	30%	25%	23%	17%	14%	9%	19%	15%
Nausea	30%	42%	18%	17%	24%	22%	**9%***	**45%***
Vomiting	22%	38%	4%	9%	0%	4%	5%	0%
Coughing	56%	50%	23%	26%	29%	26%	19%	20%
Wheezing	26%	33%	23%	17%	14%	13%	14%	15%
Can relieve bloat	56%	50%	59%	65%	52%	61%	57%	65%
Eats normal diet	69%	71%	41%	39%	38%	39%	33%	30%
Diarrhoea	NA	NA	14%	26%	19%	26%	24%	30%
Unable to belch	NA	NA	**18%****	**56%****	**9%*****	**43%*****	14%	30%
Increased flatus	NA	NA	77%	83%	76%	83%	86%	85%

*P = 0.015; **P = 0.013; ***P = 0.017. All data are % patients interviewed at each time point. No statistically significant differences were demonstrated between the two groups ($P \geq 0.05$ at all follow-up intervals) except where indicated. AP, anterior partial fundoplication; NA, not applicable; PP, posterior partial fundoplication.

Table 4 Dysphagia assessment

Variable	Preoperative		Post-operative					
			At 3 months		At 6 months		At 12 months	
	AP (n = 23)	PP (n = 24)	AP (n = 22)	PP (n = 23)	AP (n = 21)	PP (n = 23)	AP (n = 22)	PP (n = 22)
Dysphagia								
Lumpy solids	35%	58%	41%	26%	33%	17%	33%	15%
Soft solids	13%	25%	14%	9%	9%	4%	5%	0%
Liquids	9%	21%	14%	13%	19%	13%	9%	5%
Visual analogue scale								
Solids	2.0 (0.7–3.3)	3.8 (2.3–5.3)	3.9 (2.6–5.1)	2.9 (1.5–4.2)	2.2 (1.0–3.5)	2.0 (0.9–3.1)	3.3 (1.8–4.8)	2.2 (1.0–3.3)
Liquids	0.8 (0.1–1.8)	0.9 (0.1–1.8)	1.2 (0.2–2.3)	1.0 (0.3–1.7)	1.0 (0.2–1.8)	0.9 (0.2–1.6)	1.2 (0.4–2.0)	0.4 (0–0.8)
Dysphagia score								
Overall result	6.5 (2.0–11.1)	11.2 (6.3–16.2)	10.9 (7.1–14.6)	10.3 (5.5–15.1)	10.7 (6.3–15.1)	7.0 (3.6–10.4)	10.6 (5.5–15.7)	5.7 (2.7–8.7)
Scored 0 only	65%	38%	23%	30%	33%	39%	29%	35%

All data are given as percentages or mean (95% CIs). No statistically significant differences were demonstrated between the two groups ($P \geq 0.05$ at all follow up intervals) except where indicated. AP, anterior partial fundoplication; NA, not applicable; PP, posterior partial fundoplication.

Table 5 Oesophageal manometry outcomes

Variable	Type of fundoplication		P-value
	Anterior	Posterior	
Preoperative			
LOS resting pressure (mmHg)	11.2 (6.2–16.1)	11.7 (6.5–16.9)	0.991
LOS residual relaxation pressure (mmHg)	2.9 (0.9–4.9)	2.6 (1.3–3.9)	0.737
% with resting LOSP <10 mmHg	61%	61%	1.000
Post-operative			
LOS resting pressure (mmHg)	25.2 (12.9–37.4)	19.8 (13.5–26.1)	0.742
LOS residual relaxation pressure (mmHg)	8.2 (3.8–12.5)	7.0 (4.0–10.0)	0.936
% with resting LOSP <10 mmHg	85%	71%	0.648

All data are expressed as % or mean (95% CIs). LOS, lower oesophageal sphincter; LOSP, lower oesophageal sphincter pressure.

Completeness of clinical follow-up was 95.7% at 3 months, 95.7% at 6 months and 93.6% at 12 months. Two patients were not contactable during early follow-up. One was not willing to be interviewed using the questionnaire, but did indicate he was happy with his outcome. Another patient withdrew due to communication problems associated with a previous laryngectomy. One patient did not contribute data at 12 months as her husband had just died.

Tables 2–4 and 6 summarize the clinical outcomes. Significant differences were seen for nausea, belching and heartburn. All other outcomes were similar. In the posterior group, more patients

Table 6 Outcome scores, satisfaction score and Visick grading

Variable	Preoperative		Post-operative					
			3 months		6 months		12 months	
	AP (n = 23)	PP (n = 24)	AP (n = 22)	PP (n = 23)	AP (n = 21)	PP (n = 23)	AP (n = 22)	PP (n = 22)
Outcome								
Excellent	NA	NA	36%	48%	38%	56%	24%	45%
Good	NA	NA	55%	43%	48%	27%	57%	40%
Fair	NA	NA	4%	9%	5%	17%	14%	15%
Poor	NA	NA	4%	0%	9%	0%	5%	0%
Modified Visick grade								
1	4%	0%	14%	35%	14%	30%	14%	25%
2	9%	4%	68%	57%	72%	48%	57%	40%
3	44%	17%	5%	4%	0%	4%	10%	20%
4	43%	79%	9%	4%	14%	18%	14%	15%
5	NA	NA	5%	0%	0%	0	5%	0%
Satisfaction score								
Mean score	NA	NA	8.7	8.8	8.8	8.5	7.8	8.6
95% CI	NA	NA	(7.6 to 9.7)	(8.1 to 9.5)	(7.9 to 9.7)	(7.5 to 9.4)	(6.5 to 9.2)	(7.7 to 9.5)
Would have the operation again	NA	NA	91%	100%	90%	96%	86%	85%

All data are expressed as %. No statistically significant differences were demonstrated between the two groups ($P \geq 0.05$ at all follow up intervals) except where indicated. AP, anterior partial fundoplication; NA, not applicable; PP, posterior partial fundoplication.

reported nausea at 12 months, and more reported they were unable to belch at 3 and 6 months. Heartburn outcomes are summarized in Tables 2 and 3. For most questions, the outcomes were similar at 3 and 6 months. However, the heartburn score was higher in the anterior group at 12 months (Table 2). There were no significant differences for dysphagia (Table 4). Satisfaction with the outcome was similar for the two groups (Table 6). No patients underwent revision surgery during the follow-up period.

Endoscopy was undertaken at 6 months in 32 (68%) patients, oesophageal manometry in 27 (57%) and pH monitoring in 26 (55%). At endoscopy, two patients in the anterior group had a 'loose' fundoplication. One of these also had a small sliding hiatus hernia. The fundoplication appeared intact in all patients in the posterior group. No significant differences were seen for manometry outcomes (Table 5). Of the patients who underwent pH studies, three had abnormal acid exposure: posterior group – 1, anterior group – 2. Only one (anterior group) reported reflux symptoms, and all three reported high satisfaction scores (8, 9 and 10). The median percentage time for pH < 4 was 0.05% in the anterior group versus 0.30% in the posterior group ($P = 0.668$).

Discussion

Despite the good control of reflux achieved by Nissen fundoplication, the occurrence of undesirable side effects in some patients has led to the procedure being modified. Partial fundoplications probably offer the best opportunity to reduce side effects without compromising reflux control. Level 1 evidence from meta-analyses of randomized trials supports the use of posterior and anterior partial fundoplications as alternatives to the Nissen procedure,[6,8] but comparisons between the different partial fundoplications are limited.

Thirteen randomized trials have compared posterior versus Nissen fundoplication.[4–7] In general, these have shown equivalent reflux control, with the larger trials showing less wind-related side effects after posterior fundoplication. However, only two trials demonstrate less dysphagia following posterior partial fundoplication,[5,7] both at relatively short-term follow-up. Five randomized trials have compared anterior 180° partial versus Nissen fundoplication,[1,2,8] These trials also report similar control of reflux for anterior 180° partial versus Nissen fundoplication, but less dysphagia and wind related side effects. Two other trials have compared anterior 90° partial with Nissen fundoplication,[3,9] and shown similar overall satisfaction, but a trade-off between better reflux control following Nissen versus less side effects following anterior 90° fundoplication.

As the trials of partial versus Nissen fundoplication suggest good outcomes for both partial fundoplication variants, the next step is to compare anterior versus posterior partial fundoplication. Two trials have done this.[10,11] A trial from Sweden enrolled 95 patients to anterior 120° versus posterior fundoplication,[10] and the results at 5 years showed similar satisfaction, but better reflux control following posterior offset against less side effects following anterior fundoplication.[10] The anterior 120° partial fundoplication was different to the anterior 180° variant performed in the current study in which the fundus was sutured to the right hiatal pillar. A second trial from Sheffield, UK, compared anterior 180° versus posterior partial fundoplication,[11] and showed less dysphagia following anterior 180° fundoplication at 3 months, offset by a higher proportion of patients in the anterior fundoplication group reporting early heartburn symptoms. A weakness of that trial was the incomplete follow-up at 12 months.

Our findings support the observations from these two studies. At up to 12 months, we identified similar levels of satisfaction, but a trade-off between reflux versus side effects. Inability to belch was more common after posterior fundoplication, but the heartburn scores were higher after anterior 180° partial fundoplication at 12 months, consistent with the trend towards higher pH scores. Dysphagia rates were similar between the two groups at all time points.

A weakness of our study was the failure to recruit 100 patients. Hence, some analyses might be underpowered. The reasons for this were complex. We originally established a protocol to randomize to Nissen versus anterior versus posterior fundoplication. Consensus was sought from across Australia, and enthusiasm was expressed for

the original protocol. However, most surgeons had difficulty achieving equipoise for all three procedures and were unwilling to randomize. To address this, the Nissen arm was dropped, and the trial was changed to the reported two-arm trial. While it was hoped that recruitment would be easier, other factors led to slow recruitment, including a progressive shift from surgery for reflux to surgery for very large hiatus hernia.[15] Despite this, the results are consistent with the other trials, and the data should contribute to future metanalyses of trials of different partial fundoplication techniques.

We have shown similar high satisfaction with both types of partial fundoplication, but a trade-off between reflux symptoms versus side effects. When considered alongside other trials of Nissen versus the various forms of partial fundoplication, there is probably a spectrum of outcomes ranging from Nissen to posterior to anterior partial fundoplication, and a progressive trade-off between reflux control versus side effects across this spectrum. All trials show good rates of satisfaction no matter what the fundoplication type, and this lends support to the concept of a tailored approach to antireflux surgery, in which each individual patient preferences can be balanced against the risk of reflux versus possible side effects.

Acknowledgements

This trial was supported by grants from the National Health and Medical Research Council of Australia. We are grateful for the assistance of Tanya Irvine, Lorelle Smith and Janet Sullivan who contributed to data collection, and Ann Schloithe who assisted with statistical analysis.

References

1. Broeders JA, Roks DJ, Jamieson GG *et al*. Five year outcome after laparoscopic anterior partial versus Nissen fundoplication – four randomized trials. *Ann. Surg.* 2012; **255**: 637–42.
2. Cai W, Watson DI, Lally CJ *et al*. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180 partial fundoplication. *Br. J. Surg.* 2008; **95**: 1501–5.
3. Nijjar RS, Watson DI, Jamieson GG *et al*. Five-year follow-up of a multicenter, double-blind randomized clinical trial of laparoscopic Nissen vs anterior 90 degrees partial fundoplication. *Arch. Surg.* 2010; **145**: 552–7.
4. Mardani J, Lundell L, Engström C. Total or posterior partial fundoplication in the treatment of GERD: results of a randomized trial after 2 decades of follow-up. *Ann. Surg.* 2011; **253**: 875–8.
5. Strate U, Emmermann A, Fibbe C *et al*. Laparoscopic fundoplication: Nissen versus Toupet. Two-year outcome of a prospective randomized study of 200 patients regarding preoperative esophageal motility. *Surg. Endosc.* 2008; **22**: 21–30.
6. Broeders JA, Mauritz FA, Ahmed Ali U *et al*. Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. *Br. J. Surg.* 2010; **97**: 1318–30.
7. Koch OO, Kaindlstorfer A, Antoniou SA *et al*. Laparoscopic Nissen versus Toupet fundoplication: objective and subjective results of a prospective randomized trial. *Surg. Endosc.* 2012; **26**: 413–22.
8. Broeders JA, Roks DJ, Ali UA *et al*. Laparoscopic anterior 180° versus Nissen fundoplication for gastroesophageal reflux Disease – systematic review and meta-analysis of randomized clinical trials. *Ann. Surg.* 2013; **257**: 850–9.
9. Watson DI, Devitt PG, Smith L, Jamieson GG. Anterior 90(partial vs Nissen fundoplication – 5 year follow-up of a single-centre randomized trial. *J. Gastrointest. Surg.* 2012; **16**: 1653–8.
10. Engstrom C, Lonroth H, Mardani J, Lundell L. An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. *World J. Surg.* 2007; **31**: 1221–5.
11. Khan M, Smythe A, Globe J *et al*. Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease. *ANZ J. Surg.* 2010; **80**: 500–5.
12. Gatenby PAC, Bright T, Watson DI. Anterior 180 degree partial fundoplication – how I do it. *J. Gastrointest. Surg.* 2012; **16**: 2297–303.
13. Watson DI, Pike GK, Baigrie RJ *et al*. Prospective double blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann. Surg.* 1997; **226**: 642–52.
14. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J. Clin. Gastroenterol.* 1992; **14**: 99–100.
15. Engstrom C, Cai W, Irvine T *et al*. Twenty years of experience with laparoscopic antireflux surgery. *Br. J. Surg.* 2012; **99**: 1415–21.

2.8 Repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh

---

Wijnhoven BPL & Watson DI. Laparoscopic repair of a giant hiatus hernia - How I do it. *J Gastrointest Surg* (2008) **12**:1459-1464.

This paper described in detail the surgical technique for laparoscopic repair of very large hiatus hernia.

Watson DI, Thompson SK, Devitt PG, Smith L, Woods SD, Aly A, Gan S, Game PA, Jamieson GG. Laparoscopic repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh - a randomized controlled trial. *Ann Surg* (2015) **261**:282-289.

This paper reported the clinical and objective outcomes at 12 months (short term) follow-up from a randomized trial comparing laparoscopic repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh.

Koetje J, Irvine T, Thompson SK, Devitt PG, Woods SD, Aly A, Jamieson GG, Watson DI. Quality of life following repair of large hiatal hernia is improved but not influenced by use of mesh: Results from a randomized controlled trial. to *World J Surg* (2015) **39**:1465-1473.

This paper reported early quality of life outcomes from the same trial.

J Gastrointest Surg (2008) 12:1459–1464
DOI 10.1007/s11605-008-0473-3

Laparoscopic Repair of a Giant Hiatus Hernia—How I Do It

Bas P. L. Wijnhoven · David I. Watson

Received: 24 October 2007 / Accepted: 7 January 2008 / Published online: 23 January 2008

Abstract The laparoscopic approach is now the technique of choice for the repair of large hiatus hernia. It is associated with a low risk of complications. However, controversy exists as to the optimal technique for laparoscopic repair. In this paper, we describe our approach. This entails full dissection of the hernia sac from the mediastinum, hiatal repair with posteriorly placed sutures, and then construction of an appropriate fundoplication. Whether the use of mesh for hiatal repair will reduce the risk of subsequent reintervention and not add any new risks is, however, unclear. For this reason, we believe that the mesh should only be used in appropriately designed clinical trials, and for now, the standard approach to laparoscopic repair of a large hiatus hernia is sutured repair.

Keywords Laparoscopic surgery · Hiatus hernia · Paraesophageal hernia · Esophagus · Fundoplication

Introduction

Soon after introduction of the laparoscopic Nissen fundoplication, surgeons began to report experience with laparoscopic repair of large hiatus hernias, and this approach is now considered to be the technique of choice for the repair of large hiatus hernia.[1] This has led to low morbidity and mortality rates, even in the older patients. However, there is still a significant risk of recurrent, although frequently asymptomatic, herniation at longer-term follow-up. Hence, controversy exists regarding what is the optimal technique for laparoscopic repair of a large hiatus hernia. In this paper, we describe our approach to the laparoscopic repair of large hiatus hernias and discuss some alternative techniques and new developments.

B. P. L. Wijnhoven · D. I. Watson (✉)
Department of Surgery, Flinders Medical Centre, Flinders University,
Room 3D211,
Bedford Park, South Australia 5042, Australia
e-mail: david.watson@flinders.edu.au

Surgical Procedure

Preoperative Workup

A careful history of the patients' symptoms is taken, with emphasis on reflux, regurgitation, dysphagia, and (postprandial) chest pain. In the elective setting, we routinely perform a barium-swallow X-ray and upper gastrointestinal endoscopy to delineate the relevant anatomy, the degree, if present, of gastroesophageal reflux, and other pathology. Further assessment with esophageal manometry or pH monitoring is not routine as we usually add an anterior 90° partial fundoplication to the repair (discussed later). However, if a Nissen fundoplication is to be added to repair of a large hiatus hernia, esophageal manometry and pH monitoring should be undertaken to confirm reflux and adequate esophageal body peristalsis.

Theater Setup

A nasogastric tube is not routinely passed, although it can be placed temporarily intraoperatively, as needed, to decompress the stomach if it is found to be full of gas at laparoscopy. The patient is positioned in the lithotomy position with the legs extended in stirrups (French position) and 20 to 30° head up (reverse Trendelenburg). The video monitor is placed at the patient's eye level and in line with

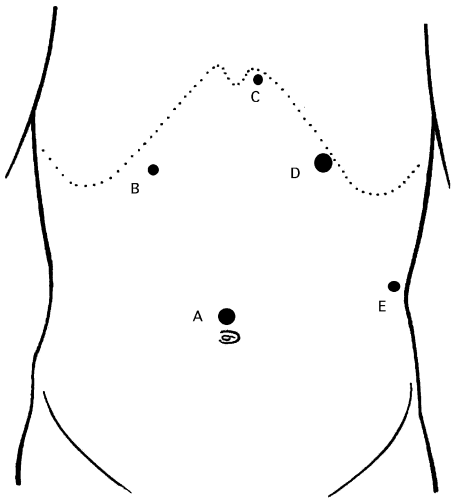


Figure 1 Port placement: *A*, camera port; *B*, *D*, surgeon's operating ports; *C*, liver retractor insertion site; *E*, port for assistant's retractor.

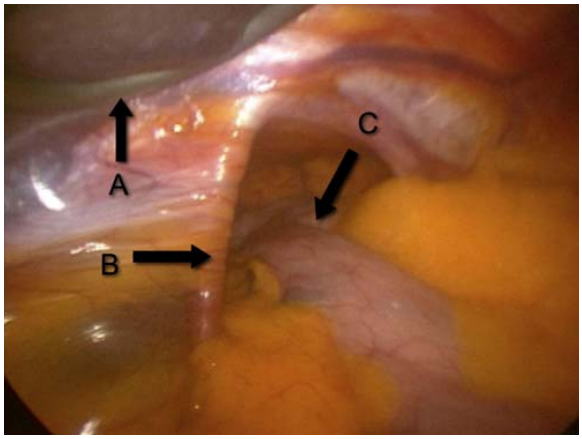


Figure 3 The initial laparoscopic view—a large paraesophageal hernia with more than 50% of the stomach in the chest via a large hiatal defect is seen. The apex of the liver retractor (*A*) is seen lifting the liver anteriorly. *B*, The hiatal rim; *C*, intrathoracic component of the stomach.

the operating surgeon who stands between the legs of the patient. The surgeon's assistant stands at the patient's left side.

The instrumentation used is fairly simple. We use two 11-mm and two 5-mm trocars (port placement is shown in Fig. 1). Instrumentation consists of two atraumatic grasping instruments, a diathermy hook, and a needle holder for the operating surgeon. A toothed grasping instrument is used initially by the assistant surgeon and an atraumatic grasping instrument later in the procedure. The assistant also controls a 30° laparoscope, and a pair of scissors is used for cutting sutures. The most important instrument is the Nathanson liver retractor (Figs. 2 and 3—Cook Medical Technology, Eight Mile Plains, Queensland, Australia). This provides a safe, stable elevation of the liver. We do not use a harmonic scalpel or similar technology.

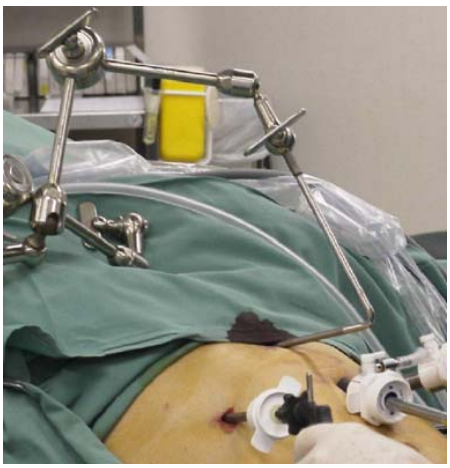


Figure 2 External view of liver retractor held in position by an "iron intern."

Operative Technique

An 11-mm port is introduced immediately supraumbilically using an open insertion technique (Fig. 1), and pneumoperitoneum is established. The liver retractor is introduced via a 5-mm stab wound, which is placed as high as possible in the angle between the xiphoid and the apex of the left costal margin, to the left side of the falciform ligament. With this device, the left lobe of the liver is retracted upward and slightly to the right, to expose the hiatal defect. Good exposure is usually obtained even in patients with a fatty liver. Three further ports are placed next: a 5-mm port immediately subcostal in the right midclavicular line, an 11-mm trocar immediately subcostal in the left midclavicular line, and a 5-mm port in the anterior left axillary line approximately 3 to 4 cm below the costal margin.

The size of the hernia and the contents of the hernia sac are first inspected (Fig. 3). However, no attempt is made to reduce the contents of the hernia, as this is usually not feasible in very large hernias until the hernia sac has been fully dissected. This is because the upper part of the stomach is incorporated into the posterior wall of the sac. Hence, the first part of the operation should be to fully dissect the hernia sac from the mediastinum. As this is undertaken, the contents (stomach and sometimes bowel) progressively reduce into the abdomen, and a sufficient intra-abdominal length of the esophagus is usually evident. We have only rarely encountered a short esophagus (two patients in nearly 400 laparoscopic procedures), and we

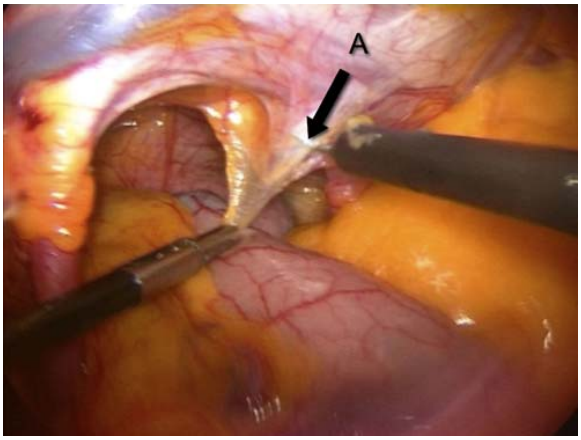


Figure 4 Division of the first layer of the hernia sac (peritoneum), commencing anterolaterally on the left side, close to and just inside the hiatal rim (*A*)

would not undertake an esophageal lengthening procedure (Collis gastroplasty) at an initial operation.

The first step is to divide the lesser omentum to expose the right hiatal pillar within the lesser sac. During this maneuver, the hepatic branch of the vagus nerve is usually divided, although occasionally, this nerve can be spared. If an aberrant left hepatic artery is encountered, this can be divided between clips or spared as necessary. Next, we commence dissection of the sac at its neck by dividing the layers of the hernia sac, close to but 0.5–1 cm inside the hiatal rim. Our preference is to commence this dissection anterolaterally on the left side of the hiatus (Fig. 4). Two layers need to be divided to enter the correct plane. The first of these is the peritoneum, and beneath this is a fascial layer composed of attenuated phreno-esophageal ligament. Once the correct plane is entered, the assistant uses a toothed grasping instrument to pull the cut edge of the hernia sac into the abdomen.

The plane of dissection is then extended across the front of the hiatus toward the right pillar and posteriorly along the left pillar. It is important for the assistant to pull firmly down on the sac as this maneuver gradually reduces the sac contents. The retraction is toward the right lower abdomen when dissecting the left pillar and to the left lower side when dissecting the right pillar. When dividing the sac from the hiatal rim, the dissection must be maintained 0.5 to 1 cm inside the hiatal rim to avoid excising the fascial coverings, which protect the muscle fibers at the hiatal rim (Fig. 5).

Dissection alternates between the left and right sides of the hiatus, and the sac is gradually reduced into the abdomen (Fig. 6). At this time, the hernia sac is dissected in the mediastinum using predominantly blunt dissection, although the diathermy hook is used if small blood vessels are encountered. If dissection is in the correct plane, separation of the sac from the mediastinum is usually very easy and bloodless. It is also mandatory to dissect any posterior sac (which is often present) from the mediastinum and to fully expose behind the esophagus. Next, an atraumatic grasping instrument held in the surgeon's left hand is passed from right to left behind the esophagus. We then pass a long linen tape through the 11-mm left upper abdominal port to this instrument, pull the tape behind the esophagus, pass it back to the instrument passing through the left upper abdominal port, and remove both ends of the tape through the left upper abdominal port. This port is removed over the tape and then resited so that the two ends of the tape pass through the wound, adjacent but not through the left upper abdominal port. The ends of the tape are secured at the level of the skin with a clamp. Traction

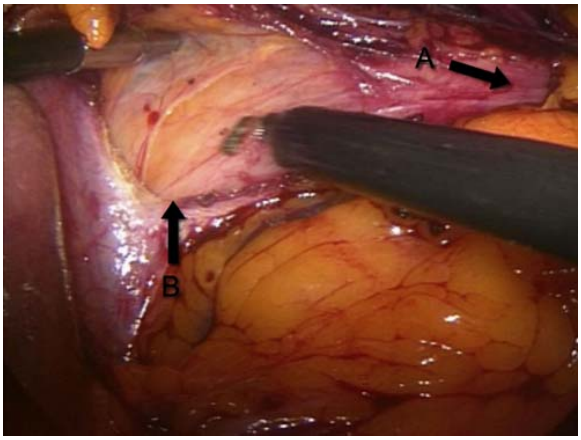


Figure 5 Once the correct plane is entered, the assistant pulls the edge of the sac (*A*) into the abdomen, and the plane of dissection is extended across the front of the hiatus toward the right pillar (*B*).

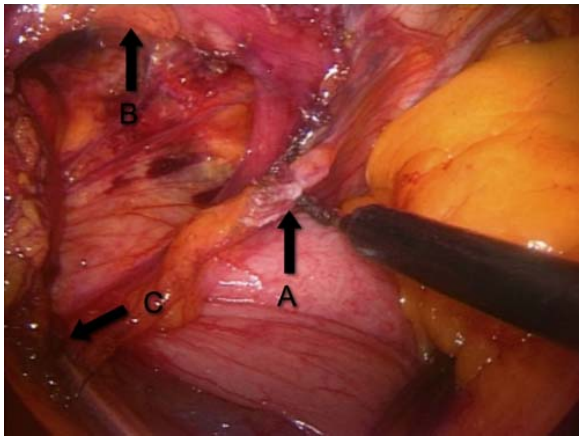


Figure 6 Dissection continues down the left pillar close to the stomach (*A*) as shown (*B*, apex of esophageal hiatus; *C*, edge of sac retracted to right side).

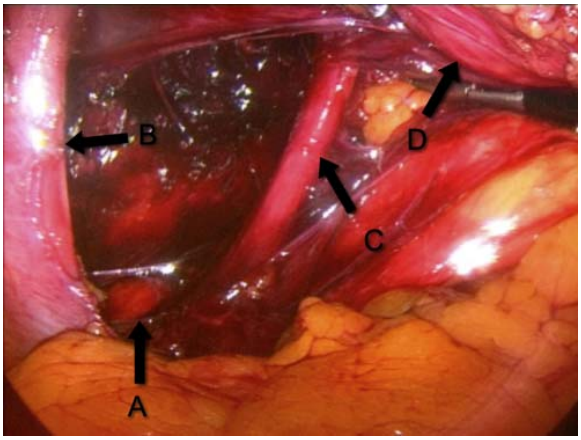


Figure 7 Dissection of the right and left pillar behind the esophagus is continued posteriorly to the decussation (*A*), and a "window" is developed behind the esophagus (*B*, right pillar; *C*, left pillar; *D*, posterior wall of the esophagus).

can then be applied to the tape, either from outside the abdomen or using a grasping instrument inside the abdomen. The esophagus can then be elevated anteriorly and retracted from the mediastinum, and this provides a better view of the hiatus, facilitating further dissection of the posterior aspects of the hernia sac to the base of the right and left pillars and behind the esophagus.

Any posterior component of the hernia sac must now be fully mobilized and brought intra-abdominally. This can be very large in some patients. A window is then created behind the esophagus exposing the left hiatal pillar from the right side (Fig. 7). It is important to undertake sufficient dissection to enable the posterior confluence of the hiatal pillars to be fully identified and for no hernia sac to lie anterior to this. In the process of posterior dissection, we routinely dissect the posterior vagal nerve away from the esophagus, so that it lies close to the confluence of the pillars.

The hiatus is next repaired with sutures. The left and right pillars are approximated with three or more interrupted figures of eight stitches (nonresorbable; monofilament sutures) commencing posteriorly and working anteriorly in 5-mm steps, until the hiatus is reduced to a diameter of approximately 30 mm (Fig. 8). If the repair appears to be under excessive tension, additional sutures can be placed in the anterior hiatus. We have always been able to obtain a satisfactory repair, although we are careful to preserve the fascial coverings over the left and right pillars. An intraesophageal bougie is not usually used to calibrate the hiatal repair, and we only use a bougie if a Nissen fundoplication is added to the procedure.

Once the hiatus is adequately narrowed, we add either an anterior 90° partial fundoplication, an anterior 180° fundoplication, or a Nissen fundoplication to the procedure. If reflux symptoms are the main indication for surgery, we perform an anterior 180° or a Nissen fundoplication, with the final choice based on preoperative esophageal motility testing and patient preference. If mechanical symptoms such as dysphagia or chest pain predominate, then we usually add an anterior 90° partial fundoplication, as this provides additional stability to the hernia repair and adds an antireflux effect but with minimal side effects. The details of the partial fundoplication procedures have been described in detail elsewhere.[2,3]

The anterior 90° partial fundoplication commences with an esophagopexy suture between the right posterolateral aspect of the distal esophagus 2 cm above the esophagogastric junction and the right hiatal pillar near the most anterior hiatal repair suture. Next, the gastric fundus is

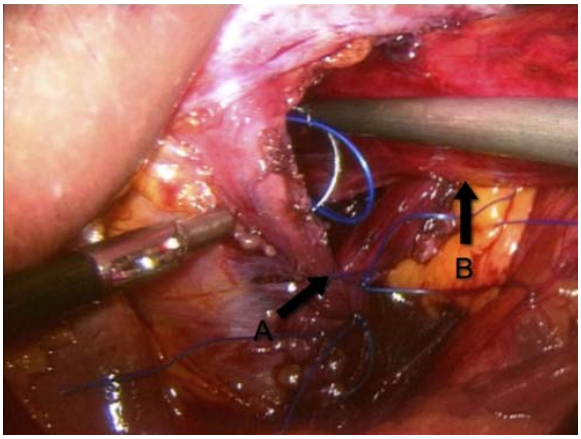


Figure 8 The hiatus is repaired with a series of interrupted sutures (*A*, hiatal repair sutures, *B*, esophagus).

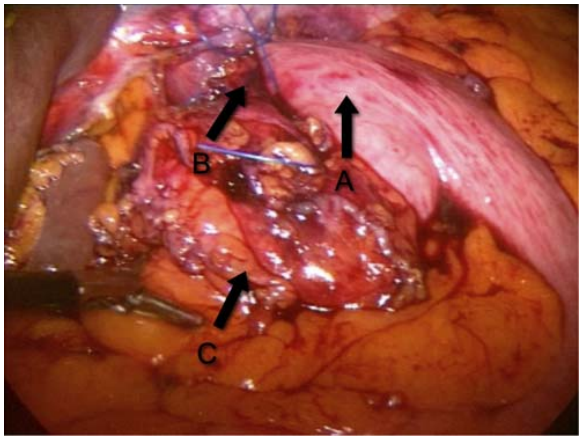


Figure 9 Completed anterior 90° partial fundoplication. *A*, Fundoplication covering left anterolateral esophagus; *B*, right anterolateral esophageal wall; *C*, empty hernia sac, reduced from mediastinum.

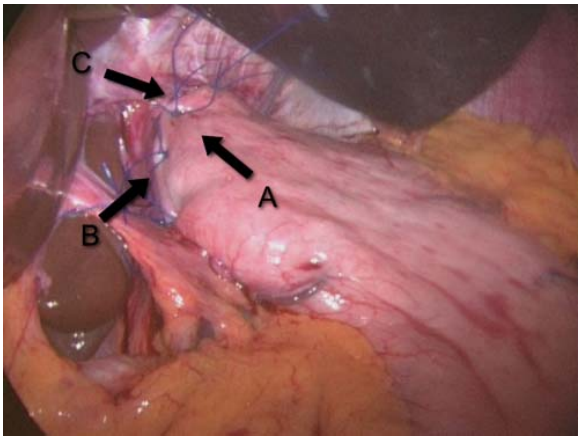


Figure 10 Completed anterior 180° partial fundoplication (*A*, fundoplication covering anterior esophagus; *B*, fundus sutured to right hiatal pillar; *C*, fundus sutured to apex of hiatus).

approximated to the left side of the esophagus using two sutures to accentuate the angle of His. The uppermost of these sutures also incorporates the left hiatal pillar.

The gastric fundus is then sutured loosely over the front of the esophagus, and this suture incorporates the apex of the hiatus and the anterior esophagus. Finally, the inferior edge of the fundal fold lying in front of the abdominal esophagus is sutured to the anterior esophagus to produce a loose fundoplication, which covers the left antero-lateral side of the esophagus (Fig. 9). It also provides three points of fixation between the esophagus and the diaphragm.

For a laparoscopic anterior 180° partial fundoplication,[3] the anterior wall of the gastric fundus is sutured to the right lateral wall of the distal esophagus and to the right hiatal pillar (with three interrupted stitches). The fundus is also sutured to the apex of the esophageal hiatus with two additional interrupted stitches (Fig. 10). If a Nissen fundoplication is added, we construct a loose 360° fundoplication using the anterior wall of the fundus of the stomach.[4] The wrap is calibrated using a 52-Fr bougie, and the short gastric vessels are not divided. The fundoplication is not sutured to the diaphragm.

Our standard approach to hiatal repair does not include reinforcement with mesh. Repair with a range of different techniques and mesh types have been described. However, there is little standardization of practice in this area. Hence, our current practice is to reinforce the hiatal repair with mesh only within the context of a randomized trial, which compares hiatal repair with sutures, with sutures reinforced with an on-lay resorbable or nonresorbable mesh. If mesh is added, we first repair the hiatus with sutures as described above. We then place a 3×5-cm piece of mesh across the hiatus repair, away from the esophageal wall, and secure this in place using either sutures or a hernia tacker (Fig. 11). The mesh is placed loosely to reinforce the posterior sutures, and the mesh is not placed around the anterior or lateral aspects of the hiatal rim.

Intraoperative Complications

Bleeding from the liver can occur because of local trauma from the liver retractor or direct surgical trauma. Bleeding from the liver is usually minor and has almost never required direct intervention. The Nathanson liver retractor also minimizes this problem. Bleeding from the short gastric vessels can occur with division of the vessels when creating a Nissen fundoplication. We no longer divide these vessels.[5]

The inability to reduce a large hiatus hernia, dense adhesions, and iatrogenic perforations of the esophagus or stomach can be other reasons for open surgery. Perforation of the esophagus or stomach has been described in several series.[6,7] This can occur with direct damage to the wall of the esophagus during dissection. In general, we avoid using ultrasonic shears or electrocautery when dissecting the esophageal wall and prefer a blunt dissection approach to minimize this risk. Another cause of esophageal perforation is injury when passing a bougie. We usually avoid using a bougie when undertaking repair of a large hiatus hernia, as it is not necessary when adding an anterior partial fundoplication. We do, however, use a bougie when constructing a Nissen fundoplication, and great care should be taken when passing the bougie in these patients.

Intraoperative pneumothoraces are documented in approximately 3–5% of patients. This is usually due to direct injury to the pleura when dissecting the hiatal sac from the mediastinum, and injury of the left pleural membrane is more likely than injury to the other side. Pneumothorax usually causes a few intraoperative problems, and the CO_2

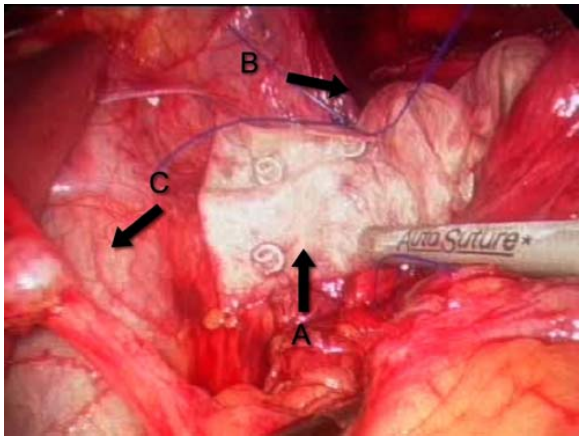


Figure 11 Posterior placement of absorbable mesh (*A*). The mesh is fixed to the hiatal repair with a hernia tacker (*B*, most anterior hiatal repair suture; *C*, inferior vena cava).

gas in the pleural cavity resolves spontaneously without the need for further intervention in most patients.[8]

Postoperative Care

A nasogastric tube is avoided. Thromboembolism prophylaxis is routinely used. Antiemetics are routinely given intraoperatively to minimize the risk of early postoperative retching and vomiting. Long-acting local anesthetic is injected at all wound sites, and opioid analgesics are avoided if possible. We routinely arrange a barium-swallow X-ray on the first day after surgery. If any early problems are identified (such as acute reherniation), early identification facilitates early repair in the first few postoperative days. The X-ray also provides a baseline for comparison should any future problems arise.

Patients are allowed to drink liquids immediately after the operation, and a vitamized/pureed diet is usually commenced on the first postoperative day. Discharge is usually on the first or second postoperative day. The pureed diet is continued for 4 weeks until the first outpatient visit, and after this, a normal diet is gradually resumed as tolerated. Mild symptoms of dysphagia are treated conservatively, and these usually resolve by 6 to 8 weeks.

Outcome

There are now several published studies that report the outcome of laparoscopic repair of large paraesophageal hernias. Anatomical recurrence rates, as judged by radiologic examination, range from 5 to 40%.[6] Clinically significant recurrence, i.e., anatomical recurrence with symptoms requiring reintervention, is much less common, as many patients with an anatomical recurrence are asymptomatic, and the presence of symptoms does not predict the presence of anatomical recurrence.[6,8] Overall satisfaction with laparoscopic repair of large hiatus hernia is high with 80–90% of patients reporting the outcome of their operation to be good or excellent.[6,9] Quality of life is also improved significantly after operation.[10]

Whether the use of mesh to reinforce the hiatal repair or to obtain a tension-free repair will reduce the recurrence rate and symptomatic outcome is still unclear. Three randomized controlled trials have compared the results of procedures with mesh and with no mesh.[11–13] Although the results of these trials appear to be promising, follow-up remains short term, and the primary outcome measure in all studies was the radiological appearance, not the clinical outcome.

It remains to be seen as to whether reinforcement of hiatus hernia repair with mesh will reduce the risk of later reintervention and at the same time not add any new risks or complications. Until this is clear, we believe that mesh should only be used in appropriately designed clinical trials. For now, the standard approach to laparoscopic repair of very large hiatus hernia is sutured repair, and the overall clinical outcome for this approach is very good in most patients.

References

1. Stylopoulos N, Rattner DW. The history of hiatal hernia surgery: from Bowditch to laparoscopy. Ann Surg 2005;241(1):185–193.
2. Krysztopik RJ, Jamieson GG, Devitt PG, Watson DI. A further modification of fundoplication. 90 degrees anterior fundoplication. Surg Endosc 2002;16(10):1446–1451.
3. Watson DI, Liu JF, Devitt PG, Game PA, Jamieson GG. Outcome of laparoscopic anterior 180-degree partial fundoplication for gastroesophageal reflux disease. J Gastrointest Surg 2000;4(5):486–492.
4. Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. Ann Surg 1994;220(2):137–145.
5. Catarci M, Gentileschi P, Papi C, Carrara A, Marrese R, Gaspari AL, Grassi GB. Evidence-based appraisal of antireflux fundoplication. Ann Surg 2004;239(3):325–337.
6. Aly A, Munt J, Jamieson GG, Ludemann R, Devitt PG, Watson DI. Laparoscopic repair of large hiatal hernias. Br J Surg 2005;92(5):648–653.
7. Watson DI, Davies N, Devitt PG, Jamieson GG. Importance of dissection of the hernial sac in laparoscopic surgery for large hiatal hernias. Arch Surg 1999;134(10):1069–1073.
8. Donkervoort SC, Bais JE, Rijnhart-de Jong H, Gooszen HG. Impact of anatomical wrap position on the outcome of Nissen fundoplication. Br J Surg 2003;90(7):854–859.
9. Pierre AF, Luketich JD, Fernando HC, Christie NA, Buenaventura PO, Litle VR, Schauer PR. Results of laparoscopic repair of giant paraesophageal hernias: 200 consecutive patients. Ann Thorac Surg 2002;74(6):1909–1915. discussion 1915–1906.
10. Parameswaran R, Ali A, Velmurugan S, Adjepong SE, Sigurdsson A. Laparoscopic repair of large paraesophageal hiatus hernia: quality of life and durability. Surg Endosc 2006;20(8):1221–1224.
11. Frantzides CT, Madan AK, Carlson MA, Stavropoulos GP. A prospective, randomized trial of laparoscopic polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. Arch Surg 2002;137(6):649–652.
12. Granderath FA, Schweiger UM, Kamolz T, Asche KU, Pointner R. Laparoscopic Nissen fundoplication with prosthetic hiatal closure reduces postoperative intrathoracic wrap herniation: preliminary results of a prospective randomized functional and clinical study. Arch Surg 2005;140(1):40–48.
13. Oelschlager BK, Pellegrini CA, Hunter J, Soper N, Brunt M, Sheppard B, Jobe B, Polissar N, Mitsumori L, Nelson J, Swanstrom L. Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. Ann Surg 2006;244(4):481–490.

RANDOMIZED CONTROLLED TRIAL

Laparoscopic Repair of Very Large Hiatus Hernia With Sutures Versus Absorbable Mesh Versus Nonabsorbable Mesh

A Randomized Controlled Trial

David I. Watson, MD, MBBS, FRACS, Sarah K. Thompson, MD, PhD, FRCSC, FRACS,† Peter G. Devitt, MS,† Lorelle Smith, BNurs,*† Simon D. Woods, MBBS, FRACS,‡ Ahmad Aly, MBBS, MS, FRACS,§ Susan Gan, MBBS, FRACS,* Philip A. Game, MBBS, FRCS, FRACS,† and Glyn G. Jamieson, MS, MBBS, FRCS, FACS, FRACS†*

Objective: Determine whether absorbable or nonabsorbable mesh in repair of large hiatus hernias reduces the risk of recurrence, compared with suture repair.

Background: Repair of large hiatus hernia is associated with radiological recurrence rates of up to 30%, and to improve outcomes mesh repair has been recommended. Previous trials have shown less short-term recurrence with mesh, but adverse outcomes limit mesh use.

Methods: Multicentre prospective double blind randomized controlled trial of 3 methods of repair: sutures versus absorbable mesh versus nonabsorbable mesh. Primary outcome—hernia recurrence assessed by barium meal radiology and endoscopy at 6 months. Secondary outcomes—clinical symptom scores at 1, 3, 6, and 12 months.

Results: A total of 126 patients enrolled: 43 sutures, 41 absorbable mesh, and 42 nonabsorbable mesh. Among them, 96.0% were followed up to 12 months, with objective follow-up data in 92.9%. A recurrent hernia (any size) was identified in 23.1% after suture repair, 30.8% after absorbable mesh, and 12.8% after nonabsorbable mesh ($P = 0.161$). Clinical outcomes were similar, except less heartburn at 3 and 6 months and less bloating at 12 months with nonabsorbable mesh; more heartburn at 3 months, odynophagia at 1 month, nausea at 3 and 12 months, wheezing at 6 months; and inability to belch at 12 months after absorbable mesh. The magnitudes of the clinical differences were small.

Conclusions: No significant differences were seen for recurrent hiatus hernia, and the clinical differences were unlikely to be clinically significant. Overall outcomes after sutured repair were similar to mesh repair.

Keywords: hiatus hernia, laparoscopy, mesh repair, randomized controlled trial

(*Ann Surg* 2015;261:282–289)

Laparoscopic surgery for the treatment of patients with a very large hiatus hernia is now standard clinical practice. This problem occurs most commonly in elderly patients, and in the early days of laparoscopic antireflux surgery it represented less than 10% of the antireflux surgery and hiatus hernia repair workload.[1] However, as laparoscopic techniques for repair have become more reliable, surgeons have been referred more patients with very large hiatus hernias, and in recent years the number of patients with this problem has increased greatly, now comprising approximately 50% of the laparoscopic antireflux surgery workload in our practices.[1] In the 1990s, the standard approach to laparoscopic repair of very large hiatus hernias entailed complete dissection of the hernia sac from the mediastinum, hiatal repair with sutures, and a fundoplication.[2,3] Although good clinical outcomes were reported after laparoscopic repair, and clinical success rates of approximately 90% have been described,[2,3] later studies, which utilized barium meal radiology follow-up, demonstrated that suture repair alone is associated with radiological recurrence rates of approximately 25% to 30%, although only 5% of these patients actually develop symptoms from the recurrent hernia.[4] Nevertheless, concern remains that patients with an asymptomatic recurrence could develop problems later.

Mesh repair has been suggested as a strategy to prevent hernia recurrence, as it applies the principles of groin hernia repair, that is, tension-free repair with prosthetic reinforcement, and it is technically straightforward to perform laparoscopically. Although good results have been reported from case series of mesh repair, some surgeons are concerned that the potential advantages of mesh repair might be offset by the risk of the mesh eroding into the esophageal lumen, and other complications.[5] Difficulties also occur when assessing the outcomes of mesh repair, as there is great variability between mesh types and configurations, and little standardization of surgical techniques.

