Evaluation of Swallowing in Critically Ill Tracheostomy Patients using High-Resolution Pharyngeal Manometry

by

Dr Sanith Cheriyan, MBBS

Thesis
Submitted to Flinders University
for the degree of

Masters of Surgery
College of Public Health and Medicine
September 2021

I. Table of Contents

II. List of Tables

III. List of Figures

IV. List of Abbreviations

APACHE II	Acute Physiology and Chronic Health Evaluation II
CCI	Charlson Comorbidity Index
COVID-19	Coronavirus disease 2019
ETT	Endotracheal Tube
FESS	Fibre-optic Endoscopic Evaluation of Swallowing
FOIS	Functional Oral Intake Score
HRPM	High-Resolution Pharyngeal Manometry
ICCU	Intensive and Critical Care Unit
IQR	Inter-quartile range
LOS	Length of Stay
NGT	Nasogastric Tube
NTS	Nucleus Tractus Solitarus
PMSV	Passy-Muir Speaking Valve
PPE	Personal Protective Equipment
PROM	Patient-Reported Outcome Measures
ROI	Region of Interest
UES	Upper Esophageal Sphincter
VFSS	Videofluoroscopic Swallow Study

HRPM Abbreviations

BPT	Bolus Pressure Time
CI	Contractile Integral
DCL	Distension to Contraction Latency
HPCI	Hypopharyngeal Contractile Integral
IBP	Hypopharyngeal Intrabolus pressure
MCI	Mesopharyngeal Contractile Integral
PCI	Proximal Esophageal Contractile Integral
Peak P	Hypopharyngeal Peak Pressure
PhCI	Pharyngeal Contractile Integral

SRI	Swallow Risk Index
UES BP	UES Basal Pressure
UES IRP	UES Integrated Relaxation Pressure
UES Max Adm	UES Maximum Admittance
UES Peak P	UES Peak Pressure
UES RT	UES Relaxation Time
UESCI	UES Contractile Integral
VCI	Velopharyngeal Contractile Integral

V. Thesis Summary

Background:

Tracheostomies are a common life-prolonging procedure, performed in critically unwell patients. The incidence of dysphagia in patients with a tracheostomy has been reported to be up to 90% (Skoretz, Riopelle et al. 2020). Historically, studies have used qualitative assessment tools in heterogenous tracheostomised cohorts, resulting in a lack of consensus on the biomechanical impact a tracheostomy has on swallowing. High-resolution pharyngeal manometry (HRPM) uses a transnasal catheter and recording system, it provides an alternative method to quantitatively assess the swallowing pathway across the pharynx and esophagus. This pilot study aimed to objectively assess biomechanical swallow metrics in those with a tracheostomy compared to healthy age-matched controls; and, to assess the change in swallow metrics across three tracheostomy conditions.

Methods:

A prospective cohort study was conducted at Flinders Medical Centre (South Australia). Tracheostomised patients were recruited who had no history of pre-existing dysphagia and no known structural or neurological conditions associated with dysphagia were recruited. Patients swallow function was tested across a variety of bolus and tracheostomy conditions (cuff up, cuff down and a Passy-Muir speaking valve). Data was collected using a high-resolution pharyngeal manometer, analysed on SwallowGateway™ (www.swallowgateway.com) and compared to a normative dataset of healthy age-matched controls.

Results:

56 patients were screened, 11 patients were eligible, of which 9 were tested (5 males); with a total of 108 swallows analysed. Compared to age-matched controls, tracheostomy patients had a higher Swallow Risk Index (a marker of disordered swallowing) with altered upper esophageal sphincter (UES) metrics (UES IBP, UES IRP and UES RT) and elevated pharyngeal pressures. Although there were no significant differences

demonstrated across the tracheostomy cuff conditions; certain trends were observed. Cuff inflation resulted in further elevation of IBP, SRI and PhCI compared to other cuff conditions and placement of the PMSV improved UES relaxation pressures.

Conclusion:

This pilot study demonstrated that HRPM is a safe, instrumental swallow assessment tool in critically ill patients. A tracheostomy has a biomechanical impact on the swallowing pathway, possibly attributable to UES dysfunction, secondary to anchorage of the tracheostomy to the anterior neck resulting in reduced hyolaryngeal excursion. Cuff inflation showed signs of worsening a patient's swallow, however insertion of the PMSV showed signs of improving UES function.

VI. Declaration

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

Sanith Cheriyan

October 2021

VII. Acknowledgement

Throughout the writing of this thesis, I have received a great deal of support and assistance. The work described in this thesis was performed under the Otorhinolaryngology, Head and Neck Surgery and Intensive and Critical Care Department at Flinders Medical Centre, Bedford Park, South Australia.

I would like to express my deepest appreciation to my supervisors. Associate Professor Eng Hooi Ooi, thank you for giving me the opportunity to do research in your department, providing insightful feedback that has pushed me to sharpen my thinking and brought my work to a higher level. Professor Taher Omari, thank you for your expertise and guidance and for opening my eyes to the world of High-Resolution Manometry, a skill I would like to continue to use. Associate Professor Shailesh Bihari, thank you for assisting in the recruitment of intensive care patients and providing assistance when I ran into difficulties. Dr Charmaine Woods, thank you for helping me with all facets of this thesis, you have been truly remarkable in helping make the world of research easier to navigate and understand. The completion of my thesis would not have been possible without the energy, time and resources you have all donated. Thank you.

I'm extremely grateful to Mistyka Schar, thank you for assisting with the initial start-up of the pilot and being the conduit between technical HRPM and its clinical and practical relevance, all whilst doing your own higher degree. To Dr Lucy Huang and Dr Nuwan Dharmawardana, thank you for your support, assistance and advice throughout this process. Further acknowledgment to the ICCU consultants, registrars and nurses for their assistance in identifying and recruiting participants.

Finally, I would like to express my sincere gratitude to my parents and my brother, Ronith, in Sydney for their support and advice. I would also like to thank my extended family including my grandparents in India. Finally, I would like to thank my partner, Bronwyn, for her support and being understanding during all the late nights of writing this thesis.

This thesis would not have been possible without everyone's support and advice. Thank you.