Three randomized trial have examined the impact of mesh repair of the esophageal hiatus, 2 in the context of very large hiatus hernia.[6–9] In 1 study, Frantzides et al[6] enrolled 72 patients to undergo repair with sutures versus a piece of polytetrafluoroethylene mesh and the results at median 2.5 years follow-up showed a reduction in hernia recurrence from 22% to 0%. In another study, Oelschlager et al[7] reported 6-month outcomes from a multicenter trial of 108 patients who underwent repair with sutures versus an absorbable mesh, and hernia recurrence was reduced from 24% to 9% at short-term follow-up. Later follow-up, however, revealed no outcome differences.[8]

Currently, there remains uncertainty about the preferred technique for repair of very large hiatus hernia, with surgeons disagreeing about whether or not to use mesh, and if mesh is used, what type of mesh and what configuration is optimal. To inform this debate, we conducted a multicenter prospective double-blinded randomized trial designed to determine the effectiveness of mesh repair for very large hiatus hernia. In this study, we compared a sutured repair technique with 2 different mesh types—absorbable versus nonabsorbable, with posterior placement of mesh for hiatal repair.

From the *Flinders Medical Centre, Department of Surgery, Flinders University, Bedford Park, South Australia, Australia; †Royal Adelaide Hospital, Discipline of Surgery, University of Adelaide, Adelaide, South Australia, Australia; ‡Cabrini Hospital, Malvern, Victoria, Australia; and §Department of Surgery, Austin Hospital, University of Melbourne, Heidelberg, Victoria, Australia.

Disclosure: This randomized trial was supported by Research Project Grants from the National Health and Medical Research Council (NHMRC) of Australia (Grant numbers 375111 and 1022722). This trial is registered with the Australia and New Zealand Clinical Trials Registry ACTRN12605000725662. The authors declare no conflicts of interest.

Reprints: David I. Watson, MD, MBBS, FRACS, Flinders Medical Centre, Department of Surgery, Flinders University, Room 3D211, Bedford Park, South Australia 5042, Australia. E-mail: david.watson@flinders.edu.au.

ISSN: 0003-4932/14/26102-0282
DOI: 10.1097/SLA.0000000000000842

METHODS

In this multicentre prospective double-blind randomized controlled trial, 3 laparoscopic methods for repair of very large hiatus hernia were compared; repair using sutures alone versus sutures and absorbable mesh versus sutures and nonabsorbable mesh. The study tested the hypothesis that the incidence of postoperative hiatus hernia would be reduced by the addition of mesh reinforcement to a standardized suture repair technique, with the primary outcome determined by the integrity of the hiatal repair assessed by barium meal radiology and upper gastrointestinal endoscopy.

Trial Design

The trial was undertaken at 4 centers in Adelaide and Melbourne, Australia. All surgery was performed by or directly supervised by 1 of 9 upper gastrointestinal surgeons and undertaken within a university teaching hospital or an associated private hospital. All individuals undergoing elective laparoscopic repair of a very large hiatus hernia, irrespective of age, were considered for entry. A very large hiatus hernia was defined as containing at least 50% of the stomach. Patients were excluded if they had undergone previous surgery involving the stomach or the esophagogastric junction, or if they required any additional procedure in addition to hiatus hernia repair.

Patients were consented before surgery and randomized 1:1:1 in the operating room after commencing the operation to 1 of 3 groups:

1. Repair using sutures alone
2. Repair using sutures reinforced by absorbable mesh (4 ply Surgisis ES, Cook Biotech, Indiana)
3. Repair using sutures reinforced by nonabsorbable mesh (TiMesh, PFM Medical, Köln, Germany).

Randomization was undertaken by opening a sealed envelope. The envelopes were prepared before commencing the trial and shuffled independently by 2 research nurses. More envelopes were prepared than needed to ensure that the randomization could not be anticipated by the operating surgeon. Patients were not told which operation variant was performed, and clinical follow-up was undertaken by a research nurse who was blinded to the surgical procedure. Objective follow-up investigations were also performed in a blinded fashion.

Preoperative workup included endoscopy and barium meal radiology. Esophageal manometry and pH monitoring was used selectively in patients with significant reflux symptoms, but often omitted in patients in whom the indication for surgery was mechanical symptoms resulting from the very large hernia in whom an anterior partial fundoplication was planned as a gastropexy.

Operating Technique

Before commencing the trial, surgical techniques were standardized across sites after a consensus meeting between the participating surgeons, and exchange of videos of the standard operating techniques. Laparoscopic repair was commenced in a similar fashion. The initial steps entailed full dissection of the hiatus hernia sac from the mediastinum, and complete reduction of the sac's contents into the abdomen.[10] An esophageal lengthening procedure was never added. The hiatal defect was narrowed to a diameter of approximately 2.5 cm using posterior hiatal sutures, supplemented by additional anterior hiatal sutures if needed to achieve an adequate closure. In patients randomized to 1 of the 2 mesh repair groups, a rectangular piece of mesh (Surgisis or TiMesh) measuring 2- to 3-cm high × 4- to 5-cm wide was cut and placed over the posterior hiatal repair sutures and the hiatal pillars, but not around the esophagus. The mesh overlapped the left and right hiatal pillars behind the esophagus and did not encircle the esophagus. It was anchored in place using either sutures or a mechanical "tacker" (ProTack, Covidien, New Haven, CT). The mesh repair aimed to reinforce the sutured hiatal repair, and it applied a similar technique to that reported by Granderath et al,[9] but using a larger piece of mesh. A fundoplication was then constructed in all patients, with the choice of the fundoplication type at the operating surgeon's discretion. If any laparoscopic procedure was converted to an open procedure, the randomization schedule was still followed, and if any procedure varied from the trial allocation, the patient remained in the trial and their allocated group for subsequent (intention to treat) analysis.

Postoperative Care

After surgery, patients were allowed oral fluids on the day of surgery, and soft food the next day. Barium meal radiology was performed routinely before discharge, to detect any early problems amenable to early laparoscopic reintervention, and to confirm integrity of hiatal repair at the time of discharge. If the appearances were unsatisfactory, the operation site was reinspected laparoscopically and action taken on the basis of the findings.

Follow-up Assessment

The primary outcome for the trial was recurrence of hiatus hernia. Hernia recurrence was determined 6 months after surgery using 2 objective investigations—barium meal radiology and upper gastrointestinal endoscopy. A recurrent hiatus hernia was defined as any evidence of stomach above the level of the diaphragm, irrespective of size. A subgroup of patients with a recurrent hernia, which was of 2 cm or greater vertical height was also identified. The results of barium meal radiology were reported by radiologists blinded to the details of the hiatal repair technique, and reporting was checked by experienced upper gastrointestinal surgeons. Endoscopy was also undertaken in a blinded fashion by upper gastrointestinal surgeons who were experienced in assessing esophagogastric anatomy after antireflux surgery.

Secondary outcomes were clinical symptom scores, and clinical recurrence of the hernia leading to reintervention. Symptoms were assessed 1, 3, 6, and 12 months after surgery, and analysis and data collection aimed to identify postoperative reflux symptoms, postoperative side effects, and overall satisfaction with the outcome after surgery. To evaluate these outcomes, all patients were interviewed before surgery and at 1, 3, 6, and 12 months after surgery and using a structured questionnaire. Longer-term follow-up is continuing, and outcomes will be reported when available. The structured questionnaire was similar to a questionnaire used in other studies reported by our group.[11] Follow-up data were collected by telephone interview by research nurses based in Adelaide. The presence or absence of the following symptoms was sought: heartburn, chest pain, epigastric pain, regurgitation, dysphagia for lumpy solids, soft solids and liquids, odynophagia, early satiety, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing and wheezing, and diarrhea. The ability to relieve bloating and whether a normal diet was being consumed was also determined.

Zero to 10 analog scales (0 = no symptoms, 10 = severe symptoms) were used to assess heartburn, dysphagia for liquids, and dysphagia for solids. A validated dysphagia score (0 = no dysphagia, 45 = severe dysphagia), which combines information about difficulty swallowing 9 types of liquids and solids, was also applied.[12] Overall outcome was determined using 3 previously described scores.[11] Patients ranked the outcome of surgery using a modified Visick grading (score 1 to 5, 1 = no symptoms, 5 = worse after surgery), an outcome score (excellent, good, fair, or poor), and an analog satisfaction score (0 = dissatisfied, 10 = satisfied). A quality-of-life assessment was

also performed using the SF-36 questionnaire, but these data will be analyzed and reported elsewhere.

Statistics and Sample size

Before commencing the trial, a power calculation determined that 126 patients (42 per group) would be required to demonstrate a 25% difference (30% vs 5%) between groups for radiological recurrence of hiatus hernia, at a significance level of $P < 0.05$ and power of 80%. The proposed magnitude of difference was based on reported outcome differences from the randomized trial reported by Frantzides et al,[6] and objective outcome studies reported by us[4] and others.[13] The sample size was also determined to be sufficient to demonstrate a 13% difference (18% vs 5%) for a 2-way comparison of mesh versus suture repair. All data were entered into a computerized database (Filemaker Pro, version 12, Filemaker, Inc., Santa Clara, CA). Data were analyzed within the database or exported to GraphPad Prism Version 6.0 (GraphPad Software, Inc., San Diego, CA) for statistical testing. Analyses were undertaken on an intention-to-treat basis with patients classified according to randomization. The 3 groups were compared separately. The χ^2 test was used to evaluate 3×2 contingency tables. Comparison of continuous data sets was undertaken using 1-way analysis of variance.

The protocol for this trial was approved by the Southern Adelaide Clinical Human Research Ethics Committee and the Clinical Research Ethics Committees for all other participating hospitals.

RESULTS

From February 2006 to September 2012, 126 patients were enrolled in the trial. Forty-three were randomized to undergo repair using sutures alone, 41 repair with absorbable mesh (Surgisis) and 42 nonabsorbable mesh (TiMesh). Of the 126 patients entered, 117 (92.9%) were interviewed 1 month after surgery, 118 (93.7%) at 3 months, 122 (96.8%) at 6 months, and 121 (96.0%) at 12 months. Objective follow-up data were available for 117 (92.9%) at 6 months follow-up. Follow-up is summarized in Figure 1. No patient withdrew from the study. Missing data were the result of an inability to contact patients at specific follow-up intervals. One patient in the suture repair group died 7 days after surgery (see later).

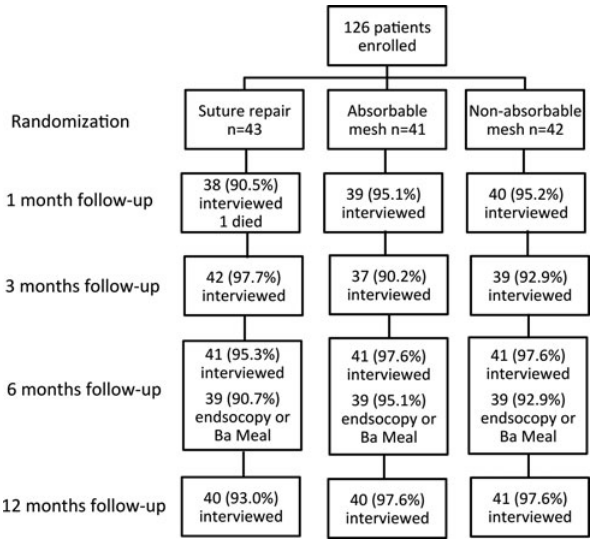


FIGURE 1. CONSORT diagram summarizing recruitment and follow-up compliance.

Preoperative Assessment

The preoperative demographic details for the 3 groups of patients were similar, and are summarized in Table 1. Preoperative symptom scores are summarized in Tables 2 to 6. Less patients in the TiMesh group reported heartburn or chest pain symptoms before surgery. The mean chest pain score was also lower in this group (Table 3), and more patients in the TiMesh group reported a Visick score of 1 or 2 before surgery (Table 6). All other preoperative symptoms were similar for the 3 groups.

Surgery

As randomization occurred in the operating room, all patients underwent surgery. One patient randomized to repair with TiMesh underwent a sutured repair only and the nonabsorbable mesh was not placed. The operating surgeon for that patient encountered a very wide hiatus, with the aorta encompassing the area where the left hiatal pillar is usually found, and was not able to suture a piece of mesh in place. All other patients underwent surgery according to the randomization schedule. Operating time and the number of sutures used for hiatal repair were similar for all 3 groups (Table 7). A fundoplication was added in all patients, and in all but 2 a partial fundoplication was constructed.

Two (1.6%) patients were thought to have a shortened esophagus at surgery—1 in the suture repair group and 1 in the TiMesh group. An esophageal lengthening procedure was not performed in any patient enrolled in the trial. Two procedures were converted to open surgery, both in the suture repair group, because of a bleeding short gastric blood vessel and intra-abdominal obesity respectively. Intra-operative complications are listed in Table 8. One patient in the Surgisis group experienced an esophageal perforation during placement of an esophageal bougie. This was initially sutured but then managed with a temporary esophageal stent inserted on the 10th day after surgery.

Early Hospital Outcomes

The mean length of stay after surgery was similar for the 3 groups (Sutures—4.2 days, Surgisis—4.3, TiMesh—4.3). Postoperative complications occurred in a similar proportion of patients in all groups and are summarized in Table 8. Four patients underwent early laparoscopic reoperation in the suture repair group, and 1 patient died suddenly 7 days after surgery following a presumed pulmonary embolus or myocardial infarct. In the Surgisis group, 1 patient experienced an esophageal perforation, which was initially repaired with sutures but eventually required placement of a temporary esophageal stent 10 days later. In the TiMesh group, 3 patients underwent early reoperation, with 1 of these converted to an open procedure to excise part of the gastric fundus, which was perforated at the site of the fundoplication sutures. Both of the patients thought to have a shortened esophagus developed an acute hiatus hernia and underwent early revision surgery with rerepair of the hiatus. Both subsequently had an excellent clinical outcome and did not have a hernia when assessed objectively at 6 months. Two (1.6%) late revision procedures were performed, 1 for a recurrent hiatus hernia after suture repair and 1 for dysphagia after repair with TiMesh.

Objective Postoperative Investigations

The outcomes for the objective assessment with barium meal radiology and endoscopy are summarized in Table 9. There were no statistically significant differences in the rate of recurrent hiatus hernia between the 3 groups for any comparisons. Of patients, 100 (79.4%) underwent barium meal radiology at 6 months, 100 (79.4%) underwent endoscopy, and 117 (92.9%) underwent at least 1 of these 2 investigations. Using barium meal radiology, a recurrent hiatus hernia

TABLE 1. Preoperative Parameters

	Randomization			
Variable	**Suture Repair**	**Surgisis**	**TiMesh**	***P***
Age (yrs)	67.8 (64.7–70.9)	68.0 (65.1–70.9)	68.1 (64.7–71.5)	0.991
Sex (M:F)	14:29	10:31	16:26	0.403
Height (cm)	1.65 (1.63–1.70)	1.64 (1.61–1.68)	1.66 (1.63–1.70)	0.556
Weight (kg)	82.5 (77.3–87.7)	78.7 (74.0–83.4)	79.4 (73.7–85.0)	0.516
BMI (kg/m^2)	29.6 (28.0–31.2)	29.4 (27.8–31.0)	28.5 (26.6–30.5)	0.663
Duration of symptoms (yrs)	9.7 (6.2–13.1)	10.2 (5.9–14.2)	7.3 (4.6–10.0)	0.496

All data are expressed as mean (95% confidence intervals) or n (%). Analysis of variance used to compare continuous data sets, χ^2 test used to assess categorical variables.

TABLE 2. Assessment of Heartburn Using 0 to 10 Visual Analog Scale

	Sutures	**Surgisis**	**TiMesh**	***P***
Preoperative	2.24 (1.29–3.20)	2.05 (1.18–2.92)	1.65 (0.86–2.44)	0.614
Postoperative (mo)				
1	0.58 (0.092–1.07)	0.69 (0.027–1.36)	0.73(0.098–1.35)	0.936
3	0.45 (0.062–0.84)	1.57 (0.60–2.54)	0.38 (−0.19 to 0.96)	0.022
6	1.49 (0.58–2.40)	1.44 (0.48–2.40)	0.17 (−0.092 to 0.44)	0.024
12	1.10 (0.45–1.76)	1.28 (0.37–2.20)	0.55 (0.059–1.04)	0.303

All data are expressed as mean (95% confidence intervals).

TABLE 3. Assessment of Chest Pain Using 0 to 10 Visual Analog Scale

	Sutures	**Surgisis**	**TiMesh**	***P***
Preoperative	2.88 (1.74–4.02)	4.35 (3.13–5.57)	1.45 (0.57–2.31)	0.0013
Postoperative (mo)				
1	1.34 (0.52–2.22)	1.36 (0.52–2.20)	1.13 (0.29–1.97)	0.903
3	1.19 (0.39–1.99)	1.60 (0.67–2.52)	0.74 (0.03–1.46)	0.343
6	0.83 (0.26–1.40)	1.20 (0.46–1.94)	0.54 (−0.05 to 1.12)	0.329
12	0.82 (0.14–1.51)	1.10 (0.37–1.83)	0.38 (−1.04 to 0.85)	0.261

All data are expressed as mean (95% confidence intervals).

of any size was identified in 22 (22.0%), and a hernia measuring 2 or more cm in length was identified in only 3 (3.0%). Using endoscopy, a recurrent hiatus hernia of any size was identified in 32 (32.0%), and a hernia measuring 2 or more cm in length was identified in 8 (8.0%). The objective outcome data for both tests was combined for a reanalysis, which prioritized the barium meal outcome assessment and supplemented the endoscopy outcome assessment in the patients who had not undergone a barium meal radiology. With this analysis, a recurrent hiatus hernia of any size was identified in 26 (22.2%), and a hernia measuring 2 or more cm in length was identified in 5 (4.3%) patients. When this definition of hernia recurrence was used to compare Mesh repair (both mesh types) versus repair with only sutures, the rate of hernia recurrence was 17/78 (21.8%) versus 9/39 (23.1%; $P = 1.00$, Fisher's exact test), and 2/78 (2.6%) versus 3/39 (7.7%; $P = 0.329$) for hernias measuring 2 cm or more in length.

One- to 12-Month Postoperative Clinical Outcome

The clinical follow-up outcomes at 1, 3, 6, and 12 months are summarized in Tables 2 to 6. Heartburn analog symptom scores were significantly lower in the TiMesh group at 3 and 6 months, with higher scores in the Surgisis group (Table 2). Chest pain and dysphagia scores were similar at all follow-up points (Tables 3 and 5). A range of other symptom scores were significantly worse in the Surgisis group—odynophagia at 1 month, nausea at 3 and 12 months, wheezing at 6 months, and inability to belch at 12 months (Table 4). In addition, the patients in the TiMesh group were less likely to report bloating at 12 months. Scores of overall satisfaction were similar for all 3 groups (Table 6). None of the 5 patients with a postoperative hernia of 2 cm or more in length identified primarily by barium meal (supplemented by endoscopy assessment in those who did not undergo barium meal) underwent revision surgery within the follow-up period. Four of the 5 reported an excellent clinical outcome at 12 months, with satisfaction scores of 8, 9, 9, and 10, and no significant symptoms. One of the 5 patients (Surgisis group) reported bloating and chest pain, and a satisfaction score of 5. At 12 months follow-up, this patient was being considered for possible revision surgery.

DISCUSSION

The reports of good early outcomes for hiatal repair with mesh in randomized trials of mesh versus sutured repair of large hiatus hernias has encouraged the wider use of mesh for repair for very large hiatus hernias, despite concerns about the risk of mesh erosion and added difficulties if subsequent surgical revision is required. At follow-up of up to 12 months, our trial identified no major differences for mesh versus sutured repair of very large hiatus hernias. In particular, no significant differences were seen between the 3 repair types for the primary study outcome of hernia recurrence measured by barium meal radiology and endoscopy. The secondary outcomes that were

TABLE 4. Preoperative and Postoperative Symptoms Assessed Using Yes Versus No Questions

	Preoperative			1 mo			3 mo			6 mo			12 mo		
Symptom	**Sutures**	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**
Heartburn	**66.7%**	**63.4%**	**40.5%***	15.8%	10.3%	15.0%	14.3%	24.3%	5.1%	31.7%	20.0%	12.2%	25.0%	27.5%	14.6%
Chest pain	**45.2%**	**61.0%**	31.0%†	26.3%	25.6%	17.5%	19.0%	21.6%	12.8%	14.6%	22.5%	9.8%	15.0%	15.0%	4.9%
Epigastric pain	50.0%	53.7%	54.8%	21.1%	35.9%	35.0%	21.4%	37.8%	20.5%	31.7%	25.0%	29.3%	25.0%	27.5%	12.2%
Regurgitation	66.7%	51.2%	61.9%	2.6%	12.8%	12.5%	9.5%	21.6%	10.3%	26.8%	17.5%	12.2%	15.0%	25.0%	17.1%
Odynophagia	14.3%	9.8%	4.8%	**0%**	**7.7%**	0%‡	2.4%	5.4%	2.6%	4.9%	5.0%	2.4%	2.5%	2.5%	0%
Early Satiety	54.8%	54.8%	50.0%	52.6%	56.4%	60.0%	57.1%	37.8%	41.0%	46.3%	47.5%	39.0%	45.0%	50.0%	29.3%
Epigastric bloat	64.3%	70.7%	47.6%	39.5%	30.8%	32.5%	35.7%	40.5%	17.9%	39.0%	37.5%	19.5%	**42.5%**	**42.5%**	19.5%‖
Anorexia	33.3%	24.4%	23.8%	31.6%	35.9%	30.0%	21.4%	18.9%	20.5%	12.2%	17.5%	14.6%	12.5%	20.0%	4.9%
Nausea	35.7%	24.4%	50.0%	26.3%	15.4%	15.0%	**4.8%**	**27.0%**	10.3%§	12.2%	22.5%	17.1%	**15.0%**	**27.5%**	4.9%**
Vomiting	21.4%	31.7%	31.0%	2.6%	7.7%	5.0%	2.4%	5.4%	0%	9.8%	12.5%	4.9%	7.5%	15.0%	2.4%
Coughing	38.1%	41.5%	26.2%	8.3%	7.7%	7.5%	11.9%	5.4%	10.3%	14.6%	17.5%	17.1%	12.5%	17.5%	9.8%
Wheezing	28.6%	22.0%	11.9%	2.6%	5.1%	5.0%	7.1%	5.4%	7.7%	**0%**	**15.0%**	7.3%¶	7.5%	17.5%	9.8%
Can relieve bloat	69.0%	47.5%	55.0%	73.7%	66.7%	60.0%	71.4%	54.1%	74.4%	73.2%	67.5%	75.6%	**92.5%**	**72.5%**	97.5%††
Eats normal diet	59.5%	50.0%	65.0%	42.1%	30.8%	25.0%	83.3%	70.3%	82.1%	75.6%	77.5%	87.8%	92.5%	85.0%	95.0%
Diarrhea	NA	NA		28.9%	15.4%	27.5%	16.7%	13.5%	7.7%	19.5%	27.5%	12.2%	25.0%	17.5%	19.5%
Increased flatus	NA	NA		57.9%	64.1%	55.0%	66.7%	62.2%	56.4%	58.5%	62.5%	48.8%	57.5%	47.5%	41.5%

All data indicate percentage of patients interviewed at each time point. No statistically significant differences were demonstrated between the 3 groups ($P \geq 0.05$ at all follow-up intervals) except where indicated. All P's < 0.05 are highlighted in bold.

*$P = 0.031$, †$P = 0.023$, ‡$P = 0.046$, §$P = 0.0119$, ¶$P = 0.0328$, ‖$P = 0.0424$, **$P = 0.0197$, ††$P = 0.0017$.

TABLE 5. Dysphagia Assessment

	Preoperative			1 mo			3 mo			6 mo			12 mo		
	Sutures	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**	**Sutures**	**Surgisis**	**TiMesh**
Dysphagia															
Lumpy solids	42.9%	41.5%	31.0%	18.4%	30.8%	12.5%	23.8%	24.3%	15.4%	19.5%	15.0%	9.8%	15.0%	17.5%	19.5%
Soft solids	14.3%	19.5%	11.9%	5.3%	7.7%	5.0%	7.1%	5.4%	5.1%	0%	5.0%	4.9%	2.5%	5.0%	2.4%
Liquids	11.9%	19.5%	14.3%	7.9%	7.7%	7.5%	7.1%	0%	2.6%	0%	10.0%	0%	2.5%	5.0%	0%
Visual analog scale															
Solids	2.7 (1.6–3.8)	3.2 (2.1–4.4)	2.2 (1.1–3.3)	1.4 (0.5–2.2)	2.3 (1.2–3.5)	1.3 (0.4–2.2)	1.8 (0.9–2.6)	1.6 (0.7–2.5)	1.4 (0.3–2.4)	1.3 (0.15–2.2)	1.2 (0.5–1.9)	1.1 (0.3–1.8)	1.1 (0.4–1.9)	1.5 (0.7–2.2)	1.1 (0.3–1.8)
Liquids	0.9 (0.1–1.6)	1.4 (0.6–2.2)	1.0 (0.2–1.8)	0.3 (−0.2 to 0.8)	0.7 (0.2–1.3)	0.4 (−0.1 to 0.9)	0.3 (−0.1 to 0.7)	0.5 (−0.1 to 1.2)	0.3 (−0.1 to 0.7)	0.2 (−0.04 to 0.5)	0.5 (0.04–0.9)	0.07 (−0.1 to 0.2)	0.3 (−0.1 to 0.7)	0.5 (0.1–0.9)	0.0 (0.0–0.0)
Dysphagia score (0–45)															
Overall score	6.9 (3.9–10.0)	8.8 (5.3–12.4)	8.7 (4.5–13.0)	11.7 (7.8–15.6)	18.7 (14.9–22.5)	17.6 (14.2–20.9)	5.1 (2.7–7.5)	7.2 (3.5–11.0)	4.2 (1.3–7.1)	4.8 (2.3–7.4)	4.9 (1.9–7.8)	4.2 (1.5–6.9)	2.9 (1.0–4.8)	4.8 (1.9–7.8)	2.4 (0.8–4.0)
Scored 0 only	52.4%	47.5%	62.5%	44.7%	20.5%	20.0%	54.8%	56.8%	74.4%	61.0%	67.5%	70.7%	75.0%	62.5%	75.0%

All data indicate percentages or mean (95% confidence intervals).

No statistically significant differences were demonstrated between groups ($P \geq 0.05$ at all follow-up intervals).

TABLE 6. Outcome Scores, Satisfaction Score and Visick Grading

	Preoperative			1 mo			3 mo			6 mo			12 mo		
	Sutures	Surgisis	TiMesh	Sutures	Surgisis	TiMesh	Sutures	Surgisis	TiMesh	Sutures	Surgisis	TiMesh	Sutures	Surgisis	TiMesh
Outcome															
Excellent or Good	N/A	N/A	N/A	86.8%	79.5%	77.5%	95.2%	86.5%	89.7%	85.4%	87.5%	92.7%	90.0%	79.5%	95.0%
Fair or Poor	N/A	N/A	N/A	13.2%	20.5%	22.5%	4.8%	13.5%	10.3%	14.6%	12.5%	7.3%	10.0%	20.5%	5.0%
Modified Visick grade															
1&2	28.6%	15.0%	50.0%*	78.9%	79.5%	77.5%	92.9%	75.7%	87.2%	82.9%	85.0%	90.2%	87.5%	79.5%	95.0%
3, 4 & 5	71.4%	85.0%	50.0%*	21.1%	20.5%	22.5%	7.1%	24.3%	12.8%	17.1%	15.0%	9.8%	12.5%	20.5%	5.0%
Satisfaction score															
Mean score	N/A	N/A	N/A	8.6	8.3	8.5	9.4	8.6	9.2	8.3	8.4	9.5	8.8	8.2	9.4
95% confidence interval	N/A	N/A	N/A	(8.0–9.3)	(7.5–9.1)	(7.7–9.2)	(9.1–9.7)	(7.7–9.5)	(8.6–9.8)	(7.5–9.1)	(7.6–9.2)	(9.1–9.9)	(8.3–9.4)	(7.3–9.2)	(9.0–9.8)
Correct decision to have operation	N/A	N/A	N/A	97.4%	97.3%	97.5%	97.6%	94.6%	100%	92.7%	97.5%	97.6%	97.5%	90.0%	97.5%

All data given as percentages or mean (95% confidence intervals). No statistically significant differences were demonstrated between groups ($P \geq 0.05$ at all follow-up intervals), except $^{*}P = 0.0030$.
N/A indicates not applicable.

measured by the clinical questionnaire also revealed no major differences in overall outcome, although there were some statistically significant differences between heartburn scores, and the incidences of nausea and bloating, with the outcomes pointing toward a somewhat poorer clinical outcome after repair with Surgisis, and a better outcome for TiMesh due to less bloating issues. However, most clinical outcomes were similar for all 3 repair types, and the differences were probably insufficient to support any claim that one particular technique was better then the others.

The outcomes from our study differ from those reported in the 3 other published randomized trials of mesh versus sutured repair, which all reported a reduced incidence of hiatus hernia after mesh repair. In the study reported by Frantzides et al,[6] the incidence of hernia recurrence at median 2.5 years follow-up was reduced from 22% to 0%. Oelschlager et al[7] reported a reduction from 24% to 9% at 6 months follow-up, and Granderath et al[9] reported a reduction from 26% to 8% at 12 months. In Frantzides et al's trial, patients underwent repair using a piece of polytetrafluoroethylene mesh that encircled the esophagus. The 0% recurrence rate after mesh repair in this study was not replicated in the other trials, perhaps reflecting the encirclement of the esophagus by the mesh prosthesis. However, many surgeons remain reluctant to place mesh fully around the esophagus because of the perceived risks of mesh erosion and hiatal fibrosis at longer term follow-up.[5] Unfortunately, because late follow-up from this study has not been reported, Frantzides et al's results have not addressed this issue.

Oelschlager et al[7] used Surgisis to reinforce the hiatus posteriorly and around the sides of the esophagus. In their trial, the early results at 6 months follow-up appeared promising.[7] However, a subsequent report of 5 years follow-up revealed very high recurrence rates of 59% versus 54% in the 2 groups and provided little support for repair with absorbable mesh.[8] In this trial, Oelschlager et al defined a hiatus hernia to be present if it exceeded 2 cm in vertical length. This was different to our study, in which as we included all hernias, irrespective of their size. When a similar definition of hernia size 2 cm or more was applied in our trial, the "hernia" recurrence rate was substantially lower (Table 9), and only 5 patients were identified by barium meal radiology (supplemented by endoscopy) to have a hernia larger than 2 cm.

Granderath et al's randomized trial included patients undergoing laparoscopic Nissen fundoplication for gastroesophageal reflux with or without a hiatus hernia and enrolled a different set of patients to those included in the other 2 trials and our current trial.[9] Hence, it did not directly address the issue of how best to repair a large hiatus hernia. Their technique did, however, entail a posterior hiatal repair with sutures, which was reinforced by an on-lay of a 3 cm × 1 cm piece of polypropylene mesh, a similar approach to that used in our trial, although we used a larger piece of mesh. Their main outcome measure was the incidence of fundoplication migration into the mediastinum, and in their control group this occurred in 26% of patients. In a report from an earlier randomized trial conducted in our Departments, we identified a much lower 6% incidence of fundoplication migration using barium meal radiology 6 months after surgery in patients who underwent a sutured hiatal repair with no mesh.[11]

Three patients in the suture repair group in the current trial underwent early laparoscopic reoperation for an acute hiatus hernia, and one required revision for a hiatus hernia at 7 months, compared to 1 early recurrence in the nonabsorbable mesh group and none in the absorbable mesh group. This was offset, however, by a higher number of patients in the absorbable mesh groups found to have a hiatus hernia at 6 months, and a more revision procedures for a tight hiatal repair in the nonabsorbable mesh group. When all of these outcomes are considered together, the risk of adverse outcomes seemed to be

TABLE 7. Perioperative Outcomes

	Randomization			
	Suture Repair	**Surgisis**	**TiMesh**	***P***
Operating time (min)	111.8 (91.0–132.7)	110.3 (96.7–123.9)	111.8 (102.2–132.1)	0.831
No. sutures used for hiatal repair	4.93 (4.37–5.49)	4.75 (4.41–5.36)	4.71 (4.06–5.36)	0.817
Fundoplication type	1—Nissen 5—Posterior partial 37—Anterior partial	0—Nissen 4—Posterior partial 37—Anterior partial	1—Nissen 8—Posterior partial 33—Anterior partial	

Data are expressed as mean (95% confidence intervals).

TABLE 8. Complications and Reoperations

	Randomization		
	Suture Repair	**Surgisis**	**TiMesh**
Intraoperative complications	2—Pneumothorax 1—Bleed from short gastric	1—Pneumothorax 1—Esophageal perforation	1—Minor splenic injury
Major complications and revision operations (30 d)	1—Tight hiatal repair (early reoperation) 3—Acute hiatus hernia (laparoscopic reoperation) 1—Death-day 7	1—Esophageal perforation (stent on day 10)	2—Tight hiatal repair (early reoperation) 1—Acute hiatus hernia and gastric perforation (open reoperation)
Revision operations after 30 d	1—Recurrent hiatus hernia (reoperation at 7 mo)	Nil	1—Dysphagia (reoperation at 8 mo)

TABLE 9. Radiology and Endoscopy Outcomes at 6 Months Follow-up

	Sutures	**Surgisis**	**TiMesh**	***P***
Barium meal radiology				
Studied	31 (72.1%)	34 (82.9%)	35 (83.3%)	
Hiatus hernia—any size	7 (22.6%)	11 (32.4%)	4 (11.4%)	0.110
Hiatus hernia—2 cm+	1 (3.2%)	2 (5.9%)	0 (0.0%)	0.357
Endoscopy				
Studied	31 (72.1%)	34 (82.9%)	35 (83.3%)	
Hiatus hernia—any size	11 (35.5%)	13 (37.1%)	8 (22.9%)	0.346
Hiatus hernia—2 cm+	2 (6.5%)	3 (8.8%)	2 (5.6%)	0.858
Barium meal radiology and endoscopy				
Underwent barium meal radiology or Endoscopy	39 (90.7%)	39 (95.1%)	39 (92.9%)	
Hiatus hernia—any size (barium meal radiology outcome prioritized)	9 (23.1%)	12 (30.8%)	5 (12.8%)	0.161
Hiatus hernia—2 cm+ (barium meal radiology outcome prioritized)	3 (7.9%)	2 (5.9%)	0 (0.0%)	0.223

All data are expressed as n (%) unless otherwise indicated.

similar for all repair types. Furthermore, we have always applied a low threshold for early laparoscopic reexploration of the operative site within the first few days, and our experience has confirmed that correction of potential problems identified by contrast radiology in the first few days, has a minimal impact on recovery, and minimizes the risk of later more difficult revision surgery.[14]

There are several factors that might impact on recurrence rate after laparoscopic repair of a very large hiatus hernia, including surgeon experience and technique. Our trial was commenced in 2006, and the surgeons contributing patients all had substantial prior experience with the techniques used in the trial. In addition, care was taken to preserve the fascial coverings over the edges of the hiatus as these provide support for hiatal repair sutures.[2] If not protected, the hiatal muscle can be exposed and the hiatal defect can be enlarged by the process of hiatal dissection until it cannot be closed without mesh. In our trial, the hiatus was closed adequately by sutures in all patients.

Strengths of our trial include a very high rate of clinical and objective follow-up, blinding of the patients and the follow-up process, and few exclusions. The trial was run across multiple sites in the public and private sectors in Australia and the results should be generalizable, at least in the Australian context where repair of very large hiatus hernias is usually undertaken by experienced upper gastrointestinal surgeons. Limiting the generalizability of the results, however, is the testing of only 1 mesh configuration. However, the configuration was similar to that used in 2 of the 3 previous randomized trials. When establishing the protocol for the trial, there was no enthusiasm in Australia for encircling the esophagus with mesh as some surgeons had encountered problems with mesh erosion and hiatal fibrosis in patients in whom the technique described by Frantzides et al[6] had been used. For this reason, posteriorly placed mesh reinforcement of a sutured hiatal repair was the most acceptable approach for the participating surgeons. However, care should be taken before trying to extrapolate the results of our trial to mesh repair using different mesh shapes and different mesh placement techniques.

The follow-up in our trial is currently limited to 12 months, and the outcomes from Oelschlager et al's trial do suggest that results can

change with more extended follow-up,[8] so longer term follow-up to confirm our initial findings is also needed. This is underway. Further barium meal radiology and endoscopy examinations are scheduled for 3 to 4 years after surgery, and the outcomes will be reported when they become available. Another potential weakness is that a large number of clinical outcomes were evaluated, and there is a risk of false-positive *P* values with multiple data analyses. However, the trend data and positive *P* values consistently pointed to a somewhat poorer clinical outcome in the group of patients who underwent repair with Surgisis, although the magnitude of these differences are unlikely to be clinically significant. With a larger trial, however, the trend toward a higher hernia recurrence rate after Surgisis repair might have become statistically significant.

The outcomes of our trial have shown no significant differences for the assessed primary outcome—recurrent hiatus hernia at radiology or endoscopy, and in general, the clinical outcome differences between the 3 techniques were small and unlikely to be clinically significant. The rate of recurrent hiatus hernia measuring 2 cm or greater in size was low across all groups. The results of this randomized trial do not add support for the routine use of mesh repair of very large hiatus hernias.

ACKNOWLEDGMENTS

The authors thank Tanya Irvine, Nicky Carney, and Lorraine Sheehan-Hennessy, who contributed to data collection.

REFERENCES

1. Engström C, Cai W, Irvine T, et al. Twenty years of experience with laparoscopic antireflux surgery. *Br J Surg.* 2012;99:1415–1421.
2. Watson DI, Davies N, Devitt PG, et al. Importance of dissection of the hernial sac in laparoscopic surgery for very large hiatus hernias. *Arch Surg.* 1999;134:1069–1073.
3. Edye M, Salky B, Posner A, et al. Sac excision is essential to adequate laparoscopic repair of paraesophageal hernia. *Surg Endosc*. 1998;12:1259–1263.
4. Aly A, Munt J, Jamieson GG, et al. Laparoscopic repair of large hiatal hernia. *Br J Surg.* 2005;92:648–653.
5. Frantzides CT, Carlson MA, Loizides S, et al. Hiatal hernia repair with mesh: a survey of SAGES members. *Surg Endosc*. 2010;24:1017–1024.
6. Frantzides CT, Madan AK, Carlson MA, Stavropoulos GP. A prospective, randomized trial of laparoscopic polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. *Arch Surg.* 2002;137:649–652.
7. Oelschlager BK, Pellegrini CA, Hunter J, et al. Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. *Ann Surg.* 2006;244:481–490.
8. Oelschlager BK, Pellegrini CA, Hunter JG, et al. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. *J Am Coll Surg*. 2011;213:461–468.
9. Granderath FA, Schweiger UM, Kamolz T, et al. Laparoscopic Nissen fundoplication with prosthetic hiatal closure reduce postoperative intrathoracic wrap herniation. *Arch Surg.* 2005;140:40–48.
10. Gatenby PAC, Bright T, Watson DI. Anterior 180 degree partial fundoplication: how I do it. *J Gastrointest Surg.* 2012;16:2297–2303.
11. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg.* 1997;226:642–652.
12. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol.* 1992;14:99–100.
13. Hashemi M, Peters JH, DeMeester TR, et al. Laparoscopic repair of large type III hiatal hernia: objective followup reveals high recurrence rate. *J Am Coll Surg*. 2000;190:553–560.
14. Tsunoda S, Jamieson GG, Devitt PG, et al. Early reoperation after laparoscopic fundoplication: the importance of routine postoperative contrast studies. *World J Surg.* 2010:34;79–84.

World J Surg (2015) 39:1465–1473
DOI 10.1007/s00268-015-2970-3

ORIGINAL SCIENTIFIC REPORT

Quality of Life Following Repair of Large Hiatal Hernia is Improved but not Influenced by Use of Mesh: Results From a Randomized Controlled Trial

Jan H. Koetje · Tanya Irvine · Sarah K. Thompson · Peter G. Devitt · Simon D. Woods · Ahmad Aly · Glyn G. Jamieson · David I. Watson

Published online: 5 February 2015

Abstract

Introduction Laparoscopic surgery is the treatment of choice for repair of large hiatus hernia, but can be followed by recurrence. Repair with prosthetic mesh has been recommended to prevent recurrence, although complications following mesh repair have generated disagreement about whether or not mesh should be used. The early objective and clinical results of a randomized trial of repair with mesh versus sutures have been reported, and revealed few differences. In the current study, we evaluated quality of life outcomes within this trial at follow-up to 2 years.

Methods In a multicenter prospective double-blind randomized trial three methods for repair of large hiatus hernia were compared: sutures versus repair with absorbable mesh (Surgisis) versus non-absorbable (Timesh). Quality of life assessment using the Short-Form 36 (SF-36) questionnaire was undertaken at 3, 6, 12 and 24 months after surgery. SF-36 outcomes (8 individual scales and 2 composite scales) were determined for each group, and compared between groups, and across different follow-up points.

Results 126 patients were enrolled—43 sutures, 41 absorbable mesh and 42 non-absorbable mesh. 115 (91.3 %) completed a preoperative questionnaire, and 113 (89.7 %) completed the post-operative questionnaire at 3 months, 116 (92.1 %) at 6 months, 114 (90.5 %) at 12 months, and 91 (72.2 %) at 24 months. The SF-36 Physical and Mental Component Scores (PCS and MCS) improved significantly following surgery, and this improvement was sustained across 24 months follow-up ($p < 0.001$ for PCS and MCS at each follow-up point). There were no significant differences between the groups for the component scores or the eight SF-36 subscale scores at each follow-up time. 29 individuals had a recurrence at 6 months follow-up, of which 9 were symptomatic. The PCS were higher in patients with recurrence versus without ($p < 0.01$), and in patients with a symptomatic recurrence versus asymptomatic recurrence versus no recurrence ($p = 0.001$).

Conclusion SF-36 measured quality of life improved significantly after repair of large hiatal hernia at up to 2 years follow-up, and there were no differences in outcome for the different repair techniques. The use of mesh versus no mesh in repair of large hiatal hernia did not influence quality of life.

J. H. Koetje · T. Irvine · D. I. Watson (✉)
Flinders University Department of Surgery, Room 3D211, Flinders Medical Centre, Bedford Park, SA 5042, Australia
e-mail: david.watson@flinders.edu.au

S. K. Thompson · P. G. Devitt · G. G. Jamieson
University of Adelaide Discipline of Surgery, Royal Adelaide Hospital, Adelaide, SA, Australia

S. D. Woods
Cabrini Hospital, Malvern, VIC, Australia

A. Aly
Department of Surgery, Austin Hospital, University of Melbourne, Heidelberg, VIC, Australia

Introduction

Laparoscopic approaches are standard for the surgical treatment of gastro-esophageal reflux disease and hiatus hernia, and achieve good clinical outcomes in most patients [1, 2]. A subgroup undergoing surgery present with a very large hiatus hernia, and when more than 50 % of the stomach herniates the stomach can rotate and lead to mechanical symptoms including chest pain, early satiety, dysphagia, vomiting, and gastric volvulus.

A standard approach to laparoscopic repair of very large hiatus hernias entails complete dissection of the hernia sac from the mediastinum, hiatal repair with posteriorly placed sutures, followed by construction of a fundoplication [3]. Initial clinical outcomes following this approach are good, but objective follow-up using barium meal X-ray has demonstrated radiological recurrence rates of 25–45 % at late follow-up, although less than 5 % of patients actually develop symptoms from a recurrent hernia [4–6]. However, there are concerns that radiological hernia recurrences could become symptomatic or progress to complications at later follow-up [4–6], and for this reason "tension-free" repair techniques using prosthetic mesh have been proposed [7]. Whilst uncontrolled studies suggest mesh reinforcement might be followed by lower recurrence rates [7–9], the use of mesh can also be followed by significant complications such as erosion of mesh into the esophageal or gastric lumen, and surgery to deal with this can lead to esophagectomy [10, 11]. Absorbable biomeshes are advocated by some surgeons for hiatal hernia repair to avoid mesh erosion [12].

To date, only a few randomized controlled trials have compared mesh versus sutures for repair of large hiatal hernias. Frantzides et al. and Oeschlager et al. both reported reductions in hernia recurrence at short-term follow-up [12, 13], although at later follow-up Oeschlager et al. identified no differences [14]. We recently reported the outcomes for a trial which randomized 126 patients to repair with sutures versus absorbable versus non-absorbable mesh, and showed no differences in hernia recurrence rates at 12 months follow-up for patients undergoing sutured versus mesh repair [15]. All previous papers reporting outcomes from randomized trials have focused on objective investigations and hernia recurrence rates.

There can, however, be differences between objectively assessed surgical outcomes and patient reported outcomes. It is also known that quality of life is impaired in patients suffering gastro-esophageal reflux [16–18], and improves following laparoscopic antireflux surgery [19, 20]. In our randomized trial of large hiatus hernia repair with sutures versus absorbable mesh versus non-absorbable mesh, we also measured quality of life using the Short-Form 36 (SF-36) questionnaire, a widely used and well-validated questionnaire which evaluates general well-being and functional status [21, 22]. In this paper, we evaluated the impact of three different methods of repair of large hiatal hernia on changes in SF-36 measured quality of life within the setting of a randomized controlled trial.

Methods

In a prospective double-blind randomized controlled trial, we compared three laparoscopic methods of repair of very large hiatus hernias: repair using sutures versus Biomesh versus non-absorbable mesh. The full details of the trial protocol and the objective and clinical symptom outcomes to 12 months follow-up have been reported elsewhere [15]. In the current study, we determined the impact of the three different methods on SF-36 measured quality of life at follow-up of up to 2 years.

Summary of trial protocol

The trial was undertaken in four centres in Adelaide and Melbourne, Australia, with surgery performed or supervised by one of nine surgeons. Individuals undergoing elective laparoscopic repair of a very large hiatus hernia were enrolled, with a very large hiatus hernia defined as containing at least 50 % of the stomach. Patients were randomized 1:1:1 to repair using sutures versus repair using sutures reinforced by absorbable mesh (4 ply Surgisis® ES, Cook Biotech, Indiana, USA) versus repair using sutures reinforced by non-absorbable mesh (Timesh®, PFM Medical, Köln, Germany). Patients were blinded to the operation variant and clinical follow-up was undertaken by a research nurse who was also blinded to the procedure type.