1 INTRODUCTION

Swallowing is an important complex biomechanical and physiological behaviour that is a universally critical process (Sasegbon and Hamdy 2017). The aim of swallowing is to allow the transit of solids and liquids to travel safely from the oral cavity into the stomach for further digestion, eventually supplying the nutritional demands of our body. Eating and drinking are pleasurable activities that have a significant positive impact on an individual's quality of life (Li, Minagi et al. 2017). Therefore, normal swallowing is integral in supplying the nutrition for our metabolically active bodies and providing quality of life (Sasegbon and Hamdy 2017).

Swallowing and breathing are interdependent processes that share anatomical regions and biomechanical regulations (Skoretz, Riopelle et al. 2020). Dysphagia or disordered swallowing is a symptom, and therefore it highlights the presence of an underlying condition or impairment to the normal swallowing pathway (Kuhlemeier 1994, Rofes, Arreola et al. 2011). Disruption to this pathway has the potential to cause malnutrition and aspiration pneumonia, which results in increased mortality, morbidity and health care costs (Jaradeh 1994). A tracheostomy is a common procedure performed in critically unwell patients, in which an artificial airway is created by opening the anterior cervical trachea to the skin to facilitate mechanical ventilation (Raimonde, Westhoven et al. 2020). Given the shared complex anatomy and biomechanical processes, dysphagia and a tracheostomy often co-exist in those with critical illnesses (Skoretz, Riopelle et al. 2020).

This thesis will assess swallowing biomechanics in the presence of a tracheostomy in patients with critical illnesses using high-resolution pharyngeal manometry. In order to understand the impact of a tracheostomy on swallowing function, the following section will present an overview of the anatomy and physiology relevant to swallowing and its assessment, the role of a tracheostomy and its association with dysphagia.

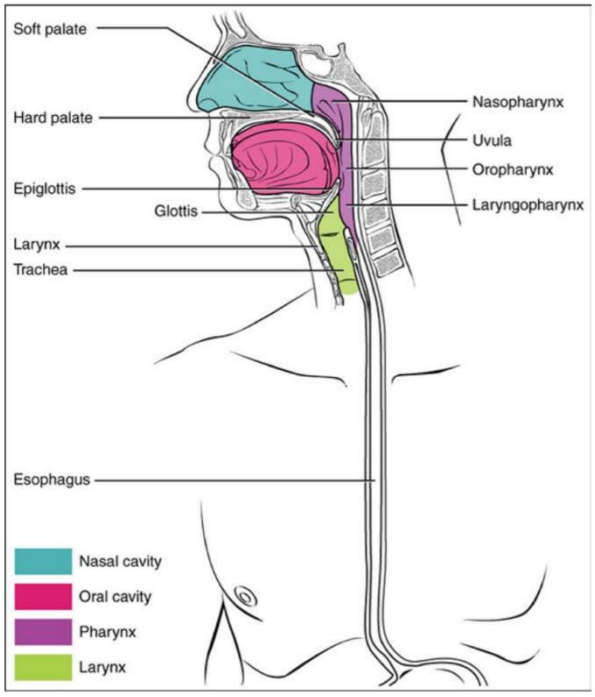
1.1 SWALLOWING

Swallowing is a complex event which involves the safe transport of a bolus from the oral cavity into the stomach through the pharynx and esophagus within a short period of time (Logemann 1998). It involves the volitional and reflexive activity of over 30 muscles and nerves to produce coordinated movements (Matsuo and Palmer 2008, Panara, Ramezanpour Ahangar et al. 2020).

1.1.1. ANATOMY OF SWALLOWING

The bolus of food travels from the oral cavity, through the pharynx and subsequently the esophagus, avoiding spillage into the larynx and trachea to finally enter the stomach (Figure 1). This is a rapid process, as the bolus travels through the pharynx in less than 1 second, with a velocity of up to 40 cm/second (Dua, Ren et al. 1997).

Figure 1 Anatomical segments of the pharynx



Various anatomical segments involved in swallowing: the oral cavity, pharynx and esophagus. The pharynx is divided into the nasopharynx (known as the velopharynx), oropharynx (known as the mesopharynx) and the laryngopharynx (known as the hypopharynx) (Sasegbon and Hamdy 2017)

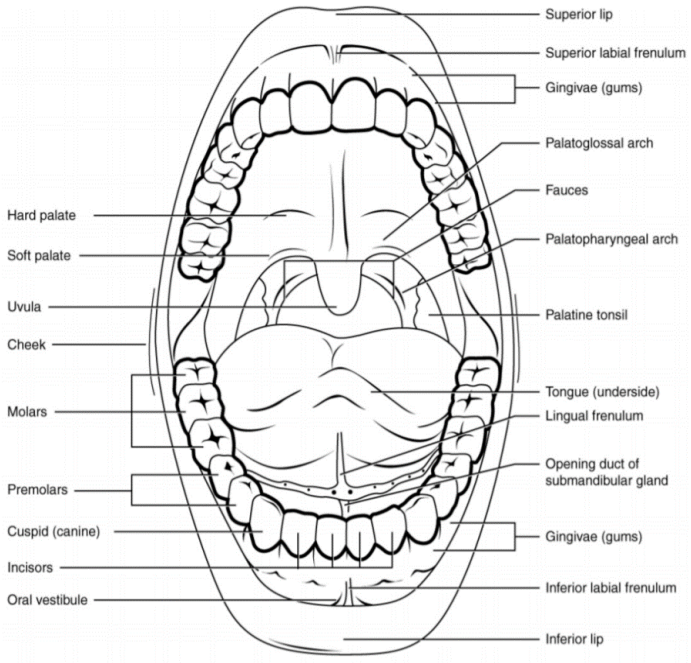
1.1.1.1 Oral Cavity

The oral cavity is responsible for containment and preparation of the food bolus through mastication and trituration with saliva. Saliva helps soften and digest food, making mastication easier; in addition, it lubricates the bolus facilitating transport through the pharynx (Pedersen, Bardow et al. 2002, Kupirovic, Elmadfa et al. 2017). The oral cavity contains various structures - these include the lips and teeth anteriorly, the hard palate, soft palate and uvula superiorly, the mandible and floor of mouth inferiorly and fauces posteriorly; which subdivides the oral cavity from the oropharynx (Logemann 1983) (Figure 2).

1.1.1.2 Teeth

An adult has 32 permanent teeth, which mechanically alter the consistency of solid food making digestion and pharyngeal transit easier. The food is contained within the oral cavity by the action of the buccinators and the orbicularis oris to seal the lips. Teeth provide sensory information about the nature of the bolus. All teeth are innervated by branches of the trigeminal nerve (maxillary and mandibular branches) (Logemann 1983, Moore, Dalley et al. 2013).

Figure 2 Anterior view of the oral cavity



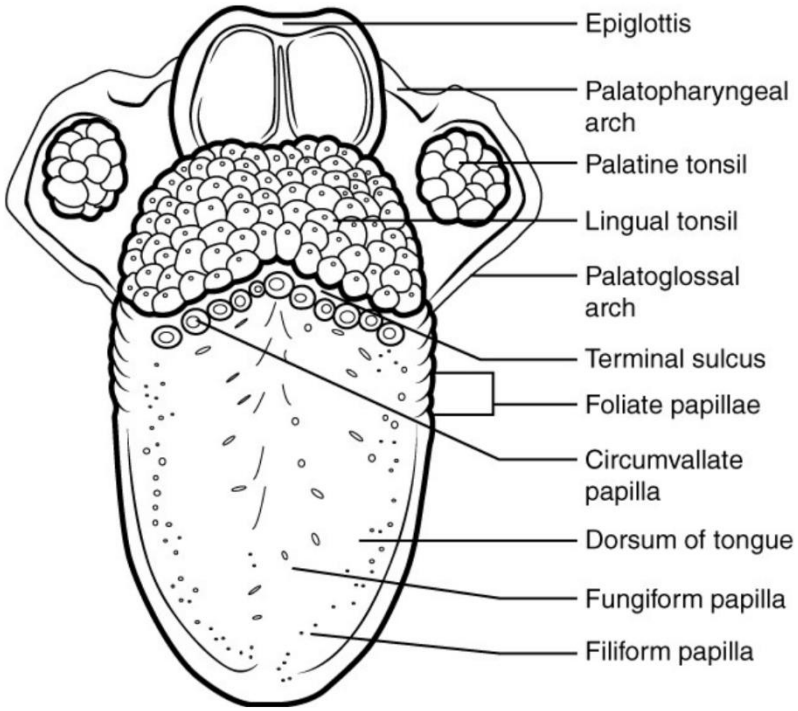
View of the structures within the oral cavity; these include the teeth, tongue, soft and hard palate, uvula and the fauces (Betts 2017)

1.1.1.3 Tongue

The tongue assists with the movement of processed food within the oral cavity and, for the purposes of swallowing, it is divided into an oral and a pharyngeal part (Logemann 1983). The oral tongue ends at the circumvallate papillae; here it becomes the pharyngeal portion, also known as the tongue base with the tongue muscles attached to the hyoid bone (Corbin-Lewis and Liss 2014) (Figure 3). The oral tongue is under voluntary control during the oral stages of swallowing (Logemann 1983). The pharyngeal portion is under involuntary control coordinated by the brainstem and is active during the pharyngeal stage of swallowing (Logemann 1983).

The tongue is composed of intrinsic (within the tongue) and extrinsic (outside the tongue) muscles. The intrinsic muscles include the longitudinalis inferior and superior, transversus linguae and verticalis linguae; and are named based on the direction of the muscle fibres (Moore, Dalley et al. 2013). Intrinsic muscles allow the size and shape of the tongue to be manipulated and changed; this is in contrast to the four-paired extrinsic muscles which change the position of the tongue within the oral cavity. Simplistically, hyoglossus contraction causes depression and retraction of the tongue whilst styloglossus retracts and elevates the tongue. Genioglossus is slightly more complex, as the inferior fibres protrude the tongue, whilst the superior fibres retract and depress the tongue tip and the middle fibres depress the tongue (Logemann 1983). Most intrinsic and extrinsic muscles are innervated by the hypoglossal nerve (Moore, Dalley et al. 2013). The palatoglossus is an extrinsic muscle, innervated by the vagus nerve, elevating the posterior aspect of the tongue against the soft palate.

Figure 3 Dorsal tongue



View of the tongue demonstrating the oral and pharyngeal portions, demarcated by the circumvallate papilla (Betts 2017)

1.1.1.4 Soft palate

The soft palate is also known as the velum and lies over the posterior tongue (Figure 2). This is an important anatomical relationship, as it prevents premature bolus spillage from the oral cavity into the larynx by contraction of the palatoglossus; furthermore, it allows closure of the velopharynx during swallowing to prevent nasal regurgitation. Velopharyngeal closure is achieved by movement of the palatopharyngeus, levator and tensor veli palantini and the superior pharyngeal constrictor. The soft palate musculature is innervated by the vagal branch of the pharyngeal plexus, however, the tensor veli palantini is supplied by a branch of the trigeminal nerve (Logemann 1983, Moore, Dalley et al. 2013).

1.1.1.5 Pharynx

The pharynx is a tube-like structure that extends from the posterior aspect of the nasal cavity, inferiorly to the upper esophageal sphincter (Corbin-Lewis and Liss 2014). The pharynx is divided into the nasopharynx, oropharynx and the laryngopharynx (also known as the hypopharynx) (Figure 1 and 4). The nasopharynx is the

posterior aspect of the nasal cavity and can be separated from the oropharynx with velopharyngeal closure; it is only involved in breathing and speech (Betts 2017). The oropharynx is the region behind the anterior fauces (also known as the anterior tonsil pillar) and extends to the level of the hyoid bone or approximately the level of the third cervical vertebrae (C3). The hypopharynx is the region behind the larynx and extends from the hyoid bone to the esophagus, which lies at the level of C6 (Corbin-Lewis and Liss 2014). The nasopharynx, oropharynx and hypopharynx are key structures as they share a common passage for both breathing and digestion.

The pharynx comprises of three semicircular muscles called the superior, middle and inferior pharyngeal constrictor (Corbin-Lewis and Liss 2014) (Figure 4). The pharyngeal constrictors arise from the skull base and the posterior pharyngeal wall (known as the posterior pharyngeal raphe) and attach to bony and cartilaginous structures anteriorly (Logemann 1983). These muscles sequentially contract to reduce the diameter of the pharynx and subsequently drive food inferiorly into the stomach (Corbin-Lewis and Liss 2014, Plural Publishing 2016). The inferior constrictor is the strongest pharyngeal muscle; it extends inferiorly to form the cricopharyngeus which is part of the upper esophageal sphincter (UES). The pharynx is mostly innervated by the pharyngeal branch of the vagus nerve, however this will be discussed in depth in Chapter 1.1.2 (Last and McMinn 1994).