Surgical techniques were standardised, and included full dissection of the hernia sac from the mediastinum, and complete reduction of the sac's contents into the abdomen [1, 3]. Esophageal lengthening procedures were not added. The hiatal defect was narrowed using posterior hiatal sutures, supplemented by anterior hiatal sutures if needed. When randomized to mesh repair, a rectangular piece of mesh (Surgisis or Timesh) measuring 2–3 cm high × 4–5 cm wide was placed over the posterior hiatal repair sutures and the hiatal pillars (but not encircling the esophagus), and anchored in place using either sutures or a mechanical "tacker". A fundoplication was then added. If any procedure varied from the trial allocation, the patient remained in the allocated group for intention to treat analysis.

Follow-up and quality of life assessment

Follow-up using Barium meal X-ray, upper gastrointestinal endoscopy and clinical symptom scores has been reported elsewhere [15]. Symptom scores were obtained with a

Table 1 Parameters measured by SF36

Concept	Summary
Physical functioning	Extent to which health limits physical activities
Role functioning—physical	Extent to which physical healthy interferes with work or other daily activities
Bodily pain	Intensity of pain and effect of pain on normal work
General health	Personal evaluation of health
Vitality	Feeling energetic
Social functioning	Extent to which physical health or emotions interfere with social activities
Role functioning—emotional	Extent to which emotional problems interfere with work or daily activities
Mental health	General mental health
Reported health transition	Evaluation of current health compared to 1 year ago

Visual Analogue Scale (VAS) of 0–10, by a 'blinded' research nurse using a structured questionnaire 3, 6, 12 and 24 months after surgery. In addition, patients completed SF-36 Quality of Life (QoL) questionnaires before surgery and at the same follow-up time points.

The SF-36 questionnaire is a widely used and well-validated questionnaire (23,24), consisting of 36 items. The questionnaire is summarised in Table 1. Thirty five questions contribute to eight subscales, and the other question stands alone and assesses "Reported Health Transition" (RHT). The scores of the eight subscales and the RHT question are each converted into a 0–100 score. A higher score indicates a better QoL on that subscale. The subscales can also be converted into two summarising component scales: a "Physical Component Scale" (PCS) and a "Mental Component Scale" (MCS). The PCS and the MCS have been validated by Ware et al. [22]. The component scales provide summary overviews of the SF-36 outcomes.

For calculation of the PCS and MCS, the 8 subscales are standardised using a z score transformation: population means are subtracted from the subscale scores, and this difference is divided by the standard deviations of the norm population. The computed z scores are then aggregated into the physical and mental component scales. Each SF-36 subscale z score is multiplied by its respective physical factor score coefficient and the eight products are summed. Similarly, this is done for the mental component scale by using the mental factor score coefficients. The last step is transforming each component score to norm-based scoring. This is accomplished by multiplying each aggregate component scale score by 10 and adding the resulting product to 50. To provide a comparable study population for our study, population norm scores were derived from the Australian population aged 65–74 years, with equal numbers of males and females collected by the Australian Bureau of Statistics in 1995.

For data analysis, pre- and post-operative PCS and MCS scores as well as the individual sub-scales were compared for the overall population to assess changes in quality of life before versus after hiatal hernia repair, and also for the three trial groups separately to determine differences in quality of life between the different repair techniques at each follow-up point.

Recurrence of hiatal hernia

As part of the trial protocol, patients underwent objective assessment using upper gastrointestinal endoscopy and barium meal radiology 6 months after surgery. The presence or absence of a recurrent hiatus hernia was determined, and patients with a recurrence were classified as symptomatic or asymptomatic based on symptom scores. Barium meal radiology was reported by radiologists blinded to the hiatal repair technique, and endoscopy was undertaken in a blinded fashion by upper gastrointestinal surgeons experienced in assessing anatomy after fundoplication. A recurrent hiatus hernia was defined as any evidence of the stomach sitting above the level of the diaphragm, irrespective of size. A symptomatic recurrent hiatus hernia was defined as (1) objective evidence of a recurrent hernia, and (2) heartburn symptoms scored as 3 or greater using a 0–10 analogue scale (details published elsewhere [15]). PCS and MCS scores determined 6 months after surgery in patients with a recurrence were compared to scores in patients without recurrence. PCS and MCS scores in patients with a symptomatic recurrence were compared to scores in patients with asymptomatic recurrence, and also to those without recurrence.

Statistics and ethics

All analyses were performed on an intention-to-treat basis, with all patients remaining in their initial allocated trial group for data analysis. Parametrically distributed data were analysed using Paired Samples t tests, One-way ANOVA tests and Student t tests. Non-parametric data

were analysed using Kruskal–Wallis tests and Mann–Whitney *U* tests. Statistical analyses were performed using IBM's Statistical Package for Social Sciences (SPSS), version 19 for Apple Macintosh OS (IBM corp., Armonk, New York, USA). A p value of less than 0.05 was considered to be statistically significant.

The protocol for this study was approved by the Human Research Ethics Committee at each participating hospital. The study was conducted in accordance with the World Medical Association declaration of Helsinki (revised 1989), and the National Health and Medical Research Council of Australia's guidelines on human experimentation.

Results

From July 2006 to September 2012, 126 patients were enrolled in the randomized trial. Forty three were randomized to undergo hiatal repair with sutures ('Sutures only' cohort), 41 to repair with Surgisis ('Biomesh' cohort), and 42 to repair with Timesh ('Timesh' cohort). As reported elsewhere [15] baseline characteristics were comparable for the three study groups.

115 (91.3 %) completed a preoperative SF-36 questionnaire, 113 (89.7 %) a questionnaire at 3 months, 116 (92.1 %) at 6 months, 114 (90.5 %) at 12 months, and 91 (72.2 %) at 24 months. Data analysis was undertaken using a paired analysis comparing baseline preoperative scores versus postoperative scores. Hence, data was only analysed for patients who completed both the preoperative questionnaire and at least one of the postoperative questionnaires. This yielded 105 (83.3 %) patients who completed preoperative and 3 months postoperative questionnaires, 106 (84.1 %) preoperative and 6 months postoperative questionnaires, 104 (82.5 %) preoperative and 12 months postoperative questionnaires, and 83 (65.9 %) who completed both the preoperative and the 24 months postoperative SF-36 questionnaire. Completion rates were comparable for the three groups. Missing data were due to inability to contact patients at specific time points or because patients chose not to complete and return the questionnaire.

Physical and Mental Component Score outcomes

Figures 1 and 2 summarise the outcomes for the PCS and MCS scores. For the entire trial cohort the post-operative PCS and MCS scores were significantly higher than the pre-operative scores at all follow-up points (Paired t tests; $p < 0.001$ for PCS and MCS at each follow-up point). When the trial groups were compared separately, the PCS scores for all three groups improved significantly at 3, 6, 12 and 24 months postoperatively compared to the pre-operative scores ($p < 0.001$–0.044). The follow-up MCS scores were not significantly different ($p > 0.05$) to the pre-operative scores at all time points in the 'Sutures only' group. In the 'Biomesh' group, the MCS score was significantly higher at 12 months ($p = 0.012$, posthoc alpha $= 0.013$) but not at other time points, whereas in the

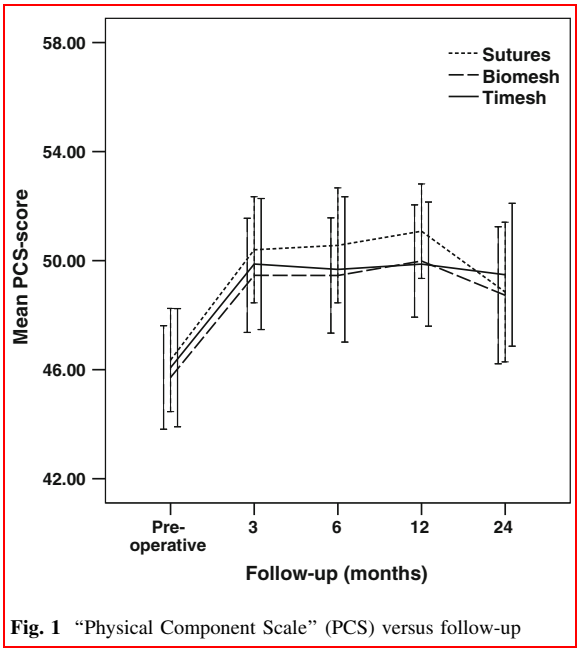


Fig. 1 "Physical Component Scale" (PCS) versus follow-up

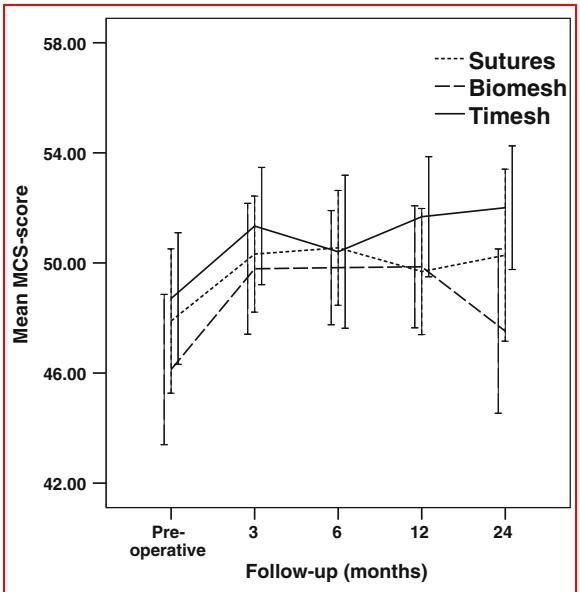


Fig. 2 "Mental Component Scale" (MCS) versus follow-up

'Timesh' group the MCS scores were significantly higher at 12 and 24 months, but not at 3 and 6 months ($p = 0.028$, $p = 0.168$, $p < 0.001$, $p < 0.001$ respectively).

When the 3 trial groups were compared at each time point, there were no significant differences between the three groups for either the PCS or the MCS scores [One-Way ANOVA comparing the three cohorts pre-operative versus postoperative scores (3, 6, 12 and 24 months)].

SF-36 subscale outcomes

The SF-36 subscale outcomes are summarised in Figs. 3, 4, 5, 6, 7, 8, 9, 10 and 11. There were no significant differences between the three groups with respect to the pre-operative scores for each of the eight subscales of the SF-36, with the exception of the 'sutures only' versus the 'Biomesh' group for the "Reported Health Transition" scale ($p = 0.003$, Mann–Whitney U, post hoc correction alpha $= 0.017$). All eight subscales of the SF-36 improved significantly at 3, 6, and 12 months following surgery, compared to the respective pre-operative scores. Seven subscales also improved significantly at 24 months, but not the "Role Functioning-Emotional" scale. There were no significant differences between the three trial groups for scores at any postoperative follow-up time point.

Recurrence

Twenty nine patients were found to have a recurrent hiatus hernia (any size) 6 months after surgery. Nine (31 %) of

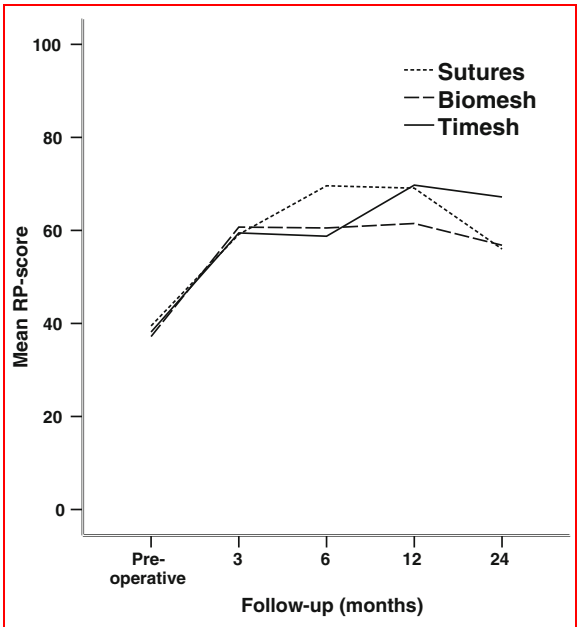


Fig. 4 SF-36 "role functioning—physical" (RP) scores

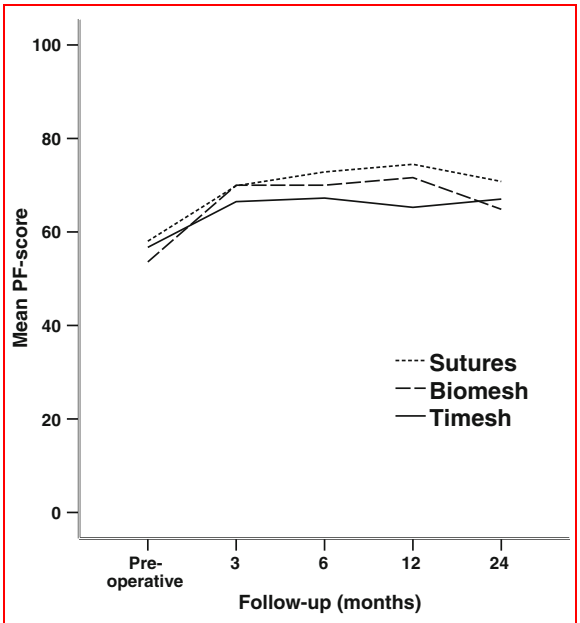


Fig. 3 SF-36 "physical functioning" (PF) scores

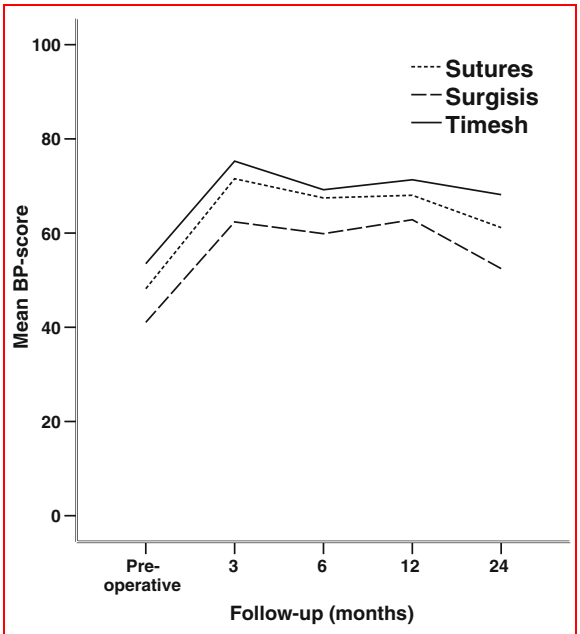


Fig. 5 SF-36 "bodily pain" (BP) scores

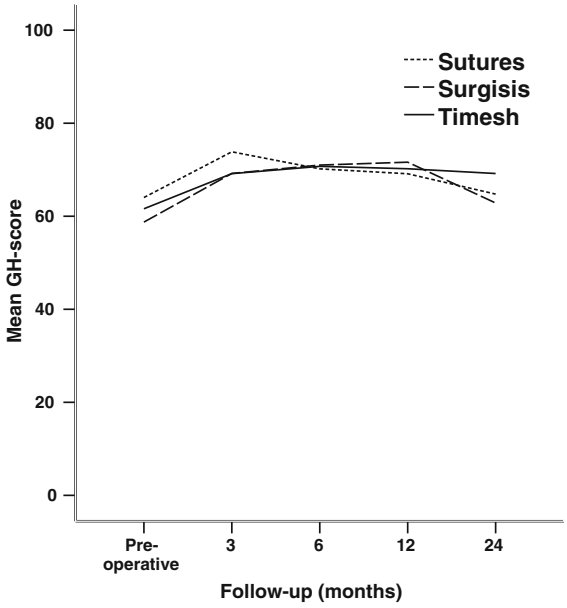


Fig. 6 SF-36 "general health" (GH) scores

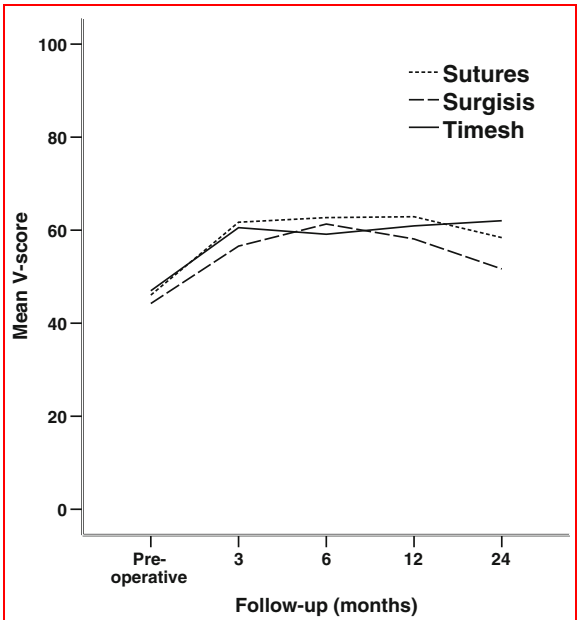


Fig. 7 SF-36 "vitality" (V) scores

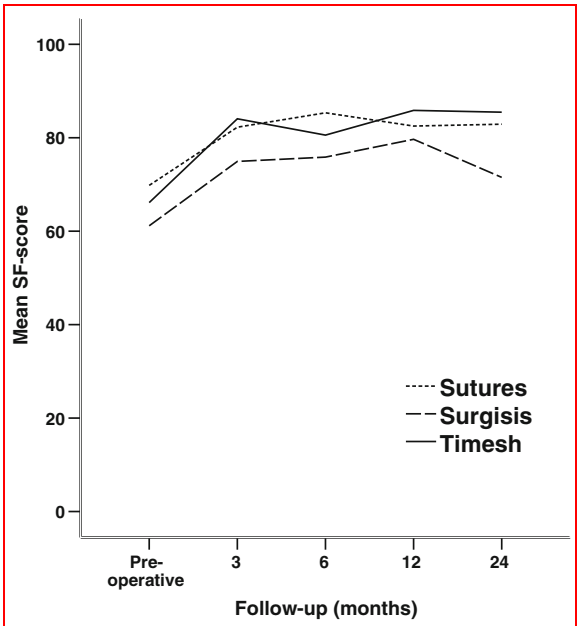


Fig. 8 SF-36 "social functioning" (SF) scores

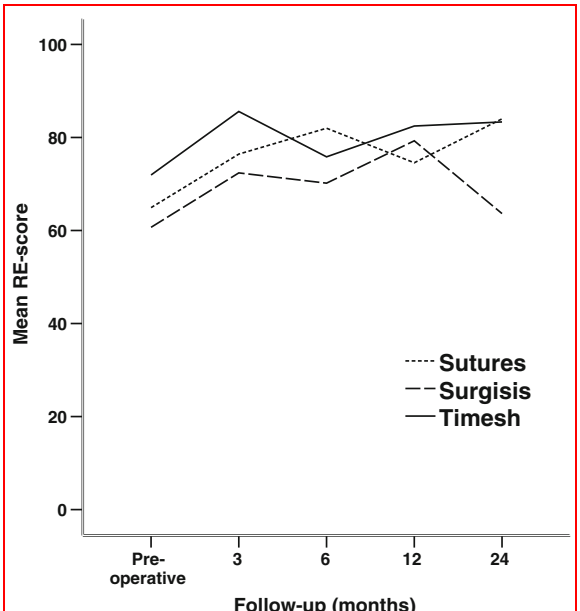


Fig. 9 SF-36 "role functioning—emotional" (RE) scores

these were symptomatic. Patients with a recurrent hernia had significantly lower PCS scores, compared to patients without recurrence (46.9 vs. 51.2; $p < 0.01$). For the MCS scores, however, there was no significant difference for recurrence versus no-recurrence (48.8 vs. 50.7; $p = 0.213$). For the 3-way comparison of symptomatic versus asymptomatic recurrence versus no recurrence, patients with

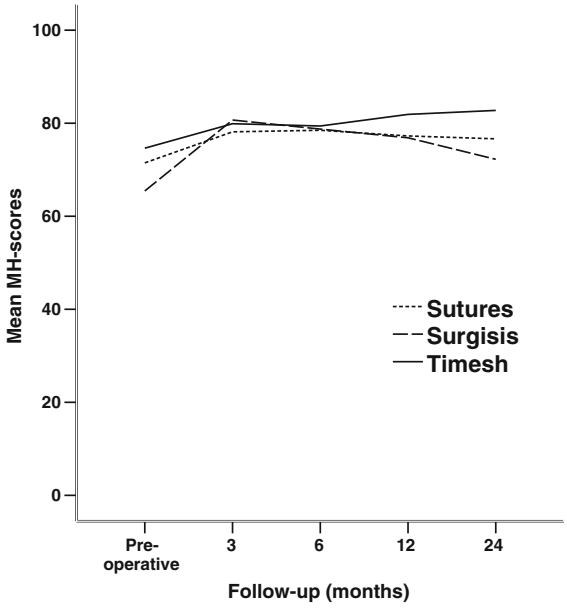


Fig. 10 SF-36 "mental health" (MH) scores

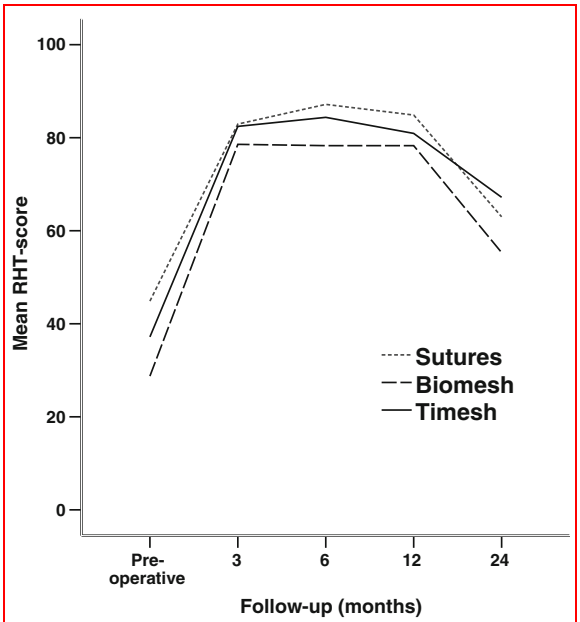


Fig. 11 SF-36 "reported health transition" (RHT) scores

symptomatic recurrences had significantly lower PCS scores ($p = 0.001$), whereas for the MCS scores there was no difference ($p = 0.453$).

Discussion

Laparoscopic approaches are now the standard surgical approach to repair of very large hiatus hernias. However, the choice of laparoscopic repair techniques can vary between different groups, and consensus is yet to be reached about the role of mesh versus sutured repair, synthetic versus biological meshes, and mesh configurations—encircling versus placed posteriorly. In our randomized trial we compared 3 different approaches to repair, including sutures versus synthetic versus biological mesh. We recently reported no significant differences for hernia recurrence or clinical outcomes for the 3 repair methods in the trial [15], and these results were similar to the late follow-up outcomes reported previously by Oelschlager et al. [14]. In both our trial and Oelschlager's trial the mesh configuration reinforced the hiatal repair posteriorly, a different technique to that used by Frantzides et al. who fully encircled the esophagus with mesh [13]. Our decision to use a posterior mesh reinforcement technique was based on encouraging early trial outcomes from both Oelschlager et al. [14] and Granderath et al. [23], as well as concern that encircling the esophagus with mesh might increase the risk of mesh erosion [11].

Previous reports from randomized trials [14, 23], and other studies [4, 6, 10] have all focussed on clinical and objective outcome parameters. However, quality of life is an alternative patient reported outcome, which reflects the general well-being and the functional status of patients. It also provides complementary information which informs surgical outcomes, and provides a perspective that might be more relevant to the individual patient [24]. In our randomized trial we used the Short-Form 36 (SF-36) questionnaire to assess general quality of life across various follow-up points. The SF-36 questionnaire is a general quality of life, rather than a disease specific quality of life questionnaire, and it has been widely validated in a range of different countries and language groups [25, 26]. It has been used elsewhere to evaluate quality of life following laparoscopic surgery, including laparoscopic anti-reflux surgery [20, 22].

Our current study revealed a general improvement in quality of life following laparoscopic repair of large hiatus hernias, and this manifested at all follow-up time points from 3 months to 2 years. Apart from the "Role Functioning-Emotional" subscale at 24 months follow-up, there was a significant improvement in all subscales of the SF-36 questionnaire, the two composite scales and the Reported Health Transition at 3, 6, 12, and 24 months postoperatively, when compared to the pre-operative scores. This confirms the effectiveness of laparoscopic repair of large hiatal hernias, and supports other studies that have shown

good clinical and objective outcomes following this surgery [14, 15].

When comparing quality of life improvements across the different trial cohorts, however, no significant differences were seen between the three groups at each follow-up point, although following surgery, the SF-36 scores did improve in a similar fashion in each group. This suggested that each surgical technique (Sutures vs. Surgisis vs. Ti-mesh) yielded a similar improvement in quality of life, and these results are consistent with the lack of significant clinical and objective outcome differences that we have reported elsewhere [15].

Recurrence of hiatus hernia was the primary outcome of this trial, and this outcome has been reported in detail elsewhere [15]. Analysis of this outcome versus quality of life revealed significantly lower quality of life scores in patients with a recurrence compared to those without. However, this was seen solely for the physical component score, not for the mental component score. In the same manner, patients with a symptomatic recurrence had a poorer quality of life outcome compared to those with an asymptomatic recurrence, again only for the physical component score.

After considering the lack of differences seen for quality of life, clinical outcomes and objective outcomes for mesh versus sutured repair of very large hiatus hernia in our randomized trial, and the lack of significant differences for mesh versus sutured repair in the 5 year outcomes reported by Oelschlager [14], we now find it difficult to use mesh for the repair of very large hiatus hernias. It could be argued that the alternative technique of completely encircling the esophagus with mesh might yield a different outcome. However, the data supporting this approach is only from the trial reported by Frantzides et al. in 2002 which enrolled 72 patients and then followed them for a median 2.5 years [13]. Good results at late follow-up, or other trials have not been reported, and are needed to confirm the safety of encircling the esophagus with polytetrafluoroethylene mesh. Others have reported significant problems with mesh erosion which we would prefer to avoid [11].

Overall quality of life was significantly better at up to 2 years follow-up after laparoscopic repair of very large hiatal hernias, with or without posteriorly placed mesh. Whilst the use of mesh did not improve the quality of life, the overall data from this trial has revealed a sustained improvement in quality of life following laparoscopic repair of very large hiatus hernia, and this supports the liberal use of surgical repair of large hiatus hernia in this cohort of patients. However, recurrence of hiatus hernia did impact on physically related aspects of quality of life. Longer follow-up will be required to confirm the durability of these outcomes.

Acknowledgments This randomized trial was supported by Research Project Grants from the National Health and Medical Research Council (NHMRC) of Australia—Grant numbers 375111 and 1022722. We are grateful for the assistance of Ms Lorelle Smith, Ms Nicky Carney and Ms Lorraine Sheehan-Hennessy who contributed to data collection, and Drs Susan Gan and Philip Game who helped with enrolment of patients into the randomized trial. This trial is registered with the Australia and New Zealand Clinical Trials Registry ACTRN12605000725662.

References

1. Watson DI, Davies N, Devitt PG, Jamieson GG (1999) Importance of dissection of the hernial sac in laparoscopic surgery for large hiatal hernias. Arch Surg 134:1069–1073
2. Andujar JJ, Papasavas PK, Birdas T et al (2004) Laparoscopic repair of large paraesophageal hernia is associated with a low incidence of recurrence and reoperation. Surg Endosc 18:444–447
3. Wijnhoven BP, Watson DI (2008) Laparoscopic repair of a giant hiatus hernia—how I do it. J Gastrointest Surg 12:1459–1464
4. Hashemi M, Peters JH, DeMeester TR, Huprich JE, Quek M, Hagen JA et al (2000) Laparoscopic repair of large type III hiatal hernia: objective followup reveals high recurrence rate. J Am Coll Surg 190:553–560
5. Smith GS, Isaacson JR, Draganic BD, Baladas HG, Falk GL (2004) Symptomatic and radiological follow-up after paraesophageal hernia repair. Dis Esophagus 17:279–284
6. Aly A, Munt J, Jamieson GG, Ludemann R, Devitt PG, Watson DI (2005) Laparoscopic repair of large hiatal hernias. Br J Surg 92:648–653
7. Carlson MA, Richards CG, Frantzides CT (1999) Laparoscopic prosthetic reinforcement of hiatal herniorrhaphy. Dig Surg 16:407–410
8. Granderath FA, Carlson MA, Champion JK, Szold A, Basso N, Pointner R et al (2006) Prosthetic closure of the esophageal hiatus in large hiatal hernia repair and laparoscopic antireflux surgery. Surg Endosc 20:367–379
9. Furnee E, Hazebroek E (2013) Mesh in laparoscopic large hiatal hernia repair: a systematic review of the literature. Surg Endosc 27:3998–4008
10. Hazebroek EJ, Leibman S, Smith GS (2009) Erosion of a composite PTFE/ePTFE mesh after hiatal hernia repair. Surg Laparosc Endosc Percutan Tech 19:175–177
11. Stadlhuber RJ, Sherif AE, Mittal SK, Fitzgibbons RJ Jr, Michael Brunt L, Hunter JG et al (2009) Mesh complications after prosthetic reinforcement of hiatal closure: a 28-case series. Surg Endosc 23:1219–1226
12. Oelschlager BK, Pellegrini CA, Hunter J, Soper N, Brunt M, Sheppard B et al (2006) Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. Ann Surg 244:481–490
13. Frantzides CT, Madan AK, Carlson MA, Stavropoulos GP (2002) A prospective, randomized trial of laparoscopic polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. Arch Surg 137:649–652
14. Oelschlager BK, Pellegrini CA, Hunter JG et al (2011) Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. J Am Coll Surg 213:461–468
15. Watson DI, Thompson SK, Devitt PG et al (2015) Laparoscopic repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh—a randomized controlled trial. Ann Surg 261:282–289

16. Kamolz T, Pointner R, Velanovich V (2003) The impact of gastroesophageal reflux disease on quality of life. Surg Endosc 17:1193–1199
17. Kaplan-Machlis B, Spiegler GE, Revicki DA (1999) Health-related quality of life in primary care patients with gastroesophageal reflux disease. Ann Pharmacother 33:1032–1036
18. Revicki DA, Wood M, Maton PN, Sorensen S (1998) The impact of gastroesophageal reflux disease on health-related quality of life. Am J Med 104:252–258
19. Kamolz T, Wykypiel H Jr, Bammer T, Pointner R (1998) Quality of life after laparoscopic antireflux surgery-Nissen fundoplication. Chirurg 69:947–950
20. Granderath FA, Kamolz T, Schweiger UM, Pointner R (2002) Quality of life, surgical outcome, and patient satisfaction three years after laparoscopic Nissen fundoplication. World J Surg 26:1234–1238. doi:10.1007/s00268-002-6416-3
21. Ware JE Jr (1992) Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 30:473–483
22. Woodcock SA, Watson DI, Lally C, Archer S, Bessell JR, Booth M et al (2006) Quality of life following laparoscopic anterior 90 degrees versus Nissen fundoplication: results from a multicenter randomized trial. World J Surg 30:1856–1863.doi:10.1007/s00268-005-0623-7
23. Granderath FA, Schweiger UM, Kamolz T et al (2005) Laparoscopic Nissen fundoplication with prosthetic hiatal closure reduces postoperative intrathoracic wrap herniation: preliminary results of a prospective randomized functional and clinical study. Arch Surg 140:40–48
24. Kamolz T, Granderath F, Pointner R (2003) Laparoscopic antireflux surgery: disease-related quality of life assessment before and after surgery in GERD patients with and without Barrett's esophagus. Surg Endosc 17:880–885
25. Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T et al (1992) Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ 305:160–164
26. Ware JE Jr., Kosinski M, Bayliss MS, McHorney CA, Rogers WH, Raczek A (1995) Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary of results from the Medical Outcomes Study. Med Care 33(4 Suppl):AS264–AS279

SECTION 3

LONG-TERM OUTCOMES FOLLOWING SURGERY FOR GASTRO-OESOPHAGEAL REFLUX AND HIATUS HERNIA

3.1 Late outcome following Nissen fundoplication

Lafullarde T, Watson DI, Jamieson GG, Myers JC, Game PA & Devitt PG. Laparoscopic Nissen fundoplication – 5 year results and beyond. *Arch Surg* (2001) **136**:180-184.

This paper reported clinical outcomes at 5 to 8 years follow-up following laparoscopic Nissen fundoplication in a larger cohort of patients who underwent surgery for gastro-oesophageal reflux in Adelaide.

Kelly J, Watson DI, Chin K, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication – clinical outcomes at 10 years. *J Am Coll Surg* (2007) **205**:570-575.

This paper reported 10 year clinical follow-up outcomes following laparoscopic Nissen fundoplication in a larger cohort of patients who underwent surgery for gastro-oesophageal reflux in Adelaide.

Engström C, Cai W, Irvine T, Devitt PG, Thompson SK, Game PA, Bessell JR, Jamieson GG, Watson DI. Twenty years of experience with laparoscopic antireflux surgery. *Br J Surg* (2012) **99**:1415-1421.

This paper reported clinical follow-up outcomes following laparoscopic fundoplication for gastro-oesophageal reflux in a cohort of 2,261 patients who underwent surgery for gastro-oesophageal reflux across a 20 year period in Adelaide.

ORIGINAL ARTICLE

Laparoscopic Nissen Fundoplication

Five-Year Results and Beyond

Thiery Lafullarde, MD; David I. Watson, MD, FRACS; Glyn G. Jamieson, MS, FACS, FRACS, FRCS; Jennifer C. Myers, BSc; Philip A. Game, MBBS, FRCS, FRACS; Peter G. Devitt, MS, FRCS, FRACS

Hypothesis: Laparoscopic Nissen fundoplication provides long-term relief of symptoms of gastroesophageal reflux disease.

Design: Prospectively evaluated case series.

Setting: University teaching hospital.

Patients: From September 1991 to December 1999, we performed more than 900 laparoscopic antireflux procedures. The outcome for patients who underwent surgery between September 1991 and June 1994 (178 cases) was determined. This included all patients having laparoscopic Nissen fundoplication, from the first procedure onward.

Interventions: Long-term follow-up for 5 or more years after laparoscopic Nissen fundoplication was obtained by an independent investigator who interviewed patients using a structured questionnaire.

Main Outcome Measures: Prospective evaluation of clinical symptoms using a structured questionnaire.

Results: Outcome data covering a period of 5 or more years after surgery was available for 176 patients (99%), with 2 patients lost to follow-up. Nine patients died (8 of unrelated causes) at some stage following surgery, and the outcome was difficult to determine in 1 patient with cerebral palsy. Hence, questionnaire data were available for 166 patients at a median follow-up of 6 years (range, 5-8 years). Three patients (1.7%) underwent revision surgery for recurrent reflux; 87% of the 176 patients remained free of significant reflux. Reoperation was required for dysphagia in 7 patients (3.9%), 2 for a tight wrap and 5 for a tight diaphragmatic hiatus. In addition, reoperation was necessary for a paraesophageal hiatus hernia in 13 patients (7.3%). Of the reoperations, 56% were performed within 12 months of the original procedure, and 22% during the second year of follow-up. Further surgery was uncommon after 2 years. The long-term outcome was considered "good or excellent" by 90% of patients.

Conclusions: The long-term outcome of laparoscopic Nissen fundoplication is similar to that following open fundoplication. Good results are obtained in most patients.

Arch Surg. 2001;136:180-184

From the University of Adelaide Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia.

LAPAROSCOPIC antireflux surgery is a relatively recent innovation, and outcomes reported to date have predominantly involved short-term results, with a few reports including the medium-term follow-up of patients for up to 3 years after surgery.[1,2] There have been no published reports on follow-up outcomes covering a period of 5 or more years after laparoscopic antireflux surgery. Even in the era of open fundoplication, reports of outcomes beyond a 5-year period were few, and none achieved follow-up rates of more than 90%. Most of these rates were in the range of 40% to 60%.[3-8]

Short-term follow-up has suggested that laparoscopic techniques are likely to achieve similar results to open fundoplication for the correction of gastroesophageal reflux,[1,9] and for this reason it has been assumed that long-term outcomes would support the same conclusion. However, differences between laparoscopic and open techniques have led to a new spectrum of complications,[10,11] and an increased incidence of short-term dysphagia following laparoscopic fundoplication has been suggested based on 1 recent randomized controlled trial.[12] Therefore, it is important that satisfactory long-term outcomes can be demonstrated for the laparoscopic approach because one cannot assume that short-term efficacy will translate into long-term effectiveness. Hence, we have evaluated the outcome for the laparoscopic Nissen procedure in a large group of patients

PATIENTS AND METHODS

Follow-up data for a period of 5 or more years was sought for all patients undergoing a laparoscopic Nissen fundoplication between September 1991 and June 1994 at the University of Adelaide Department of Surgery at the Royal Adelaide Hospital in Adelaide, South Australia. This included every patient having the laparoscopic procedure since its inception in our institution in September 1991. During this period, all patients admitted for antireflux surgery were offered a laparoscopic approach, irrespective of any difficulties perceived by preoperative assessment such as obesity, large hiatal hernia, previous upper abdominal surgery, esophageal stricturing, or Barrett esophagus. Gastroesophageal reflux was initially diagnosed by the presence of endoscopic esophagitis in patients with typical reflux symptoms, and 24-hour pH monitoring was used to confirm the diagnosis of reflux in patients with atypical symptoms or who did not have endoscopic evidence of esophagitis.

Information about the preoperative assessment and management, surgical procedure, and postoperative outcome for each patient was collected prospectively and stored on a computerized database. Postoperative clinical follow-up was obtained through a standardized questionnaire administered by a nonclinical investigator both 3 months and 12 months following surgery and annually thereafter. This questionnaire was initially mailed to each patient. If it was not returned, the patient was located, and data were collected by telephone interview using the same structured questionnaire. A concerted effort was made to obtain follow-up information for every patient who had undergone surgery, in an attempt to complete follow-up at the 5-year interval.

The presence or absence of heartburn and liquid- and solid-food dysphagia, as well as patient satisfaction with the procedure, was graded from 0 to 10 (0=no symptoms; 10=severe symptoms) using visual analog scales. The presence or absence of gaseous bloating, the ability to belch, the ability to relieve abdominal distension, and the ability to eat a normal diet, and patients' opinions on whether they would undergo the same procedure again under similar circumstances, were also determined. Details of adverse outcomes such as hospital readmission, complications, or surgical revision were recorded. Esophageal manometry, pH monitoring, and endoscopy tended to be performed postoperatively in symptomatic patients with clinical indications, although manometry was sought in the early phase of this series as a method of objective follow-up. The results of this follow-up have been reported previously.[13,14] All data analysis was performed on an intention-to-treat basis, and patients whose laparoscopic operation was converted to an open procedure, as well as those requiring later surgical revision, remained in the overall patient group for data analysis.

This surgical technique has previously been described in detail.[13] Five trocars were sited in the upper abdominal wall. In the initial procedure, Veress needle insufflation at the left costal margin was used, and a single laparoscopic grasping instrument was used to retract the left lobe of the liver. Both pillars of the esophageal hiatus were dissected using electrocautery to expose the distal esophagus. Posterior hiatal repair was not performed routinely until 1994. Prior to this, it was performed only in patients with a moderate or larger hiatus hernia. In some patients, short gastric vessels were divided between clips as part of a randomized trial.[15] In all patients, irrespective of whether these vessels were divided or not, a short, loose total fundoplication was constructed, calibrated over a 52F bougie within the lumen of the esophagus. Three interrupted polypropylene sutures were used to secure a total fundoplication of between 1.5 and 2 cm in length.

who have been followed prospectively for at least 5 years after their original operation.

RESULTS

From September 1991 to June 1994, 178 laparoscopic Nissen fundoplication procedures were performed by 6 different surgeons associated with the University of Adelaide Department of Surgery at the Royal Adelaide Hospital or by surgical trainees supervised by 1 of these surgeons. Hiatal repair was performed selectively for the first 153 procedures and routinely for the last 25, and although short gastric vessel division was not routinely performed, the last 30 patients were enrolled in a prospective randomized trial that compared division vs nondivision of these vessels.[15]

This report includes our early learning experience, and 21 (12%) of these procedures required conversion from a laparoscopic to an open approach for the following reasons: intra-abdominal obesity restricting surgical access and obscuring anatomy (9 patients), inability to reduce a very large hiatal hernia (6 patients), dense upper abdominal adhesions (3 patients), and technical difficulties with esophageal dissection because of periesophagitis (3 patients).

Long-term outcome data (beyond 5 years) was obtained for 176 patients (99%), with follow-up ranging from 5 to 8 years (median, 6 years). Two patients could not be contacted for follow-up purposes. One of these is an itinerant alcoholic of "no fixed abode" who was last seen in a beachside town on the coast of South Australia, and the other patient is hiding from his ex-wife, 3000 km away, somewhere in the Australian state of Queensland, and is said to be living in fear for his life. Since undergoing the operation, 9 patients have died; however, only 1 of these deaths was related to the laparoscopic procedure. This patient died following the development of thrombosis of the superior mesenteric and celiac arteries in the immediate postoperative period. Full details of this case have been reported.[16] Four patients died of disseminated carcinoma (1 each of cancer of the prostate, colon, lung, and esophagus), 3 of ischemic heart disease, and 1 of "old age." Another patient has severe cerebral palsy, and communication with her has been difficult, rendering symptomatic assessment unreliable. As far as could be determined, her results have been positive. However, she was excluded from data analysis because she could not be interviewed with the standardized questionnaire. Hence, standardized clinical follow-up

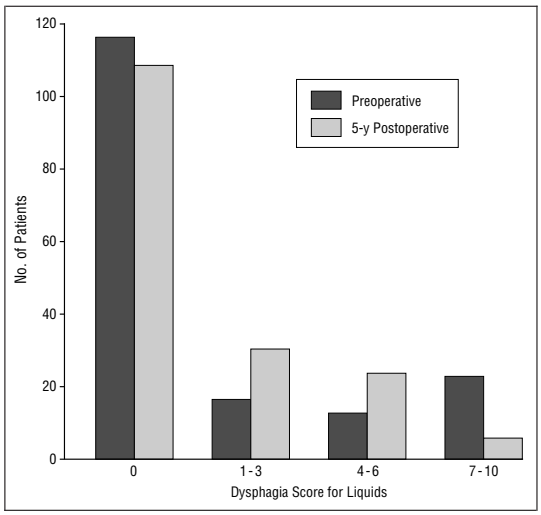


Figure 1. *Preoperative and postoperative dysphagia with liquids (P<.001, χ^2 test).*

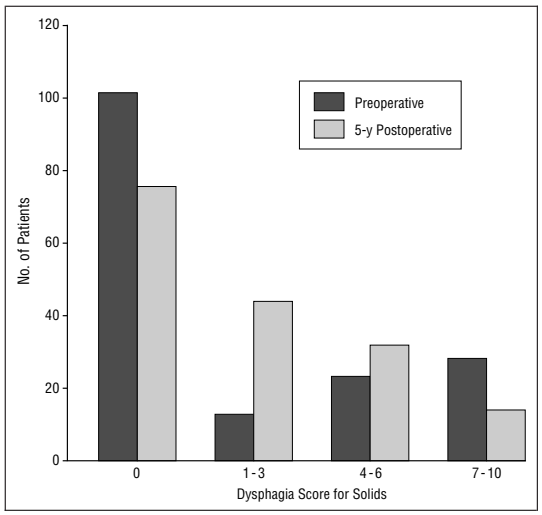


Figure 2. *Preoperative and postoperative dysphagia with solid food (P<.001, χ^2 test).*

data at 5 or more years after surgery were available for 166 patients.

A further surgical procedure was required for 27 patients (15%) because of a problem that developed after the original fundoplication. Thirteen of these procedures were for the repair of a paraesophageal hiatus hernia,[10] 7 were for dysphagia (5 because of a tight esophageal hiatus,[11] and 2 for conversion of the Nissen fundoplication to a posterior partial fundoplication procedure), 3 were for recurrent reflux (wrap undone), 3 were because of a technical error resulting in gastric obstruction (creation of an exaggerated bilobed stomach[13]), and 1 patient underwent multiple laparotomies because of mesenteric thrombosis. Another patient (not included in the total) underwent an esophagectomy following the development of severe dysplasia in a segment of Barrett esophagus. Reoperation was performed within a year of the initial procedure in 15 (56%) of the patients, in the second postoperative year in 6 patients (22%), and beyond 2 years in the remaining 6 patients (22%). Thus, at 5 to 8 years' follow-up, 78% of reoperations had been performed within 2 years of the original procedure. Early postoperative dysphagia sufficient to require endoscopic dilatation occurred in an additional 9 patients (5%). Eight patients were successfully managed with a single dilatation procedure, and 1 patient underwent several dilatations before adequate swallowing was achieved. None of these patients had preoperative endoscopic evidence of an esophageal stricture, although 2 patients did experience preoperative dysphagia of similar severity to what they experienced postoperatively.

In the 166 patients for whom clinical follow-up was obtained at 5 or more years after surgery, 100 patients (60%) had no heartburn, and 45 (27%) had occasional minor episodes of heartburn (heartburn score 1, 2, or 3). Fifteen patients (9%) reported a heartburn score of 4 to 6, and 6 patients (4%) graded their heartburn as 7 or higher (significant troublesome heartburn). Most patients reported a heartburn score of 7 or higher before surgery. Hence, 87% of patients were free of significant reflux symptoms at 5 or more years' follow-up. Regular acid suppression medication for "reflux" symptoms is being taken by 18 patients (11%), who are included in the groups experiencing more severe symptoms described previously.

Figure 1 and **Figure 2** summarize the dysphagia scores for liquids and solids, respectively. More patients had severe dysphagia with liquids (score, 7-10) before surgery than after ($P<.001$, χ^2 test), although a greater number of patients had milder degrees of dysphagia with liquids (scores, 1-3, 4-6) at long-term follow-up. The overall number of patients with dysphagia with liquids was similar before and after surgery. Although there was a significant reduction in the number of patients with severe dysphagia (scores 7-10) with solids following surgery ($P<.001$, χ^2 test), fewer patients were totally free of dysphagia with solids, and a greater number reported mild dysphagia (scores, 1-3) at 5 years after surgery.