1.1.1.6 Upper Esophageal Sphincter

The UES is continuous with the inferior constrictor. It is a high-pressure region, that anatomically separates the pharynx from the esophagus (Murry, Carrau et al. 2020). The UES is formed by the cervical esophagus, inferior pharyngeal constrictor and predominantly, the cricopharyngeus (Figure 5). The anterior aspect of the UES is formed by the posterior surface of the cricoid and arytenoid cartilages and inter-arytenoid muscles superiorly (Sivarao and Goyal 2000). The UES is innervated by branches of the vagus, glossopharyngeal and ansa cervicalis (Mittal 2011).

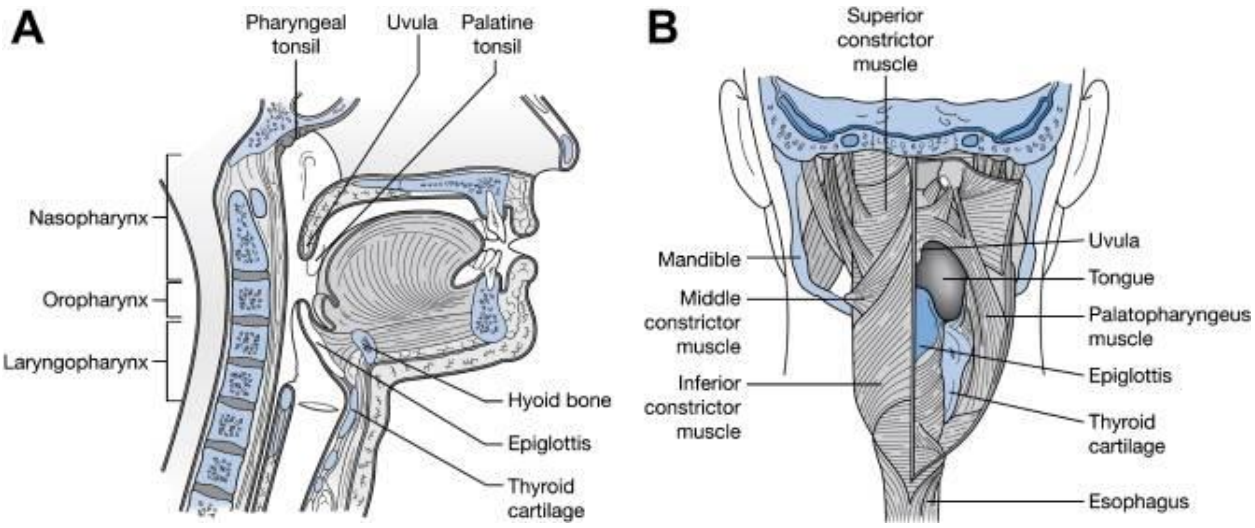
The UES is tonically contracted at rest; this prevents the inhalation of air into the esophagus with respiration and prevents the entry of refluxed materials into the hypopharynx (Sivarao and Goyal 2000, Carrau, Murry et

al. 2016). Intermittently, the UES is able to relax and open to allow the entry of food into the esophagus. UES relaxation occurs due to the 1) relaxation of the inferior pharyngeal constrictor, 2) forward and anterior excursion of the hyo-laryngeal complex due to contraction of the suprahyoid muscles and 3) the distracting force of the bolus itself (Sivarao and Goyal 2000). The inability of the UES to sufficiently relax results in impaired entry of the swallowed bolus into the esophagus.

1.1.1.1 The Esophagus

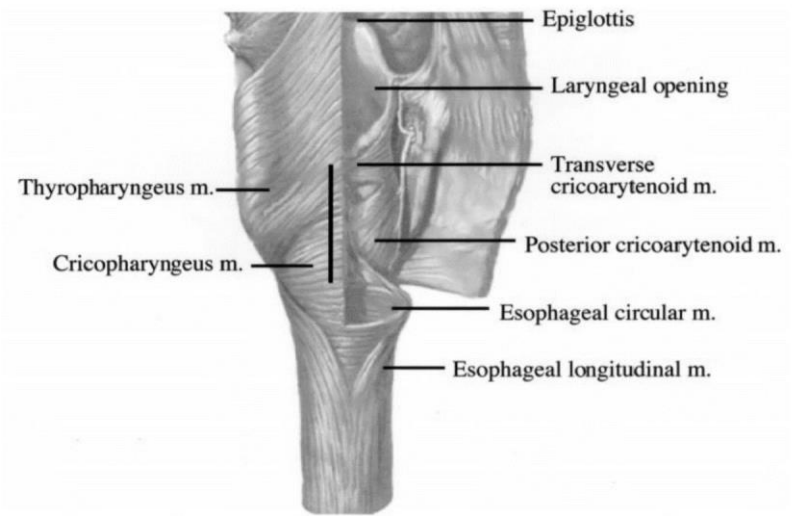
The esophagus is a muscular tube, approximately 25 centimetres in length, connecting the pharynx to the stomach (Last and McMinn 1994). The esophagus has an outer longitudinal and an inner circular layer which is skeletal muscle in the upper third, whilst the lower two-third is smooth muscle (Figure 5) (Last and McMinn 1994). The primary role of the esophagus is to facilitate the transit of ingested food into the stomach, which occurs through peristalsis (Carrau, Murry et al. 2016, Plural Publishing 2016). Peristalsis is the sequential contraction of the esophagus; where ingested food is propelled inferiorly by contraction above the bolus and simultaneous relaxation below it (Murry, Carrau et al. 2020). This action allows food to travel and enter the stomach for further digestion.

Figure 4 Relationship of the pharyngeal constrictors



Diagrammatic depiction of the oral cavity and the pharynx in the lateral (A) and posterior-anterior view (B) (Matsuo and Palmer 2008). Demonstrating the anatomical relationship of the pharyngeal constrictors to the skull base, midline and esophagus.

Figure 5 Dorsal view of the upper esophageal sphincter and the esophagus



The UES is composed of the cervical esophagus and the inferior pharyngeal constrictor muscles. The thyropharyngeus and cricopharyngeus muscles make up the inferior pharyngeal constrictor.

The vertical line demonstrates the extent of the high pressure zone of the UES (Sivarao and Goyal 2000)

1.1.2. NEUROANATOMY AND NEURO-REGULATION OF SWALLOWING

There are five cranial nerves responsible for swallowing (Matsuo and Palmer 2008). The trigeminal, facial, glossopharyngeal, vagal and hypoglossal nerve are responsible for the motor and sensory control of swallowing (Table 1) (Sasegbon and Hamdy 2017).

Table 1 Cranial nerves involved in the swallowing reflex

Cranial nerve	Function	Muscles innervated
Trigeminal nerve (CN V)	CN V has both sensory and motor components. It receives sensation from the anterior two-thirds of the tongue, the lower lip, mucous membranes of the cheek and the teeth of the lower jaw. CN V supplies the muscles of mastication.	Anterior belly of digastric Masseter Medial and lateral pterygoids Mylohyoid Temporalis Tensor veli palatini
Facial nerve (CN VII)	The motor component assists with hyoid elevation through action of the stylohyoid and posterior belly of digastric muscle. Taste from the anterior two-thirds of the tongue is supplied by the chorda tympani.	Facial muscles Posterior belly of digastric Stylohyoid
Glossopharyngeal nerve (CN IX)	CN IX provides sensation and receives taste from the posterior one-third of the tongue. It also receives sensation from the palatine tonsils and oropharynx. It forms part of the pharyngeal plexus	Stylopharyngeus
Vagus nerve (CN X)	The recurrent laryngeal nerve supplies all muscles of the larynx (apart from the cricothyroid) and receives sensation from the mucous membranes of the larynx and cervical segments of the esophagus. The pharyngeal plexus is formed by the pharyngeal branch, external branch of the superior laryngeal nerve and glossopharyngeal nerve to supply the mucous membrane of the pharynx and most of the muscles of the soft palate.	Cricopharyngeus Intrinsic laryngeal muscles Levator veli palatine Palatopharyngeus Pharyngeal constrictors Salpingopharyngeus
Hypoglossal nerve (CN XII)	Supplies all the intrinsic and most of the extrinsic muscles of the tongue	Intrinsic tongue muscles Hyoglossus Geniohyoid Genioglossus Styloglossus Thyrohyoid

Table derived from Anatomy and physiology of feeding and swallowing: normal and abnormal (Matsuo and Palmer 2008, Sasegbon and Hamdy 2017)

The oral phase of swallowing is mostly under voluntary control, whilst the pharyngeal and esophageal stages are reflexive (Sasegbon and Hamdy 2017). As the bolus moves through the oral cavity and the pharynx it stimulates various sensory receptors; which relay information to a region in the brainstem reticular formation known as the nucleus tractus solitarius (NTS) (Corbin-Lewis and Liss 2014). The NTS is commonly known as the swallowing centre or the swallowing pattern generator. Once activated, the swallowing centre generates inhibitory or excitatory signals to the nucleus ambiguus which innervates muscles of the soft palate, pharynx, larynx and upper esophagus through the action of the glossopharyngeal, vagus and spinal accessory nerve (Corbin-Lewis and Liss 2014, Baker and Lui 2019). This pathway is known as the pharyngeal swallowing reflex.

There are specific points within the pharynx that act as a trigger for the NTS to modulate this reflex; this includes the anterior pillars, base of tongue, valleculae, pyriform sinuses and the larynx (Logemann 1983, Corbin-Lewis and Liss 2014). Sensory stimuli across these points can alter the pharyngeal swallowing reflex. Therefore, variations in the bolus consistency, volume, viscosity, texture and even taste can modulate the timing and pattern of the swallowing sequence (Barlow 2009, Corbin-Lewis and Liss 2014).

1.1.3. PHYSIOLOGY AND BIOMECHANICS OF SWALLOWING

1.1.3.1. Models of swallowing

A swallow is described according to the position of the bolus – oral, pharyngeal and esophageal (Dodds, Stewart et al. 1990, Sasegbon and Hamdy 2017). Although similar, there are two models that describe a swallow; the Four-Stage model is used to describe the movement of a liquid bolus (Matsuo and Palmer 2008), however, it has limited utility in describing bolus formation and movement in solids, therefore the Process Model of Feeding is used for solids (Palmer, Rudin et al. 1992, Dua, Ren et al. 1997, Hiiemae and Palmer 1999) (Figure 6 and 7).

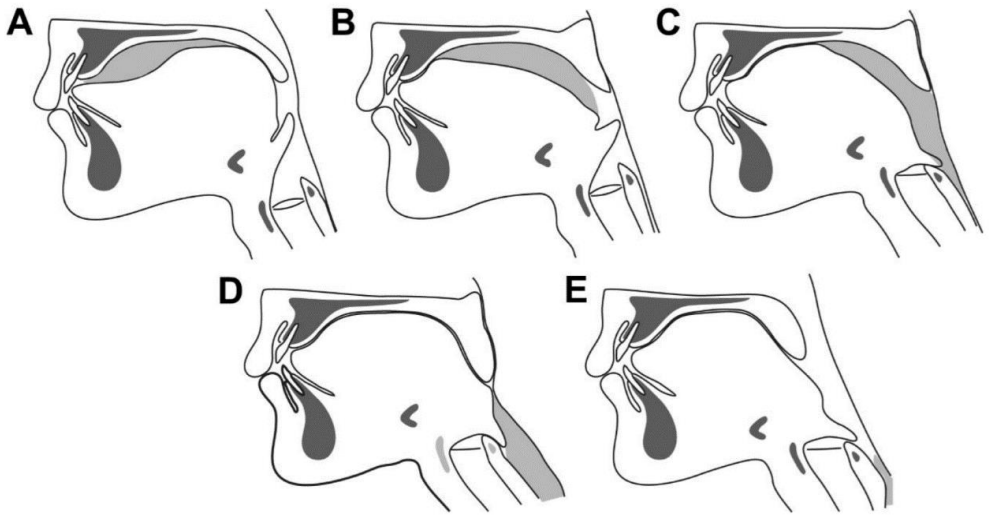
The oral stage is divided into an oral preparatory and propulsive stage in the four-stage model; whilst in the Process Model the oral stage is broken into Stage I transport, food processing followed by Stage II transport (Table 2) (Figure 6 and 7). The subsequent pharyngeal and esophageal stages are the same across both models.