At 5 years' follow-up, 72% of patients claimed that they were able to belch. Occasional epigastric bloating after eating was experienced by 66% of all patients, and 71% of this subgroup were able to relieve this symptom by belching. Certain foods were avoided by 11% of patients because of dysphagia or food intolerance. Overall patient satisfaction with the procedure produced a mean satisfaction score of 8.2 (of 10). In similar circumstances, 90% of patients said that they would repeat their operation.

COMMENT

Laparoscopic antireflux surgery is a relatively recent innovation, with most published series describing short-term follow-up,[17-19] and relatively few series reporting medium-term outcomes with follow-up for 2 to 3 years after surgery.[1,2] No previous studies have reported long-term (5-year) follow-up for a large group of patients who have

undergone a laparoscopic antireflux procedure. However, the long-term outcome of this operation will ultimately determine its place in the treatment armamentarium for gastroesophageal reflux, and it is essential to demonstrate an acceptable long-term outcome rather than simply to assume that because short-term results are acceptable, long-term results will be equally good. This is of particular relevance to laparoscopic antireflux surgery because the introduction of this new technique was associated with unexpected complications, such as an increased incidence of paraesophageal hiatus herniation.[10] Previous experience with open antireflux surgery had failed to predict many of these problems. Hence, we cannot be certain that long-term results can be extrapolated from short- to medium-term follow-up.

The long-term outcome for open Nissen fundoplication has been reported previously.[3-8] Although widely quoted, the study of DeMeester et al,[3] which demonstrated a positive outcome for 91% of patients undergoing open Nissen fundoplication, extrapolated a 10-year outcome through an actuarial analysis with a series that reported an average follow-up of 45 months. Long-term data is provided by various Scandinavian series.[4-6] Lundell et al[5] reported a 12% dysphagia rate and a 10% reflux rate for open Nissen fundoplication at 5 years' follow-up within their randomized trial of Nissen vs posterior partial fundoplication. Johansson et al[4] also reported a 21% dysphagia rate, 18% recurrent reflux rate, and 84% overall success rate for Nissen fundoplication at 5 years' follow-up, whereas Luostarinen et al[6] reported an overall success rate of 76% at 20 years' follow-up. However, complete follow-up was not obtained for each of these series, with Lundell et al reporting a follow-up rate of 37% at 5 years; Johansson et al, 85% at 5 years; and Luostarinen et al, 87% at 20 years. No previous follow-up studies after antireflux surgery have achieved close to a 100% follow-up rate.

To achieve a minimum of 5 years' follow-up for laparoscopic Nissen fundoplication, we attempted interviews with every patient who underwent this procedure between September 1991 and July 1994, generating a series of 178 laparoscopic Nissen fundoplications. We previously reported that there is a learning curve for this operation; the results of a surgeon inexperienced with this procedure are associated with a poorer outcome, a higher conversion rate, and a higher reoperation rate.[20] Outcomes improve once surgeons have gained this learning experience.[9] We opted to include this factor in our current study because those problems usually appeared at short-term follow-up, and the current study is primarily of long-term outcome. Hence, the 12% conversion rate to open surgery and the reoperation rate of 15% are both high, reflecting this initial learning experience. We now achieve a conversion rate of approximately 2%[21] and a much lower reoperation rate.[9] Although it could be argued that we should not have included "converted" cases in our follow-up analysis, we believe that it is better to include all patients who underwent an attempted laparoscopic procedure and to analyze the data on an intention-to-treat basis. Selectively omitting this group, who tended to be less satisfied with the outcome of their original procedure, could artificially enhance the quality of the overall outcome, and this should be avoided.

Reoperation for paraesophageal hiatus herniation was common initially, and we have discussed this in detail elsewhere.[10] This was a technical problem caused by our failure to routinely narrow the esophageal hiatus (we had not regularly performed hiatal repair during open surgery). Since routinely narrowing the hiatus, the problem of postoperative herniation is now much less common. Similarly, the issue of a tight hiatus caused by fibrosis has become infrequent as we have made adjustments to our surgical technique.[11] Approximately three quarters of all revision procedures were required within 2 years of the original operation, suggesting that many of the previous studies with shorter follow-up after laparoscopic antireflux procedures are reporting data that can reasonably be extrapolated to 5 years' follow-up.

Postoperative dysphagia is often difficult to assess because the outcome reported depends on who asks about it (eg, surgeon vs independent investigator), how the questions are constructed, and the scoring system used. For this reason, it is better to consider data that compare the same patients at different time intervals (as we have done here) or comparative data from randomized trials. Within the current study, it is clear from Figure 1 that the incidence and severity of dysphagia with liquids was not influenced by laparoscopic Nissen fundoplication and that the number of patients with severe dysphagia with liquids at 5 years was less than the number reporting this problem before surgery. For dysphagia with solid food, there were also less patients with severe dysphagia 5 years after surgery than before surgery. However, more patients reported minor dysphagia with solids at 5 years follow-up than before surgery, and this was caused by an increase in the number of patients with mild dysphagia with solids. Although severe dysphagia was less common, there were more patients overall with dysphagia after surgery, even though it was not usually troublesome and did not require any dietary modification.

Of importance for the assessment of laparoscopic Nissen fundoplication is its ability to abolish reflux symptoms, particularly heartburn. This symptom was not experienced after surgery by 60% of patients. The 27% of patients with a score of 3 or less reported an occasional episode of mild heartburn that did not require medication. Moderate heartburn was reported by 9% of patients, and 4% reported severe heartburn. The outcomes are similar to those following open Nissen fundoplication, suggesting that the laparoscopic approach does not compromise reflux control. Of interest, overall patient satisfaction following surgery was high, with 90% of patients satisfied with their long-term outcome. However, our follow-up is clinical only, and objective follow-up using either pH or endoscopic studies was not sought. It is certainly possible that a few patients who claimed relief of reflux symptoms might demonstrate abnormalities if they underwent either pH monitoring or endoscopy. On the other hand, some of the patients who claimed to experience symptomatic reflux following surgery had no objective evidence of reflux when they underwent postoperative testing. For this reason,

in a clinical practice setting, the symptoms experienced by patients ultimately determine the success or failure of the operations we perform, not the outcome of follow-up tests or the surgeon's opinion about technical success. Hence, we believe that laparoscopic Nissen fundoplication is an effective long-term treatment for gastroesophageal reflux disease, yielding similar results to open fundoplication but with the short-term advantages of quicker recovery and reduced wound-related morbidity.

Corresponding author: David I. Watson, MD, FRACS, University of Adelaide Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia (e-mail: david.watson@.adelaide.edu.au).

REFERENCES

1. Trus TL, Laycock WS, Branum G, Waring JP, Mauren S, Hunter JG. Intermediate follow-up of laparoscopic antireflux surgery. *Am J Surg.* 1996;171:32-35.
2. Anvari M, Allen C. Laparoscopic Nissen fundoplication: two-year comprehensive follow-up of a technique of minimal paraesophageal dissection. *Ann Surg.* 1998;227:25-32.
3. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease: evaluation of primary repair in 100 consecutive patients. *Ann Surg.* 1986;204:9-20.
4. Johansson J, Johnsson F, Joelsson B, Floren CH, Walther B. Outcome 5 years after 360° fundoplication for gastro-oesophageal reflux disease. *Br J Surg.* 1993; 80:46-49.
5. Lundell L, Abrahamsson H, Ruth M, Rydberg L, Lonroth H, Olbe L. Long-term results of a prospective randomized comparison of total fundic wrap (Nissen-Rossetti) or semifundoplication (Toupet) for gastro-oesophageal reflux. *Br J Surg.* 1996;83:830-835.
6. Luostarinen M, Isolauri J, Laitinen J, et al. Fate of Nissen fundoplication after 20 years: a clinical, endoscopical, and functional analysis. *Gut.* 1993;34:1015-1020.
7. Martinez de Haro LF, Ortiz A, Parrilla P, Garcia Marcilla JA, Aguayo JL, Morales G. Long-term results of Nissen fundoplication in reflux esophagitis without strictures. *Dig Dis Sci.* 1992;37:523-537.
8. Grande L, Toledo-Pimentel V, Manterola C, et al. Value of Nissen fundoplication in patients with gastro-oesophageal reflux judged by long-term symptom control. *Br J Surg.* 1994;81:548-550.
9. Watson DI, Jamieson GG, Baigrie RJ, Mathew G, Devitt PG, Game PA. Laparoscopic surgery for gastro-oesophageal reflux: beyond the learning curve. *Br J Surg.* 1996;83:1284-1287.
10. Watson DI, Jamieson GG, Devitt PG, Mitchell PC, Game PA. Paraoesophageal hiatus hernia: an important complication of laparoscopic Nissen fundoplication. *Br J Surg.* 1995;82:521-523.
11. Watson DI, Jamieson GG, Mitchell PC, Devitt PG, Britten-Jones R. Stenosis of the esophageal hiatus following laparoscopic fundoplication. *Arch Surg.* 1995; 130:1014-1016.
12. Bais JE, Bartelsman JF, Bonjer HJ, et al. Laparoscopic or conventional Nissen fundoplication for gastro-oesophageal reflux disease: randomised clinical trial. *Lancet.* 2000;355:170-174.
13. Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. *Ann Surg.* 1994;220:137-145.
14. Mathew G, Watson DI, Myers JC, Holloway RH, Jamieson GG. Oesophageal motility before and after laparoscopic Nissen fundoplication. *Br J Surg.* 1997;84: 1465-1469.
15. Watson DI, Pike GK, Baigrie RJ, et al. Prospective double-blind randomised trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg.* 1997;226:642-652.
16. Mitchell PC, Jamieson GG. Coeliac axis and mesenteric arterial thrombosis following laparoscopic Nissen fundoplication. *Aust N Z J Surg.* 1994;64:728-730.
17. Gotley DC, Smithers BM, Rhodes M, Menzies B, Branicki FJ, Nathanson L. Laparoscopic Nissen fundoplication: 200 consecutive cases. *Gut.* 1996;38:487-491.
18. Anvari M, Allen C, Borm A. Laparoscopic Nissen fundoplication is a satisfactory alternative to long-term omeprazole therapy. *Br J Surg.* 1995;82:938-942.
19. Hunter JG, Trus TL, Barum GD, Waring JP. A physiologic approach to laparoscopic fundoplication for gastroesophageal reflux disease. *Ann Surg.* 1996;223: 673-687.
20. Watson DI, Baigrie RJ, Jamieson GG. A learning curve for laparoscopic fundoplication: definable, avoidable, or a waste of time? *Ann Surg.* 1996;224:198-203.
21. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. A prospective randomised double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg.* 1999;86:123-130.

IN OTHER AMA JOURNALS

ARCHIVES OF INTERNAL MEDICINE

The Heart and Estrogen/Progestin Replacement Study Revisited: Hormone Replacement Therapy Produced Net Harm, Consistent With the Observational Data

John A. Blakely, BA, MD, FRCPC

Lower coronary event rates in women receiving hormone replacement therapy (HRT) have led to a presumption of benefit. The Heart and Estrogen/Progestin Replacement Study, a large randomized trial, observed a 1.4% first year excess of coronary events, well beyond the plausible play of chance on the expected effect. Over the duration of the study, event totals were similar, but patients treated with HRT experienced them earlier, with a net loss of patient-months of event-free survival. The point at which the lower event rate in hormone-treated patients would fully repay the first year loss, with constant rates, is almost double the trial duration (of 4.1 years). Since patients in the trial were preselected for satisfactory adherence to therapy, the net benefit in practice is likely to be even less. Had the patients in the Heart and Estrogen/Progestin Replacement Study been recruited to an observational study at various intervals over the first 5 years after starting HRT, the apparent risk reduction over 5 years would have been between 21% and 34%. A previous meta-analysis of trials of HRT for other indications also shows net harm. Women with or at high risk of coronary heart disease should not start HRT. There is a risk that women without coronary heart disease might experience even greater net harm from HRT. The late benefit is necessarily limited, as it cannot exceed the event rate. The mechanism of the early loss is unknown; if it were reduced proportionately less than the late benefit, considerable net harm could result. (*2000;160:2897-2900*)

Corresponding author: John A Blakely, BA, MD, FRCPC, Sunnybrook and Women's College Health Sciences Centre, 2075 Bayview Ave, Room H121, Toronto, Ontario, Canada M4N 3M5 (e-mail: john.blakely@utoronto.ca).

Laparoscopic Nissen Fundoplication: Clinical Outcomes at 10 Years

Jamie J Kelly, BM, FRCS, David I Watson, MD, FRACS, Kin Fah Chin, BM, FRCS, Peter G Devitt, MS, FRCS, FRACS, Philip A Game, MBBS, FRCS, FRACS, Glyn G Jamieson, MS, FRACS

BACKGROUND: Laparoscopic Nissen fundoplication is now the most common operative procedure for treatment of gastroesophageal reflux disease, although longterm clinical outcomes after this procedure remain uncertain.

STUDY DESIGN: Outcomes for 250 patients who underwent Nissen (total) fundoplication at least 10 years ago (September 1991 to August 1995) were determined prospectively using a structured questionnaire that evaluated clinical symptom scores for heartburn, dysphagia, and satisfaction with clinical outcomes.

RESULTS: Clinical followup data for at least 10 years (120 to 167 months) after operation were available for 226 patients, an additional 21 patients had died, making outcomes for 247 patients (99%). Of the three (1%) remaining patients, one was lost to followup and dementia developed in two. One hundred eighty-seven (83%) patients were highly satisfied with the clinical outcomes. One hundred eighty-nine (84%) had good or excellent control of heartburn. Symptom scores for heartburn, dysphagia, and overall satisfaction were unchanged from 5-year followup data. Forty-two (17%) patients underwent revision operations, 28 (22%) were in the first 125 patients and 14 (11%) in the subsequent 125 patients. Antireflux medication use increased gradually, resulting in 47 (21%) patients using medication at 10 years. Of 21 deaths, 1 was postoperative and the remaining 20 were similar to that predicted for a matched population. A high preoperative heartburn score correlated with high patient satisfaction and lower dysphagia score at 10 or more years ($p = 0.038$ and $p = 0.041$, respectively).

CONCLUSIONS: Laparoscopic Nissen fundoplication is an effective longterm treatment for gastroesophageal reflux disease. (J Am Coll Surg 2007;205:570–575. © 2007 by the American College of Surgeons)

Laparoscopic fundoplication is an accepted treatment option for gastroesophageal reflux, but reported followup has rarely exceeded 5 years. The only previous reports of outcomes data solely beyond 10 years were a series of 25 patients who were followed for 20 years after undergoing an open Nissen fundoplication, and a recent report of 100 patients who underwent operations in 1993.[1,2] Good-to-excellent outcomes were reported in 55% and 90% of patients, respectively, in these two series. Laparoscopic fundoplication became available in the early 1990s. It should now be possible to determine 10-year outcomes for laparoscopic techniques in larger groups of patients.

More recently, longterm efficacy and risk of side effects, such as dysphagia, after fundoplication have been questioned.[3] In particular, Spechler and colleagues[4] reported that > 50% of postfundoplication patients continue to use antireflux medication, and that there is substantially reduced longterm survival in patients who undergo fundoplication because of an increased rate of cardiac deaths during followup. To investigate these issues more, we prospectively determined the clinical outcomes for patients who had undergone laparoscopic Nissen fundoplication at 10 years after operation.

METHODS

Late outcomes were determined for 250 patients who underwent Laparoscopic Nissen fundoplication between September 1, 1991 and August 1, 1995 at the Royal Adelaide Hospital or associated private hospitals. The study group

Competing Interests Declared: None.

Received March 30, 2007; Revised May 14, 2007; Accepted May 22, 2007.
From the Discipline of Surgery, University of Adelaide, Royal Adelaide Hospital, Adelaide, South Australia (Kelly, Chin, Devitt, Game, Jamieson) and Department of Surgery, Flinders University, Flinders Medical Centre, Bedford Park, South Australia (Kelly, Watson).
Correspondence address: David I Watson, MD, FRACS, Department of Surgery, Flinders University, Room 3D211, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia. email: david.watson@flinders.edu.au

ISSN 1072-7515/07/$32.00
doi:10.1016/j.jamcollsurg.2007.05.024

Table 1. Satisfaction as Measured Using a 0−10 Analogue Scale

Satisfaction score*	5 Years (%)	10+ Years (%)
0−3	6	7
4−6	9	10
7−9	39	40
10	46	43

*0, unsatisfied; 10, highly satisfied.

Table 2. Heartburn as Measured Using a 0−10 Analogue Scale

Heartburn score*	5 Years (%)	10+ Years (%)
0	60	63
1−3	27	21
4−6	9	9
7−10	4	7

*0, no symptoms; 10, severe symptoms.

included the first patient to undergo a laparoscopic antireflux operation in our unit, and all subsequent patients who underwent a laparoscopic procedure. One hundred fifty-three (61%) patients were male and 97 (39%) were female. Ages ranged from 15 to 91 years (median 46 years), and patients weighed from 37 to 123 kg (median 80 kg). Gastroesophageal reflux was confirmed before operation by the presence of ulcerative esophagitis (Savary-Miller grade 1 or higher) at endoscopy or abnormal 24-hour pH monitoring ($pH < 4$ for $> 7\%$ of the study period, or $pH < 4$ between 4% and 7% of the study with $> 50\%$ correlation between reflux episodes and symptoms). One hundred forty-four (58%) of the patients were investigated with pH monitoring before operation, and 234 (94%) underwent assessment with esophageal manometry. All patients were consuming some form of acid-suppression therapy before operation, and $> 90\%$ (226) of patients had reflux symptoms (heartburn, regurgitation, or both) that were poorly controlled by medical therapy.

Operations were undertaken by two or more of a group of six consultant surgeons and three senior upper gastrointestinal surgery fellows. The operative technique has been described previously.[5] Before 1994, hiatal repair was performed in patients with a moderate or large hiatus hernia (this was our earlier practice for open operation) only. From 1994 onward, all patients underwent routine posterior hiatal repair. One hundred twenty-six (50%) of patients included in this study underwent hiatal repair. Sixty-three (25%) patients had their short gastric vessels divided during the operation, the majority as part of a randomized controlled trial. In the remaining patients, vessels were not divided. A short, loose 360° fundoplication was constructed and secured using three nonabsorbable sutures. A 52F intraesophageal bougie was used in all procedures.

After operation, followup was conducted using a standardized questionnaire. This was administered by an independent nonclinical investigator at 3 and 12 months after operation and annually thereafter. Information was collected prospectively, and managed on a computerized database. Presence or absence of heartburn and dysphagia for liquids and solids was graded using previously described analogue scales from 0 to 10 (0, no symptoms; 10, severe symptoms).[6] Patient satisfaction was measured using an analogue scale (0, unsatisfied; 10, highly satisfied). Presence or absence of various side effects was also determined. Patients were also asked whether or not they thought their original decision to undergo the procedure was correct or not.

All patients who underwent laparoscopic Nissen fundoplication were included in this study, and patients who subsequently underwent revision operations remained in the overall patient group. Ten-plus years of followup data were gathered and compared with baseline and 5-year followup data. Statistical evaluation was undertaken using the SPSS statistical package (SPSS, Inc). Mann-Whitney U test was used to compare nonparametric data sets, Wilcoxon test was used to compare paired data sets, and chi-square test was used to analyze contingency tables.

RESULTS

A minimum of 10 years (range 120 to 167 months) clinical followup data were obtained for 226 patients. An additional 21 patients died within 10 years of operation. Outcomes were available for 247 patients (99% overall 10+ years of followup). Of the remaining three patients, one had emigrated and was lost to followup, and dementia developed in two and they were unable to provide accurate clinical followup information. No patient refused followup in this study. One patient who had previously been reported to be lost to followup at 5 years was found by 10 years, and contributed clinical data to this study.[7]

Overall satisfaction with outcomes is summarized in Table 1. Eighty-three percent of patients were highly satisfied with outcomes at 10+ years (analogue score 7 to 10). No marked differences were seen between the 5- and 10+-year satisfaction scores (mean 8.4 [median 9] at 5 years, 8.1 [median 9] at 10 years, $p = 0.894$—Wilcoxon matched pairs). When patients were asked at 10 years whether they thought their original decision to undergo the operation was correct, 83% replied yes, 15% replied no, and 2% were unsure.

Table 2 summarizes the outcomes for heartburn. Eighty-four percent of patients had good or excellent (score 0 to 3) control of heartburn at 10 or more years. No marked differences were seen between the 5 and 10+ year scores

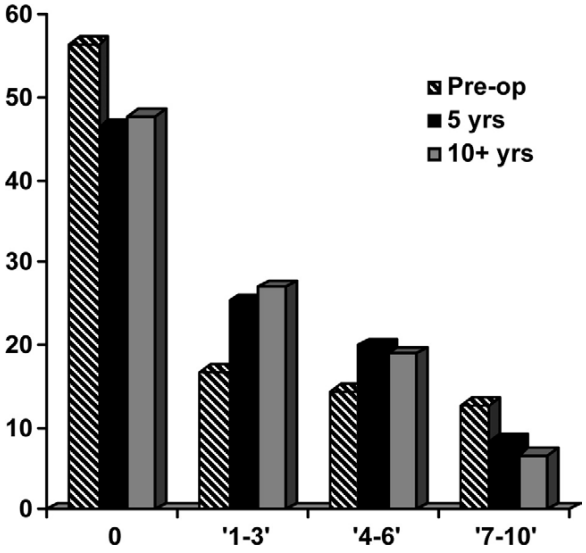


Figure 1. Dysphagia scores for liquids (% patients before and after operation with various dysphagia scores).

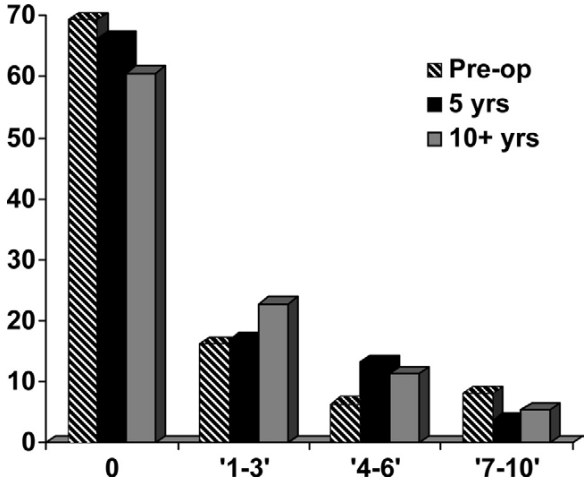


Figure 2. Dysphagia scores for solids (% patients before and after operation with various dysphagia scores).

(mean 1.2 [median 0] at 5 yrs, 1.4 [median 0] at 10 years; p = 0.269—Wilcoxon matched pairs test).

Figures 1 and 2 summarize dysphagia for liquids and solids before, at 5 years, and 10 or more years after Nissen fundoplication. Overall dysphagia scores were similar before and after operation. Mean dysphagia score for liquids was 1.7 (median 0) before operation versus 1.3 (median 0) at 5 years versus 1.3 (median 0) at 10+ years. Corresponding mean scores for solids were 2.6 (median 0), 2.1 (median 1), and 1.9 (median 0), respectively. No marked differences in outcomes were seen between the 5- and 10-year followup points for either liquids (p = 0.626—Wilcoxon) or solids (p = 0.162—Wilcoxon). In patients included in this study, hiatal repair was performed selectively. One hundred ten patients did not have the hiatus repaired. In these patients, mean dysphagia scores were 1.2 (median 0) for liquids and 1.6 (median 0) for solids. In 106 patients who underwent hiatal repair, mean dysphagia scores were 1.4 (median 0) and 2.2 (median 2), respectively, for liquids and solids. Dysphagia scores for solids were considerably less at 10+ years in patients who did not undergo hiatal repair (p = 0.0498—Mann-Whitney U test). Postprandial bloating was present in 60% of patients at both 5- and 10-year followup.

Thirty-eight (15%) patients who were followed for 10 or more years underwent an additional procedure during the followup period. An additional four patients who had died during followup had also undergone surgical revision. Forty-two (17%) of 250 patients underwent surgical revision within 10 years of their original Nissen fundoplication. Table 3 summarizes the reasons for additional operations. Fifteen of these procedures were performed within 3 months of the original Nissen fundoplication operation, 6 between 3 months and 1 years, 11 between 1 and 5 years, and 10 between 5 and 10 years after operation (Fig. 3). One

Table 3. Reasons for Additional Operations

Reason	n
Recurrent hiatus hernia	15
Dysphagia	15
Recurrent reflux	11
Postoperative bleeding	1

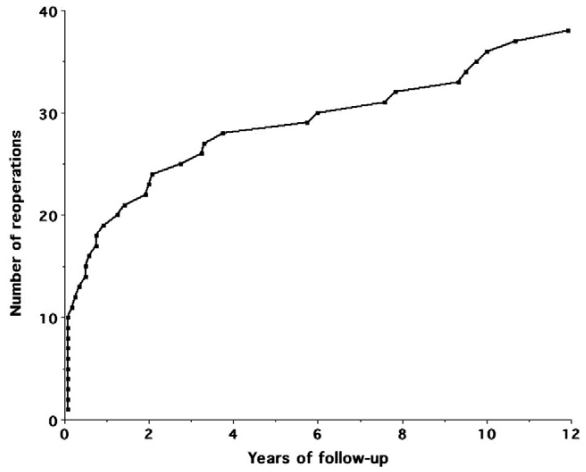


Figure 3. Cumulative number of revision operations versus length of followup.

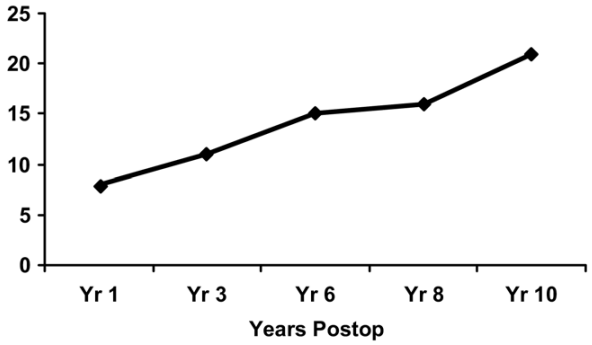


Figure 4. Percentage of patients consuming antireflux medication versus length of followup.

patient underwent operation for bleeding from a short gastric vessel within the first 24 hours after operation. Nine of 12 patients who had revision operations for dysphagia did so within 1 month of their original operation. Chronologically, 28 (22%) of the first 125 patients underwent a revision operation, compared with 14 (11%) of the second 125. Overall likelihood of undergoing revision operation was not influenced by whether or not the short gastric vessels were divided at the original procedure. All of the reoperations for recurrent reflux entailed formation of a new Nissen fundoplication.

Forty-seven patients (21%) were using some form of antireflux medication at 10 or more years after operation. Thirty-four (15%) of these patients were using either a proton pump inhibitor or a H_2 receptor antagonist, and 13 (6%) were using simple antacids. Figure 4 demonstrates a gradual increase in medication consumption as followup lengthened. Patients who were taking antireflux medication substantially worse clinical outcomes (mean heartburn score 4.1 versus 0.7 [medians 4 versus 0]) for all other patients [$p = 0.0001$ Mann-Whitney U test]), mean satisfaction score 6.0 versus 8.7 (medians 7 versus 9) for all other patients ($p = 0.0001$; Mann-Whitney U test). Recurrent reflux after a surgical revision procedure for recurrent reflux developed in three of the patients who were taking proton pump inhibitors at 10-year followup. This was a proportion similar to that of patients in the overall study group, who were using medication 10 years after operation.

There was 1 postoperative death in this series (described previously[8]), and 20 later deaths during the 10-year followup period. Causes of death are listed in Table 4. The number of deaths observed in our group of patients was one more than was predicted in an age- and gender-matched group of South Australians over the same time period (as calculated from death rates published by Australian Bureau of Statistics, available at http://www.abs.gov.au). Only one of the seven cancer deaths was a result of adenocarcinoma of gastroesophageal junction.

Table 4. Cause of Deaths During Late Followup (Postoperative Death Excluded)

Cause of death	n
Carcinoma	7
Myocardial infarction	3
Cerebrovascular accident	2
Medication overdose (suicide)	2
Car accident	1
Liver failure	1
Pancreatitis	1
Gunshot	1
Pneumonia	1
Unknown	1

A regression analysis for outcomes measures of analogue satisfaction, heartburn, and dysphagia scores was carried out against various preoperative or intraoperative measures: age, weight, gender, dysphagia scores to liquids and solids, heartburn score, esophagitis, lower esophageal sphincter pressure, percentage time below pH 4 (when pH studies done), hiatal repair, division of short gastric vessels, and number of sutures used to construct the fundoplication. When using satisfaction as the outcomes measure, the only major factor that correlated with outcomes was the preoperative heartburn score ($p = 0.038$). A high preoperative score correlated with high patient satisfaction at 10 or more years after operation. Dysphagia for solids also correlated with the preoperative heartburn score ($p = 0.041$). A high preoperative heartburn score was associated with a lower dysphagia score at 10 or more years. None of the factors correlated with outcomes when tested against heartburn as the primary outcomes measure.

DISCUSSION

The goals of antireflux operation are to achieve control of reflux symptoms with minimum risk and without adding any longterm side effects to the patient undergoing the procedure. Our results have shown that at least 10 years after operation, $> 80\%$ of patients who undergo laparoscopic Nissen fundoplication are highly satisfied with their situation, and no longer experience reflux symptoms. This adds weight to similar findings reported by Dallemagne and colleagues[2] from a smaller case series.

In our series, most clinical outcomes were stable beyond 5-year followup. The level of postoperative dysphagia and bloating symptoms at 10 years was very similar to that reported at 5-year followup. This suggests that if good outcomes are achieved at 5-year followup, there is a low risk of recurrent reflux or other problems arising at later followup

Nissen fundoplication. Offsetting this was the gradual increase in use of antireflux medication over time. This could be, in part, because of a low but continuing risk of recurrence of reflux. The rate of recurrence of reflux is probably less than the consumption of medication suggests. Lord and colleagues[9] in 2002 showed that only 24% of patients who were on antireflux medication for reflux symptoms after fundoplication actually had reflux when tested using 24-hour pH monitoring. We and others have also shown that "reflux-like" symptoms after fundoplication correlate poorly with outcomes of pH studies, with reflux confirmed in only 20% to 30% of patients who report postoperative reflux symptoms.[10-13] Other reasons for patients using acid suppression include counterbalancing adverse effects of corticosteroid therapy or nonsteroidal antiinflammatory agents, and prescriptions for other dyspeptic or functional symptoms. Some patients even continue to take medications when all reflux symptoms have been abolished by operation.[14] In our series, only 21% of patients were taking antireflux medication at 10 years. This is considerably less than the 62% at 8 years reported by Spechler and colleagues.[4]

The rate of revisional operations in this series is high. This is almost certainly because the experience reported includes our initial learning curve, which can be observed by examining the patients in chronologic order.[15] The first 125 patients required 28 reoperations, compared with the second 125 patients, for whom only 14 revision procedures were required. This difference is almost certainly a result of the learning curve. We were one of the first groups in the world to perform laparoscopic antireflux operations.[5] During this early experience, we audited our outcomes and modified our technique in response to problems that had arisen during earlier cases. For example, we reported our observation of an increased incidence of postoperative paraesophageal hiatus hernia after procedures in which the esophageal hiatus had not been routinely repaired.[16] Subsequent application of routine hiatal repair was followed by a substantial reduction in the rate of surgical revision for this problem. It is likely that the lower reoperation rate in the second half of our experience is a better reflection of longterm outcomes after laparoscopic Nissen fundoplication. Also influencing the revision rate is the fact that all surgeons in our unit have a policy to take the patients with severe early dysphagia back to the operating room for reexploration within the first few days of operation. This protocol minimized the risk of a possibly more difficult procedure in the subsequent weeks. Nine early revision procedures were performed for this reason and it could be argued that such early intervention might not have always been necessary. Commonly quoted figures at around 5 years for revisional operation are 3% to 7%,[17-19] and a 10-year late revision rate of around 5% is likely to be more representative of current outcomes.

One unexpected finding of our study was the lower dysphagia rate in patients in whom the hiatus was not repaired. The role of hiatal closure in dysphagia has not been adequately assessed, although a small study of seven patients after fundoplication has shown changes in the hiatal canal associated with delayed emptying of a liquid bolus.[20] It might be that high-resolution esophageal manometry will be helpful in providing insights here.[21] Failure to narrow the hiatus was not associated with an excessive rate of revisional operation, despite the fact that we have previously reported a higher rate of revision for postoperative paraesophageal hiatus hernia on patients in whom the hiatus was not repaired.[16] One might speculate that this could be because any reduction in risk of postoperative hiatus hernia achieved by routine hiatal repair might be offset by a greater risk of early revision for dysphagia. It is now well-understood that not all postfundoplication dysphagia is a result of problems with fundoplication, and dysphagia can follow development of a tight diaphragmatic hiatus.[22]

Spechler and colleagues,[4] in their 2001 report, suggested there might be an increase in the death rate from cardiovascular events after antireflux operation, and that this could be a reason to avoid operation for reflux. The death rate in our study was identical to the predicted death rate for an age- and gender-matched group of patients in our community, and this supports similar findings in Dallemagne and colleagues'[2] study. The high death rate in Spechler and colleagues' Veterans Affairs' study remains an unexplained finding, and is at variance to mortality rates reported in most of the literature on laparoscopic fundoplication.

In conclusion, laparoscopic Nissen fundoplication appears to be a safe and relatively effective longterm treatment for gastroesophageal reflux disease. Once the learning curve has been passed, the number of patients requiring revisional operations is low. Nevertheless, low surgical revision and longterm dysphagia rates should not deter surgeons from continually trying to improve clinical outcomes for patients undergoing operation for gastroesophageal reflux.

Author Contributions

Study conception and design: Watson, Devitt, Game, Jamieson

Acquisition of data: Kelly, Watson, Chin

Analysis and interpretation of data: Kelly, Watson, Chin, Jamieson

Drafting of manuscript: Kelly, Watson, Jamieson

Critical revision: Watson, Devitt, Game, Jamieson

REFERENCES

1. Luostarinen M, Isolauri J, Laitinen J, et al. Fate of Nissen fundoplication after 20 years. A clinical, endoscopical, and functional analysis. Gut 1993;34:1015–1020.
2. Dallemagne B, Weerts J, Markiewicz S, et al. Clinical results of laparoscopic fundoplication at ten years after surgery. Surg Endosc 2006;20:159–165.
3. Dominitz JA, Dire CA, Billingsley KG, Todd-Stenberg JA. Complications and antireflux medication use after antireflux surgery. Clin Gastroenterol Hepatol 2006;4:299–305.
4. Spechler SJ, Lee E, Ahnen D, et al. Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial. JAMA 2001; 285:2331–2338.
5. Jamieson GG, Watson DI, Britten-Jones R, et al. Laparoscopic Nissen fundoplication. Ann Surg 1994;220:137–145.
6. Watson DI, Jamieson GG, Devitt PG, et al. Paraoesophageal hiatus hernia: an important complication of laparoscopic Nissen fundoplication. Br J Surg 1995;82:521–523.
7. Lafullarde T, Watson DI, Jamieson GG, et al. Laparoscopic Nissen fundoplication: five-year results and beyond. Arch Surg 2001;136:180–184.
8. Yau P, Watson DI, Devitt PG, et al. Early reoperation following laparoscopic antireflux surgery. Am J Surg 2000;179:172–176.
9. Lord RV, Kaminski A, Oberg S, et al. Absence of gastroesophageal reflux disease in a majority of patients taking acid suppression medications after Nissen fundoplication. J Gastrointest Surg 2002;6:3–9.
10. Draaisma WA, Rijnhart-de Jong HG, Broeders IA, et al. Five-year subjective and objective results of laparoscopic and conventional Nissen fundoplication: a randomized trial. Ann Surg 2006;244:34–41.
11. Thompson SK, Jamieson GG, Myers JC, et al. Recurrent heartburn after laparoscopic fundoplication is not always recurrent reflux. J Gastroint Surg 2007;11:642–647.
12. Galvani C, Fisichella PM, Gorodner MV, et al. Symptoms are a poor indicator of reflux status after fundoplication for gastroesophageal reflux disease: role of esophageal functions tests. Arch Surg 2003;138:514–518.
13. Khajanchee YS, O'Rourke RW, Lockhart B, et al. Postoperative symptoms and failure after antireflux surgery. Arch Surg 2002; 137:1008–1013.
14. Papasavas PK, Keenan RJ, Yeaney WW, et al. Effectiveness of laparoscopic fundoplication in relieving the symptoms of gastroesophageal reflux disease (GERD) and eliminating antireflux medical therapy. Surg Endosc 2003;17:1200–1205.
15. Watson DI, Baigrie RJ, Jamieson GG. A learning curve for laparoscopic fundoplication. Definable, avoidable, or a waste of time? Ann Surg 1996;224:198–203.
16. Mitchell PC, Jamieson GG. Coeliac axis and mesenteric arterial thrombosis following laparoscopic Nissen fundoplication. Aust NZ J Surg 1994;64:728–730.
17. Eubanks TR, Omelanczuk P, Richards C, et al. Outcomes of laparoscopic antireflux procedures. Am J Surg 2000;179:391–395.
18. Rothenberg SS. The first decade's experience with laparoscopic Nissen fundoplication in infants and children. J Pediatr Surg 2005;40:142–146.
19. Pessaux P, Arnaud JP, Delattre JF, et al. Laparoscopic antireflux surgery: five-year results and beyond in 1340 patients. Arch Surg 2005;140:946–951.
20. Ghosh SK, Kahrilas PJ, Zaki T, et al. The mechanical basis of impaired esophageal emptying postfundoplication. Am J Physiol Gastrointest Liver Physiol 2005;289:G21–G35.
21. Pandolfino JE, Zhang QG, Ghosh SK, et al. Transient lower esophageal sphincter relaxations and reflux: mechanistic analysis using concurrent fluoroscopy and high-resolution manometry. Gastroenterology 2006;131:1725–1733.
22. Watson DI, Jamieson GG, Mitchell PC, et al. Stenosis of the esophageal hiatus following laparoscopic fundoplication. Arch Surg 1995;130:1014–1016.

Original article

Twenty years of experience with laparoscopic antireflux surgery

C. Engström[2,3], W. Cai[2], T. Irvine[2], P. G. Devitt[1], S. K. Thompson[1], P. A. Game[1], J. R. Bessell[2], G. G. Jamieson[1] and D. I. Watson[2]

[1]University of Adelaide Discipline of Surgery, Royal Adelaide Hospital, Adelaide, and Flinders University Department of Surgery[2], Flinders Medical Centre, Bedford Park, South Australia, Australia, and [3]Department of Surgery, Sahlgrenska University Hospital, Göteborg, Sweden
Correspondence to: Professor D. I. Watson, Flinders University Department of Surgery, Room 3D211, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia (e-mail: david.watson@flinders.edu.au)

Background: There are few reports of large patient cohorts with long-term follow-up after laparoscopic antireflux surgery. This study was undertaken to evaluate changes in surgical practice and outcomes for laparoscopic antireflux surgery over a 20-year period.

Methods: A standardized questionnaire, prospectively applied annually, was used to determine outcome for all patients undergoing laparoscopic fundoplication in two centres since commencing this procedure in 1991. Visual analogue scales ranging from 0 to 10 were used to assess symptoms of heartburn, dysphagia and satisfaction with overall outcome. Data were analysed to determine outcome across 20 years.

Results: From 1991 to 2010, 2261 consecutive patients underwent laparoscopic fundoplication at the authors' institutions. Follow-up ranged from 1 to 19 (mean 7·6) years. Conversion to open surgery occurred in 73 operations (3·2 per cent). Revisional surgery was performed in 216 patients (9·6 per cent), within 12 months of the original operation in 116. There was a shift from Nissen to partial fundoplication across 20 years, and a recent decline in operations for reflux, offset by an increase in surgery for large hiatus hernia. Dysphagia and satisfaction scores were stable, and heartburn scores rose slightly across 15 years of follow-up. Heartburn scores were slightly higher and reoperation for reflux was more common after anterior partial fundoplication ($P = 0{\cdot}005$), whereas dysphagia scores were lower and reoperation for dysphagia was less common ($P < 0{\cdot}001$). At 10 years, satisfaction with outcome was similar for all fundoplication types.

Conclusion: Laparoscopic Nissen and partial fundoplications proved to be durable and achieved good long-term outcomes. At earlier follow-up, dysphagia was less common but reflux more common after anterior partial fundoplication, although differences had largely disappeared by 10 years.

Paper accepted 1 June 2012
Published online in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.8870

Introduction

Laparoscopic antireflux surgery was first described in 1991[1,2]. Good outcomes were reported initially, although early critics of this approach highlighted the lack of long-term outcomes. The weight of evidence now confirms that laparoscopic Nissen fundoplication is an effective treatment for gastro-oesophageal reflux disease[3,4]. However, postfundoplication side-effects have encouraged various modifications to Nissen's procedure and the development of partial fundoplications[5–7].

The first laparoscopic antireflux procedure undertaken in the authors' units was performed in 1991. This entailed a modified Nissen fundoplication technique. Initially the hiatus was not repaired routinely or the short gastric blood vessels divided routinely. Outcome data were collected in a standardized manner and audit analysis of postoperative outcomes led to incremental changes to the operative technique. Some of these modifications were then evaluated in prospective randomized trials[8–11]. The results of these trials suggested that division of the short gastric blood vessels during laparoscopic Nissen fundoplication is generally not necessary, and that laparoscopic anterior 180° partial fundoplication achieves equivalent control of reflux but with fewer side-effects at early and late follow-up.

Similar outcomes have been reported from trials conducted elsewhere[12].

However, these randomized trials have looked only at specific aspects of surgical technique, rather than the bigger picture, which can be evaluated only by measuring outcomes in all patients undergoing antireflux surgery. Hence, this study evaluated the overall experience with laparoscopic antireflux surgery in the authors' units since commencing the procedure in 1991. The aim of the study was prospectively to measure and document outcomes in a large cohort of patients undergoing antireflux surgery, and to identify changes in antireflux surgery practice and their impact on outcome over two decades.

Methods

All patients who underwent an attempted laparoscopic fundoplication for gastro-oesophageal reflux and/or a large hiatus hernia at the Royal Adelaide Hospital, Flinders Medical Centre and associated private hospitals in Adelaide, South Australia, from October 1991 (when the first laparoscopic fundoplication was attempted) until December 2010 were included in this study. Procedures were performed by either a consultant upper gastrointestinal surgeon or an upper gastrointestinal surgery fellow working under direct supervision. Preoperative, operative and postoperative outcome data were collected prospectively for all patients, and data were managed on a computerized database.

During the study period all primary antireflux procedures were commenced using the laparoscopic approach, and from 1992 onwards no patient underwent a primary open antireflux procedure. Operative techniques included total 360° (Nissen), posterior 270°, anterior 180° and anterior 90° partial fundoplications. These techniques have all been described in detail elsewhere[5,6,13]. Following an initially high rate of postoperative hiatus hernia, posterior hiatal repair was used routinely for all fundoplications from 1994 onwards[14]. Nissen fundoplication entailed the construction of a loose 360° total fundoplication after selective division of the short gastric vessels. A 50–52-Fr bougie was used to calibrate the fundoplication and ensure it was not too tight. Anterior 180° partial fundoplication involved suturing the anterior fundus across the front of the oesophagus, and anchoring it to the wall of the oesophagus and the hiatal rim, including the right hiatal pillar. Anterior 90° partial fundoplication entailed suturing the anterior fundus to the left side of the oesophagus and left hiatal pillar, and then halfway across the front of the oesophagus, with anchorage to the wall of the oesophagus and the apex of the hiatal rim. Both types of partial fundoplication aimed to stabilize the distal oesophagus in the abdomen, and to anchor the fundus to the oesophagus and the hiatal rim.

After surgery, patients were followed using a standardized set of questions that were applied at fixed time points. Follow-up was managed by a team of research nurses. A questionnaire was mailed to all patients at 3 and 12 months, and annually thereafter. If this questionnaire was not returned and the location of the patient was known, the questionnaire was administered by a research nurse by telephone. Patients were asked questions about symptoms of heartburn, postoperative dysphagia for liquids and solids, and overall satisfaction with the outcome following surgery. These outcomes were assessed using a visual analogue scale (VAS) ranging from 0 to 10[8–10]. For the assessment of heartburn, dysphagia for liquids and dysphagia for solids, 0 indicated no symptoms and 10 indicated severe symptoms. For the assessment of overall satisfaction the scale was reversed, so that 0 indicated dissatisfied and 10 highly satisfied. In general, symptom scores of 0–3 indicated either no symptoms or minor symptoms that did not interfere with quality of life, whereas 4–6 indicated moderate and 7–10 severe symptoms. A satisfaction score of 7–10 indicated a high level of satisfaction with the overall outcome, 4–6 a moderate level of satisfaction, and 0–3 a low level of satisfaction.

Patients were also asked to answer yes or no to the question whether or not they thought they had made the correct decision to undergo their original surgery, and also whether or not they were consuming antisecretory medication, irrespective of the indication.

Data on symptom scores were analysed at each year of follow-up. The decision question and use of proton pump inhibitor (PPI) medication were analysed at 5 and 10 years' follow-up for each fundoplication type.

Statistical analysis

Continuous data, expressed as mean(s.d.), were compared using the Mann–Whitney *U* test, and categorical variables by means of the χ^2 test. InStat® version 3.1a (GraphPad Software, La Jolla, California, USA) was used for analysis of symptom scores.

Results

A total of 2261 patients underwent an attempted laparoscopic fundoplication and were included in this study; 1108 (49·0 per cent) were male and 1153 (51·0 per cent) female. Mean age was 52·4(15·5) (range 15–95) years. Mean weight was 82·7(17·2) (range 40–160) kg and mean body mass index was 28·9(5·7) (range 15·6–60·2) kg/m^2. The mean duration of symptoms before surgery was 8·5(9·4) years.