Table 2 Models of swallowing

	Four-stage model (liquids)		**Process model of feeding (solids)**	
1. Oral	Preparatory	The bolus is sealed within the oral cavity (by the hard palate and posterior tongue) to prevent spillage	Stage I transport	Solid food is directed laterally to the occlusion surfaces of the molars
	Propulsive	Posterior tongue falls to direct the bolus to move into the oropharynx	Food processing	Food is mechanically reduced in size and softened. This requires coordination between the tongue, soft palate and cheek
			Stage II transport	The bolus is propelled posteriorly and allow to accumulate on the base of tongue and/or vallecula
2. Pharyngeal	The soft palate is elevated to seal the nasopharynx and the base of tongue is retracted against the pharyngeal wall to guide the bolus posteriorly. The pharyngeal constrictors sequentially contract, guiding the bolus inferiorly			
3. Esophageal	During a swallow, the UES relaxes which allows bolus entry into the esophagus and subsequently the stomach with lower esophageal sphincter relaxation.			

Table derived from Anatomy and physiology of feeding and swallowing: normal and abnormal (Matsuo and Palmer 2008)

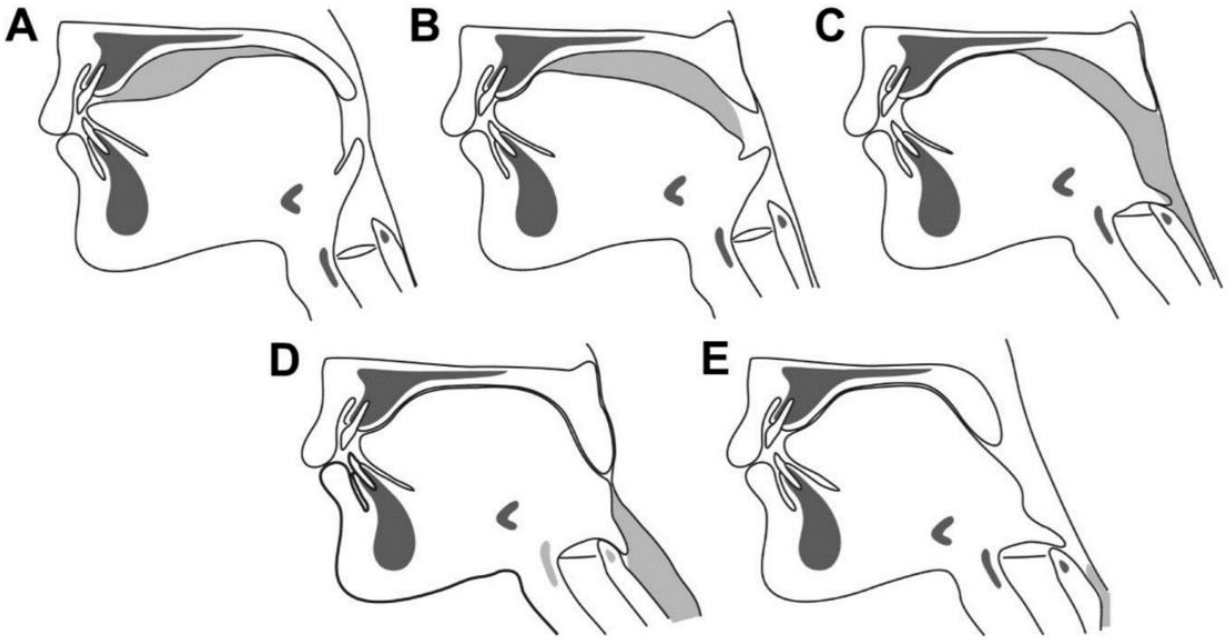
Figure 6 Four-stage process model



Diagrammatic representation of the four-stage process of swallowing a liquid bolus.
Oral preparatory stage (A), oral propulsive stage (B), pharyngeal stage (C and D) and esophageal stage (E)

Image from Anatomy and physiology of feeding and swallowing: normal and abnormal (Matsuo and Palmer 2008)

Figure 7 Oral phase of the Process Model of Feeding



Diagrammatic representation of the Process Model of feeding for swallowing a solid bolus.
Food is triturated and subsequently pushed into the oropharynx by movement of the tongue (A-C). The bolus is left to accumulate in the vallecula whilst food processing occurs, prior to the pharyngeal stage (D-E).

Image from Anatomy and physiology of feeding and swallowing: normal and abnormal (Matsuo and Palmer 2008)

1.1.3.2. Mechanics of the pharyngeal stage of swallowing

The pharyngeal phase of swallowing can be mechanistically divided into various anatomical segments; this allows easier biomechanical analysis of disordered swallowing (Table 3) (Dua, Ren et al. 1997, Logemann 1998, Jones, Meisner et al. 2018).

Table 3 Mechanistic actions

Anatomical segments	Muscles and mechanistic action
Velopharynx	The superior pharyngeal constrictor, levator veli palatini, musculus uvulae and palatopharyngeus assist in elevating the soft palate to seal the nasopharynx. This prevents regurgitation into the nasopharynx
Oropharynx	The tongue base pushes the bolus against the posterior pharyngeal wall; this results in positive pressure on the 'tail' of the bolus. Sequential contraction from the pharyngeal constrictors guides the bolus towards the UES and esophagus. Muscles involved include the palatoglossus, hyoglossus and pharyngeal constrictors.
Hypopharynx	Various protective mechanisms generate a negative pressure that direct the bolus away from the larynx and towards the esophagus; therefore, preventing aspiration.
Upper Esophageal Sphincter	The UES is tonically contracted at rest. The cricopharyngeus and the circular skeletal segment of the cervical esophagus relax to allow bolus entry. UES opening is further assisted through movement of the laryngeal framework (Chapter 1.1.4.2)

The pharynx and larynx are complex, shared structures that facilitate both deglutition and respiration; they work synergistically to guide the bolus safely into the esophagus, minimising the risk of aspiration during swallowing.

1.1.4. COORDINATION OF SWALLOWING AND RESPIRATION

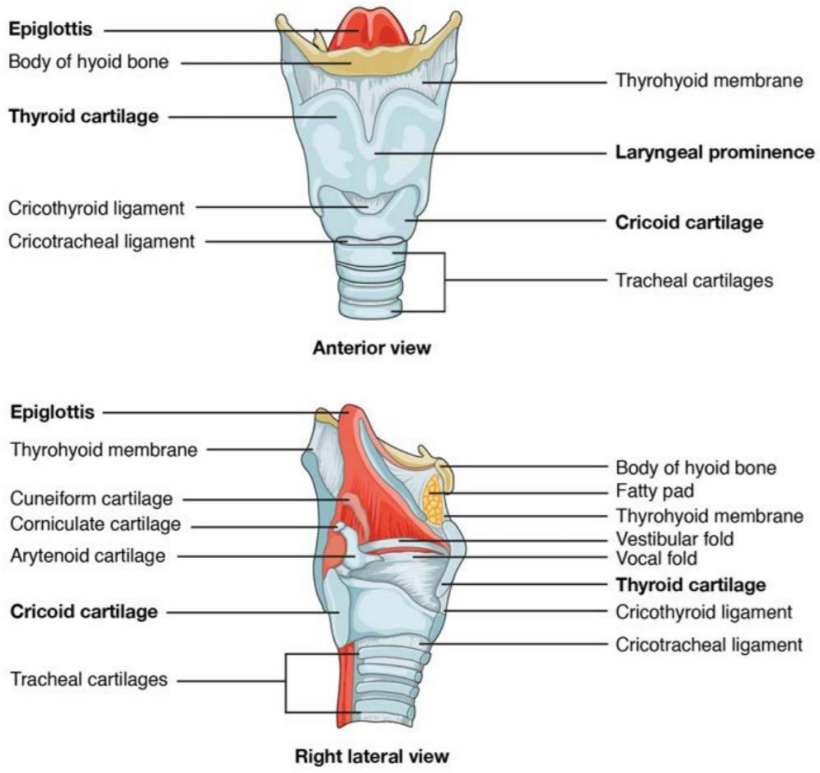
1.1.4.1. The larynx

The larynx is a mucosal-lined, cartilaginous structure that lies inferior and anterior to the hypopharynx. It is composed of interacting muscles, cartilages and ligaments which connects the pharynx to the trachea (Carrau,

Murry et al. 2016). The basic role of the larynx is airway protection and respiration; however, in humans, its function has evolved to include phonation (Carrau, Murry et al. 2016).

The larynx is composed of three cartilage pairs (arytenoids, cuneiform and corniculate) and three single cartilages (epiglottis, thyroid and cricoid) (Figure 8) (Last and McMinn 1994, Armstrong and Netterville 1995). The thyroid cartilage is the largest cartilage and along with the cricoid, which sits inferiorly, it provides the general framework for the larynx. The cuneiform and corniculate cartilages lie on top of the arytenoid, which itself, rests on top of the cricoid cartilage (Tarrazona and Deslauriers 2007).

Figure 8 Cartilaginous and bony anatomy of the larynx



Anterior and lateral view demonstrating the bony and cartilaginous relationship of the larynx. The framework created by the larynx and the hyoid bone is known as the hyo-laryngeal complex.

Image from Open Stax College, Anatomy & Physiology (Betts 2017)

1.1.4.2. Laryngeal protective mechanisms during swallowing

The larynx and pharynx synergistically work to prevent aspiration by guiding the bolus towards the esophagus. These protective mechanisms include 1) the glottic reflex in which the vocal cords adduct to seal entry into the airway, 2) forward tilting of the arytenoids towards the epiglottic base, 3) anterior and superior movement of the hyo-laryngeal complex controlled by the suprahyoid and thyrohyoid muscles and 4) epiglottic retroflexion to seal the laryngeal vestibule (Shaker, Dodds et al. 1990, Logemann, Kahrilas et al. 1992, Ohmae, Logemann et al. 1995). Superior movement of the hyo-laryngeal complex, whilst preventing aspiration, also facilitates UES opening through relaxation of cricopharyngeus (Figure 9) (Cook, Dodds et al. 1989, Shaw, Cook et al. 1995, Ertekin and Aydogdu 2002).