Perioperative outcomes

The mean duration of operation was 81(5) (range 20–260) min. Some 2188 operations (96·8 per cent) were completed laparoscopically and 73 (3·2 per cent) were converted to an open surgical procedure. A total of 1209 patients (53·5 per cent) underwent a Nissen fundoplication, 977 (43·2 per cent) an anterior partial fundoplication (612 anterior 180°, 365 anterior 90°) and 63 (2·8 per cent) a posterior partial fundoplication. Nine patients (0·4 per cent) underwent repair of a large hiatus hernia without a fundoplication. Because of intraoperative complications, three procedures (0·1 per cent) were converted to a resection procedure (2 oesophagectomy, 1 partial gastrectomy).

The short gastric blood vessels were divided in 265 patients (11·7 per cent), all of whom had a Nissen fundoplication. They were never divided during a partial fundoplication. Before mid-1994 the hiatus was not repaired routinely except in patients with a significant hiatus hernia. However, from mid-1994, hiatal repair was routine. A 52-Fr intraoesophageal bougie was used to calibrate the fundoplication in 1528 patients (67·6 per cent). It was used routinely for Nissen fundoplication, but omitted in many partial fundoplication procedures.

The mean postoperative hospital stay was 3(3) days. Three patients died during the hospital admission (in-hospital mortality rate 0·1 per cent), two following repair of a very large hiatus hernia (complications of oesophageal perforation 1, myocardial infarction 1) and one after a procedure for reflux (ischaemic gut due to mesenteric artery thrombosis). Mean follow-up was 7·6(4·7) (range 1–19) years.

Revisional surgery

A total of 216 patients (9·6 per cent) underwent revisional surgery at some stage. One hundred and sixteen of the revisions were undertaken within 12 months of the original operation. In this group, the commonest indications were dysphagia (62, 53·4 per cent) and hiatus hernia (26, 22·4 per cent). Other reasons for early reoperation in 28 patients included: recurrent reflux (11), oesophageal perforation or leakage (6), sepsis (4), abdominal pain (3), bleeding (2), wound dehiscence (1) and mesenteric artery thrombosis (1).

Revision 12 months or more after the original surgery was undertaken in 100 patients. The commonest reasons for later revision were: dysphagia (25, 25·0 per cent), hiatus hernia (24, 24·0 per cent) and recurrent reflux (47, 47·0 per cent). Other reasons in four patients included bloating (3) and abdominal pain (1). Revisional surgery was undertaken beyond 10 years in ten (1·4 per cent) of 703 patients followed for more than 10 years. Four of these very late reoperations were for symptoms of recurrent reflux.

Overall, reoperation was undertaken in 11·8 per cent of patients (143 of 1209) after Nissen fundoplication, in 6·0 per cent (37 of 612) after anterior 180° partial fundoplication, in 8·2 per cent (30 of 365) after anterior 90° partial fundoplication, and in 6 per cent of patients (4 of 63) after posterior partial fundoplication. The reoperation rate was significantly higher in patients who underwent a Nissen fundoplication ($P = 0·005$).

Reasons for reoperation in relation to the original fundoplication type are summarized in *Table 1*. Compared with Nissen fundoplication, reoperation for recurrent reflux was significantly more common after both types of anterior partial fundoplication (3·1 and 4·9 per cent for 180° and 90° respectively *versus* 1·7 per cent; $P = 0·005$), but much less frequently undertaken for dysphagia (1·0 and 0·8 per cent *versus* 6·3 per cent; $P < 0·001$).

Changing workload

Fig. 1 shows the number of laparoscopic fundoplications performed each year according to the indication for surgery. Initially, from 1992 to 1998, there was a rapid increase in the number of laparoscopic fundoplications undertaken for gastro-oesophageal reflux, but subsequently there was a slow decline in the number of operations each year for this indication. This decline was offset by an increase in the number of operations performed for repair of a very large hiatus hernia; the proportion of patients undergoing surgery for a very large hiatus hernia reached 50 per cent of the total caseload in 2010. The conversion rate to open surgery declined with experience from 14 per cent in 1992 to approximately 2 per cent in the late 1990s, and to zero for the last 5 years.

Fig. 2 shows the different types of fundoplication. From the late 1990s there was a reduction in the number of Nissen fundoplications, offset by an increase

Table 1 Reasons for reoperation in relation to type of fundoplication at the original surgery

	Nissen ($n = 1209$)	Anterior 180° ($n = 612$)	Anterior 90° ($n = 365$)	Posterior partial ($n = 63$)	P*
Recurrent reflux	20 (1·7)	19 (3·1)	18 (4·9)	1 (2·0)	0·005
Dysphagia	76 (6·3)	6 (1·0)	3 (0·8)	2 (3·0)	< 0·001
Hiatus hernia	38 (3·1)	8 (1·3)	7 (1·9)	1 (2·0)	0·089
Other reason	9 (0·7)	4 (0·7)	2 (0·5)	0 (0)	
Total (all reasons)	143 (11·8)	37 (6·0)	30 (8·2)	4 (6·0)	0·005

Values in parentheses are percentages. *Nissen *versus* anterior 180° *versus* anterior 90° *versus* posterior fundoplication (χ^2 test).

in the number of anterior partial fundoplications. Anterior partial fundoplication is now the commonest procedure performed, entailing more than 80 per cent of the current workload.

Long-term clinical outcomes

Fig. 3 shows the mean VAS scores for heartburn, dysphagia and satisfaction at each year of follow-up for all fundoplication types, across the first 15 years after surgery. All scores were reasonably stable up to 15 years' follow-up. There was a slight rise in heartburn scores as follow-up lengthened, although the extent of the increase was unlikely to be clinically significant. Dysphagia scores were stable and did not improve at late follow-up. Overall satisfaction remained stable and high across the first 15 years.

Fig. 4 shows mean heartburn scores at each year of follow-up for each of the three commonest fundoplication

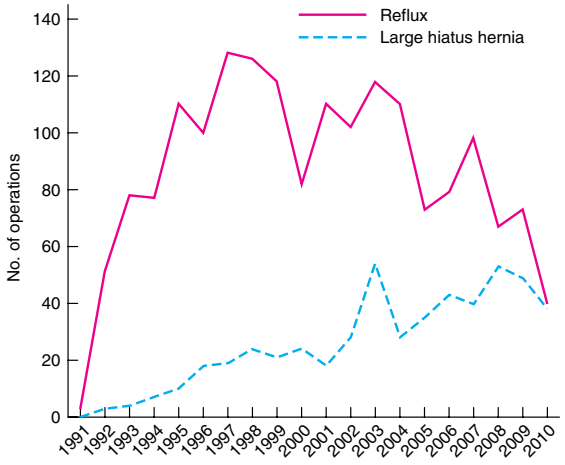


Fig. 1 Number of laparoscopic operations performed for gastro-oesophageal reflux and large hiatus hernia from 1991 to 2010

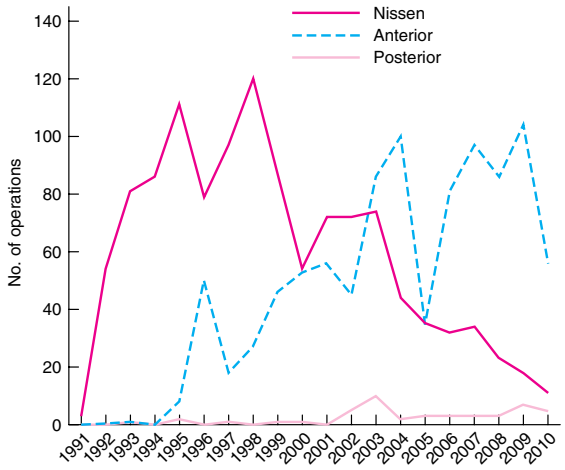


Fig. 2 Number of laparoscopic fundoplications performed each year from 1991 to 2010 by fundoplication subtype: Nissen fundoplication, anterior (90° and 180°) partial fundoplication and posterior partial fundoplication

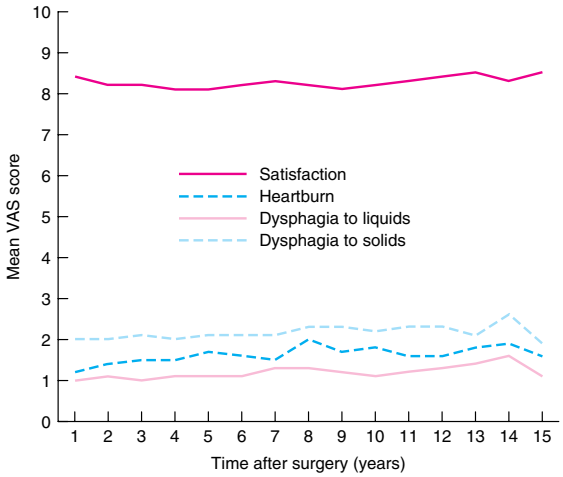


Fig. 3 Mean scores on a visual analogue scale (VAS) from 0 to 10 for heartburn, dysphagia and satisfaction at each year of follow-up for the first 15 years

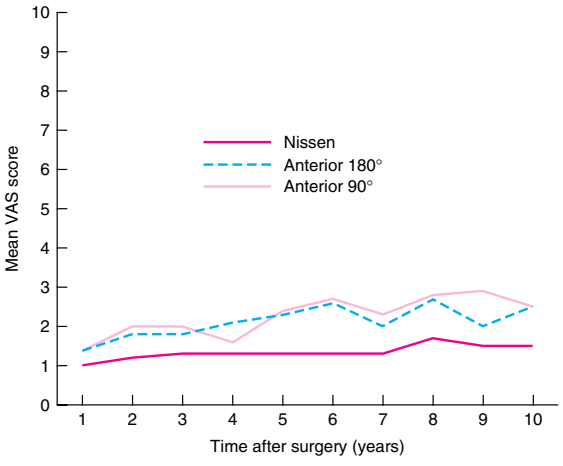


Fig. 4 Mean visual analogue scale (VAS) scores for heartburn after different fundoplication types at each year of follow-up for the first 10 years

types. This analysis was limited to the first 10 years of follow-up because anterior 90° fundoplications were started later in the series, and an insufficient number were followed beyond 10 years. The heartburn scores remained fairly stable across the first 10 years, although there tended to be a gradual increase as follow-up lengthened for all fundoplication types. However, the scores remained low at 10 years' follow-up compared with preoperative symptom scores, suggesting that effective reflux control was achieved in most patients by all fundoplication variants. PPIs were used at 5 years' follow-up by 8·8 per cent after Nissen fundoplication, 23·4 per cent after anterior 180° partial and 26·2 per cent after anterior 90° partial fundoplication ($P < 0·001$). Respective values at 10 years were 19·7, 29·7 and 30·1 per cent ($P = 0·027$).

Fig. 5 summarizes dysphagia scores for solids for each fundoplication type over the first 10 years of follow-up. The dysphagia score for solids after Nissen fundoplication remained stable across the 10 years. Although the scores for anterior 180° and 90° partial fundoplication were initially lower, they increased gradually with time. At 10 years' follow-up scores were identical to those reported following Nissen fundoplication.

The dysphagia scores for liquids followed a similar pattern. They were stable following Nissen fundoplication across the first 10 years of follow-up. Scores were similarly lower after anterior partial fundoplication during the first 5 years of follow-up, but rose to the same level as those following Nissen fundoplication by 10 years.

Satisfaction scores were generally stable for all fundoplication types across the first 10 years of follow-up, with similar scores for Nissen and anterior 180° partial fundoplication at each year of follow-up. Satisfaction scores following anterior 90° partial fundoplication were lower than those for the other fundoplication types at 5–8 years' follow-up, but by 10 years were similar to satisfaction scores for the other fundoplication types.

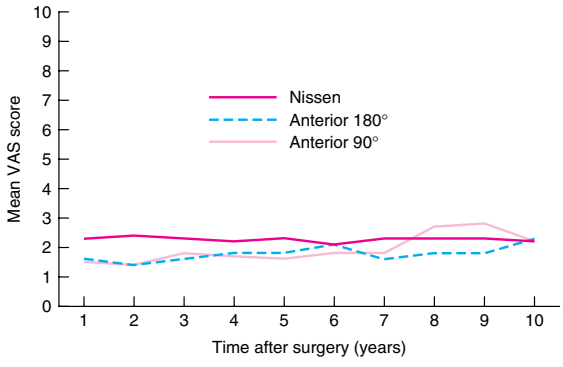


Fig. 5 Mean visual analogue scale (VAS) scores for dysphagia for solid food after different fundoplication types at each year of follow-up for the first 10 years

The overall success rate at 5-year follow-up, determined as the proportion of patients who answered 'yes' to the question addressing the correctness of the original decision to undergo antireflux surgery, was 87·0 per cent after Nissen fundoplication, 89·7 per cent after anterior 180° partial and 88·1 per cent after anterior 90° partial fundoplication ($P = 0·527$). At 10 years' follow-up the success rates were 90·8, 94·1 and 91·8 per cent respectively ($P = 0·573$).

Discussion

Since the introduction of laparoscopic techniques for Nissen fundoplication in 1991[1,2,13], many centres have accumulated large experiences. This, in combination with prospective audit of outcome data, has provided a better understanding of how best to undertake antireflux surgery, facilitating modifications to surgical procedures used for the treatment of gastro-oesophageal reflux. The authors of the present study have evaluated modifications to the original laparoscopic Nissen fundoplication technique in a series of prospective randomized trials[8–11], and have also performed more than 1700 laparoscopic antireflux procedures outside these trials. Evaluation of prospective outcomes from the overall experience has led to changes in practice, and allowed outcomes to be determined across two decades.

Following the introduction of laparoscopic fundoplication, a progressive increase in surgical workload occurred in the authors' institution from 1991 to 1995. From 1992 onwards, all primary antireflux procedures were attempted laparoscopically. The increase in workload after this time appeared to be due to a larger number of referrals, generated by a combination of increased patient demand and redistribution of workload from general surgeons to specialist upper gastrointestinal surgeons. For much of the next 12 years the rate of surgery remained stable, although it peaked in 2003 and declined slightly thereafter.

It is possible that a reduction in the rate of referral for antireflux surgery is now being seen, a pattern that has been reported in Europe and the USA[15,16]. It is also possible that in Australia laparoscopic fundoplication is now transitioning from a subspecialty operation to a more routine procedure, being undertaken by a larger number of surgeons, and that this has led to fewer operations being captured within the authors' database. This view is supported by a recent analysis of Australian population

data, which suggested that the rate of surgery for gastro-oesophageal reflux is still increasing slowly[17]. However, any decline in surgery for reflux in the authors' units has been offset by a steady increase in the number of patients undergoing surgery for large hiatus hernia. These patients now represent 50 per cent of the laparoscopic fundoplication workload. This trend probably reflects the perception that laparoscopic repair can now be achieved safely and reliably, as well as the ageing of the Australian population. The decline since 2005 to a very low rate of conversion to open surgery supports the view that these procedures can be reliably performed laparoscopically.

The surgical technique of fundoplication has evolved over time. Changes were made as data emerged from outcome audits and clinical trials. For instance, when laparoscopic fundoplication was commenced, hiatal repair was undertaken only in patients who had what the operating surgeon considered at that time to be a major hiatus hernia. However, in mid-1994, following a study that demonstrated a fivefold increased risk of further surgery for postoperative hiatus hernia in patients in whom the hiatus had not been repaired, routine hiatal repair was instituted[14]. From 1996 a series of prospective randomized trials evaluated various techniques for laparoscopic anterior partial fundoplication *versus* Nissen fundoplication[9–11]. As the outcomes from these trials emerged and confidence was developed in the long-term efficacy[18], the partial fundoplication technique was used for an increasing proportion of patients undergoing surgery for reflux. Hence, the proportion of Nissen fundoplications declined from nearly 100 per cent to fewer than 20 per cent of all fundoplications over recent years in the present series.

Revisional operations were undertaken in 9·6 per cent of patients in this series. More than half were done in the first 12 months after surgery, and very few more than 5 years after the original fundoplication. Some of the reinterventions, especially those undertaken within the first 12 months, could have been related to early learning curve issues, as well as technical problems such as failure to undertake routine hiatal repair during the first 200 procedures, or the opposite problem of overtightening the oesophageal hiatus during posterior hiatal repair[19]. However, reintervention for either recurrent reflux or persistent dysphagia is probably still inevitable in a proportion of patients, and it is likely that similar reintervention rates will occur elsewhere. The data from this study suggest that reintervention is infrequently required beyond 5 years' follow-up.

The patient-reported clinical scores for heartburn and dysphagia were stable over 15 years' follow-up, and satisfaction remained high at late follow-up. Any deterioration in reflux control over time was fairly minimal, and the data support the proposal that laparoscopic antireflux surgery achieves effective reflux control in most patients at late follow-up. This is supported by the stable satisfaction scores across extended follow-up. Interestingly, the dysphagia scores did not improve over time. The scores after Nissen fundoplication remained stable, and those after anterior partial fundoplication actually increased slightly to equivalence with Nissen fundoplication by 10 years' follow-up. These data do not support the idea that postfundoplication dysphagia improves beyond 12 months. Rather, it suggests that troublesome dysphagia at 12 months might require active reintervention to achieve resolution.

Other outcomes, including heartburn and satisfaction scores, and the overall success rate, were also similar for all fundoplication subtypes at 10 years' follow-up. Both the anterior 90° and 180° partial fundoplication procedures were associated with slightly higher heartburn scores compared with Nissen fundoplication, and there was a slow increase in these scores over time. However, the magnitude of the differences was small, and probably none was clinically important. It should also be noted that the heartburn scores and PPI use do not provide objective evidence of recurrent gastro-oesophageal reflux. Rather the score is a patient-reported score for the symptom of 'heartburn', which relies on how each individual interprets this symptom. Other studies have shown that only 30–35 per cent of PPI use after antireflux surgery is actually for recurrent gastro-oesophageal reflux[20]. Nevertheless, previous studies have demonstrated that the heartburn score does correlate with reflux[8–11], and it provides one way of comparing different procedure types and measuring changes in outcome over time. Furthermore, these data are supported by the higher surgical revision rate for recurrent reflux, and the higher rate of PPI use after anterior partial fundoplication. Although it would be desirable to validate these outcomes with pH monitoring, good compliance with repeated objective outcome measures, such as 24-h pH monitoring, is not feasible for the purpose of this study, and the present clinical results are more indicative of longer-term outcomes.

Overall, the outcomes in the present study are consistent with those reported in previous randomized trials[9–12]. Overall satisfaction following surgery was similar for Nissen and anterior partial fundoplication, and 5 years after surgery there was some trade-off between heartburn control and postoperative dysphagia, with the advantages and disadvantages for these procedures balancing to achieve similar rates of satisfaction. These differences seemed

to disappear by 10 years, and satisfaction rates were approximately 90 per cent for all fundoplication types at late follow-up. These outcomes are consistent with the higher surgical revision rate for dysphagia, and the lower revision rate for recurrent reflux following Nissen fundoplication. Based on these data, anterior 180° partial fundoplication is now offered to patients thought to be at high risk of side-effects following Nissen fundoplication, a choice of anterior 180° or Nissen fundoplication for those deemed to be at a lower risk of side-effects, and an anterior 90° partial fundoplication to more elderly patients undergoing surgery primarily for a very large hiatus hernia.

Acknowledgements

The authors thank Ms Lorelle Smith, Ms Carolyn Lally, Ms Janet Sullivan and Ms Nicky Carney for their assistance with follow-up of patients after laparoscopic fundoplication. Some of the follow-up in this study was supported by Research Project Grants from the National Health and Medical Research Council of Australia (grant numbers 157986 and 375111).

Disclosure: The authors declare no conflict of interest.

References

1 Dallemagne B, Weerts JM, Jehaes C, Markiewicz S, Lombard R. Laparoscopic Nissen fundoplication: preliminary report. *Surg Laparosc Endosc* 1991; **1**: 138–143.
2 Geagea T. Laparoscopic Nissen's fundoplication: preliminary report on ten cases. *Surg Endosc* 1991; **5**: 170–173.
3 Kelly JJ, Watson DI, Chin KF, Devitt PG, Game PA, Jamieson GG. Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. *J Am Coll Surg* 2007; **205**: 570–575.
4 Cowgill SM, Gillman R, Kraemer E, Al-Saadi S, Villadolid D, Rosemurgy A. Ten-year follow up after laparoscopic Nissen fundoplication for gastroesophageal reflux disease. *Am Surg* 2007; **73**: 748–752.
5 Watson DI, Liu JF, Devitt PG, Game PA, Jamieson GG. Outcome of laparoscopic anterior 180-degree partial fundoplication for gastroesophageal reflux disease. *J Gastrointest Surg* 2000; **4**: 486–492.
6 Krysztopik RJ, Jamieson GG, Devitt PG, Watson DI. A further modification of fundoplication. 90 degrees anterior fundoplication. *Surg Endosc* 2002; **16**: 1446–1451.
7 O'Reilly MJ, Mullins SG, Saye WB, Pinto SE, Falkner PT. Laparoscopic posterior partial fundoplication: analysis of 100 consecutive cases. *J Laparoendosc Surg* 1996; **6**: 141–150.
8 Yang H, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG. Randomized trial of division *versus* nondivision of the short gastric vessels during laparoscopic Nissen fundoplication: 10-year outcomes. *Ann Surg* 2008; **247**: 38–42.
9 Ludemann R, Watson DI, Jamieson GG, Game PA, Devitt PG. Five-year follow-up of a randomized clinical trial of laparoscopic total *versus* anterior 180 degrees fundoplication. *Br J Surg* 2005; **92**: 240–243.
10 Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M *et al.*; International Society for Diseases of the Esophagus – Australasian Section. Multicenter, prospective, double-blind, randomized trial of laparoscopic Nissen *vs* anterior 90 degrees partial fundoplication. *Arch Surg* 2004; **139**: 1160–1167.
11 Spence GM, Watson DI, Jamieson GG, Lally CJ, Devitt PG. Single center prospective randomized trial of laparoscopic Nissen *versus* anterior 90 degrees fundoplication. *J Gastrointest Surg* 2006; **10**: 698–705.
12 Hagedorn C, Jonson C, Lonroth H, Ruth M, Thune A, Lundell L. Efficacy of an anterior as compared to a posterior laparoscopic partial fundoplication: results of a randomized controlled clinical trial. *Ann Surg* 2003; **238**: 189–196.
13 Jamieson GG, Watson DI, Britten-Jones R, Mitchell PC, Anvari M. Laparoscopic Nissen fundoplication. *Ann Surg* 1994; **220**: 137–145.
14 Watson DI, Jamieson GG, Devitt PG, Mitchell PC, Game PA. Paraesophageal hiatus hernia: an important complication of laparoscopic Nissen fundoplication. *Br J Surg* 1995; **82**: 521–523.
15 Statens Beredning för Medicinsk Utvärdering (SBU). *Dyspepsi och reflex. En systematisk litteraturöversikt*. *SBU-rapport nr* 185. SBU: Stockholm, 2007.
16 Finks JF, Wei YL, Barmier JD. The rise and fall of antireflux surgery in the United States. *Surg Endosc* 2006; **20**: 1698–1701.
17 Jay AP, Watson DI. Changing work patterns for benign upper gastrointestinal and biliary disease: 1994–2007. *ANZ J Surg* 2010; **80**: 519–525.
18 Chen Z, Thompson SK, Jamieson GG, Devitt PG, Game PA, Watson DI. Anterior 180-degree partial fundoplication: a 16 year experience with 548 patients. *J Am Coll Surg* 2011; **212**: 827–834.
19 Watson DI, Jamieson GG, Mitchell PC, Devitt PG, Britten-Jones R. Stenosis of the esophageal hiatus following laparoscopic fundoplication. *Arch Surg* 1995; **130**: 1014–1016.
20 Wijnhoven BPL, Lally CJ, Kelly JJ, Myers JC, Watson DI. Use of antireflux medication after antireflux surgery. *J Gastrointest Surg* 2008; **12**: 510–517.

3.2 Late outcome following anterior 180 degree partial fundoplication

---

Rice S, Watson DI, Lally CJ, Devitt PG, Game PA & Jamieson GG. Laparoscopic anterior 180-degree partial fundoplication - 5 year results and beyond. *Arch Surg* (2006) **141**:271-275.

This paper reported 5 to 11 year clinical follow-up outcomes for 117 patients who underwent laparoscopic anterior 180 degree partial fundoplication for gastro-oesophageal reflux.

Chen Z, Thompson SK, Jamieson GG, Devitt PG, Game PA, Watson DI. Anterior 180 degree partial fundoplication – a 16 year experience with 548 patients. *J Am Coll Surg* (2011) **212**:827-834.

This paper reported clinical follow-up to 10 years in 548 patients who underwent laparoscopic anterior 180 degree partial fundoplication for gastro-oesophageal reflux.

ORIGINAL ARTICLE

Laparoscopic Anterior 180° Partial Fundoplication

Five-Year Results and Beyond

Sam Rice, BMBS; David I. Watson, MBBS, MD, FRACS; Carolyn J. Lally, RN, RM; Peter G. Devitt, MBBS, MS, FRCS, FRACS; Philip A. Game, MBBS, FRCS, FRACS; Glyn G. Jamieson, MBBS, MS, FRCS, FRACS

Hypothesis: Laparoscopic anterior 180° partial fundoplication provides good long-term relief for symptoms of gastroesophageal reflux disease and is associated with few adverse effects.

Design: Prospectively evaluated case series.

Setting: University teaching hospital.

Patients: The late clinical outcome was determined for all patients who had undergone a laparoscopic anterior 180° partial fundoplication by us between August 1, 1993, and November 30, 1999.

Interventions: Long-term (≥5 years') follow-up after laparoscopic anterior 180° partial fundoplication was obtained using a structured questionnaire.

Main Outcome Measures: Overall satisfaction and the symptoms of heartburn and dysphagia were assessed using analog scales, and the presence or absence of other adverse outcomes was also determined.

Results: One hundred seventeen procedures were performed. The outcome at 5 to 11 years' (mean, 6.4 years') follow-up was determined for 113 patients (97%). Twelve patients (11%) died of unrelated causes during follow-up, and 1 patient underwent esophagectomy. Further surgery was undertaken in 12 patients (11%): 8 for recurrent reflux, 3 for a symptomatic hiatal hernia, and 1 for dysphagia. For 100 patients with clinical outcome data at late follow-up, gastroesophageal reflux symptoms were significantly improved following surgery and were well controlled in 80 patients. The incidence and severity of dysphagia were reduced after surgery. Normal belching was preserved in 91 patients, and almost all patients were able to eat normally. The overall outcome of surgery was rated as satisfactory, with 95 patients reporting that they considered their original decision to undergo surgery correct.

Conclusions: Laparoscopic anterior 180° partial fundoplication is an effective procedure for the surgical treatment of gastroesophageal reflux and is associated with a high rate of patient satisfaction at late follow-up. Compared with Nissen fundoplication, however, it is likely to be associated with a higher risk of recurrent reflux, although this is balanced by a lower rate of adverse effects.

Arch Surg. 2006;141:271-275

Author Affiliations: Department of Surgery, Flinders University, Flinders Medical Centre, Bedford Park (Drs Rice and Watson and Ms Lally), and Department of Surgery, University of Adelaide, Royal Adelaide Hospital, Adelaide (Ms Lally and Drs Devitt, Game, and Jamieson), Australia.

FUNDOPLICATION HAS A WELL-established role in the treatment of gastroesophageal reflux disease. It is well accepted that a Nissen fundoplication performed using an open surgical technique achieves a good long-term outcome for most patients undergoing surgery for gastroesophageal reflux.[1,2] With the development of laparoscopic approaches, most surgeons now perform a laparoscopic Nissen fundoplication procedure. At both short- and long-term follow-up, this approach has been shown to be at least equivalent to the previous open operation.[3-5]

Unfortunately, however, some patients undergoing Nissen fundoplication are troubled by adverse effects, including persistent dysphagia, gas bloat, and the inability to belch.[2] Because of these problems, anterior and posterior partial fundoplication techniques were developed.[6-8] Randomized trials[8-11] have shown that the partial fundoplication techniques are associated with a reduced incidence of adverse effects and with good reflux control at short-term follow-up. In addition, a recent systematic review[12] concluded that the partial fundoplication techniques were associated with a reduced risk of reoperation for problems such as dysphagia. It also stated that long-term follow-up is needed after laparoscopic partial fundoplication, because short-term efficacy does not necessarily translate into long-term effectiveness.[6,12]

Reports of long-term outcomes (≥5 years) are few, often with only moderate follow-up rates.[1,13] Our group previously

reported the outcome for a cohort of patients who underwent a laparoscopic Nissen fundoplication 5 to 8 years earlier.[3] In that study, the outcome was determined for 99% of the study cohort. We also reported 5-year outcomes from 2 randomized trials,[9,14] with similar rates of follow-up. One of those studies compared anterior 180° partial fundoplication with Nissen fundoplication, with the results suggesting advantages for the partial fundoplication procedure at 5 years.[9] Nevertheless, the long-term efficacy of anterior 180° partial fundoplication remains under scrutiny, and it is important to determine and report the long-term outcome. In the present study, we determined the outcome for a larger group of patients who had undergone a laparoscopic anterior 180° partial fundoplication procedure at least 5 years earlier.

METHODS

Since commencing laparoscopic antireflux surgery in 1991, all of our patients undergoing this procedure have been followed up prospectively. Clinical data have been stored in a database, which was used to identify patients who had undergone a laparoscopic anterior 180° partial fundoplication at least 5 years earlier. These patients underwent surgery between August 1, 1993, and November 30, 1999, primarily at the Royal Adelaide Hospital and associated private hospitals in Adelaide, Australia. The operative technique for laparoscopic anterior 180° partial fundoplication has been described in detail previously.[6] It entails laparoscopic hiatal dissection, posterior hiatal repair, and suturing of the anterior wall of the gastric fundus and the right lateral wall of the distal esophagus to the right hiatal pillar and the apex of the esophageal hiatus, to stabilize a length of intra-abdominal esophagus and to cover the anterior aspect of the intra-abdominal esophagus with the gastric fundus.

During the study, all patients who underwent a primary antireflux procedure were treated with a laparoscopic approach to fundoplication, irrespective of any perceived difficulties at preoperative assessment such as obesity, large hiatal hernia, previous upper abdominal surgery, esophageal stricturing, or Barrett esophagus. Esophageal manometry was performed before surgery in all patients. Some patients were selected to undergo an anterior 180° partial fundoplication because they had poor esophageal motility, some underwent the procedure as part of a previously reported randomized trial,[9] and still others specifically selected the procedure. Most patients who did not undergo an anterior 180° partial fundoplication underwent a laparoscopic Nissen procedure. More than 90% of the patients underwent surgery because of troublesome reflux symptoms that were not adequately controlled with standard acid-suppression medication.

Preoperative, operative, and postoperative outcome data for each patient were collected prospectively and stored in a computerized database (FileMaker Pro, Version 5.5; FileMaker, Inc, Santa Clara, Calif). Postoperative clinical follow-up information was obtained by using a standardized questionnaire, which was administered by a research nurse at 3 months and then yearly after surgery. This questionnaire was initially mailed to each patient. If the questionnaire was not returned, it was sent a second time. If the second follow-up attempt failed, further attempts were made to locate the patient so that data could be collected by telephone interview using the same structured questionnaire. A concerted effort was made to obtain follow-up information for every patient who had undergone surgery, in an attempt to achieve complete follow-up.

The presence or absence of heartburn, dysphagia for liquids, and dysphagia for solid food were assessed using 0-to-10 visual analog scales (in which 0 indicates no symptoms; 10, severe symptoms). Overall satisfaction with the outcome of the procedure was also determined using a 0-to-10 visual analog scale (0 indicates totally dissatisfied; 10, totally satisfied). The presence or absence of abdominal bloating and the abilities to belch, to relieve abdominal distention by belching, and to eat a normal diet were determined with yes/no questions. Patients' opinions of whether they thought they had made the correct decision to undergo surgery were also sought.

Details about adverse outcomes, including postoperative complications, hospital readmissions, and surgical revision, were also recorded. Postoperative esophageal manometry, 24-hour ambulatory pH monitoring, and endoscopy were generally performed only in symptomatic patients. For this reason, these data were not formally analyzed in this report. They were, however, taken into consideration when determining whether patients had developed recurrent reflux during follow-up.

Outcome data were analyzed to determine the long-term clinical efficacy of the anterior 180° partial fundoplication procedure, as well as the incidence of adverse outcomes and overall satisfaction with the surgical outcome.

RESULTS

From August 1, 1993, to November 30, 1999, 117 laparoscopic anterior 180° partial fundoplication procedures were performed by us or under our supervision. These patients constituted the study group. During the same period, we performed a laparoscopic Nissen fundoplication in an additional 487 patients.

Of the 117 study group patients, 109 procedures (93%) were completed laparoscopically and 8 (7%) were converted to an open operation. The reasons for conversion were the inability to reduce a large hiatal hernia, dense upper abdominal adhesions, an enlarged fatty liver, and esophageal perforation during esophageal dissection (in 2 patients each).

The long-term outcome (minimum, 5 years' follow-up) was determined for 113 patients (97%), and follow-up for these patients ranged between 5 and 11 years (mean, 6.4 years). Follow-up data were not available for 4 patients who could not be located at the time of the present study. Since undergoing the anterior fundoplication, 12 (11%) of the 113 patients died during follow-up. None of the deaths were linked to the laparoscopic procedure. The causes of death were disseminated carcinoma (5 patients [3 colonic, 2 lung]), myocardial infarction (1 patient), cerebrovascular accident (1 patient), bicycle accident (1 patient), suicide (1 patient), "old age" (2 patients), and complications of an open esophageal mucosectomy procedure for severe dysplasia in Barrett esophagus (1 patient).

One additional patient underwent an esophagectomy for an early-stage (T1) esophageal cancer in Barrett esophagus, which developed 4 years after the anterior partial fundoplication procedure. That patient's original anterior partial fundoplication failed and he underwent an open Nissen fundoplication 1 year later. As of this writing (9 years after the original anterior partial fundoplication and 5 years after the esophagectomy), he is alive and well.

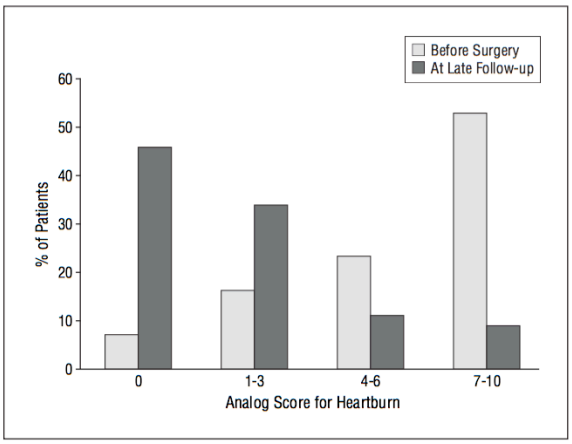


Figure 1. Analog scores for heartburn before surgery and at late follow-up (5-11 years after surgery). Scores ranged from 0 (no heartburn) to 10 (severe heartburn).

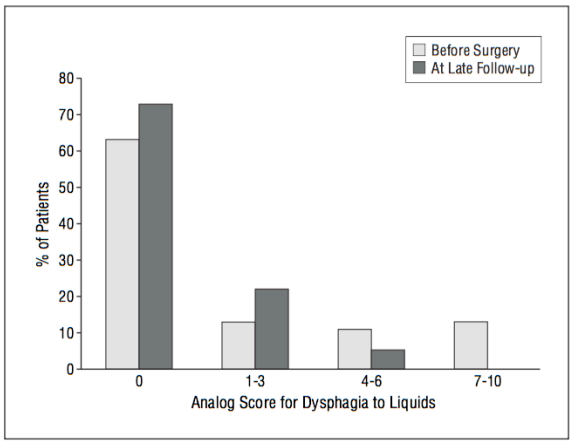


Figure 2. Analog scores for dysphagia to liquids before surgery and at late follow-up (5-11 years after surgery). Scores ranged from 0 (no dysphagia) to 10 (severe dysphagia).

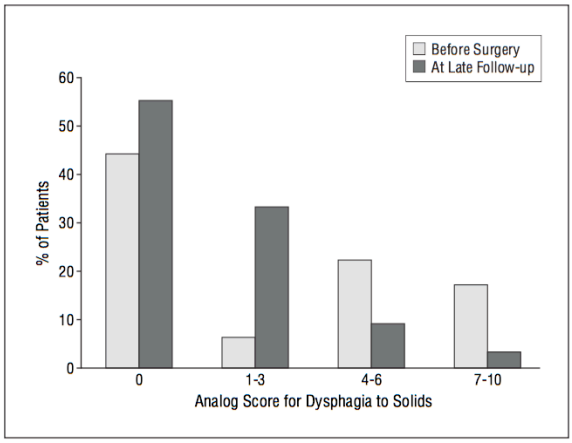


Figure 3. Analog scores for dysphagia to solids before surgery and at late follow-up (5-11 years after surgery). Scores ranged from 0 (no dysphagia) to 10 (severe dysphagia).

Further surgical procedures were undertaken in 12 patients (11%). Two of these were performed immediately using a laparoscopic approach: one at day 3 for an acute para-esophageal hiatal hernia, and the other at day 7 for acute dysphagia. In the latter patient, the esophageal hiatus was widened by removing 1 hiatal repair suture. Eight procedures (7%) were performed for recurrent reflux between 8 months and 6 years (median, 4 years) after the original fundoplication. All procedures entailed conversion to a Nissen fundoplication: 6 were completed using a laparoscopic technique and 2, by an open technique. Two more open-technique reoperations were undertaken for repair of a para-esophageal hiatal hernia at 2 and 3 years after the original anterior partial fundoplication. In addition, early postoperative dysphagia sufficient to require endoscopic dilatation occurred in 2 other patients. One of these patients was successfully treated with a single dilatation procedure, and the other underwent several dilatations before adequate swallowing was achieved.

Clinical outcome data at 5 to 11 years after surgery (late follow-up) were available for 100 patients. This group of patients excludes the 12 patients who died, the patient who underwent esophagectomy, and the 4 patients who were unavailable for follow-up. Gastroesophageal reflux symptoms were well controlled in most patients at late follow-up. When they reported heartburn using the analog scale, 46 patients had a postoperative score of 0 (no heartburn); 34 had a score of 1, 2, or 3 (occasional minor episodes of heartburn); 11 reported a score of 4 to 6 (moderate heartburn symptoms; and 9 gave a score of 7 or higher (significant troublesome heartburn). Most patients reported a moderate-to-severe heartburn score before surgery. **Figure 1** compares the symptom of heartburn before surgery with that at late follow-up. Twenty-two patients were taking acid-suppressing medications (proton pump inhibitors [12 patients], histamine$_2$ receptor antagonists [10 patients]) for "reflux" symptoms at late follow-up. All of these patients reported symptoms of heartburn.

At late postoperative follow-up, patients were less likely to describe dysphagia to liquids and solids compared with preoperative scores (**Figure 2** and **Figure 3**). Overall, fewer patients reported dysphagia after surgery than had before surgery. The overall data demonstrated a reduction in dysphagia after surgery.

At late follow-up, 91 patients were able to belch normally. Occasional epigastric bloating after eating was reported by 52 patients, and 37 of this subgroup (71%) were able to relieve this by belching. Some food types were avoided by 14 patients because of either food intolerance or dysphagia. The mean overall satisfaction score was 8.4 (median score, 9). Forty-five reported a satisfaction score of 10; 35, a score of 7 to 9; 17, a score of 4 to 6; and 3, a score of 3 or less. Ninety-five patients reported that they believed their original decision to undergo surgery was correct.

COMMENT

Since Nissen's[15] original description, the 360° total fundoplication has been the most common surgical procedure used for the treatment of gastroesophageal reflux. Although initially performed using an open abdominal

or thoracic surgical approach, most Nissen fundoplications are now performed laparoscopically. Previous reports[1,13] of long-term outcome following open Nissen fundoplication have confirmed a success rate of approximately 90% at 5 to 10 years after surgery. More recently, longer outcomes following laparoscopic Nissen fundoplication have also been reported.[4,16,17] Our group previously described the 5- to 8-year follow-up outcomes for 176 patients who had undergone a laparoscopic Nissen fundoplication.[3] In that series, clinical outcome data were obtained for 99% of patients. Reflux was well controlled in 87% of patients, and 90% considered the overall outcome to be good or excellent. Similar outcomes have been reported by others,[4,16,17] although follow-up has been less complete in those reports.

It is now widely accepted that the Nissen fundoplication achieves an effective barrier to reflux in most patients at medium to long-term follow-up. Unfortunately, however, the new antireflux barrier is more effective than the lower esophageal sphincter in normal patients, which means that some patients will be troubled by adverse effects following surgery, such as persistent dysphagia, flatulence, gas bloat, and the inability to belch.[14,18] In some of these patients, the adverse effects are sufficiently troublesome to interfere with quality of life, which can result in a poor overall outcome despite the fundoplication having provided effective control of the reflux symptoms.

For this reason, anterior and posterior partial fundoplication variants have been developed with the aim of reducing the incidence of adverse effects while still achieving effective control of gastroesophageal reflux symptoms. Previous randomized trials[8,10,11] comparing a posterior partial fundoplication with a Nissen fundoplication have demonstrated a reduced incidence of gas-related adverse effects such as flatulence and abdominal bloating. However, whether patients who underwent a posterior partial fundoplication experience less dysphagia is less clear from these reports. Only 1 trial[10] showed a reduced incidence of dysphagia, and this was at 4 months' follow-up, with longer follow-up yet to be reported.

Ten years ago, we recognized the potential for an anterior fundoplication to achieve effective reflux control but with fewer adverse effects than either Nissen fundoplication or posterior partial fundoplication. Our group previously described the technique of laparoscopic anterior 180° partial fundoplication and reported short-term outcomes in an uncontrolled case series.[6] We also compared this procedure with a Nissen fundoplication in a prospective randomized trial.[19] Early clinical outcomes have been promising, with anterior partial fundoplication associated with a significantly reduced incidence of both dysphagia and gas-related adverse effects compared with Nissen fundoplication. One valid criticism of those early studies, however, was that only short-term follow-up was reported, and longer-term outcomes were required to prove the effectiveness of anterior 180° partial fundoplication as an antireflux procedure.

Our group recently reported the 5-year outcomes from a randomized trial of anterior 180° partial fundoplication vs Nissen fundoplication.[9] The results of that trial confirmed the efficacy of the anterior 180° partial fundoplication at 5 years and showed a reduced rate of adverse effects and a high rate of patient satisfaction with the partial fundoplication procedure. The present study was undertaken to determine the long-term outcome (minimum follow-up, 5 years) in a larger group of patients who underwent a laparoscopic anterior 180° partial fundoplication. Our results show that the anterior 180° partial fundoplication is an effective procedure. Reflux remained well controlled in approximately 80% of patients at late follow-up, with less than 10% reporting an analog heartburn score of 7 or greater. Twenty-two percent of patients were receiving antisecretory medication at late follow-up in our study, although this rate is similar to that reported in most other late follow-up studies after Nissen fundoplication.[3,20]

Surprisingly, not all patients with recurrent reflux at late follow-up were unhappy with their outcome. Almost all of the patients who underwent surgery in the present series had poorly controlled, troublesome reflux symptoms before surgery, despite using proton pump inhibitors. The symptoms of some of the patients who developed recurrent reflux after surgery, however, were fully controlled by acid-suppression medication, whereas these medications had been ineffective before surgery. Hence, this subgroup of patients with recurrent reflux regarded themselves as having benefited from surgery. Many of these patients rated the overall clinical outcome highly, which probably explains why 95% of patients were highly satisfied with the outcome of the surgery, even though full control of reflux by the operation alone was achieved in only 80%. Overall, it is reasonable to conclude that anterior 180° partial fundoplication achieved a satisfactory rate of overall success at 5 to 11 years' follow-up.

In general, the other clinical outcomes investigated in the present study improved after surgery. Dysphagia was less common and less severe at late follow-up compared with preoperative dysphagia, and most patients were able to belch effectively. Epigastric bloating was less common after surgery, and most patients could eat a normal diet. These findings confirm that anterior 180° partial fundoplication is associated with a low rate of adverse effects after surgery, supporting the contention that there is a trade-off between the risk of recurrent reflux and the risk of adverse effects associated with antireflux procedures. For many patients, such a trade-off is acceptable.

When evaluating the outcome of surgery for gastroesophageal reflux, it is important to consider the completeness of clinical follow-up. In the era of open antireflux surgery, most follow-up studies failed to determine the outcome for more than 20% of their patients.[1,13,21] In general, case series of patients undergoing laparoscopic antireflux surgery have similar rates of follow-up.[4,17] The exceptions are the 99% follow-up rate in our previously reported 5- to 8-year follow-up after laparoscopic Nissen fundoplication,[3] and the 100% and 98% 5-year follow-up rates in 2 of our randomized trials.[9,14] Analysis of data from one of those randomized trials demonstrated that clinical outcomes may appear to be better than they really are if complete or near-complete follow-up is not obtained.[22] Patients who do not respond to initial follow-up attempts are more likely than patients who volunteer for follow-up studies to have a poor outcome. For

this reason, studies without high follow-up rates are at risk of underreporting adverse outcomes. A strength of the present study is that a late clinical outcome was determined for 97% of our patients with evaluable data.

However, the results reported herein should be interpreted with some caution. It is not appropriate to directly compare these results with outcomes for Nissen fundoplication reported elsewhere because some selection bias was involved with these patients that was not in the randomized trials. Nevertheless, the outcomes are at least consistent with the outcome at 5 years in the previously reported randomized controlled trial of anterior 180° partial fundoplication vs Nissen fundoplication.[9] Therefore, the larger patient cohort and longer follow-up in the present study support the contention that laparoscopic anterior 180° partial fundoplication is an appropriate procedure for patients with gastroesophageal reflux.

Our study might also be criticized for not reporting objective outcome data. Patients were not systematically reevaluated with esophageal manometry, pH monitoring, or endoscopy at late follow-up, and we have therefore limited our report to clinical outcomes. Ultimately, however, the measure of success after a surgical procedure is determined by the patient's view of the outcome rather than by the results of various investigations.

We conclude, therefore, that laparoscopic anterior 180° partial fundoplication is an appropriate procedure for patients undergoing surgery for gastroesophageal reflux. Patients offered this procedure should be informed that the procedure is associated with a higher risk of recurrent reflux at late follow-up after surgery than is Nissen fundoplication. However, they should also be made aware that the risk is offset by a lower risk of adverse effects, and for this reason the overall satisfaction with the procedure at late follow-up is high.

Accepted for Publication: May 2, 2005.
Correspondence: David I. Watson, MBBS, MD, FRACS, Department of Surgery, Flinders University, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia (david.watson@flinders.edu.au).
Acknowledgment: We thank Nicky Ascott for invaluable assistance with data collection for this study.

REFERENCES

1. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease: evaluation of primary repair in 100 consecutive patients. *Ann Surg*. 1986;204:9-20.
2. Crookes PF, DeMeester TR. Does Toupet fundoplication out-perform the Nissen procedure as the operation of choice for gastro-esophageal reflux disease? *Dis Esophagus*. 1994;7:265-267.
3. Lafullarde T, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG. Laparoscopic Nissen fundoplication: five-year results and beyond. *Arch Surg*. 2001; 136:180-184.
4. Bammer T, Hinder RA, Klaus A, Klingler PJ. Five- to eight-year outcome of the first laparoscopic Nissen fundoplications. *J Gastrointest Surg*. 2001;5:42-48.
5. Gotley DC, Smithers BM, Rhodes M, Menzies B, Branicki FJ, Nathanson L. Laparoscopic Nissen fundoplication—200 consecutive cases. *Gut*. 1996;38: 487-491.
6. Watson DI, Liu JF, Devitt PG, Game PA, Jamieson GG. Outcome of laparoscopic anterior 180-degree partial fundoplication for gastroesophageal reflux disease. *J Gastrointest Surg*. 2000;4:486-492.
7. Watson A, Jenkinson LR, Ball CS, Barlow AP, Norris TL. A more physiological alternative to total fundoplication for the surgical correction of resistant gastro-oesophageal reflux. *Br J Surg*. 1991;78:1088-1094.
8. Hagedorn C, Lonroth H, Rydberg L, Ruth M, Lundell L. Long-term efficacy of total (Nissen-Rossetti) and posterior partial (Toupet) fundoplication: results of a randomized clinical trial. *J Gastrointest Surg*. 2002;6:540-545.
9. Ludemann R, Watson DI, Jamieson GG, Game PA, Devitt PG. Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180° fundoplication. *Br J Surg*. 2005;92:240-243.
10. Zornig C, Strate U, Fibbe C, Emmermann A, Layer P. Nissen vs Toupet laparoscopic fundoplication. *Surg Endosc*. 2002;16:758-766.
11. Walker SJ, Holt S, Sanderson CJ, Stoddard CJ. Comparison of Nissen total and Lind partial transabdominal fundoplication in the treatment of gastro-oesophageal reflux. *Br J Surg*. 1992;79:410-414.
12. Catarci M, Gentileschi P, Papi C, et al. Evidence-based appraisal of antireflux fundoplication. *Ann Surg*. 2004;239:325-337.
13. Luostarinen M. Nissen fundoplication for reflux esophagitis: long-term clinical and endoscopic results in 109 of 127 consecutive patients. *Ann Surg*. 1993; 217:329-337.
14. O'Boyle CJ, Watson DI, Jamieson GG, Myers JC, Game PA, Devitt PG. Division of short gastric vessels at laparoscopic Nissen fundoplication: a prospective double-blind randomized trial with 5-year follow-up. *Ann Surg*. 2002;235:165-170.
15. Nissen R. Eine einfache operation zur Beeinflussung der Refluxoesophagitis. *Schweiz Med Wochenschr*. 1956;86(suppl 20):590-592.
16. Granderath FA, Kamolz T, Schweiger UM, et al. Long-term results of laparoscopic antireflux surgery. *Surg Endosc*. 2002;16:753-757.
17. Booth MI, Jones L, Stratford J, Dehn TC. Results of laparoscopic Nissen fundoplication at 2-8 years after surgery. *Br J Surg*. 2002;89:476-481.
18. Watson DI, Jamieson GG. Antireflux surgery in the laparoscopic era. *Br J Surg*. 1998;85:1173-1184.
19. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg*. 1999;86:123-130.
20. Lord RV, Kaminski A, Oberg S, et al. Absence of gastroesophageal reflux disease in a majority of patients taking acid suppression medications after Nissen fundoplication. *J Gastrointest Surg*. 2002;6:3-9.
21. Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. *World J Surg*. 1977;1:439-444.
22. Ludemann R, Watson DI, Jamieson GG. Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication. *Am J Surg*. 2003; 186:143-147.

Anterior 180-Degree Partial Fundoplication: A 16-Year Experience with 548 Patients

Zhen Chen, MD, Sarah K Thompson, MD, FRCSC, FRACS, Glyn G Jamieson, MS, FRACS, Peter G Devitt, MS, FRCS, FRACS, Philip A Game, MBBS, FRCS, FRACS, David I Watson, MD, FRACS

BACKGROUND: Previous randomized studies have shown that laparoscopic anterior 180-degree partial fundoplication achieves good control of gastroesophageal reflux, and with fewer side effects compared with Nissen fundoplication. Late clinical outcomes, however, remain uncertain, and outcomes from large series have not been reported.

STUDY DESIGN: From August 1993 to November 2009, we performed 548 laparoscopic anterior 180-degree partial fundoplications. Perioperative data and clinical outcomes were determined prospectively using a structured questionnaire that evaluated heartburn, dysphagia, and satisfaction with clinical outcomes. Early and late clinical outcomes were evaluated in the overall group, and separately for patients with and without a large hiatus hernia.

RESULTS: Five hundred and forty-eight patients (243 men, 305 women) underwent surgery, 380 primarily for gastroesophageal reflux and 168 with a large hiatus hernia. Fourteen patients (2.6%) underwent reoperation within 7 days of their original procedure, and later reoperation was required in 17 (3.1%) patients. Patients undergoing surgery for a large hiatus hernia were more likely to have a postoperative complication develop (13.7% versus 2.1%), more likely to undergo surgical revision in the first postoperative week (6.0% versus 1.1%), and less likely to undergo later revision (0.6% versus 4.2%), compared with patients undergoing surgery predominantly for reflux. Three-month, 1-, 5-, and 10-year follow-up was available for 511, 462, 233, and 89 patients, respectively. Heartburn and dysphagia scores were significantly improved at all postoperative time points compared with preoperative scores ($p < 0.0001$). Overall satisfaction with the outcomes of surgery remained stable across 10 years of follow-up.

CONCLUSIONS: Laparoscopic anterior 180-degree partial fundoplication is an effective and durable alternative to Nissen fundoplication for the surgical treatment of gastroesophageal reflux. (J Am Coll Surg 2011;212:827–834. © 2011 by the American College of Surgeons)

Fundoplication has a well-established role in the treatment of gastroesophageal reflux disease and hiatus hernia, and with the development of laparoscopic approaches, it has become a widely accepted treatment. Many studies report short- and long-term outcomes after laparoscopic Nissen fundoplication, and outcomes are equivalent to the equivalent open procedure.[1-4] However, in some patients, Nissen fundoplication can be followed by troublesome side effects, including dysphagia, gas bloat, and inability to belch.[5,6] To minimize the risk of these problems, anterior and posterior partial fundoplication techniques have been developed.[7,8]

Five- and 10-year[9,10] clinical outcomes from a prospective randomized trial of anterior 180-degree partial versus Nissen fundoplication undertaken in our department suggest that anterior 180-degree partial fundoplication is as effective as the Nissen procedure. However, the outcomes from other randomized trials[11-13] suggest poorer reflux control after anterior partial fundoplication. Baigrie and colleagues compared anterior 180-degree partial with Nissen fundoplication and showed somewhat poorer reflux control, which was offset by fewer side effects.[12] This resulted in equivalent overall patient satisfaction for both procedures. Engstrom and colleagues compared anterior 120-degree partial fundoplication with Nissen fundoplication, and also showed more reflux after the anterior 120-degree partial fundoplication.[11] Khan and colleagues also reported

Disclosure Information: Nothing to disclose.

Received October 12, 2010; Revised December 17, 2010; Accepted December 21, 2010.

From the Department of Surgery, Flinders University, Flinders Medical Centre, Bedford Park (Chen, Watson) and Discipline of Surgery, University of Adelaide, Adelaide (Thompson, Jamieson, Devitt, Game), South Australia, Australia.

Correspondence address: David I Watson, MD, FRACS, Department of Surgery, Flinders University, Room 3D211, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia. email: david.watson@flinders.edu.au

ISSN 1072-7515/11/$36.00
doi:10.1016/j.jamcollsurg.2010.12.051

poorer reflux control after anterior 180-degree partial fundoplication, compared with a posterior partial fundoplication, although again offset by fewer side effects after anterior partial fundoplication.[13] In our department, we coordinated a multicenter trial of anterior 90-degree partial fundoplication versus Nissen fundoplication, and this also showed more reflux symptoms at up to 5 years follow-up after anterior 90-degree fundoplication, offset by fewer side effects.[14] The anterior 90-degree and 120-degree partial fundoplications evaluated in these trials[11,14] were different from the anterior 180-degree partial fundoplication evaluated in our original study, the option we currently favor.

Although many surgeons argue about the relative merits of different fundoplication variants, most agree that long-term efficacy after anterior partial fundoplication has remained uncertain, and no study has reported long-term outcomes in a large cohort of patients for this procedure. Our current study was undertaken to address this issue. In it we evaluated the clinical efficacy of laparoscopic anterior 180-degree fundoplication in a large cohort of patients who underwent surgery during a period of 16 years.

METHODS

All patients who underwent primary laparoscopic anterior 180-degree fundoplication for either gastroesophageal reflux or a large hiatus hernia at the Royal Adelaide Hospital, Flinders Medical Centre and associated private hospitals in Adelaide, South Australia were included in this study. Patients were excluded if their first procedure was a revision operation. Patients were followed prospectively using a standardized prospective approach to data collection. The operative technique for laparoscopic anterior 180-degree partial fundoplication has been described in detail previously.[15] The key steps entailed laparoscopic hiatal dissection, posterior hiatal repair, and suturing of the anterior wall of the gastric fundus to the right lateral wall of the distal esophagus and the right hiatal pillar, with additional sutures between the fundoplication and the anterior aspects of the esophageal hiatus. In many procedures, the medial aspect of the gastric fundus was also sutured to the left side of the esophagus. The procedure creates a flap valve by stabilizing a length of intra-abdominal esophagus, recreating the angle of His, and fully covering the anterior aspect of the intra-abdominal esophagus with the anterior gastric fundus.

Preoperatively, gastroesophageal reflux disease was confirmed by 24-hour pH monitoring or gastroscopy, and esophageal manometry was performed routinely to evaluate esophageal motility. Some patients were selected for anterior 180-degree partial fundoplication because of poor esophageal motility, some underwent the procedure within a previously reported randomized trial,[9,10] and others, after discussion with their surgeons, deliberately chose this procedure. The principal indication for surgery was persistent troublesome reflux symptoms that were not adequately controlled by proton pump inhibitor medication.

Preoperative, operative, and postoperative outcomes data for each patient were collected prospectively and stored in a computerized database (FileMaker Pro; FileMaker Inc). Postoperative clinical follow-up was obtained using a standardized questionnaire that was administered by a research nurse, either by telephone or mail-out, 3 and 12 months after surgery and annually thereafter, using questions and analogue scores that have been described previously.[2,6,9,10]

The presence or absence of heartburn, dysphagia for liquids, and dysphagia for solid food were assessed using 0 to 10 analogue scales (0 = no symptoms to 10 = severe symptoms). Overall satisfaction with the outcomes of the procedure was also determined using a 0 to 10 analogue scale (0 = totally dissatisfied to 10 = satisfied). Presence or absence of abdominal bloating and the abilities to belch, relieve abdominal distention by belching, and eat a normal diet were determined using yes/no questions. Patients were also asked whether or not they thought their original decision to undergo the procedure was correct or not. Details about adverse outcomes, including postoperative complications, hospital readmissions, and surgical revision, were also recorded. Postoperative esophageal manometry, 24-hour ambulatory pH monitoring, and endoscopy were generally performed in symptomatic patients only, and data from these studies were only used to support the contention or otherwise of recurrent reflux in symptomatic individuals.

All patients who underwent a primary laparoscopic anterior 180-degree fundoplication were included in this study. Patients who underwent a subsequent revision operation remained in the overall group for data analysis. Data were analyzed to determine clinical outcomes at baseline, 3 months, 1 year, 5 years, and 10+ years follow-up. Analysis was undertaken for the entire group of patients and for subsets with versus without a large hiatus hernia, defined as a hernia containing $\geq$50% of the stomach at the time of surgery. Statistical evaluation was undertaken using the SPSS statistical package (SPSS, Inc). Mann-Whitney U test was used to compare nonparametric data sets. Fisher's exact test was used to determine significance of 2×2 contingency tables.

RESULTS

From August 1, 1993, to November 30, 2009, 548 laparoscopic anterior 180-degree partial fundoplications were

Table 1. Demographic and Perioperative Factors in Patients Undergoing Laparoscopic Anterior 180-Degree Partial Fundoplication

	All patients	Large hiatus hernia	Reflux (no large hernia)
n (%)	548	168 (30.7)	380 (69.3)
Male-to-female ratio	243:305	56:112	187:193
Age (y), median (range)	56 (10–95)	65 (40–95)	51 (10–81)
Hiatal repair method, n (%)			
Posterior sutures	452 (82.5)	110 (65.5)	342 (90.0)
Anterior sutures	21 (3.8)	0 (0.0)	21 (5.5)
Anterior and posterior sutures	66 (12.0)	58 (34.5)	8 (2.1)
No sutures	9 (2.0)	0 (0.0)	0 (2.4)
Mesh added to sutures, n (%)	20 (3.6)	20 (11.9)	0 (0.0)
Operating time (min), median (range)	60 (20–270)	95 (30–270)	50 (20–181)
Complications, n (%)	30 (5.5)	21 (12.5)	9 (2.4)
Mortality, n (%)	1 (0.2)	1 (0.6)	0 (0.0)

performed. During the same time period, we also performed an additional 1,637 laparoscopic procedures for reflux (ie, Nissen, posterior and anterior 90-degree partial wraps). Two hundred and forty-three (44.3%) of the patients in this study were men and 305 (55.7%) were women. Median age at surgery was 55 years (range 10 to 95 years). One hundred and sixty-eight (30.7%) patients with a large hiatus hernia containing ≥50% of the stomach and 380 (69.3%) without a large hiatus hernia underwent surgery primarily for symptomatic gastroesophageal reflux. Demographic details and perioperative parameters are summarized in Tables 1, 2, and 3. The ratio of male to female patients was similar in the group undergoing surgery primarily for reflux, although the male-to-female ratio was 1:2 for patients with a large hiatus hernia.

Hiatal repair was performed in 539 (98.4%) patients overall, and in 100% of the patients with a large hiatus hernia (Table 1). Across the whole study group, repair was undertaken with posterior hiatal sutures in 82.5%. In the subgroup with a large hiatus hernia, 65.5% underwent repair using posterior hiatal sutures, and in the other 34.5% repair used a combination of anterior and posterior hiatal sutures. In 11.9% of patients with a large hiatus hernia, the sutured repair was reinforced posteriorly with a mesh onlay using either Timesh (GfE Medizintechnik) or Surgisis (Cook Australia). In patients without a large hernia, posterior hiatal repair was undertaken in 90%, anterior hiatal repair in 5.5%, and combination of anterior and posterior sutures in 2.1%.

Five hundred and forty-three (97.4%) procedures were completed laparoscopically, and 14 (2.6%) were converted to an open operation. Reasons for conversion are summarized in Table 2. The likelihood of conversion to open surgery was similar for patients with versus without a large hiatus hernia. Median operating time was 60 minutes for the full cohort, but longer in patients who had a large hiatus hernia (median 95 versus 50 minutes). Postoperative hospital stay ranged from 1 to 21 days (median 2 days).

Postoperative complications occurred in 31 (5.7%) patients (Table 3). Complications were more common in patients with a large hiatus hernia (13.7% versus 2.1%; $p < 0.0001$). Many of the complications were minor and did not delay hospital discharge. These included respiratory infection (n = 10), wound infection (n =1), and urinary retention (n = 2). However, more serious complications that required surgical reintervention or a longer stay in hospital occurred in 18 (3.3%). These included dysphagia requiring early revision (n = 2), intra-abdominal sepsis

Table 2. Conversion to Open Surgery During Laparoscopic Anterior 180-Degree Partial Fundoplication

	All patients (n = 548)		Large hiatus hernia (n = 168)		Reflux (no large hernia) (n = 380)	
Reason for conversion	n	%	n	%	n	%
Dense upper abdominal adhesions	5	0.9	0	0.0	5	1.3
Perforated esophagus	2	0.4	1	0.6	1	0.3
Perforated stomach	1	0.2	0	0.0	1	0.3
Unable to reduce hiatus hernia	5	0.9	5	3.0	0	0.0
Hepatomegaly	1	0.2	0	0.0	1	0.3
Total	14	2.6	6	3.6	8	2.1

Table 3. Complications in Patients Undergoing Laparoscopic Anterior 180-Degree Partial Fundoplication

	All patients (n = 548)		Large hiatus hernia (n = 168)		Reflux (no large hernia) (n = 380)	
Complication	**n**	**%**	**n**	**%**	**n**	**%**
Pneumonia	10	1.8	8	4.8	2	0.5
Severe dysphagia	2	0.4	1	0.6	1	0.3
Wound infection	1	0.2	1	0.6	0	0.0
Intra-abdominal sepsis	2	0.4	1	0.6	1	0.3
Pulmonary embolism	2	0.4	1	0.6	1	0.3
Myocardial infarction	2	0.4	2	1.2	0	0.0
Acute hiatus hernia	10	1.8	8	4.8	2	0.5
Urinary retention	2	0.4	1	0.6	1	0.3
Total complications	31	5.7	23	13.7	8	2.1

(n = 2), pulmonary embolism (n = 2), myocardial infarction (n = 2), and acute hiatus hernia (n = 10). Major complications arose in 5 (1.3%) patients undergoing surgery for reflux versus 13 (7.7%) of patients with a large hiatus hernia. One patient died (perioperative mortality 0.2%) after a perioperative myocardial infarct 13 days after surgery for a large hiatus hernia. This patient was 83 years old at surgery, had presented with intermittent gastric volvulus, and underwent concurrent repair of a giant hiatus hernia (intrathoracic stomach). No patients died after surgery in the group undergoing surgery primarily for gastroesophageal reflux.

Reoperation after fundoplication is summarized in Table 4. Fourteen patients (2.6%) underwent early reoperation (within the first 7 days of the original procedure). Ten (1.8%) of these early reoperations were for repair of an acute paraesophageal hiatal hernia, 2 (0.4%) were for severe dysphagia requiring revision of a tight hiatal repair, and 2 (0.4%) entailed re-exploration for presumed sepsis—in both patients no gastrointestinal perforation or other evidence of sepsis was found. Thirteen of the reoperative procedures were performed laparoscopically and 1 (undertaken for possible sepsis) was converted to open surgery. Early reoperation was significantly less likely in patients undergoing surgery for reflux (1.1% versus 6.0%; p = 0.0018). The difference between the 2 groups was largely due to a difference in the rate of reoperation for an acute hiatus hernia.

In an additional 17 (3.1%) patients, a later reoperation was undertaken between 8 and 123 months (median 25 months) after the original procedure (Table 4). Overall, 31 (5.7%) patients underwent a revision or re-exploration procedure at some stage. Of the 17 late revision procedures, 11 were performed within 3 years of the initial surgery and 6 were after the first 3-year follow-up. Fifteen (91.7%) of the late revision procedures were attempted laparoscopically. Eleven (73.3%) of these were completed laparoscopically and 4 (26.7%) were converted to open surgery. Two patients, both of whom underwent revision before 1996, had a planned open revision procedure. Recurrent gastroesophageal reflux was the most common indication for late surgical revision, accounting for 13 (76.5%) of 17 proce-

Table 4. Reoperation after Laparoscopic Anterior 180-Degree Partial Fundoplication

	All patients (n = 548)		Large hiatus hernia (n = 168)		Reflux (no large hernia) (n = 380)	
Reason for reoperation	**n**	**%**	**n**	**%**	**n**	**%**
Early reoperation						
Dysphagia	2	0.4	1	0.6	1	0.3
Acute hiatus hernia	10	1.8	8	4.8	2	0.5
Intra-abdominal sepsis	2	0.4	1	0.6	1	0.3
Subtotal, early reoperations	14	2.6	10	6.0	4	1.1
Late reoperation						
Paraesophageal hernia	3	0.5	1	0.6	2	0.5
Recurrent reflux	13	2.4	0	0.0	13	3.4
Reversal for bloating	1	0.2	0	0.0	1	0.3
Subtotal, late reoperations	17	3.1	1	0.6	16	4.2
Total, all reoperations	31	5.7	11	6.5	20	5.3

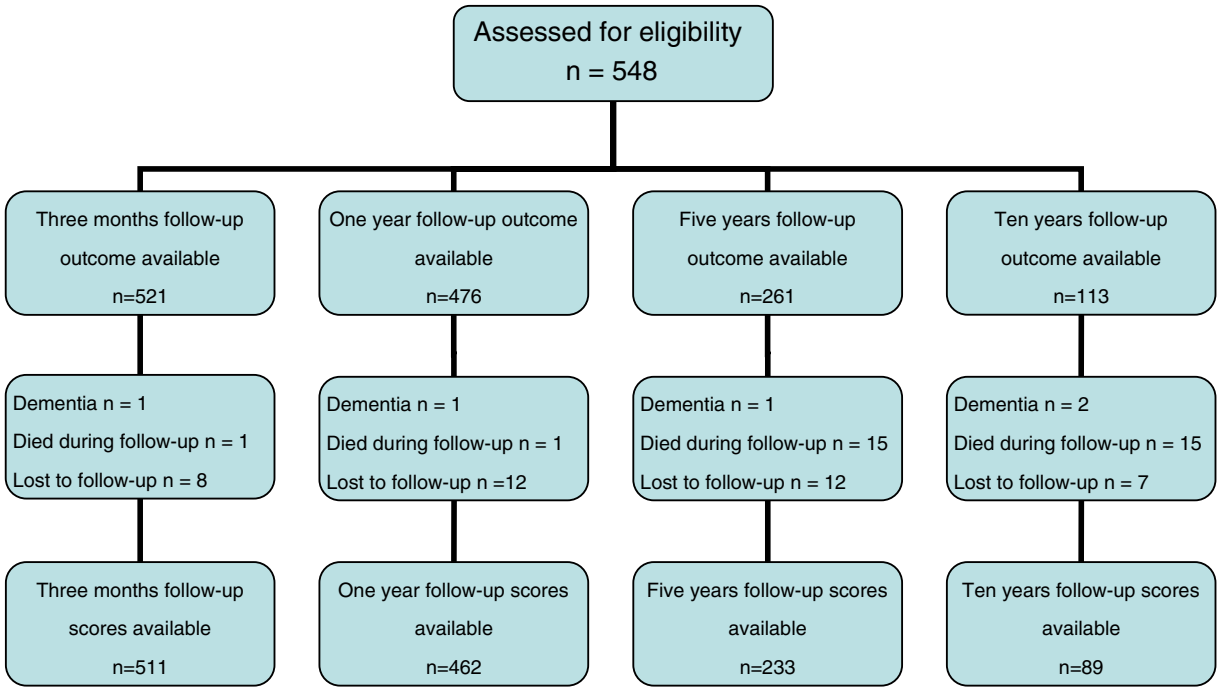


Figure 1. Flow diagram summarizing follow-up.

dures. All patients who underwent revision surgery had objective evidence of recurrent reflux demonstrated by 24-hour pH monitoring. Late revision was more likely after surgery for reflux in patients without a large hiatus hernia (4.2% versus 0.6%; $p = 0.029$), primarily due to the 13 revision operations for recurrent reflux in this group. Of the patients undergoing revision for recurrent reflux, a Nissen fundoplication was performed in 9 and an additional anterior 180-degree partial fundoplication was performed in 4. Heartburn developed at later follow-up in 2 of the 4 patients who underwent a revision anterior 180-degree partial fundoplication, and in 1 patient who was revised to a Nissen fundoplication, severe dysphagia and bloating developed requiring additional revision back to an anterior 180-degree partial fundoplication. When all of the early and late revision procedures are considered together, the risk of additional surgical intervention was not different for patients undergoing surgery for reflux versus large hiatus hernia (5.3% versus 6.5%; $p = 0.551$).

Clinical follow-up data was available at 3 months, 1 year, 5 years, and 10 years for 511, 462, 233, and 89 patients, respectively. Figure 1 summarizes the outcomes and availability of follow-up data at each time point. Follow-up outcomes (patients not lost to follow-up) were available for 98.5% at 3 months, 97.5% at 1 year, 95.4% at 5 years, and 93.8% at 10 years. Eighty-nine patients provided follow-up data 10 to 16 years after their original surgery. Fifteen patients died during follow-up, 14 from causes unrelated to the original fundoplication. Table 5 summarizes the analogue scores for heartburn, dysphagia, and overall satisfaction with the surgical outcomes at various follow-up intervals. At all postoperative follow-up intervals, heartburn and dysphagia scores were improved considerably as compared with preoperative scores. There were no substantial differences in the postoperative dysphagia and satisfaction scores across all follow-up time points. In the overall group, heartburn scores were similar at 3 months and 1 year, but higher at 5 and 10 years as compared with earlier follow-up. Patients with a large hiatus hernia had lower preoperative heartburn scores but higher preoperative dysphagia scores. The analogue symptom and satisfaction scores were similar for patients with and without a large hiatus hernia across all follow-up time points.

At the last recorded follow-up, 455 (89.0%) patients could belch and clear gas from their stomachs. Occasional epigastric bloating symptoms after eating were reported by 148 (29.0%) patients, and 77 of these (52.0%) were able to relieve this problem by belching. Four hundred and fifty-one (88.3%) were able to eat a normal diet, and 60 (11.7%) avoided some food types because of either food intolerance or dysphagia. One hundred and ninety-six patients (38.4%) were using some sort of antisecretory medication at late follow-up, either a proton pump inhibitor or H2 blocker, although medications were used for recurrent re-

Table 5. Mean Analogue Scores for Heartburn, Dysphagia for Liquids and Solids, and Satisfaction with Surgical Outcomes

	All patients	Large hiatus hernia	Reflux (no large hernia)
Heartburn score			
Preoperative	7.2 ± 3.5	6.1 ± 3.9	7.7 ± 3.1
3 mo	1.1 ± 2.2	0.8 ± 1.9	1.0 ± 2.1
1 y	1.4 ± 2.4	1.1 ± 2.3	1.5 ± 2.2
5 y	2.3 ± 2.9	1.8 ± 2.7	2.5 ± 3.0
10+ y	2.5 ± 2.9	2.0 ± 2.8	2.5 ± 2.9
Dysphagia for liquids score			
Preoperative	2.1 ± 3.3	2.4 ± 3.4	1.9 ± 3.2
3 mo	0.8 ± 1.7	0.6 ± 1.7	0.8 ± 1.6
1 y	0.8 ± 1.7	0.7 ± 1.7	0.8 ± 1.8
5 y	0.8 ± 1.8	0.8 ± 1.5	0.9 ± 1.8
10+ y	1.1 ± 1.9	0.5 ± 1.5	1.1 ± 2.1
Dysphagia for solids score			
Preoperative	3.1 ± 3.7	4.0 ± 4.0	2.7 ± 3.6
3 mo	1.7 ± 2.3	1.3 ± 2.1	1.9 ± 2.2
1 y	1.6 ± 2.3	1.3 ± 2.2	1.7 ± 2.3
5 y	1.8 ± 2.4	1.6 ± 2.1	1.9 ± 2.5
10+ y	2.3 ± 2.7	2.8 ± 2.9	2.2 ± 2.0
Satisfaction score			
3 mo	8.7 ± 2.1	9.1 ± 1.7	8.7 ± 2.0
1 y	8.4 ± 2.4	8.8 ± 2.3	8.4 ± 2.3
5 y	8.3 ± 2.4	8.6 ± 2.2	8.1 ± 2.6
10+ y	8.4 ± 2.0	8.8 ± 1.5	8.4 ± 2.2

Values are expressed as mean ± standard deviation.
$p < 0.0001$ for comparisons between all postoperative scores versus preoperative scores, for all parameters. No significant differences ($p > 0.05$) for all comparisons between postoperative scores for dysphagia to liquids and solids, and satisfaction. $p < 0.001$ for comparison between heartburn score for "all patients" at 5 years versus 3 months and 1 year, and for 10+ years versus 3 months and 1 year.

flux symptoms in only one-third of these patients. In general, the decision to recommence antisecretory medication was made on clinical grounds only, and usually by a medical practitioner who was not part of the original surgical team. Four hundred and fifty-nine patients (89.8%) reported that they considered their original decision to undergo surgery to be correct, 41 (8.0%) considered this decision to be incorrect, and 11 (2.2%) were uncertain. Eight-one (91.0%) of the 89 patients who were followed for 10 or more years stated that they considered their original decision to undergo a fundoplication to be correct.

DISCUSSION

The goals of antireflux surgery are long-term control of reflux symptoms and no postfundoplication side effects. Since Nissen's original description,[16] a 360-degree fundoplication has been the most widely used surgical solution, and approximately 90% of patients are reported to have good long-term outcomes.[1-4] Unfortunately, some patients are troubled by unwanted side effects, in particular, dysphagia and gas-related problems,[5,6] and in some of these patients the side effects are troublesome and interfere with quality of life. This can result in poor overall outcomes, despite effective reflux control. Routine use of a partial fundoplication has been advocated as a solution for this problem.[7]

In a series of randomized controlled trials, we have evaluated different techniques for the construction of an anterior partial fundoplication[9,10,14] and, in general, we now prefer the anterior 180-degree partial fundoplication technique for primary antireflux surgery. It appears to provide a reasonable balance between the risks of postfundoplication side effects versus recurrent reflux. Lesser degrees of anterior partial fundoplication, such as 90 degrees or 120 degrees, are probably less effective in terms of long-term reflux control,[11,13,14] although this view has not been tested in a randomized controlled trial. Our current study supports our conclusion that laparoscopic anterior 180-degree partial fundoplication is an effective procedure for treatment of gastroesophageal reflux and large hiatus hernia. We have demonstrated this in a large series of patients and have shown stable results at long-term follow-up. The efficacy of this procedure, defined as the individual patient considering that surgery has been effective, was approximately 90%, which is similar to the overall success rates reported for Nissen fundoplication at 10-year follow-up.[2-4]

There are, however, some differences in outcomes after anterior 180-degree partial fundoplication compared with reported outcomes after Nissen fundoplication. Anterior partial fundoplication appears to be followed by fewer side effects, such as dysphagia and gas bloat, although this is probably offset by more reflux symptoms at later follow-up.[10] The heartburn scores in our current study were similar to those described at 10-year follow-up after anterior 180-degree partial fundoplication in our previously reported randomized trial of anterior 180-degree partial versus Nissen fundoplication (mean analogue heartburn score for the current study 2.5 versus 2.3 in the randomized trial).[10] However, the analogue heartburn scores in our current study were higher than those reported after Nissen fundoplication at 10-year follow-up in 2 previous studies from our departments (mean 2.5 versus 1.7[10] and 1.2[17]).

Interestingly, in our current study, the dysphagia scores at all follow-up intervals were lower than those reported before surgery, and this supports the contention that anterior 180-degree partial fundoplication is a good strategy for

minimizing the risk of postfundoplication dysphagia. Similar outcomes do not occur after Nissen fundoplication.[18] The level of heartburn symptoms, although greater at 5- and 10-year follow-up, was still acceptable at late follow-up, consistent with 90% of patients expressing satisfaction with longer-term surgical outcomes and stable satisfaction scores during 10+ years of follow-up.

Of note, the patient's perspective about the importance of recurrent symptoms might differ from that of surgeons and gastroenterologists. Not all patients with recurrent heartburn are actually unhappy with this symptom. Reflux symptoms in many patients are fully controlled by medications that were not effective before surgery. This might explain the discrepancy between the satisfaction rate of approximately 90% and the use of antisecretory medication in 38% of the patients in our study. In addition, previous studies have shown that most antisecretory medication use after fundoplication is not for recurrent reflux,[19] and for this reason the actual rate of recurrent reflux at late follow-up was probably <15%. Outcomes in our study were relatively stable beyond 5 years of follow-up, and surgical reintervention was uncommon beyond the first 3 years of follow-up. This suggests that if an individual reports good outcomes at later follow-up, there is a low risk of recurrent reflux or other problems arising with additional long-term follow-up.

Randomized trials have directly compared outcomes after anterior partial versus Nissen fundoplication.[9,10,12-14] These also support the conclusion that anterior partial fundoplication provides somewhat less effective long-term reflux control, offset by fewer side effects. There is, however, some inconsistency between our results and some other randomized studies that have reported poorer results after anterior partial fundoplication.[11-14] This might relate to variations in operative technique, with some procedures anchoring the gastric fundus to the anterior esophagus, not the right hiatal pillar,[11,14] and others cover the entire anterior aspect of the intra-abdominal esophagus and anchor the wrap to the right side of the diaphragmatic hiatus.[10,12] Also impacting on outcomes could be the experience of the institution. Our experience of nearly 550 patients undergoing anterior 180-degree partial fundoplication is the largest reported. Fein and colleagues recently reported 10-year outcomes for laparoscopic anterior partial fundoplication, although their series included only 22 of these procedures.[20]

Our current study evaluated clinical outcomes only. Objective evaluation with esophageal manometry, pH monitoring, or endoscopy was not undertaken except in symptomatic patients. Our previous experience has been that a considerable proportion of otherwise well patients will not consent to the use of invasive investigations for follow-up.[21,22] In addition, from the individual patient's perspective, a successful procedure is one that fixes the clinical problem and is not followed by new side effects. Such clinical outcomes can be difficult to measure using objective investigations such as pH monitoring or endoscopy.

When the subgroups of patients with and without a large hiatus hernia are considered separately, our data suggest that the group undergoing repair of a large hiatus hernia contained a higher proportion of women, were older, the operations took longer, and surgery was more likely to be followed by a complication or early reoperation for an acute hiatus hernia. On the other hand, late reoperation, beyond the early postoperative period, was less common in these patients and the conversion rate to open surgery and clinical outcomes scores were similar for patients with versus without a large hernia. Interestingly, the majority of later reoperations were for recurrent gastroesophageal reflux, and these were undertaken exclusively in patients who did not have a large hiatus hernia. The proportion of patients undergoing revision for recurrent reflux in this group was still an acceptably low 3.4%, supporting the contention that laparoscopic anterior 180-degree partial fundoplication is an appropriate surgical treatment for gastroesophageal reflux.

CONCLUSIONS

Overall, the results of our study confirm that in a large patient cohort, laparoscopic anterior 180-degree partial fundoplication is a safe, effective, and durable alternative to Nissen fundoplication for the surgical treatment of gastroesophageal reflux disease and large hiatus hernia. Results after this procedure compare very favorably with other fundoplication types.

Author Contributions

Study conception and design: Chen, Jamieson, Watson
Acquisition of data: Thompson, Jamieson, Devitt, Game, Watson
Analysis and interpretation of data: Chen, Thompson, Jamieson, Watson
Drafting of manuscript: Chen, Watson
Critical revision: Thompson, Jamieson, Devitt, Game

REFERENCES

1. Salminen PT, Hiekkanen HI, Rantala AP, Ovaska JT. Comparison of long-term outcome of laparoscopic and conventional Nissen fundoplication: a prospective randomized study with an 11-year follow-up. Ann Surg 2007;246:201–206.
2. Kelly JJ, Watson DI, Chin KF, et al. Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. J Am Coll Surg 2007; 205:570–575.

3. Dallemagne B, Weerts J, Markiewicz S, et al. Clinical results of laparoscopic fundoplication at ten years after surgery. Surg Endosc 2006;20:159–165.
4. Cowgill SM, Gillman R, Kraemer E, et al. Ten-year follow up after laparoscopic Nissen fundoplication for gastroesophageal reflux disease. Am Surg 2007;73:748–752.
5. Luostarinen M, Isolauri J, Laaitinen J, et al. Fate of Nissen fundoplication after 20 years. A clinical, endoscopical and functional analysis. Gut. 1993;34:1015–1020.
6. O'Boyle CJ, Watson DI, Jamieson GG, et al. Division of short gastric vessels at laparoscopic Nissen fundoplication—a prospective double blind randomized trial with five year follow-up. Ann Surg 2002;235:165–170.
7. Watson A, Jenkinson LR, Ball CS, et al. A more physiological alternative to total fundoplication for the surgical correction of resistant gastroesophageal reflux. Br J Surg 1991;78:1088–1094.
8. Crookes PF, DeMeester TR. Does Toupet fundoplication out-perform the Nissen procedure as the operation of choice for gastro-esophageal reflux disease? Dis Esophagus 1994;7:265–267.
9. Ludemann R, Watson DI, Jamieson GG, et al. Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180° fundoplication. Br J Surg 2005;92:240–243.
10. Cai W, Watson DI, Lally CJ, et al. Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180° partial fundoplication. Br J Surg 2008;95:1501–1505.
11. Engstrom C, Lonroth H, Mardani J, Lundell L. An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. World J Surg 2007;31:1221–1225.
12. Baigrie RJ, Cullis SN, Ndhluni AJ, Cariem A. Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. Br J Surg 2005;92:819–823.
13. Khan M, Smythe A, Globe J, et al. Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease. ANZ J Surg 2010;80:500–505.
14. Nijjar RS, Watson DI, Jamieson GG, et al. Five year follow-up of a multicentre double blind randomized clinical trial of laparoscopic Nissen versus anterior 90° partial fundoplication. Arch Surg 2010;145:552–557.
15. Watson DI, Liu JF, Devitt PG, et al. Outcome of laparoscopic anterior 180° partial fundoplication for gastro-oesophageal reflux disease. J Gastrointest Surg 2000;4:486–492.
16. Nissen R. Eine einfache operation zur Beeinflussung der Reflux oesophagitis. Schweiz Med Wochenschr 1956;86:590–592.
17. Kelly JJ, Watson DI, Chin KF, et al. Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. J Am Coll Surg 2007;205:570–575.
18. de Beaux A, Watson DI, O'Boyle C, Jamieson GG. Role of fundoplication in patient symptomatology after laparoscopic antireflux surgery. Br J Surg 2001;88:1117–1121.
19. Wijnhoven BPL, Lally CJ, Kelly JJ, et al. Use of anti-reflux medication after anti-reflux surgery. J Gastrointest Surg 2008;12:510–517.
20. Fein M, Bueter M, Thalheimer A, et al. Ten-year outcome of laparoscopic antireflux surgery. J Gastrointest Surg 2008;12:1893–1899.
21. Watson DI, Jamieson GG, Pike GK, et al. Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 1999;86:123–130.
22. Ludemann R, Watson DI, Jamieson GG. Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication. Am J Surg 2003;186:143–147.

SECTION 4

RANDOMISED TRIALS FOR ANTIREFLUX SURGERY AND HIATUS HERNIA REPAIR

The randomized controlled trials reported in the papers included in this thesis assessed progressive modifications to surgical procedures for gastro-oesophageal reflux across a period of 22 years (*Watson, Pike et al. 1997, Watson, Jamieson et al. 1999, Watson, Jamieson et al. 2001, O'Boyle, Watson et al. 2002, Ackroyd, Watson et al. 2004, Watson, Jamieson et al. 2004, Ludemann, Watson et al. 2005, Spence, Watson et al. 2006, Woodcock, Watson et al. 2006, Cai, Watson et al. 2008, Wijnhoven, Watson et al. 2008, Yang, Watson et al. 2008, Nijjar, Watson et al. 2010, Chew, Jamieson et al. 2011, Engstrom, Jamieson et al. 2011, Broeders, Roks et al. 2012, Watson, Devitt et al. 2012, Broeders, Broeders et al. 2013, Daud, Thompson et al. 2013, Koetje, Irvine et al. 2015, Watson, Thompson et al. 2015*). Collectively, these trials demonstrate that outcomes can be progressively improved by appropriate technical modifications. The trials also provide an evidence base which underpins surgical practice for antireflux surgery and hiatus hernia repair. From the starting point in 1991 when open Nissen fundoplication with division of the short gastric blood vessels was the standard antireflux procedure, the modifications tested included laparoscopic surgery *(Ackroyd, Watson et al. 2004*), non-division of the short gastric blood vessels (*Watson, Pike et al. 1997*), anterior hiatal repair (*Watson, Jamieson et al. 2001*), anterior 180 degree partial fundoplication (*Watson, Jamieson et al. 1999*), anterior 90 degree partial fundoplication (*Watson, Jamieson et al. 2004, Spence, Watson et al. 2006*), posterior partial fundoplication (*Daud, Thompson et al. 2013*) and mesh repair for very large hiatus hernia (*Watson, Thompson et al. 2015*).

Across the 22 year time span encompassed by these trials, a consistent approach to protocol development and the conduct of the series of trials has been maintained. Participants were blinded, and follow-up was by blinded research nurses who applied standardized clinical assessment questionnaires and clinical outcome scales. These assessments were similar across all of the randomized trials. In all trials, and also for the longer term outcome studies, clinical questionnaires were applied at standardized follow-up time points; 3, 6 and 12 months and then yearly beyond this time point. Consistently high rates of follow-up were achieved across all of the studies, with follow-up rates of 97-100% achieved at follow-up to 5 years (*O'Boyle, Watson et al. 2002, Ludemann, Watson et al. 2005, Wijnhoven, Watson et al. 2008, Nijjar, Watson et al. 2010, Watson, Devitt et al. 2012)*, and 93-95% in the trials in which participants have now been followed for 10 years *(Cai, Watson et al. 2008, Yang, Watson et al. 2008, Chew, Jamieson et al. 2011*). This level of follow-up completeness exceeds that achieved in most other trials addressing surgery for gastro-oesophageal reflux and

adds strength to the data reported. Confirming this Cartaci et al, in 2003, reviewed the publications from randomized trials addressing surgery for gastro-oesophageal reflux, and assessed trial design, reporting standards, completeness of follow-up, and statistical power, and rated the trials conducted in Adelaide as the highest in quality (*Catarci, Gentileschi et al. 2004*).

In addition to the standardised symptom scores used to assess clinical symptom outcomes, global outcome measures were also applied. These were designed to balance the effectiveness of surgical control of reflux symptoms against side effects and other adverse outcomes which can be associated with surgery in some individuals. Surgeons undertaking surgery for gastro-oesophageal reflux might at times focus on antireflux efficacy, and overlook side effects and other unintended consequences, whereas from the individual patient's perspective the success of surgery might be measured by balancing improved symptom control against adverse outcomes. The perspective of the treating surgeon can sometimes be different to the perspective held by individual patients.

In addition to the symptom assessments, short term outcomes in all trials were verified using relevant objective outcome measures. In general the results from these outcome measures were consistent with the clinical outcomes (*Watson, Pike et al. 1997, Watson, Jamieson et al. 1999, Watson, Jamieson et al. 2001, Watson, Jamieson et al. 2004, Broeders, Broeders et al. 2013*). It might, however, be argued that a weakness of the trials conducted is that longer term outcomes were generally not confirmed by objective assessment, with the exception of a late outcome study undertaken within a small sub-cohort from the laparoscopic anterior 180 degree partial vs. Nissen fundoplication trial (*Broeders, Broeders et al. 2013*). In general, it has not been possible for any clinical trial in this area to repeatedly perform objective follow-up with oesophageal manometry and pH studies, and compliance with a protocol requiring regular repeated assessment with investigations such as 24 hour pH monitoring has not been feasible in the Australian context.

In addition, high rates of compliance with follow-up tests such as oesophageal manometry and 24 hour pH monitoring applied at a single time point are generally difficult to achieve, and in the studies reported in this thesis compliance rates for these investigations was approximately 50-60%. These compliance rates were similar to the rates reported in other comparable randomized trials. The situation for trials evaluating

hiatus hernia repair is somewhat different, as objective follow-up requires contrast radiology or endoscopy, not oesophageal manometry and 24 hour pH monitoring. In the trial conducted to assess repair of very large hiatus hernia with vs. without mesh the statistical power calculation was based on objective outcome measures, and a much higher (93%) compliance rate was achieved with endoscopy and/or Barium meal X-ray follow-up (*Watson, Thompson et al. 2015*). These tests are usually perceived to be less unpleasant from the patient's perspective than the oesophageal function tests used in the other trials.

For the reasons discussed above the conclusions drawn from the trials which assessed surgery for gastro-oesophageal reflux are based principally on analysis of the clinical outcome scores. Clinical outcomes are relevant to patients, whereas good objectively measured outcomes (manometry and pH studies) do not always translate directly to a good clinical outcome from the individual patient's perspective. Hence, the clinical outcome assessment used in the various trials is likely to be relevant to actual clinical practice.

4.1 Laparoscopic vs. open Nissen fundoplication

Laparoscopic techniques for Nissen fundoplication were first described in 1991 (*Dallemagne, Weerts et al. 1991, Geagea 1991*), and large single centre case series were first reported in 1994 (*Hinder, Filipi et al. 1994, Jamieson, Watson et al. 1994*), including a large experience from Adelaide (*Jamieson, Watson et al. 1994*). Non-randomised comparisons between open and laparoscopic fundoplication soon followed, but relied on historical controls. These comparisons generally showed that laparoscopic fundoplication required more operating time than the equivalent open surgical procedure (*Peters, Heimbucher et al. 1995, Rattner and Brooks 1995*), that the incidence of postoperative complications was reduced, the length of postoperative hospital stay was shortened by 3–7 days, patients returned to full physical function 6–27 days quicker, and overall hospital costs were reduced. The efficacy of reflux control appeared to be similar between the two approaches.

Ten randomised controlled trials which compare laparoscopic fundoplication with its open surgical equivalent have since been reported (*Franzen T 1996, Laine, Rantala et al. 1997, Heikkinen, Haukipuro et al. 1999, Perttila, Salo et al. 1999, Bais, Bartelsman et al. 2000, Nilsson, Larsson et al. 2000, Luostarinen, Virtanen et al. 2001, Chrysos, Tsiaoussis et al. 2002, Ackroyd, Watson et al. 2004, Nilsson, Wenner*

et al. 2004, Franzen, Anderberg et al. 2005, Draaisma, Buskens et al. 2006, Draaisma, Rijnhart-de Jong et al. 2006, Hakanson, Thor et al. 2007, Salminen, Hiekkanen et al. 2007, Broeders, Rijnhart-de Jong et al. 2009, Salminen, Hurme et al. 2012), including the study included in this thesis (section 2.1) (*Ackroyd, Watson et al. 2004*). Nine of the randomized trials investigated a Nissen fundoplication and one study compared laparoscopic vs. open posterior partial fundoplication. Early outcome reports from these trials described short term follow-up extending up to 12 months, and confirmed advantages for the laparoscopic approach, although less dramatic than the advantages reported in the non-randomised studies. Longer-term outcomes from some of the trials have also been reported (*Franzen, Anderberg et al. 2005, Draaisma, Rijnhart-de Jong et al. 2006, Salminen, Hiekkanen et al. 2007, Broeders, Rijnhart-de Jong et al. 2009, Salminen, Hurme et al. 2012*).

Early reports from smaller trials (*Franzen T 1996, Heikkinen, Haukipuro et al. 1999, Perttila, Salo et al. 1999*) that enrolled 20–42 patients demonstrated equivalent short-term reflux control, shortening of the postoperative stay by about one day (3 vs. 4 median), longer operating times (extended by approximately 30 minutes), and an overall reduction in the incidence of postoperative complications following laparoscopic Nissen fundoplication. The average reduction in the length of the postoperative hospital stay by only one day was an unexpected finding, although more recent experience with enhanced recovery programs following other surgical procedures has confirmed that quicker recovery and shorter hospital stays can be achieved for many open surgical procedures (*Kahokehr, Sammour et al. 2010*). This concept was not well understood in the 1990's during the early days of laparoscopic surgery. In the trials of laparoscopic vs. open fundoplication the shorter than expected hospital stay following open fundoplication suggested that at least some of the proposed benefits of the laparoscopic approach might have also been achieved by a change in management policy to encourage earlier oral intake, avoid nasogastric tubes and encourage earlier discharge from hospital after open surgery.

Chrysos et al reported 12 month follow-up from a trial that enrolled 106 patients *(Chrysos, Tsiaoussis et al. 2002*). Both approaches achieved effective reflux control, post-fundoplication dysphagia was similar, and the laparoscopic approach was followed by less complications, a quicker recovery, and less symptoms of epigastric bloating and distension. Laine et al reported 110 patients randomised to undergo laparoscopic or open Nissen fundoplication (*Laine, Rantala et al. 1997*). Hospital stay

was halved from 6.4 to 3.2 days and patients returned to work quicker (37 vs. 15 days), but operating time was also prolonged by 31 minutes. Subsequent reports from this group described 11 and then 15-year follow-up in 86 patients (*Salminen, Hiekkanen et al. 2007, Salminen, Hurme et al. 2012*). Whilst symptom control and side-effects were similar at late follow-up and 82% of the laparoscopic surgery group were satisfied with the late outcome, the incidence of wrap disruption at endoscopic assessment was significantly higher following open surgery (40% vs. 13%) and there were 10 incisional hernias, all following the open technique. Similar outcomes were reported by Nilsson et al in a smaller trial that followed patients for 5 years (*Nilsson, Wenner et al. 2004*).

Håkanson et al enrolled 192 patients into a trial of laparoscopic vs. open posterior partial fundoplication. Their results were similar to the Nissen fundoplication trials (*Hakanson, Thor et al. 2007*). Early complications were more common after open surgery, the length of the hospital stay was longer (5 vs. 3 days) and return to work was slower (42 vs. 28 days). However, this was offset by a higher incidence of early side-effects and recurrent reflux in the laparoscopic group. At 3 years follow-up, however, there were no outcome differences, satisfaction with the surgery was similar for the two groups, and the need for re-operative surgery of any sort was not influenced by the choice of technique.

A study that created controversy in this area was published by Bais et al. in 2000 (*Bais, Bartelsman et al. 2000*). This multicentre study initially enrolled 103 patients. The early (3 months) results from this trial showed a disadvantage for the laparoscopic approach and the trial was stopped early because of an excess of adverse end-points. The investigators were criticised for terminating the trial prematurely, as it can be argued that the conclusions were misleading. The decision to stop the trial was based primarily on postoperative dysphagia within the first 3 months. Other studies have reported that most patients who undergo a Nissen fundoplication still have some dysphagia 3 months after surgery, but that this dysphagia usually subsides as time passes (*Watson, Pike et al. 1997, Luostarinen, Virtanen et al. 2001)*. A follow-up period of 3 months is too short for the end-point of dysphagia to be adequately assessed. Subsequently Bais et al restarted their trial, boosted the number of patients enrolled to 177, and then reported 5 and 10-year follow-up (*Draaisma, Rijnhart-de Jong et al. 2006, Broeders, Rijnhart-de Jong et al. 2009*). These late follow-up studies confirmed the validity of the initial critique, with no differences in symptoms or

subjective outcome demonstrated at late follow-up. In addition, 24-hour pH monitoring confirmed equivalent reflux control. At 10 years follow-up, there was a higher rate of surgical reintervention following open surgery, mainly due to an excess of incisional hernias, and the authors eventually concluded that the late results from their trial actually supported the application of laparoscopic antireflux surgery!

The outcomes from the trial included in this thesis (section 2.1) (*Ackroyd, Watson et al. 2004*) are consistent with the other published randomized trials of laparoscopic vs. open Nissen fundoplication, and add weight to the evidence supporting the laparoscopy as the preferred access method for antireflux surgery. This trial enrolled 99 patients. Operating time was longer with laparoscopic surgery (82 vs. 46 minutes), but pain was less, recovery quicker and hospital stay shorter (3 vs. 5 days) following laparoscopic Nissen fundoplication. Reflux control 12 months after surgery, measured objectively and by symptom scores, was similar for the two approaches.

Hence, all randomized trials of laparoscopic vs. open surgery for gastro-oesophageal reflux have shown consistent findings, with short and long-term advantages for the laparoscopic over the open approach in terms of reduced overall morbidity and quicker recovery, and no compromise in terms of reflux control. The only trade-off has been slightly longer operating times. Given the overall advantages of the laparoscopic approach over the open approach, laparoscopic techniques have superseded the open approach for most clinical situations.

4.2 Division vs. non-division of the short gastric blood vessels during Nissen fundoplication

Until the 1990s the issue of division vs. non-division of the short gastric vessels was rarely discussed. However, following anecdotal reports of increased problems with postoperative dysphagia following laparoscopic Nissen fundoplication without division of the short gastric vessels, this aspect of surgical technique became a much debated topic in the 1990's (*Dallemagne, Weerts et al. 1996, Hunter, Swanstrom et al. 1996*). Routine division of the short gastric vessels during fundoplication, to achieve full fundal mobilisation and thereby ensure a loose fundoplication, was claimed to be an essential step during laparoscopic (and open) Nissen fundoplication (*DeMeester, Bonavina et al. 1986*). This opinion was popularised by the publication of studies that compared more recent experience with division of the short gastric vessels with earlier historical experience with a Nissen fundoplication performed without dividing these

vessels (*Donahue PE 1977, DeMeester, Bonavina et al. 1986, Dallemagne, Weerts et al. 1996, Hunter, Swanstrom et al. 1996*). However, other uncontrolled studies of Nissen fundoplication, either with or without division of the short gastric vessels confuse the issue further, as good results have been reported whether these vessels were divided or not (*Rossetti and Hell 1977, DeMeester, Bonavina et al. 1986*). Argument has continued about the impact of division of the short gastric blood vessels on the risk of side effects, including dysphagia and bloating, as well as the risk of recurrent reflux. Proponents of vessel division argue that failure to divide the vessels adversely impacts outcomes across all of these areas.

Six randomised trials have been reported that investigate this aspect of technique, including the trial included in this thesis (section 2.2). Luostarinen et al reported the first trial to address division vs. no division of the short gastric vessels, undertaking the trial in patients undergoing open Nissen fundoplication (*Luostarinen, Koskinen et al. 1995, Luostarinen and Isolauri 1999*). Fifty patients were enrolled and a later report described outcomes at median 3-years follow-up (*Luostarinen and Isolauri 1999*). Both procedures healed endoscopic oesophagitis effectively. However, there was a trend towards a higher incidence of disruption of the fundoplication (5 vs. 2) and recurrent reflux symptoms (6 vs. 1) in patients whose short gastric vessels were divided. Further, 9 of 26 patients who underwent vessel division developed a postoperative sliding hiatus hernia, compared to only one of 24 patients whose vessels were kept intact. The likelihood of long-term dysphagia was not influenced by mobilising the gastric fundus in this trial, although bloating symptoms were more common after dividing the short gastric vessels.

The trial included in this thesis (section 2.2) was the first trial to enroll patients undergoing laparoscopic Nissen fundoplication, and it remains the largest trial to address this question (*Watson, Pike et al. 1997*). This trial enrolled 102 patients to have a laparoscopic Nissen fundoplication either with or without division of the short gastric blood vessels. The initial report published in 1997 revealed no difference in overall outcome at initial follow-up of 6 months, and failed to show any advantages for dividing the short gastric vessels during laparoscopic Nissen fundoplication (*Watson, Pike et al. 1997*). Early postoperative dysphagia symptoms were not impacted by dividing the vessels, and the outcome of objective investigations measuring oesophageal motility, oesophageal acidification, and post-surgical anatomy were similar. The subsequent reports of follow-up at 5 and 10 years, confirmed that

both procedures were equally durable in terms of reflux control, and the incidence of postoperative dysphagia remained similar *(O'Boyle, Watson et al. 2002, Yang, Watson et al. 2008*). However, at 5 years follow-up division of the short gastric vessels was associated with more flatulence and bloating symptoms, and greater difficulties with belching. Strengths of this particular trial include blinding of the participants and data collection, and a very high rate of follow-up, with 100% clinical follow-up at 5 years and 95% at 10 years.

Blomqvist et al from Sweden reported the outcome of a similar trial that enrolled 99 patients (*Blomqvist, Dalenback et al. 2000, Mardani, Lundell et al. 2009*). At 12 months and 10 years follow-up, this study also showed that dividing the short gastric vessels did not improve in the outcome. A paper reporting a study which combined this Swedish data set and the Adelaide trial data set is also included in this thesis (section 2.2) (*Engstrom, Jamieson et al. 2011*). The original data sets for both trials were combined to yield a group of 201 individuals who had been randomized 1:1 to division vs. non-division of the short gastric blood vessels. Outcome data was available for 170 patients at mean 11.5 years follow-up. Whilst equivalent reflux control and dysphagia symptoms were demonstrated in this larger group, abdominal bloating symptoms were more common following division of the short gastric vessels during laparoscopic Nissen fundoplication (72% vs. 48%. P=0.002), suggesting that vessel division might actually yield a poorer longer term outcome .

Other randomized trials have been reported by Farah et al, Kosek et al and Chrysos et al (*Chrysos, Tzortzinis et al. 2001, Farah, Grande et al. 2007, Kosek, Wykypiel et al. 2009*). These trials also report equivalent reflux control and postoperative dysphagia, irrespective of whether the short gastric vessels were divided or not. Chrysos et al also identified an increased incidence of bloating symptoms after division of the short gastric vessels (*Chrysos, Tzortzinis et al. 2001*). The belief that dividing the short gastric blood vessels will improve the outcome following laparoscopic Nissen fundoplication is actually not supported by the outcomes from any published randomized controlled trials. Furthermore, dividing the vessels actually increases the complexity of the procedure, and produced a poorer outcome in three of the six trials (including the trial included in this thesis) due to an increase in the incidence of bloating symptoms following vessel division.

4.3 Anterior vs. posterior hiatal repair during Nissen fundoplication

It is well understood that following Nissen fundoplication some patients experience ongoing problems with troublesome dysphagia, and whilst the type of fundoplication might contribute to this problem, the method of hiatal repair used to reduce the size of the oesophageal hiatus might also contribute to dysphagia in some individuals. Dysphagia has been reported following excessive perihiatal scar tissue formation which can lead to narrowing of the diaphragmatic hiatus, and this highlights the potential for post-operative dysphagia to be explained by a problem at the hiatus, despite a technically correct total fundoplication (*Watson, Jamieson et al. 1995*). In addition, post-operative barium swallow X-rays following Nissen fundoplication usually demonstrate anterior displacement of the distal oesophagus, and this angulation might be due at least in part to posterior repair of the hiatus, and this might also contribute to dysphagia. In contrast, anterior repair of the hiatus tends to push the oesophagus posteriorly, thus keeping the axis of the oesophagus straighter. Hence, we hypothesised that anterior hiatal repair might reduce the risk of post-operative dysphagia, and this was tested in the randomised trial of anterior versus posterior hiatal repair during laparoscopic Nissen fundoplication included in this thesis (section 2.3).

This study randomised 103 patients to undergo posterior vs. anterior hiatal repair. Six month outcomes (with 97% follow-up) demonstrated equivalent reflux control for both study groups, although there were more reoperations for recurrent hiatus hernia in patients who had undergone posterior hiatal repair (*Watson, Jamieson et al. 2001, Wijnhoven, Watson et al. 2008, Chew, Jamieson et al. 2011*). This was an unexpected finding, and might be due to a type II statistical error. The 9% incidence of reoperation for hiatal narrowing in the posterior repair group in this randomised trial was much higher than the incidence identified outside this trial, and in the Nissen fundoplication arms of all other randomised trials included in this thesis, reoperation for hiatal narrowing occurred at a rate of approximately 1%.

Ninety six percent of patients were available for follow-up at 5 years follow-up, and 93% at 10 years (*Wijnhoven, Watson et al. 2008, Chew, Jamieson et al. 2011)*. At 5 years the dysphagia rates were similar in both groups, and better control of reflux symptoms was identified in patients who had undergone anterior hiatal repair. At 10 years the outcomes were similar. From this trial it can be concluded that anterior hiatal repair is an appropriate method for hiatal repair, although this option is currently only

infrequently used in clinical practice. The results of this study are specific to the context of laparoscopic Nissen fundoplication, and should not be extrapolated to other scenarios such as hiatal repair during partial fundoplication, or hiatal repair during bariatric surgery. Application within the context of partial fundoplication is currently untested. Further, until this trial is replicated by other investigators, it is probably premature to recommend changing established surgical techniques.

4.4 Partial vs. total fundoplication

Because Nissen fundoplication is associated with an incidence of postoperative dysphagia, gas bloat and other gas-related symptoms such as increased flatulence, partial fundoplications where the fundus is only wrapped part way around the distal oesophagus have been recommended to minimize the risk of these side effects (*Watson, Jenkinson et al. 1991, Krysztopik, Jamieson et al. 2002*). The relative merits of the Nissen fundoplication procedure vs. various partial fundoplication variants have been debated for many years. The introduction of laparoscopic approaches heightened this controversy, and surgeons often hold fixed views about the relative merits of these competing approaches, depending on which country they trained in and where they currently practice.

Most surgeons agree that the Nissen fundoplication produces an over-competent gastro-oesophageal junction, and this is likely to contribute to at least some of the dysphagia and gas bloat problems seen in some patients after Nissen fundoplication. Most surgeons also agree that partial fundoplications are likely to reduce the risk of over-competence, although many consider that this is at the expense of a less durable antireflux repair. Hence, when considering the merits of a partial vs. Nissen fundoplication, the questions that need to be answered include; 1) does construction of a partial fundoplication minimize the risk of side effects after antireflux surgery? and 2) does a partial fundoplication provide a durable antireflux barrier, or is the risk of recurrent reflux too great a trade off to justify its use? The outcomes of many prospective randomised trials of Nissen vs. a partial fundoplication have now been reported, and comparisons can be made of Nissen vs. posterior partial fundoplication, Nissen vs. anterior partial fundoplication, and anterior vs. posterior partial fundoplication.

4.4.1 Nissen versus posterior fundoplication

Eleven randomised trials have compared Nissen vs. posterior partial fundoplication. Some of these trials contribute little to the pool of evidence as they are either small and underpowered, or only reported very short term outcomes (*Thor and Silander 1989, Walker, Holt et al. 1992, Laws, Clements et al. 1997, Chrysos, Tsiaoussis et al. 2003, Koch, Kaindlstorfer et al. 2012*). However, others make significant contributions to the evidence base.

Lundell et al reported the outcomes of the first large trial of Nissen vs. posterior (Toupet) partial fundoplication; 137 patients undergoing open antireflux surgery were enrolled. The early outcomes at 6 months follow-up for the two procedures were similar (*Lundell, Abrahamsson et al. 1991*). At 5 years follow-up reflux control and dysphagia rates were also similar, although flatulence was more common after Nissen fundoplication at 2 and 3 years but not at 4 or 5 years follow-up (*Lundell, Abrahamsson et al. 1996*). Re-operation was more common following Nissen fundoplication, with one patient in the posterior fundoplication group undergoing further surgery for severe gas bloat symptoms and five of the Nissen group undergoing reoperation for postoperative paraoesophageal herniation. A reanalysis of the data from this trial sought to answer the question of whether a tailored approach to antireflux surgery should be applied (*Rydberg, Ruth et al. 1999*). There were no demonstrable disadvantages for the Nissen procedure in those patients who had manometrically abnormal peristalsis before surgery. In 2011, minimum follow-up of 18 years was reported (*Mardani, Lundell et al. 2011*). The outcomes at this very late follow-up were equivalent, with success rates of more than 80% reported for both procedures, and no significant differences in the incidence of side effects at late follow-up, importantly suggesting that the mechanical side effects following Nissen fundoplication progressively improve with very long term follow-up.

Zornig et al reported a trial that enrolled 200 patients to either total fundoplication with division of the short gastric vessels vs. posterior fundoplication (*Zornig, Strate et al. 2002*). One hundred patients had normal preoperative oesophageal motility and 100 had ‘abnormal’ motility. At 4 months follow-up an overall good outcome was obtained in about 90% of patients in each group, and reflux control was equivalent. Short-term dysphagia was less common following posterior partial fundoplication, and no correlation was seen between preoperative oesophageal motility and outcome,

providing no support for the selective application of a partial fundoplication in patients with abnormal preoperative motility. The 2-year follow-up outcomes were similar (*Strate, Emmermann et al. 2008*). Eighty-five percent of each group was satisfied with their clinical outcome, and dysphagia remained significantly more common after Nissen fundoplication (19 vs. 8 patients).

A study from Guérin et al enrolled 140 patients (*Guerin, Betroune et al. 2007*). At 3 years follow-up 118 patients were evaluated and no outcome differences could be identified. Similarly, Booth et al enrolled 127 patients in a trial of Nissen vs. Toupet fundoplication (*Booth, Stratford et al. 2008*), Khan et al enrolled 121 patients in another trial (*Khan, Smythe et al. 2009*), and Shaw et al enrolled 100 (*Shaw, Bornman et al. 2010*). Each of these trials showed no differences in reflux control one year after surgery. Although dysphagia was more common following Nissen fundoplication in Booth et al's trial, there were no differences in the prevalence of side effects in the other trials. Subgroup analysis in Booth et al's and Shaw et al's trial did not reveal any differences between patients with or without poor preoperative oesophageal motility.

If all the data from the Nissen vs. posterior fundoplication trials is combined, the evidence supports the view that side-effects are less common following posterior partial fundoplication, particularly wind-related side-effects such as flatulence and abdominal bloating. However, the hypothesis that dysphagia is less of a problem following a posterior partial fundoplication has only been substantiated in two of the 11 trials. These data suggest that there is still room to improve outcomes for antireflux surgery, as the outcome following posterior partial fundoplication, whilst somewhat better than following Nissen fundoplication, is still less than ideal. In an attempt to further improve outcomes techniques for anterior partial fundoplication were developed and tested in further trials.

4.4.2 Rationale for anterior partial fundoplication

An anterior partial fundoplication in the form of the Dor fundoplication has been used for many decades to prevent reflux in situations where the Nissen fundoplication has been perceived to be associated with an excessive risk of dysphagia. It is commonly used to reduce the risk of reflux following cardiomyotomy for achalasia, and also in patients with very poor oesophageal peristalsis who are considered for antireflux surgery. The situation following cardiomyotomy for achalasia represents arguably the highest risk situation for any antireflux procedure - an aperistaltic oesophagus and

absent lower oesophageal sphincter tone (after surgical division). If anterior partial fundoplication is effective in these individuals, the question that should be asked is; why not use an anterior partial fundoplication for all individuals undergoing surgery for reflux?

There are anatomical considerations which might enable an anterior partial fundoplication to deliver less side effects. The construction of a Nissen fundoplication or posterior partial fundoplication entails placement of the gastric fundus behind the oesophagus, and this lifts the oesophagus anteriorly, angulating the oesophagogastric junction, whereas when the fundus is placed in front of the oesophagus when constructing an anterior partial fundoplication, the oesophagus maintains a straighter line into the stomach. This might make food bolus transit easier following anterior partial fundoplication, compared to the other variants, and account for differences in the risks of dysphagia and other side effects.

Supporting the idea of using an anterior partial fundoplication as a standard procedure for all patients undergoing surgery for gastro-oesophageal reflux, Anthony Watson in 1991 described an open surgical technique for anterior 120 degree partial fundoplication (*Watson, Jenkinson et al. 1991*). In 1995 we set out to simplify this procedure and to develop an improved laparoscopic approach. The full technical details are described in the technique publication included this thesis (section 2.4) (*Gatenby, Bright et al. 2012*). This procedure aimed to stabilize the gastro-oesophageal junction below the diaphragm, maintain an adequate length of intra-abdominal oesophagus, and create a flap valve. To do this, the gastric fundus was placed in front of the intra-abdominal oesophagus and then sutured to the right hiatal pillar and to the right side of the oesophagus. This maintains close apposition between gastric fundus and intra-abdominal oesophagus to create the flap valve which prevents reflux. As the fundus covers the anterior half of the oesophagus, the procedure was designated an “anterior 180 degree partial fundoplication”.

4.4.3 Anterior 180 degree partial fundoplication vs. Nissen fundoplication

Five trials have evaluated Nissen vs. anterior 180 degree partial fundoplication. The first of these is the study included in this thesis (section 2.4). The initial report published in 1999 was the first prospective randomised trial to compare a Nissen fundoplication with any anterior partial fundoplication technique (*Watson, Jamieson et al. 1999*). In this trial both procedures were performed laparoscopically. The study

enrolled 107 patients to undergo either Nissen or anterior partial fundoplication. Ninety eight per cent of patients were available for follow-up at 5 years (*Ludemann, Watson et al. 2005*), and 93% at 10 years (*Cai, Watson et al. 2008*). Whilst no overall outcome differences between the two procedures were demonstrated at 1 and 3 months follow-up, at 6 months patients who underwent anterior 180 degree partial fundoplication were less likely to report dysphagia for solid food, were less likely to be troubled by excessive passage of flatus, were more likely to be able to belch normally, and the overall outcome was better. The outcomes at 5 years were similar to the outcomes reported in the initial report (*Ludemann, Watson et al. 2005*). Reflux control was marginally better after total fundoplication, but this was offset by significantly less dysphagia, less abdominal bloating and better preservation of belching, resulting in a greater proportion of patients reporting a good or excellent overall outcome 5 years after anterior fundoplication (94% vs. 86%). This suggested that the trade-off between reflux vs. side effects was in favour of the partial fundoplication. At 10 years follow-up, however, there were no significant outcome differences between the two procedures, with equivalent control of reflux demonstrated, and no differences for side effects, although the post-surgical satisfaction rate was 98% following anterior vs. 90% 10 yrs after Nissen fundoplication (*Cai, Watson et al. 2008*). This lack of significant differences at late follow-up was similar to the very late follow-up outcomes seen in Lundell and colleagues trial of Nissen vs. posterior partial fundoplication (*Mardani, Lundell et al. 2011*), suggesting gradual improvement in side effects at very late follow-up after Nissen fundoplication.

Baigrie et al. from Cape Town, South Africa, reported 2-year follow-up from a similar study in which 163 patients underwent either a Nissen or anterior 180° partial fundoplication (*Baigrie, Cullis et al. 2005*). This trial demonstrated equivalent control of reflux symptoms and less dysphagia following anterior 180° partial fundoplication, although the incidence of re-operation for recurrent reflux was higher after anterior fundoplication. Cao et al reported 5 year outcomes for a similar trial which enrolled 100 patients (*Cao, Cai et al. 2012*). Reflux control was similar for the 2 procedures, and flatulence was less common after anterior 180° partial fundoplication. Raue et al reported equivalent outcomes at 18 months mean follow-up in a smaller trial which enrolled 64 patients (*Raue, Ordemann et al. 2011*). A very small trial was also reported by Chrysos et al, but contributes little as it only enrolled 12 patients in each arm (*Chrysos, Athanasakis et al. 2004*).

An analysis of merged data sets from the three randomized trials of anterior (180 or 90 degree) partial vs. Nissen fundoplication undertaken in Adelaide (included in this thesis in sections 2.4, 2.5 and 2.6), and Baigrie et al's original data set from the South African trial was subsequently undertaken, and included data from 461 individuals, of whom 270 were enrolled in trials of anterior 180 degree partial vs. Nissen fundoplication (section 2.4) (*Broeders, Roks et al. 2012*). The combined data set showed that the anterior 180 degree partial fundoplication delivered similar reflux control, but with less side effects (dysphagia, inability to belch, flatulence) compared to Nissen fundoplication. Measures of overall satisfaction were similar for the two procedures. Overall the data from the trials of anterior 180 degree vs. Nissen fundoplication confirmed effective reflux control, with less side effects following anterior 180 degree partial fundoplication, and supported the hypothesis that this procedure is effective, but with less side effects, in patients undergoing surgery for gastro-oesophageal reflux.

4.4.4 Anterior 90 degree partial fundoplication vs. Nissen fundoplication

As the trials assessing anterior 180 degree partial fundoplication have shown this to be an effective antireflux procedure, but still associated with some side effects, although occurring less commonly than after Nissen fundoplication, we further modified the anterior 180 degree fundoplication to an anterior 90 degree partial fundoplication, aiming to further reduce the incidence of post-fundoplication side effects. Initial proof of concept work was undertaken using ex vivo and in vivo models and was described in full in earlier publications *(Watson, Mathew et al. 1997, Watson, Mathew et al. 1998, Yau, Watson et al. 2000*) and in the author's earlier Doctor of Medicine thesis (1998). The construction of an anterior 90 degree partial fundoplication is described fully in the papers included in the current thesis (section 2.5) (*Krysztopik, Jamieson et al. 2002*). In brief, the anterior 90 degree partial fundoplication entails posterior hiatal repair, suturing the posterior esophagus to the right hiatal pillar, re-creation of the angle of His by suturing the fundus to the left side of the esophagus, and then construction of a fundoplication which is secured to the apex of the anterior hiatal rim, thereby covering only the left anterolateral intra-abdominal esophagus. Early clinical outcomes following this procedure appeared satisfactory, and 2 further randomized trials were initiated, both comparing the new procedure with a Nissen fundoplication *(Krysztopik, Jamieson et al. 2002, Watson, Jamieson et al. 2004, Spence, Watson et al. 2006*).

The first trial was conducted as a multicentre randomised trial in six cities in Australia and New Zealand, and 15 surgeons contributed patients to this study (section 2.5) (*Watson, Jamieson et al. 2004, Nijjar, Watson et al. 2010*). One hundred and twelve patients were enrolled. To standardise the Nissen fundoplication across all sites and achieve equipoise amongst the surgeons contributing to the trial, short gastric blood vessels were routinely divided when constructing the Nissen fundoplication. The 6 month clinical outcomes (97% follow-up) demonstrated a reduction in dysphagia and gas-related side effects, traded off against a slightly higher rate of recurrent reflux in patients who underwent anterior 90 degree fundoplication. Overall satisfaction with the outcome was higher at 6 months following anterior 90^0 fundoplication (98% vs. 88%). A quality of life analysis using the SF-36 questionnaire identified better quality of life outcomes following anterior 90 degree fundoplication at early follow-up to 6 months, but similar outcomes for the two procedures 1 and 2 years after surgery (*Woodcock, Watson et al. 2006*). At 5 years the outcomes were similar for side effects, although heartburn symptoms were better controlled following Nissen fundoplication (*Nijjar, Watson et al. 2010*). Satisfaction with the overall outcome was similar for both fundoplication types.

Concurrently in Adelaide a parallel single-centre randomised trial of anterior 90 degree partial vs. Nissen fundoplication was conducted, and this trial enrolled 79 patients (section 2.6) (*Spence, Watson et al. 2006*). This trial differed from the first trial in that it was conducted at a single site, and when constructing the Nissen fundoplication short gastric vessels were not divided. Standardisation of procedures was more certain in this trial as only 3 surgeons, working closely together, performed all the surgical procedures. Early follow-up to 12 months was obtained in 99% of patients, and similar outcomes to the first trial were seen - equivalent reflux control for both procedures, and less side effects following anterior 90^0 partial fundoplication. Five year outcome data was available for 95% of individuals, and confirmed less side effects following anterior 90^0 partial fundoplication (bloating - 32.4% vs. 80.0%; diet restrictions 5.4% vs. 21.6%), offset by a higher rate of proton pump inhibitor use (29.7% vs. 8.1%) (*Watson, Devitt et al. 2012*). Reflux symptom control and measures of overall satisfaction were not significantly different for the two procedures at 5 years.

In the recently published analysis of merged data sets from the randomized trials of anterior (180 or 90 degree) partial vs. Nissen fundoplication undertaken in Adelaide and Cape Town (section 2.4) (*Broeders, Roks et al. 2012*), the comparison of anterior 90 degree partial vs. Nissen fundoplication included 192 patients, with outcome data analysed for 172 patients at 5 years follow-up. The improved statistical power of this merged data set reinforced the earlier findings of less side effects and equivalent satisfaction outcomes following anterior 90 degree partial fundoplication, offset by higher heartburn scores in the group who had undergone the anterior 90 degree partial fundoplication. This data suggests a trade-off between reflux control vs. side effects across the spectrum of fundoplication types, and the anterior 90 degree procedure appears to offer an additional reduction in side effect risk at the likely expense of a higher risk of recurrent reflux, compared to anterior 180 degree partial fundoplication.

4.4.5 Anterior 180 degree partial fundoplication vs. posterior partial fundoplication

As the evidence from the randomized trials of Nissen vs. posterior partial and Nissen vs. anterior partial fundoplication demonstrates acceptable reflux control with reduced side effects for both partial fundoplication types, compared to the Nissen procedure, a logical question to ask is; which partial fundoplication technique is best? Comparisons against Nissen fundoplication have shown consistently less side effects following anterior partial fundoplication, whereas the results for the posterior partial vs. Nissen fundoplication trials have been less consistent, with only some trials reporting less dysphagia after posterior partial fundoplication. Randomized trials of anterior vs. posterior partial fundoplication are needed to answer this question.

To date, 3 randomised trials (including the trial in this thesis - section 2.7) (*Hagedorn, Jonson et al. 2003, Khan, Smythe et al. 2010, Daud, Thompson et al. 2013*) have compared variants of anterior vs. posterior partial fundoplication. In the first reported study, Hagedorn et al randomised 95 patients to undergo either a laparoscopic posterior (Toupet) vs. an anterior 120 degree partial fundoplication (*Hagedorn, Jonson et al. 2003, Engstrom, Ruth et al. 2005, Engstrom, Lonroth et al. 2007*). Their results showed better reflux control, but more side effects following posterior partial fundoplication. Unfortunately the clinical and objective outcomes following anterior 120 degree fundoplication in this trial were significantly worse than the outcomes from other randomised and non-randomised studies. pH monitoring was used for objective assessment of outcome, and the average exposure time to acid (pH <4) was

5.6% following anterior 120 degree partial fundoplication in their study, whereas in other studies evaluating anterior partial fundoplication variants this figure has been reported to be between 2.5% and 2.7% *(Watson, Jamieson et al. 1999, Watson, Jamieson et al. 2004*), suggesting that the procedure performed by Hagedorn et al was less effective and therefore different in someway to the procedures performed in other studies. Furthermore, the anterior 120 degree partial fundoplication may not be directly comparable to the anterior 180 degree variant discussed previously, as the anterior 120 degree fundoplication is not stabilized in the same way by anchoring it to the right hiatal pillar, a step which might be important for long term stability of anterior partial fundoplication wraps.

More recently, Khan et al reported 12 months follow-up from a trial which enrolled 103 patients to undergo anterior 180 degree vs. posterior partial fundoplication (*Khan, Smythe et al. 2010*). As the senior author on this paper was trained in Adelaide in the anterior 180 degree partial fundoplication technique, the construction of the anterior fundoplication performed in this particular trial should have been consistent with previous trials undertaken in Adelaide. In this trial, reflux control was also better following posterior partial fundoplication at 12 months follow-up, but offset by significantly more side effects. The data from this trial suggested a trade-off between recurrent reflux vs. side effects, with the overall outcome thought to favour the posterior partial fundoplication. Unfortunately, however, follow-up in this study was limited to 12 months and data was only available for 58% of the original patient cohort at 12 months. As data was not available for 42% of participants the conclusions may not be robust.

The third trial was reported recently and is detailed in this thesis (section 2.7) (*Daud, Thompson et al. 2013*). Unfortunately, it also had some methodological problems as recruitment became difficult across the duration of the trial, and the original recruitment target of 100 was not met. Forty seven patients were enrolled in this trial comparing anterior 180 degree vs. posterior 270 degree (Toupet) partial fundoplication. A high rate of follow-up was achieved, with clinical outcome data available at 12 months for 94% of participants. Outcomes were similar to the two other trials, with heartburn symptoms more likely after anterior 180 degree partial fundoplication, but wind related problems less likely. Global satisfaction measures were similar for the two procedures (85% vs. 86% satisfied at 12 months).

All 3 trials addressing anterior vs. posterior partial fundoplication demonstrated a trade off between side effects vs. reflux control for the different partial fundoplication types. However, unlike the other comparisons assessed in the randomized trials discussed earlier, the quality of the trials addressing the question of anterior vs. posterior partial fundoplication is not as good, with methodological problems seen in all 3 trials; uncertain quality of the anterior 120 degree partial fundoplication in one trial, a low rate of follow-up in the second trial, and incomplete recruitment in the third. Further trials addressing this question are needed to definitively address this comparison.

4.5 Repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh

Reports of good early outcomes for hiatal repair with mesh in randomized trials of mesh vs. sutured repair of large hiatus hernias have encouraged the wider use of mesh for repair for very large hiatus hernias, despite concerns about the risk of mesh erosion and added difficulties if subsequent surgical revision is required. This has polarized surgeons' opinions about the merits or otherwise of repairing hiatus hernia with mesh. The outcomes of randomized trials, including the trial included in this thesis (section 2.8), inform this debate. At follow-up of up to 12 months, the trial included in this thesis identified no major differences for mesh vs. sutured repair of very large hiatus hernias (*Watson, Thompson et al. 2015*). In particular, no significant differences were seen between the 3 repair types for the primary outcome of hernia recurrence assessed by barium meal radiology and endoscopy. The risk of recurrent hernia and other adverse outcomes were similar for all repair types. Secondary clinical symptom outcomes measured by a clinical questionnaire also revealed no major differences, although some statistically significant differences were seen for heartburn scores, nausea and bloating, with the outcomes pointing towards a poorer symptom outcome following repair with absorbable mesh (Surgisis), and a better outcome following repair with non-absorbable mesh (Timesh), mainly due to less bloating issues in this group.

The outcomes from the study in this thesis differed from those reported in the 3 other published randomized trials of mesh vs. sutured repair, which all reported a reduced incidence of hiatus hernia after mesh repair at short term follow-up. Frantzides et al reported that the incidence of hernia recurrence at median 2.5 years follow-up was reduced from 22% to 0% following mesh repair (*Frantzides, Madan et al. 2002*). Oelschlager et al reported a reduction from 24% to 9% at 6 months follow-up

(*Oelschlager, Pellegrini et al. 2006*), and Granderath et al reported a reduction from 26% to 8% at 12 months (*Granderath, Schweiger et al. 2005)*. In Frantzides et al's trial, patients underwent repair using a piece of polytetrafluoroethylene (PTFE) mesh that encircled the oesophagus. The 0% recurrence rate after mesh repair reported in that trial was not replicated in the other trials, and this might indicate that encirclement of the esophagus by the mesh prosthesis achieves a more reliable repair than techniques which don't fully encircle the oesophageal hiatus. However, many surgeons are reluctant to place mesh fully around the esophagus because mesh erosion and hiatal fibrosis have also been reported at longer term follow-up in other studies applying this technique (*Frantzides, Carlson et al. 2010*). Furthermore, as late follow-up from Frantzides et al's trial has not been reported, the risk of mesh erosion and other mesh related problems following repair using PTFE mesh that encircles the oesophagus is unknown.

Oelschlager et al used an absorbable mesh (Surgisis) to reinforce the hiatus posteriorly and around the sides of the esophagus. The early results at 6 months follow-up in this trial appeared promising (*Oelschlager, Pellegrini et al. 2006*). However, a subsequent report of 5 years follow-up revealed very high recurrence rates of 59% vs. 54% in both groups, and failed to support repair with an absorbable mesh (*Oelschlager, Pellegrini et al. 2011*). In this trial Oelschlager et al defined a hiatus hernia to be present if it exceeded 2cm in vertical length.

Granderath et al reported a randomized trial which included patients undergoing laparoscopic Nissen fundoplication for gastro-esophageal reflux with or without a hiatus hernia (*Granderath, Schweiger et al. 2005*); i.e. a different set of patients to those included in the other mesh repair trials, including the trial in this thesis. Hence, this study did not address the issue of how best to repair a large hiatus hernia. The technique did, however, entail posterior hiatal repair with sutures reinforced by an on-lay of a 3x1cm piece of polypropylene mesh, a similar configuration to that used in the trial in this thesis, although the latter used a larger piece of mesh. In Granderath's trial the main outcome measure was the incidence of fundoplication migration into the mediastinum, and this was reduced from 26% to 8% at 12 months by the use of mesh. Longer term data has not been reported.

Strengths of the trial conducted in Australia and reported in this thesis include a very high rate of clinical and objective follow-up, blinding of the patients and the follow-up process, and few exclusions. The trial was run across multiple sites in the public and

private sectors in Adelaide and Melbourne and the results should be generalizable within the Australian context where repair of very large hiatus hernias is usually undertaken by experienced upper gastrointestinal surgeons. Limiting the generalizability of the results, however, was the testing of only one mesh configuration. Nevertheless, this configuration was similar to that used in 2 of the 3 other randomized trials. When establishing the trial protocol there was no enthusiasm in Australia for encircling the esophagus with mesh, as some surgeons had encountered problems with mesh erosion and hiatal fibrosis in patients in whom the technique described by Frantzides et al had been used (*Frantzides, Madan et al. 2002*). Hence, posteriorly placed mesh reinforcement was the most acceptable approach for the surgeons contributing patients to this randomized trial. As that particular mesh configuration was used, this trial is relevant to mesh repair techniques which reinforce the posterior hiatal repair, but not to techniques which fully encircle the oesophagus. The follow-up in this trial is also currently limited to 12 months, and the outcomes from Oelschlager et al's trial suggest that results can change with more extended follow-up (*Oelschlager, Pellegrini et al. 2011*). Longer term follow-up is needed to confirm the initial findings. Nevertheless, the outcomes of this trial revealed no significant differences for the assessed primary outcome; recurrent hiatus hernia, and do not provide support for the routine use of mesh repair of very large hiatus hernias.

4.6 Late outcomes after surgery for gastro-oesophageal reflux and hiatus hernia

The randomized trials included in this thesis, each enrolled approximately 100 individuals, and not all patients undergoing surgery for gastro-oesophageal reflux met the selection criteria or agreed to participate in the trials. For any randomized trial, questions should be asked about the generalisability of the trial outcomes to the broader group of individuals undergoing surgery. The long term outcome studies included in this thesis (section 3.1 and 3.2) were undertaken to evaluate broader experience with laparoscopic surgery for gastro-oesophageal reflux and hiatus hernia, and the outcomes from these studies inform the generalizability of the randomized trials to clinical practice.

The paper reporting 20 year experience with antireflux surgery has demonstrated several changes in practice across 2 decades in the units contributing to the randomized trials, and these changes were consistent with appropriate application of

the evidence from the trials (*Engstrom, Cai et al. 2012*). This study showed several important trends, including:

- A steady rise in the number of operations undertaken for very large hiatus hernia to the point where this now comprises 50% of current surgical workload.
- A decline in the proportion of Nissen fundoplications performed from 100% in the early 1990's to less than 10% by the late 2000's.
- An increase in the use of anterior partial fundoplication variants to more than 90% of the operations performed by the late 2000's.

The change in preferred fundoplication type has been consistent with data from the randomized trials, and growing confidence with the longer term outcomes following these procedures. Better overall outcomes for the anterior partial fundoplication variants at short to medium term follow-up, and equivalent efficacy at late (10 years) follow-up in the randomized trials, has supported this change in clinical practice. The increase in workload associated with very large hiatus hernia also highlights the importance and opportunity for randomized trials addressing how to best repair these hernias.

The late outcome studies included in this thesis confirm good clinical outcomes following both laparoscopic Nissen and anterior 180 degree partial fundoplication at 5 to 10 years follow-up, with approximately 90% of individuals reporting a good clinical outcome at longer term follow-up (*Lafullarde, Watson et al. 2001, Rice, Watson et al. 2006, Kelly, Watson et al. 2007, Chen, Thompson et al. 2011*). These outcomes, in larger unselected cohorts, are consistent with the outcomes reported in the trials, and confirm the generalizability of the trial outcomes, at least within the practices of the surgeons performing laparoscopic antireflux surgery at Flinders Medical Centre, the Royal Adelaide Hospital and associated private hospitals in Adelaide, South Australia. These larger outcome studies also give a level of reassurance that the anterior 180 degree partial fundoplication achieves satisfactory outcomes, and is a reasonable alternative to the Nissen fundoplication, achieving good reflux control, but fewer side effects in most individuals undergoing surgery for gastro-oesophageal reflux.

4.7 Outcome assessment – clinical vs. objective measures

When considering outcomes following surgery for gastro-oesophageal reflux and hiatus hernia several different outcome assessment methods are available, and each of

these has advantages and disadvantages. These measures can be broadly categorised as either objective outcome measures, clinical symptom scores, or quality of life measures. There is currently no generally accepted gold standard for assessment of outcome, and surgeons hold different opinions about which measures should take precedence.

Objective outcome measures include 24 hour pH monitoring, oesophageal manometry, endoscopy and contrast radiology. When considering post-surgical anatomy there is broad agreement that endoscopy and contrast radiology provide accurate methods for the assessment of anatomy and the integrity of hiatus hernia repair. In the randomised trial which evaluated repair of very large hiatus hernia with vs. without mesh (section 2.8), these investigations were used to assess outcome, and reporting in the context of this trial indicated that these measures take precedence over the clinical outcome scores (*Watson et al. 2015*).

However, in the other seven randomised trials, the outcomes assessed were reflux control vs. side effects, not post-surgical anatomy. In these trials pH monitoring, oesophageal manometry, and endoscopy were used 6 months after surgery for objective assessment of outcome. Whilst these measures provide objective outcome data, they are not perfect, and in some circumstances the outcomes of these investigations can be misleading. For example, pH monitoring is used to measure acid exposure (pH<4) in the distal oesophagus, and a cut-off of pH<4 for 4% or less of the study duration is conventionally considered to be “normal” and to exclude gastro-oesophageal reflux. However, in approximately 10% of individuals with gastro-oesophageal reflux this test will be negative. Similarly, endoscopy fails to demonstrate objective evidence of reflux (ulcerative oesophagitis) in up to 50% of people with gastro-oesophageal reflux. Oesophageal manometry, measures lower oesophageal sphincter pressure and relaxation of this sphincter, as well as oesophageal body peristalsis. The outcomes of manometry assessment cannot reliably diagnose gastro-oesophageal reflux, although they contribute to an understanding of post-fundoplication physiology. Lower oesophageal sphincter pressure also fails to correlate with surgical outcomes, and has been shown to be a poor predictor of post-fundoplication outcomes, including control of gastro-oesophageal reflux (*Yang et al. 2007*).

Whilst objective investigations are informative following fundoplication, they only contribute some of the information required to adequately assess outcome within the context of the randomised trials described in this thesis. Objective measures do have the advantage of being able to be applied consistently between different individuals, and the actual outcomes are not subjective. However, a significant disadvantage for objective measures is that compliance when used for follow-following surgery is poor. In the context of randomised trials where complete follow-up is important for valid outcome assessment, reliance on incomplete objective follow-up is a serious problem. In the randomised trials described in this thesis (sections 2.1-2.7) the follow-up rates when using oesophageal manometry and pH monitoring at the single early follow-up time point of 6 months following surgery generally approximated 50-60%, although a bit higher (70-80%) when endoscopy was used. Repeated investigation using invasive objective measures across an extended period of time is not practical, and such follow-up has not been reported from anywhere in the world. The 19.8% compliance rate for manometry and pH assessment at late follow-up in the randomised trial of anterior 180 degree vs. Nissen fundoplication highlights this difficulty (*Broeders et al. 2013*). Nevertheless, the objective investigations used in the trials in this thesis did provide snapshots of early outcomes, and also provide reassurance that the clinical outcomes reported at early and late follow-up are likely to be valid.

Clinical outcomes can be assessed in many ways, and these outcomes can be influenced by the way in which questions are asked, by the person asking the question (surgeon vs independent assessor), and the assessment tool used. When surgeons undertake clinical follow-up, there is a significant risk of reporting bias (*Ludemann et al. 2003*). Follow-up bias can arise when the surgeon is aware of the nature of the procedure performed, and can also occur when patients try to please their surgeon by reporting a better outcome than the outcome they might report to a nurse or other assessor (*Ludemann et al. 2003*). To minimise the risk of bias when assessing clinical outcomes, a several steps were built into the trial protocols; 1) patients were blinded to the procedural variant, 2) outcomes were reported to a research nurse or research assistant who was also blinded, 3) a consistent set of questions and clinical outcome scales were developed and applied in the same way across all randomised trials in this thesis. At early follow-up, these outcome measures were broadly consistent with the objective outcomes at 6 months follow-up.

Clinical outcome assessment using standardised assessment scores has some advantages over objective measures of outcome. These measures can be applied repeatedly to assess outcome across time, as was achieved in the trials. From early follow-up to 10 year outcomes and beyond, compliance with clinical follow-up ranged from 93-100% across all trials in this thesis. This rate of follow-up cannot be achieved when using objective outcome measures. A previous study has shown that apparent follow-up outcomes differ for complete vs incomplete follow-up, with the outcome appearing better when follow-up is incomplete (*Ludemann et al. 2003*). In the context of this thesis, the complete or near complete follow-up in each trial supports the reliability of the trial outcomes, and is a major strength for the studies reported. No other groups have been able to achieve this level of completeness of follow-up in clinical trials assessing surgery for gastro-oesophageal reflux.

A further advantage for clinical assessment scores, is clinical relevance. The clinical assessment scores directly assess specific symptoms that are relevant to patients who have undergone surgery for gastro-oesophageal reflux – reflux symptoms, dysphagia, and flatulence/wind related side effects. Whilst objective outcomes assess outcomes relevant to reflux control, they do not directly inform the assessment of side effects following surgery. Furthermore, the clinical outcome assessment applied in the trials included an assessment of overall outcome; i.e. global satisfaction measures, which determine whether or not individuals undergoing surgery thought their operation was successful or not. Global outcome measures balanced reflux symptom control vs side effect trade-offs.

Quality of life measures can also be used and applied repeatedly. They were applied in the trials described in 2.5, 2.7 and 2.8. General and disease specific quality of life measures are available. Improvements in SF-36 measured quality of life were demonstrated in the trials of Anterior 90 degree partial fundoplication vs. Nissen fundoplication with division of the short gastric blood vessels (section 2.5), and Repair of very large hiatus hernia with sutures vs. absorbable vs. non-absorbable mesh (section 2.8). However, quality of life measures arguably added no additional information beyond that collected by the clinical outcome scores, although these measures provided a level of support to the validity of the clinical outcomes reported for these two trials.

There are strengths and weaknesses for each type of outcome assessment used in the context of surgery for gastro-oesophageal reflux, and it can be argued that a combination of measures, as applied in the randomised trials in this thesis, should yield robust outcomes that are reliable and informative. Clinical measures, however, took priority within the published papers as they appear to better assess the balance of reflux symptom control vs side effects trade-offs, they can be successfully applied repeatedly across extended periods of time, and high rates of compliance with follow-up are achievable. For these reasons, the standardised clinical outcomes are likely to be more indicative of longer-term outcomes, than incomplete follow-up using objective measures at one or 2 specific time points.

4.8 Overview and conclusions

The outcomes of the randomized trials included in this thesis have demonstrated that;

- Laparoscopic Nissen fundoplication is followed by a quicker recovery, a shorter hospital stay, and less respiratory complications than open Nissen fundoplication, but these advantages are offset by increased operating time. The laparoscopic and open approaches achieved equivalent reflux control, and side effects at 12 months follow-up.
- Division of the short gastric blood vessels during laparoscopic Nissen fundoplication is unnecessary. Division of these vessels is followed by a higher prevalence of ‘wind’ related side effects, and does not reduce the risk of dysphagia or improve any clinical outcome following Nissen fundoplication.
- Anterior hiatal repair is an effective technique for hiatal repair and achieves outcomes which are at least as good as following posterior hiatal repair during laparoscopic Nissen fundoplication.
- At 10 years follow-up anterior 180 degree partial fundoplication achieves equivalent reflux symptom control and similar overall satisfaction with the surgical outcome to Nissen fundoplication. At up to 5 years follow-up anterior 180 degree partial fundoplication is followed by less side effects than Nissen fundoplication, but side effect outcomes are similar at 10 years.
- Anterior 90 degree partial fundoplication achieves adequate reflux symptom control, and equivalent overall satisfaction with the surgical outcome compared to Nissen fundoplication at follow-up to 5 years. However, reflux symptoms are more common after anterior 90 degree partial fundoplication at up to 5 years follow-up, although side-effects are less frequent.

- At 12 months follow-up overall satisfaction with the surgical outcome is similar for anterior 180 degree partial fundoplication and posterior partial fundoplication. However, anterior 180 degree partial fundoplication is less effective for reflux symptom control, but side effects are significantly more frequent following posterior partial fundoplication.
- Posterior reinforcement of the hiatal repair with absorbable or non-absorbable mesh during laparoscopic repair of very large hiatus hernia does not reduce the risk of early (6 months) hernia recurrence. Symptom outcomes are similar at 12 months follow-up.

These outcomes are broadly consistent with outcomes reported from the other randomized trials which evaluated similar questions. When considering the evidence available from all of the reported trials, as well as the trials included in this thesis, it is reasonable to conclude that the laparoscopic approach is the preferred method of surgical access for antireflux surgery. The development of laparoscopic approaches has made surgery a more attractive option for patients with gastro-oesophageal reflux disease and hiatus hernia.

The randomized trials of division vs. non-division of the short gastric blood vessels during Nissen fundoplication have produced consistent results, with no trial supporting routine division of these vessels during Nissen fundoplication. These trials provide strong evidence that routine division of these vessels is not necessary. Furthermore, division of the short gastric vessels actually increased the likelihood of bloating side-effects in 3 of these randomized trials, further reinforcing the conclusion that division of these vessels is unnecessary.

Evidence from trials of posterior partial vs. Nissen fundoplication demonstrate advantages for the posterior partial fundoplication technique, in particular reduced gas-related side-effects, and possibly reduced post-fundoplication dysphagia. Similarly, the anterior partial vs. Nissen fundoplication trials also demonstrate reduced post-fundoplication dysphagia and less side-effects after anterior partial fundoplication. Better reflux control is likely after anterior 180 degree partial fundoplication, rather than anterior 90 degree fundoplication, although both variants achieve high rates of satisfaction in patients undergoing antireflux surgery. The trials which directly compared anterior vs. posterior partial fundoplication showed better reflux control, but more side effects after posterior partial fundoplication, although the

quality of these trials has not been as good as the trials using Nissen fundoplication as the comparator. Hence, these outcomes are probably less robust, and further trials are needed to adequately address the question of anterior vs. posterior partial fundoplication.

When all of the partial (anterior and posterior) vs. Nissen fundoplication trials are reviewed together, the evidence suggests that all fundoplication variants achieve similar (high) rates of satisfaction, but with a progressive trade-off between reflux control vs. side effects across the spectrum of fundoplication types from Nissen fundoplication to posterior partial to anterior 180 degree and then to anterior 90 degree partial fundoplication. As different individuals might prioritise the risk of adverse outcomes such as recurrent reflux vs. side effects differently, the relative risk of these outcomes, and the risk of trade-offs, can be discussed with individual patients before surgery. It is probably feasible to tailor the fundoplication type to individual patient expectations by choosing a procedure that minimizes the risk of the adverse outcomes that are of particular concern to each individual undergoing surgery.

The evidence from the various mesh trials which have evaluated techniques for repair of very large hiatus hernia is more mixed, with the trial included in this thesis identifying different short term outcomes to those reported in the other 3 trials. Some of these outcome differences might be accounted for by differences in mesh configuration and mesh types. The use of a configuration that encircles the oesophageal hiatus, might reduce the risk of hernia recurrence after repair of hiatus hernia, but the perceived risk of mesh erosion associated with this technique has meant that few surgeons, if any, in the Australian setting are willing to encircle the oesophagus with mesh. The results of the Adelaide trial are more consistent with the absorbable mesh trial reported by Oelschlager et al which identified no differences at later follow-up *(Oelschlager, Pellegrini et al. 2011*). The lack of consistency in outcomes between the various trials suggests the need for more trials in this area, as well as longer follow-up from 3 of the 4 currently reported trials.

The randomized trials in this thesis represent a significant contribution to the evidence base underpinning surgery for gastro-oesophageal reflux and hiatus hernia, and they are one of the largest single centre contributions to this body of evidence. The quality of these trials is high, with very high rates of follow-up achieved in all trials across a period of more than two decades, adding to the reliability of the data that underpin the

conclusions drawn from these trials. Whilst some trial outcomes were not unexpected; e.g. partial fundoplications are followed by less side effects, other outcomes were different to what was expected before the trials were established; e.g. short gastric vessel division is followed by a poorer outcome, and mesh repair of hiatus hernia does not impact hiatus hernia recurrence. This highlights the need to strengthen the surgical evidence base from outcomes of low quality uncontrolled case series and expert opinion, to higher level evidence from randomized controlled trials. More randomized trials will help surgeons refine other aspects of surgical technique for antireflux and hiatus hernia surgery, and similar approaches to the assessment of surgical technique should also benefit other areas of surgical practice.

SECTION 5

BIBLIOGRAPHY

References

Ackroyd, R., D. I. Watson and P. A. Game (1999). Fizzy drinks following laparoscopic Nissen fundoplication: a cautionary tale of explosive consequences. *Aust N Z J Surg* **69**: 887-888.

Ackroyd, R., D. I. Watson, A. W. Majeed, G. Troy, P. J. Treacy and C. J. Stoddard (2004). Randomized clinical trial of laparoscopic versus open fundoplication for gastro-oesophageal reflux disease. *Br J Surg* **91**: 975-982.

Aly, A., J. Munt, G. G. Jamieson, R. Ludemann, P. G. Devitt and D. I. Watson (2005). Laparoscopic repair of large hiatal hernias. *Br J Surg* **92**: 648-653.

Anvari, M., C. Allen, J. Marshall, D. Armstrong, R. Goeree, W. Ungar and C. Goldsmith (2006). A randomized controlled trial of laparoscopic nissen fundoplication versus proton pump inhibitors for treatment of patients with chronic gastroesophageal reflux disease: One-year follow-up. *Surg Innov* **13**: 238-249.

Anvari, M., C. Allen, J. Marshall, D. Armstrong, R. Goeree, W. Ungar and C. Goldsmith (2011). A randomized controlled trial of laparoscopic Nissen fundoplication versus proton pump inhibitors for the treatment of patients with chronic gastroesophageal reflux disease (GERD): 3-year outcomes. *Surg Endosc* **25**: 2547-2554.

Attwood, S. E., L. Lundell, J. G. Hatlebakk, S. Eklund, O. Junghard, J. P. Galmiche, C. Ell, R. Fiocca and T. Lind (2008). Medical or surgical management of GERD patients with Barrett's esophagus: the LOTUS trial 3-year experience. *J Gastrointest Surg* **12**: 1646-1654.

Aye, R. W., L. D. Hill, S. J. Kraemer and P. Snopkowski (1994). Early results with the laparoscopic Hill repair. *Am J Surg* **167**: 542-546.

Baigrie, R. J., S. N. Cullis, A. J. Ndhluni and A. Cariem (2005). Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. *Br J Surg* **92**: 819-823.

Bais, J. E., J. F. Bartelsman, H. J. Bonjer, M. A. Cuesta, P. M. Go, E. C. Klinkenberg-Knol, J. J. van Lanschot, J. H. Nadorp, A. J. Smout, Y. van der Graaf and H. G. Gooszen (2000). Laparoscopic or conventional Nissen fundoplication for gastro-oesophageal reflux disease: randomised clinical trial. The Netherlands Antireflux Surgery Study Group. *Lancet* **355**: 170-174.

Bate, C. M., P. W. Keeling, C. O'Morain, S. P. Wilkinson, D. N. Foster, R. A. Mountford, J. M. Temperley, R. F. Harvey, D. G. Thompson, M. Davis and et al. (1990). Comparison of omeprazole and cimetidine in reflux oesophagitis: symptomatic, endoscopic, and histological evaluations. *Gut* **31**: 968-972.

Behar, J., D. G. Sheahan, P. Biancani, H. M. Spiro and E. H. Storer (1975). Medical and surgical management of reflux esophagitis. A 38-month report of a prospective clinical trial. *N Engl J Med* **293**: 263-268.

Belsey, R. (1977). Mark IV repair of hiatal hernia by the transthoracic approach. *World J Surg* **1**: 475-481.

Blomqvist, A., J. Dalenback, C. Hagedorn, H. Lonroth, A. Hyltander and L. Lundell (2000). Impact of complete gastric fundus mobilization on outcome after laparoscopic total fundoplication. *J Gastrointest Surg* **4**: 493-500.

Booth, M. I., J. Stratford, L. Jones and T. C. Dehn (2008). Randomized clinical trial of laparoscopic total (Nissen) versus posterior partial (Toupet) fundoplication for gastro-oesophageal reflux disease based on preoperative oesophageal manometry. *Br J Surg* **95**: 57-63.

Broeders, J. A., E. A. Broeders, D. I. Watson, P. G. Devitt, R. H. Holloway and G. G. Jamieson (2013). Objective outcomes 14 years after laparoscopic anterior 180-degree partial versus nissen fundoplication: results from a randomized trial. *Ann Surg* **258**: 233-239.

Broeders, J. A., H. G. Rijnhart-de Jong, W. A. Draaisma, A. J. Bredenoord, A. J. Smout and H. G. Gooszen (2009). Ten-year outcome of laparoscopic and conventional nissen fundoplication: randomized clinical trial. *Ann Surg* **250**: 698-706.

Broeders, J. A., D. J. Roks, G. G. Jamieson, P. G. Devitt, R. J. Baigrie and D. I. Watson (2012). Five-year outcome after laparoscopic anterior partial versus Nissen fundoplication: four randomized trials. *Ann Surg* **255**: 637-642.

Cai, W., D. I. Watson, C. J. Lally, P. G. Devitt, P. A. Game and G. G. Jamieson (2008). Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180(degrees) partial fundoplication. *Br J Surg* **95**: 1501-1505.

Cao, Z., W. Cai, M. Qin, H. Zhao, P. Yue and Y. Li (2012). Randomized clinical trial of laparoscopic anterior 180 degrees partial versus 360 degrees Nissen fundoplication: 5-year results. *Dis Esophagus* **25**: 114-120.

Catarci, M., P. Gentileschi, C. Papi, A. Carrara, R. Marrese, A. L. Gaspari and G. B. Grassi (2004). Evidence-based appraisal of antireflux fundoplication. *Ann Surg* **239**: 325-337.

Chen, Z., S. K. Thompson, G. G. Jamieson, P. G. Devitt, P. A. Game and D. I. Watson (2011). Anterior 180-degree partial fundoplication: a 16-year experience with 548 patients. *J Am Coll Surg* **212**: 827-834.

Chew, C. R., G. G. Jamieson, P. G. Devitt and D. I. Watson (2011). Prospective randomized trial of laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair: late outcomes. *World J Surg* **35**: 2038-2044.

Chey, W. D., R. R. Mody, E. Q. Wu, L. Chen, S. Kothari, B. Persson, N. Beaulieu and M. Lu (2009). Treatment patterns and symptom control in patients with GERD: US community-based survey. *Curr Med Res Opin* **25**: 1869-1878.

Chrysos, E., E. Athanasakis, G. Pechlivanides, A. Tzortzinis, A. Mantides and E. Xynos (2004). The effect of total and anterior partial fundoplication on antireflux mechanisms of the gastroesophageal junction. *Am J Surg* **188**: 39-44.

Chrysos, E., J. Tsiaoussis, E. Athanasakis, O. Zoras, J. S. Vassilakis and E. Xynos (2002). Laparoscopic vs open approach for Nissen fundoplication. A comparative study. *Surg Endosc* **16**: 1679-1684.

Chrysos, E., J. Tsiaoussis, O. J. Zoras, E. Athanasakis, A. Mantides, A. Katsamouris and E. Xynos (2003). Laparoscopic surgery for gastroesophageal reflux disease patients with impaired esophageal peristalsis: total or partial fundoplication? *J Am Coll Surg* **197**: 8-15.

Chrysos, E., A. Tzortzinis, J. Tsiaoussis, H. Athanasakis, J. Vasssilakis and E. Xynos (2001). Prospective randomized trial comparing Nissen to Nissen-Rossetti technique for laparoscopic fundoplication. *Am J Surg* **182**: 215-221.

Cookson, R., C. Flood, B. Koo, D. Mahon and M. Rhodes (2005). Short-term cost effectiveness and long-term cost analysis comparing laparoscopic Nissen fundoplication with proton-pump inhibitor maintenance for gastro-oesophageal reflux disease. *Br J Surg* **92**: 700-706.

Cowgill, S. M., R. Gillman, E. Kraemer, S. Al-Saadi, D. Villadolid and A. Rosemurgy (2007). Ten-year follow up after laparoscopic Nissen fundoplication for gastroesophageal reflux disease. *Am Surg* **73**: 748-752.

Dallemagne, B., J. M. Weerts, C. Jehaes and S. Markiewicz (1996). Causes of failures of laparoscopic antireflux operations. *Surg Endosc* **10**: 305-310.

Dallemagne, B., J. M. Weerts, C. Jehaes, S. Markiewicz and R. Lombard (1991). Laparoscopic Nissen fundoplication: preliminary report. *Surg Laparosc Endosc* **1**: 138-143.

Daud, W. N., S. K. Thompson, G. G. Jamieson, P. G. Devitt, I. J. Martin and D. I. Watson (2013). Randomized controlled trial of laparoscopic anterior 180 degrees partial versus posterior 270 degrees partial fundoplication. *ANZ J Surg* DOI: 10.1111/ans.12476. (published online).

DeMeester, T. R., L. Bonavina and M. Albertucci (1986). Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. *Ann Surg* **204**: 9-20.

Dent, J. (1990). Australian clinical trials of omeprazole in the management of reflux oesophagitis. *Digestion* **47** Suppl 1: 69-71.

Donahue P. E., C. T. Bombeck (1977). The modified Nissen fundoplication – reflux prevention without gas bloat. *Chir Gastroent* **11**: 15-27.

Dor, J., P. Humbert, J. M. Paoli, M. Miorclerc and J. Aubert (1967). [Treatment of reflux by the so-called modified Heller-Nissen technic]. *Presse Med* **75**: 2563-2565.

Draaisma, W. A., E. Buskens, J. E. Bais, R. K. Simmermacher, H. G. Rijnhart-de Jong, I. A. Broeders and H. G. Gooszen (2006). Randomized clinical trial and follow-up study of cost-effectiveness of laparoscopic versus conventional Nissen fundoplication. *Br J Surg* **93**: 690-697.

Draaisma, W. A., H. G. Rijnhart-de Jong, I. A. Broeders, A. J. Smout, E. J. Furnee and H. G. Gooszen (2006). Five-year subjective and objective results of laparoscopic and conventional Nissen fundoplication: a randomized trial. *Ann Surg* **244**: 34-41.

Edye, M., B. Salky, A. Posner and A. Fierer (1998). Sac excision is essential to adequate laparoscopic repair of paraesophageal hernia. *Surg Endosc* **12**: 1259-1263.

Engstrom, C., W. Cai, T. Irvine, P. G. Devitt, S. K. Thompson, P. A. Game, J. R. Bessell, G. G. Jamieson and D. I. Watson (2012). Twenty years of experience with laparoscopic antireflux surgery. *Br J Surg* **99**: 1415-1421.

Engstrom, C., G. G. Jamieson, P. G. Devitt and D. I. Watson (2011). Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of the short gastric vessels during Nissen fundoplication. *Br J Surg* **98**: 1063-1067.

Engstrom, C., H. Lonroth, J. Mardani and L. Lundell (2007). An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. *World J Surg* **31**: 1221-1225.

Engstrom, C., M. Ruth, H. Lonroth and L. Lundell (2005). Manometric characteristics of the gastroesophageal junction after anterior versus posterior partial fundoplication. *Dis Esophagus* **18**: 31-36.

Farah, J. F., J. C. Grande, A. Goldenberg, J. C. Martinez, R. A. Lupinacci and J. Matone (2007). Randomized trial of total fundoplication and fundal mobilization with or without division of short gastric vessels: a short-term clinical evaluation. *Acta Cir Bras* **22**: 422-429.

Farrell, T. M., C. D. Smith, R. E. Metreveli, A. B. Johnson, K. D. Galloway and J. G. Hunter (1999). Fundoplication provides effective and durable symptom relief in patients with Barrett's esophagus. *Am J Surg* **178**: 18-21.

Francis, D. O., M. Goutte, J. C. Slaughter, C. G. Garrett, D. Hagaman, M. D. Holzman and M. F. Vaezi (2011). Traditional reflux parameters and not impedance monitoring predict outcome after fundoplication in extraesophageal reflux. *Laryngoscope* **121**: 1902-1909.

Frantzides, C. T., M. A. Carlson, S. Loizides, A. Papafili, M. Luu, J. Roberts, T. Zeni and A. Frantzides (2010). Hiatal hernia repair with mesh: a survey of SAGES members. *Surg Endosc* **24**: 1017-1024.

Frantzides, C. T., A. K. Madan, M. A. Carlson and G. P. Stavropoulos (2002). A prospective, randomized trial of laparoscopic polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. *Arch Surg* **137**: 649-652.

Franzen T, A. B., Tibbling L, Johansson KE. (1996). A report from a randomized study of open and laparoscopic 360° fundoplication. *Surg Endosc* **10**: 582 (abstract).

Franzen, T., B. Anderberg, M. Wiren and K. E. Johansson (2005). Long-term outcome is worse after laparoscopic than after conventional Nissen fundoplication. *Scand J Gastroenterol* **40**: 1261-1268.

Gatenby, P. A., T. Bright and D. I. Watson (2012). Anterior 180 degrees partial fundoplication - how I do it. *J Gastrointest Surg* **16**: 2297-2303.

Geagea, T. (1991). Laparoscopic Nissen's fundoplication: preliminary report on ten cases. *Surg Endosc* **5**: 170-173.

Goeree, R., R. Hopkins, J. K. Marshall, D. Armstrong, W. J. Ungar, C. Goldsmith, C. Allen and M. Anvari (2011). Cost-utility of laparoscopic Nissen fundoplication versus proton pump inhibitors for chronic and controlled gastroesophageal reflux disease: a 3-year prospective randomized controlled trial and economic evaluation. *Value Health* **14**: 263-273.

Gotley, D. C., B. M. Smithers, M. Rhodes, B. Menzies, F. J. Branicki and L. Nathanson (1996). Laparoscopic Nissen fundoplication - 200 consecutive cases. *Gut* **38**: 487-491.

Granderath, F. A., U. M. Schweiger, T. Kamolz, K. U. Asche and R. Pointner (2005). Laparoscopic Nissen fundoplication with prosthetic hiatal closure reduces postoperative intrathoracic wrap herniation: preliminary results of a prospective randomized functional and clinical study. *Arch Surg* **140**: 40-48.

Guerin, E., K. Betroune, J. Closset, A. Mehdi, J. C. Lefebvre, J. J. Houben, M. Gelin, P. Vaneukem and I. El Nakadi (2007). Nissen versus Toupet fundoplication: results of a randomized and multicenter trial. *Surg Endosc* **21**: 1985-1990.

Hagedorn, C., C. Jonson, H. Lonroth, M. Ruth, A. Thune and L. Lundell (2003). Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial. *Ann Surg* **238**: 189-196.

Hakanson, B. S., K. B. Thor, A. Thorell and O. Ljungqvist (2007). Open vs laparoscopic partial posterior fundoplication. A prospective randomized trial. *Surg Endosc* **21**: 289-298.

Heikkinen, T. J., K. Haukipuro, P. Koivukangas, A. Sorasto, R. Autio, H. Sodervik, H. Makela and A. Hulkko (1999). Comparison of costs between laparoscopic and open Nissen fundoplication: a prospective randomized study with a 3-month followup. *J Am Coll Surg* **188**: 368-376.

Hetzel, D. J., J. Dent, W. D. Reed, F. M. Narielvala, M. Mackinnon, J. H. McCarthy, B. Mitchell, B. R. Beveridge, B. H. Laurence, G. G. Gibson and et al. (1988). Healing and relapse of severe peptic esophagitis after treatment with omeprazole. *Gastroenterology* **95**: 903-912.

Hill, L. D. (1967). An effective operation for hiatal hernia: an eight year appraisal. *Ann Surg* **166**: 681-692.

Hinder, R. A., C. J. Filipi, G. Wetscher, P. Neary, T. R. DeMeester and G. Perdikis (1994). Laparoscopic Nissen fundoplication is an effective treatment for gastroesophageal reflux disease. *Ann Surg* **220**: 472-481.

Hunter, J. G., L. Swanstrom and J. P. Waring (1996). Dysphagia after laparoscopic antireflux surgery. The impact of operative technique. *Ann Surg* **224**: 51-57.

Ireland, A. C., R. H. Holloway, J. Toouli and J. Dent (1993). Mechanisms underlying the antireflux action of fundoplication. *Gut* **34**: 303-308.

Jamieson, G. G., D. I. Watson, R. Britten-Jones, P. C. Mitchell and M. Anvari (1994). Laparoscopic Nissen fundoplication. *Ann Surg* **220**: 137-145.

Jobe, B. A., K. D. Horvath and L. L. Swanstrom (1998). Postoperative function following laparoscopic collis gastroplasty for shortened esophagus. *Arch Surg* **133**: 867-874.

Johnson, A. B., M. Oddsdottir and J. G. Hunter (1998). Laparoscopic Collis gastroplasty and Nissen fundoplication. A new technique for the management of esophageal foreshortening. *Surg Endosc* **12**: 1055-1060.

Kahokehr, A., T. Sammour, K. Zargar-Shoshtari, S. Srinivasa and A. G. Hill (2010). Recovery after open and laparoscopic right hemicolectomy: a comparison. *J Surg Res* **162**: 11-16.

Kelly, J. J., D. I. Watson, K. F. Chin, P. G. Devitt, P. A. Game and G. G. Jamieson (2007). Laparoscopic Nissen fundoplication: clinical outcomes at 10 years. *J Am Coll Surg* **205**: 570-575.

Khan, M., A. Smythe, J. Globe, C. J. Stoddard and R. Ackroyd (2010). Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease. *ANZ J Surg* **80**: 500-505.

Khan, M. A., A. Smythe, J. Globe, C. J. Stoddard and R. Ackroyd (2009). Randomized controlled trial of laparoscopic Nissen versus Lind fundoplication for gastro-oesophageal reflux disease. *Scand J Gastroenterol* **44**: 269-275.

Koch, O. O., A. Kaindlstorfer, S. A. Antoniou, K. U. Asche, F. A. Granderath and R. Pointner (2012). Laparoscopic Nissen versus Toupet fundoplication: objective and subjective results of a prospective randomized trial. *Surg Endosc* **26**: 413-422.

Koetje, J. H., T. Irvine, S. K. Thompson, P. G. Devitt, S. D. Woods, A. Aly, G. G. Jamieson and D. I. Watson (2015). Quality of Life Following Repair of Large Hiatal Hernia is Improved but not Influenced by Use of Mesh: Results From a Randomized Controlled Trial. *World J Surg* **39**: 1465-1473.

Kosek, V., H. Wykypiel, H. Weiss, E. Holler, G. Wetscher, R. Margreiter and A. Klaus (2009). Division of the short gastric vessels during laparoscopic Nissen

fundoplication: clinical and functional outcome during long-term follow-up in a prospectively randomized trial. *Surg Endosc* **23**: 2208-2213.

Krysztopik, R. J., G. G. Jamieson, P. G. Devitt and D. I. Watson (2002). A further modification of fundoplication. 90 degrees anterior fundoplication. *Surg Endosc* **16**: 1446-1451.

Lafullarde, T., D. I. Watson, G. G. Jamieson, J. C. Myers, P. A. Game and P. G. Devitt (2001). Laparoscopic Nissen fundoplication: five-year results and beyond. *Arch Surg* **136**: 180-184.

Laine, S., A. Rantala, R. Gullichsen and J. Ovaska (1997). Laparoscopic vs conventional Nissen fundoplication. A prospective randomized study. *Surg Endosc* **11**: 441-444.

Laws, H. L., R. H. Clements and C. M. Swillie (1997). A randomized, prospective comparison of the Nissen fundoplication versus the Toupet fundoplication for gastroesophageal reflux disease. *Ann Surg* **225**: 647-653.

Lind, J. F., C. M. Burns and J. T. MacDougal. (1965). 'Physiological' repair for hiatus hernia – manometric study. *Arch Surg* **91**: 233-237.

Ludemann, R., D. .I. Watson and G. G. Jamieson (2003). Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication *Am J Surg* **186**; 143-147.

Ludemann, R., D. I. Watson, G. G. Jamieson, P. A. Game and P. G. Devitt (2005). Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180 degrees fundoplication. *Br J Surg* **92**: 240-243.

Lundell, L., H. Abrahamsson, M. Ruth, L. Rydberg, H. Lonroth and L. Olbe (1996). Long-term results of a prospective randomized comparison of total fundic wrap (Nissen-Rossetti) or semifundoplication (Toupet) for gastro-oesophageal reflux. *Br J Surg* **83**: 830-835.

Lundell, L., H. Abrahamsson, M. Ruth, N. Sandberg and L. C. Olbe (1991). Lower esophageal sphincter characteristics and esophageal acid exposure following partial or 360 degrees fundoplication: results of a prospective, randomized, clinical study. *World J Surg* **15**: 115-120.

Lundell, L., S. Attwood, C. Ell, R. Fiocca, J. P. Galmiche, J. Hatlebakk, T. Lind and O. Junghard (2008). Comparing laparoscopic antireflux surgery with esomeprazole in the management of patients with chronic gastro-oesophageal reflux disease: a 3-year interim analysis of the LOTUS trial. *Gut* **57**: 1207-1213.

Lundell, L., P. Miettinen, H. E. Myrvold, J. G. Hatlebakk, L. Wallin, C. Engstrom, R. Julkunen, M. Montgomery, A. Malm, T. Lind and A. Walan (2009). Comparison of outcomes twelve years after antireflux surgery or omeprazole maintenance therapy for reflux esophagitis. *Clin Gastroenterol Hepatol* **7**: 1292-1298.

Lundell, L., P. Miettinen, H. E. Myrvold, J. G. Hatlebakk, L. Wallin, A. Malm, I. Sutherland and A. Walan (2007). Seven-year follow-up of a randomized clinical trial comparing proton-pump inhibition with surgical therapy for reflux oesophagitis. *Br J Surg* **94**: 198-203.

Lundell, L., P. Miettinen, H. E. Myrvold, S. A. Pedersen, B. Liedman, J. G. Hatlebakk, R. Julkonen, K. Levander, J. Carlsson, M. Lamm and I. Wiklund (2001). Continued (5-year) followup of a randomized clinical study comparing antireflux surgery and omeprazole in gastroesophageal reflux disease. *J Am Coll Surg* **192**: 172-179.

Lundell, L., P. Miettinen, H. E. Myrvold, S. A. Pedersen, K. Thor, M. Lamm, A. Blomqvist, J. G. Hatlebakk, E. Janatuinen, K. Levander, P. Nystrom and I. Wiklund (2000). Long-term management of gastro-oesophageal reflux disease with omeprazole or open antireflux surgery: results of a prospective, randomized clinical trial. The Nordic GORD Study Group. *Eur J Gastroenterol Hepatol* **12**: 879-887.

Luostarinen, M., M. Koskinen, P. Reinikainen, J. Karvonen and J. Isolauri (1995). Two antireflux operations: floppy versus standard Nissen fundoplication. *Ann Med* **27**: 199-205.

Luostarinen, M., J. Virtanen, M. Koskinen, M. Matikainen and J. Isolauri (2001). Dysphagia and oesophageal clearance after laparoscopic versus open Nissen fundoplication. A randomized, prospective trial. *Scand J Gastroenterol* **36**: 565-571.

Luostarinen, M. E. and J. O. Isolauri (1999). Randomized trial to study the effect of fundic mobilization on long-term results of Nissen fundoplication. *Br J Surg* **86**: 614-618.

Mahon, D., M. Rhodes, B. Decadt, A. Hindmarsh, R. Lowndes, I. Beckingham, B. Koo and R. G. Newcombe (2005). Randomized clinical trial of laparoscopic Nissen fundoplication compared with proton-pump inhibitors for treatment of chronic gastro-oesophageal reflux. *Br J Surg* **92**: 695-699.

Mardani, J., L. Lundell and C. Engstrom (2011). Total or posterior partial fundoplication in the treatment of GERD: results of a randomized trial after 2 decades of follow-up. *Ann Surg* **253**: 875-878.

Mardani, J., L. Lundell, H. Lonroth, J. Dalenback and C. Engstrom (2009). Ten-year results of a randomized clinical trial of laparoscopic total fundoplication with or without division of the short gastric vessels. *Br J Surg* **96**: 61-65.

Mehta, S., J. Bennett, D. Mahon and M. Rhodes (2006). Prospective trial of laparoscopic nissen fundoplication versus proton pump inhibitor therapy for gastroesophageal reflux disease: Seven-year follow-up. *J Gastrointest Surg* **10**: 1312-1316.

Nguyen, N. T., P. R. Schauer, W. Hutson, R. Landreneau, T. Weigel, P. F. Ferson, R. J. Keenan and J. D. Luketich (1998). Preliminary results of thoracoscopic Belsey Mark IV antireflux procedure. *Surg Laparosc Endosc* **8**: 185-188.

Nijjar, R. S., D. I. Watson, G. G. Jamieson, S. Archer, J. R. Bessell, M. Booth, R. Cade, G. L. Cullingford, P. G. Devitt, D. R. Fletcher, J. Hurley, G. Kiroff, I. J. Martin, L. K. Nathanson and J. A. Windsor (2010). Five-year follow-up of a multicenter, double-blind randomized clinical trial of laparoscopic Nissen vs anterior 90 degrees partial fundoplication. *Arch Surg* **145**: 552-557.

Nilsson, G., S. Larsson and F. Johnsson (2000). Randomized clinical trial of laparoscopic versus open fundoplication: blind evaluation of recovery and discharge period. *Br J Surg* **87**: 873-878.

Nilsson, G., J. Wenner, S. Larsson and F. Johnsson (2004). Randomized clinical trial of laparoscopic versus open fundoplication for gastro-oesophageal reflux. *Br J Surg* **91**: 552-559.

Nissen, R. (1956). [A simple operation for control of reflux esophagitis]. *Schweiz Med Wochenschr* **86**(Suppl 20): 590-592.

O'Boyle, C. J., D. I. Watson, G. G. Jamieson, J. C. Myers, P. A. Game and P. G. Devitt (2002). Division of short gastric vessels at laparoscopic nissen fundoplication: a prospective double-blind randomized trial with 5-year follow-up. *Ann Surg* **235**: 165-170.

Oelschlager, B. K., C. A. Pellegrini, J. Hunter, N. Soper, M. Brunt, B. Sheppard, B. Jobe, N. Polissar, L. Mitsumori, J. Nelson and L. Swanstrom (2006). Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. *Ann Surg* **244**: 481-490.

Oelschlager, B. K., C. A. Pellegrini, J. G. Hunter, M. L. Brunt, N. J. Soper, B. C. Sheppard, N. L. Polissar, M. B. Neradilek, L. M. Mitsumori, C. A. Rohrmann and L. L. Swanstrom (2011). Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. *J Am Coll Surg* **213**: 461-468.

Ortiz, A., L. F. Martinez de Haro, P. Parrilla, G. Morales, J. Molina, J. Bermejo, R. Liron and J. Aguilar (1996). Conservative treatment versus antireflux surgery in Barrett's oesophagus: long-term results of a prospective study. *Br J Surg* **83**: 274-278.

Parrilla, P., L. F. Martinez de Haro, A. Ortiz, V. Munitiz, J. Molina, J. Bermejo and M. Canteras (2003). Long-term results of a randomized prospective study comparing medical and surgical treatment of Barrett's esophagus. *Ann Surg* **237**: 291-298.

Perttila, J., M. Salo, J. Ovaska, J. Gronroos, M. Lavonius, A. Katila, M. Lahteenmaki and K. Pulkki (1999). Immune response after laparoscopic and conventional Nissen fundoplication. *Eur J Surg* **165**: 21-28.

Peters, J. H., J. Heimbucher, W. K. Kauer, R. Incarbone, C. G. Bremner and T. R. DeMeester (1995). Clinical and physiologic comparison of laparoscopic and open Nissen fundoplication. *J Am Coll Surg* **180**: 385-393.

Ratnasingam, D., T. Irvine, S. K. Thompson and D. I. Watson (2011). Laparoscopic antireflux surgery in patients with throat symptoms: a word of caution. *World J Surg* **35**: 342-348.

Rattner, D. W. and D. C. Brooks (1995). Patient satisfaction following laparoscopic and open antireflux surgery. *Arch Surg* **130**: 289-293.

Raue, W., J. Ordemann, C. A. Jacobi, C. Menenakos, A. Buchholz and J. Hartmann (2011). Nissen versus Dor fundoplication for treatment of gastroesophageal reflux disease: a blinded randomized clinical trial. *Dig Surg* **28**: 80-86.

Rice, S., D. I. Watson, C. J. Lally, P. G. Devitt, P. A. Game and G. G. Jamieson (2006). Laparoscopic anterior 180 degrees partial fundoplication: five-year results and beyond. *Arch Surg* **141**: 271-275.

Rossetti, M. and K. Hell (1977). Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. *World J Surg* **1**: 439-443.

Rothstein, R., C. Filipi, K. Caca, R. Pruitt, K. Mergener, A. Torquati, G. Haber, Y. Chen, K. Chang, D. Wong, J. Deviere, D. Pleskow, C. Lightdale, A. Ades, R. Kozarek, W. Richards and A. Lembo (2006). Endoscopic full-thickness plication for the treatment of gastroesophageal reflux disease: A randomized, sham-controlled trial. *Gastroenterology* **131**: 704-712.

Rydberg, L., M. Ruth, H. Abrahamsson and L. Lundell (1999). Tailoring antireflux surgery: A randomized clinical trial. *World J Surg* **23**: 612-618.

Salminen, P., S. Hurme and J. Ovaska (2012). Fifteen-year outcome of laparoscopic and open Nissen fundoplication: a randomized clinical trial. *Ann Thorac Surg* **93**: 228-233.

Salminen, P. T., H. I. Hiekkanen, A. P. Rantala and J. T. Ovaska (2007). Comparison of long-term outcome of laparoscopic and conventional nissen fundoplication: a prospective randomized study with an 11-year follow-up. *Ann Surg* **246**: 201-206.

Schwartz, M. P., H. Wellink, H. G. Gooszen, J. M. Conchillo, M. Samsom and A. J. Smout (2007). Endoscopic gastroplication for the treatment of gastro-oesophageal reflux disease: a randomised, sham-controlled trial. *Gut* **56**: 20-28.

Shaw, J. M., P. C. Bornman, M. D. Callanan, I. J. Beckingham and D. C. Metz (2010). Long-term outcome of laparoscopic Nissen and laparoscopic Toupet fundoplication for gastroesophageal reflux disease: a prospective, randomized trial. *Surg Endosc* **24**: 924-932.

Spechler, S. J. (1992). Comparison of medical and surgical therapy for complicated gastroesophageal reflux disease in veterans. The Department of Veterans Affairs Gastroesophageal Reflux Disease Study Group. *N Engl J Med* **326**: 786-792.

Spechler, S. J., E. Lee, D. Ahnen, R. K. Goyal, I. Hirano, F. Ramirez, J. P. Raufman, R. Sampliner, T. Schnell, S. Sontag, Z. R. Vlahcevic, R. Young and W. Williford

(2001). Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial. *JAMA* **285**: 2331-2338.

Spence, G. M., D. I. Watson, G. G. Jamiesion, C. J. Lally and P. G. Devitt (2006). Single center prospective randomized trial of laparoscopic Nissen versus anterior 90 degrees fundoplication. *J Gastrointest Surg* **10**: 698-705.

Strate, U., A. Emmermann, C. Fibbe, P. Layer and C. Zornig (2008). Laparoscopic fundoplication: Nissen versus Toupet two-year outcome of a prospective randomized study of 200 patients regarding preoperative esophageal motility. *Surg Endosc* **22**: 21-30.

Swanstrom, L. L., D. R. Marcus and G. Q. Galloway (1996). Laparoscopic Collis gastroplasty is the treatment of choice for the shortened esophagus. *Am J Surg* **171**: 477-481.

Thompson W. E. and K. W. Heaton (1982). Heartburn and globus in apparently healthy people. *Canadian Medical Association Journal* **126**: 46-48.

Thor, K. B. and T. Silander (1989). A long-term randomized prospective trial of the Nissen procedure versus a modified Toupet technique. *Ann Surg* **210**: 719-724.

Toupet, A. (1963). [Technic of esophago-gastroplasty with phrenogastropexy used in radical treatment of hiatal hernias as a supplement to Heller's operation in cardiospasms]. *Mem Acad Chir (Paris)* **89**: 384-389.

Trus, T. L., W. S. Laycock, G. Branum, J. P. Waring, S. Mauren and J. G. Hunter (1996). Intermediate follow-up of laparoscopic antireflux surgery. *Am J Surg* **171**: 32-35.

Walker, S. J., S. Holt, C. J. Sanderson and C. J. Stoddard (192). "Comparison of Nissen total and Lind partial transabdominal fundoplication in the treatment of gastro-oesophageal reflux. *Br J Surg* **79**: 410-414.

Waring, J. P., J. G. Hunter, M. Oddsdottir, J. Wo and E. Katz (1995). The preoperative evaluation of patients considered for laparoscopic antireflux surgery. *Am J Gastroenterol* **90**: 35-38.

Watson, A., L. R. Jenkinson, C. S. Ball, A. P. Barlow and T. L. Norris (1991). A more physiological alternative to total fundoplication for the surgical correction of resistant gastro-oesophageal reflux. *Br J Surg* **78**: 1088-1094.

Watson, D. I., N. Davies, P. G. Devitt and G. G. Jamieson (1999). Importance of dissection of the hernial sac in laparoscopic surgery for large hiatal hernias. *Arch Surg* **134**: 1069-1073.

Watson, D. I., P. G. Devitt, L. Smith and G. G. Jamieson (2012). Anterior 90 degrees partial vs Nissen fundoplication - 5 year follow-up of a single-centre randomised trial. *J Gastrointest Surg* **16**: 1653-1658.

Watson, D. I., G. G. Jamieson, R. J. Baigrie, G. Mathew, P. G. Devitt, P. A. Game and R. Britten-Jones (1996). Laparoscopic surgery for gastro-oesophageal reflux: beyond the learning curve. *Br J Surg* **83**: 1284-1287.

Watson, D. I., G. G. Jamieson, P. G. Devitt, J. A. Kennedy, T. Ellis, R. Ackroyd, T. Lafullarde and P. A. Game (2001). A prospective randomized trial of laparoscopic Nissen fundoplication with anterior vs posterior hiatal repair. *Arch Surg* **136**: 745-751.

Watson, D. I., G. G. Jamieson, P. G. Devitt, P. C. Mitchell and P. A. Game (1995). Paraoesophageal hiatus hernia: an important complication of laparoscopic Nissen fundoplication. *Br J Surg* **82**: 521-523.

Watson, D. I., G. G. Jamieson, P. A. Game, R. S. Williams and P. G. Devitt (1999). Laparoscopic reoperation following failed antireflux surgery. *Br J Surg* **86**: 98-101.

Watson, D. I., G. G. Jamieson, C. Lally, S. Archer, J. R. Bessell, M. Booth, R. Cade, G. Cullingford, P. G. Devitt, D. R. Fletcher, J. Hurley, G. Kiroff, C. J. Martin, I. J. Martin, L. K. Nathanson and J. A. Windsor (2004). Multicenter, prospective, double-blind, randomized trial of laparoscopic nissen vs anterior 90 degrees partial fundoplication. *Arch Surg* **139**: 1160-1167.

Watson, D. I., G. G. Jamieson, P. C. Mitchell, P. G. Devitt and R. Britten-Jones (1995). Stenosis of the esophageal hiatus following laparoscopic fundoplication. *Arch Surg* **130**: 1014-1016.

Watson, D. I., G. G. Jamieson, G. K. Pike, N. Davies, M. Richardson and P. G. Devitt (1999). Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. *Br J Surg* **86**: 123-130.

Watson, D. I. and C. J. Lally (2009). Prevalence of symptoms and use of medication for gastroesophageal reflux in an Australian community. *World J Surg* **33**: 88-94.

Watson, D. I., G. Mathew, G. K. Pike, R. J. Baigrie and G. G. Jamieson (1998). Efficacy of anterior, posterior and total fundoplication in an experimental model. *Br J Surg* **85**: 1006-1009.

Watson, D. I., G. Mathew, G. K. Pike and G. G. Jamieson (1997). Comparison of anterior, posterior and total fundoplication using a viscera model. *Dis Esophagus* **10**: 110-114.

Watson, D. I., G. K. Pike, R. J. Baigrie, G. Mathew, P. G. Devitt, R. Britten-Jones and G. G. Jamieson (1997). Prospective double-blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. *Ann Surg* **226**: 642-652.

Watson, D. I., S. K. Thompson, P. G. Devitt, L. Smith, S. D. Woods, A. Aly, S. Gan, P. A. Game and G. G. Jamieson (2015). Laparoscopic repair of very large hiatus hernia with sutures versus absorbable mesh versus nonabsorbable mesh: a randomized controlled trial. *Ann Surg* **261**: 282-289.

Wijnhoven, B. P., D. I. Watson, P. G. Devitt, P. A. Game and G. G. Jamieson (2008). Laparoscopic Nissen fundoplication with anterior versus posterior hiatal repair: long-term results of a randomized trial. *Am J Surg* **195**: 61-65.

Woodcock, S. A., D. I. Watson, C. Lally, S. Archer, J. R. Bessell, M. Booth, R. Cade, G. L. Cullingford, P. G. Devitt, D. R. Fletcher, J. Hurley, G. G. Jamieson, G. Kiroff, C. J. Martin, I. J. Martin, L. K. Nathanson and J. A. Windsor (2006). Quality of life following laparoscopic anterior 90 degrees versus Nissen fundoplication: results from a multicenter randomized trial. *World J Surg* **30**: 1856-1863.

Yang, H., D. I. Watson, J. Kelly, C. J. Lally, J. C. Myers and G. G. Jamieson GG (2007). Esophageal manometry and clinical outcome after laparoscopic Nissen fundoplication *J Gastrointest Surg* **11**; 1126-1133.

Yang, H., D. I. Watson, C. J. Lally, P. G. Devitt, P. A. Game and G. G. Jamieson (2008). Randomized trial of division versus nondivision of the short gastric vessels during laparoscopic Nissen fundoplication: 10-year outcomes. *Ann Surg* **247**: 38-42.

Yau, P., D. I. Watson, N. Ascott, T. Lafullarde and G. G. Jamieson (2000). Efficacy of a 90 degree anterior fundoplication vs a total fundoplication in an experimental model. *Surg Endosc* **14**: 830-833.

Zornig, C., U. Strate, C. Fibbe, A. Emmermann and P. Layer (2002). Nissen vs Toupet laparoscopic fundoplication. *Surg Endosc* **16**: 758-766.