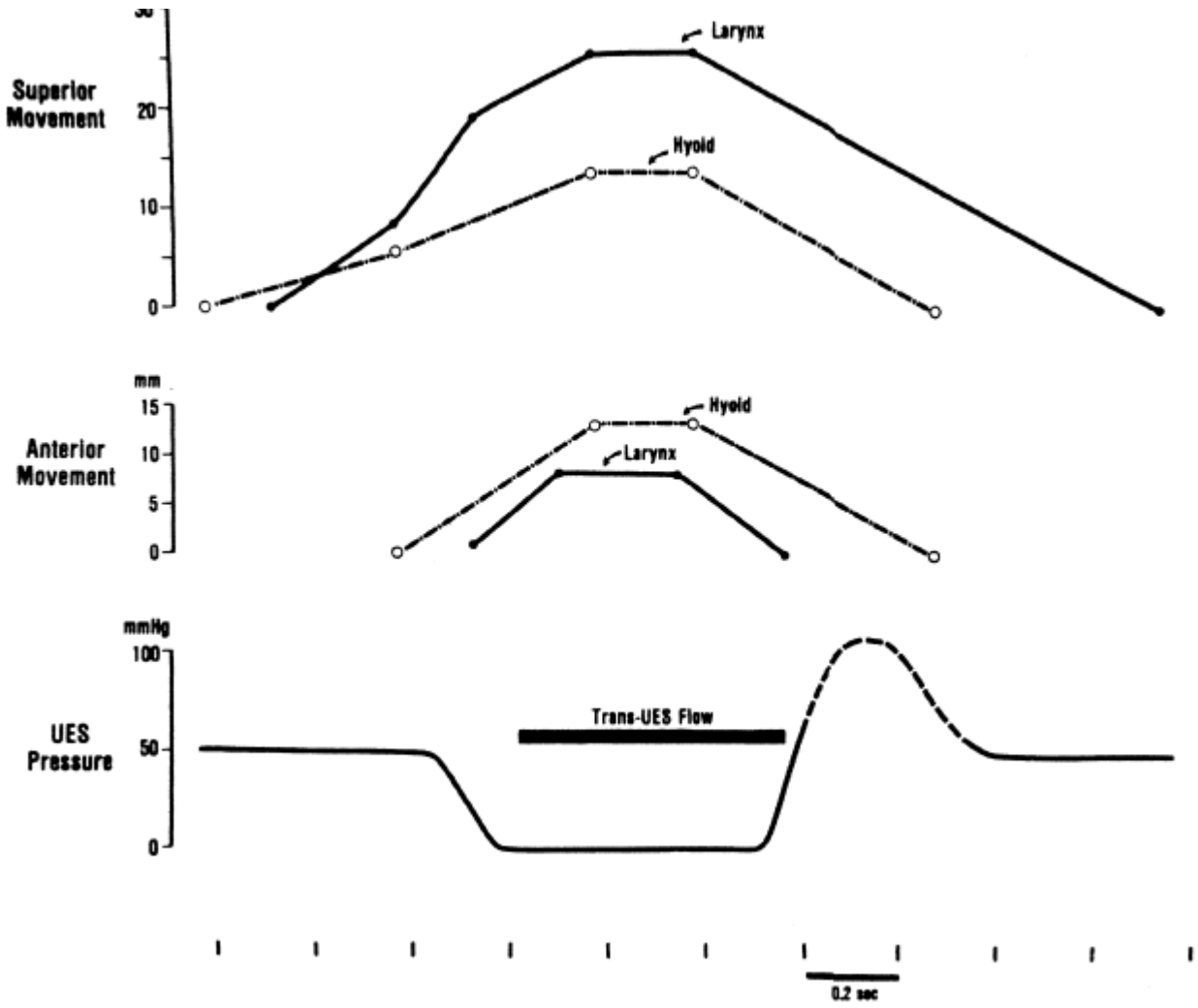
1.1.4.3. Suppression of respiration

Deglutition and respiration utilise a common tract and is therefore tightly coordinated (Matsuo and Palmer 2008). Swallowing is the dominant action, and therefore respiration is briefly ceased during swallowing (Nishino, Yonezawa et al. 1985, McFarland and Lund 1995). This pause occurs through brainstem mediated neural suppression of breathing and the physical closure of the airway through various laryngeal protective mechanisms (Nishino and Hiraga 1991).

Brain stem suppression of respiration results in swallowing apnoea which is dependent on the individual's age, bolus consistency, bolus size and whether the swallow is cued or spontaneous (Carrau, Murry et al. 2016). Swallowing usually occurs in the expiratory phase of respiration, with apnoea lasting for up to 1.5 seconds (Martin-Harris, Brodsky et al. 2005, Carrau, Murry et al. 2016). After swallowing, resumption of breathing often occurs during the expiratory phase (Shaker, Li et al. 1992, Matsuo and Palmer 2008, Carrau, Murry et al. 2016). This mechanism not only prevents inhalation of food but allows the positive pressure generated during expiration to assist with laryngeal clearance (Shaker, Li et al. 1992).

Swallowing is an intricate and complex process requiring sequential and coordinated actions. Clinical and instrumental assessments allow further evaluation into the structural and functional causes of disordered swallowing.

Figure 9 Manometric recording of hyolaryngeal movement and UES pressures during swallowing



Manometric data assessing anterosuperior movement of the hyolaryngeal complex in association to UES pressures.

Following the initiation of swallowing, vagal stimulation results in the loss of active tension within the UES resulting in a drop in resting pressures to near atmospheric levels (Asoh and Goyal 1978, Medda, Lang et al. 1997, Williams, Wallace et al. 2002).

The intra-sphincteric pressures are further reduced to sub-atmospheric levels following superior and anterior movement of the hyolaryngeal complex; this results in UES luminal wall separation with subsequent bolus flow across a large pressure gradient (Jacob, Kahrilas et al. 1989, Williams, Wallace et al. 2002).

This relaxation can last for up to one second; after which the sphincter contracts with a force higher than its baseline (as shown with the dashed UES pressure) before returning to its normal resting tone (Carrau, Murry et al. 2016).

Image from Functional anatomy and physiology of the upper esophageal sphincter (Sivarao and Goyal 2000).

1.2 EVALUATION OF SWALLOWING

Patients can be screened and evaluated to identify the presence of disordered swallowing which may result in aspiration. The purpose of a swallow assessment is to 1) identify structures and/or functional parameters affecting normal swallowing function, 2) understanding the effect impaired swallowing has on an individual and 3) minimise the impact of disordered swallowing through various strategies (De la Corte-Rodriguez and Rodriguez-Merchan 2016). Swallowing assessments involve the use of patient-reported outcome measures, clinical and instrumental swallowing assessments.

1.2.1 Patient Report Outcome Measures

Patient-Reported Outcome Measures (PROMs) are defined as a "report that comes directly from the patient about the status of a patient's health condition without amendment or interpretation" by a clinician (Snyder, Jensen et al. 2013, Patel, Sharda et al. 2017). PROMs assist with clinical decisions and research by providing patient-centred evidence on the effect of various conditions or treatments on a patient's symptoms and quality of life (Snyder, Jensen et al. 2013).

There are at least 34-dysphagia related PROM's (Patel, Sharda et al. 2017), with the first PROM being developed in 1987 to identify benign esophageal pathologies (Andersen, Madsen et al. 1987). Commonly used PROMs for oropharyngeal dysphagia are the M.D Anderson Dysphagia Inventory (also known as MDADI) (Chen, Frankowski et al. 2001), Swallowing Quality of Life questionnaire (also known as SWAL-QOL) (McHorney, Bricker et al. 2000) in those with head and neck cancer, the Sydney Swallowing Questionnaire (also known as SSQ) (Wallace, Middleton et al. 2000) in patients with mechanical and neurogenic dysphagia (Patel, Sharda et al. 2017) and the 10-Item Eating Assessment Tool (also known as EAT-10) to quantify patient-perceived symptoms and monitor treatment efficacy in a wide range of swallow disorders (Belafsky, Mouadeb et al. 2008).

PROM's are useful in understanding the impact of dysphagia on a patient's quality of life; it serves as a screening tool or a method of assessing change. There are however limitations with PROM's: 1) its use in a populations for which it has not been validated for can create potential bias or error (Logemann and Pitts

2013), 2) it can be difficult to interpret when incompletely filed (Zraick, Atcherson et al. 2012, Patel, Sharda et al. 2017) and 3) these measures are not reliable in patients with treatment or disease misconceptions, cognitive impairment or reduced literacy (Logemann and Pitts 2013). Therefore, an appropriate and validated PROM can act as a quick screening tool that can result in directing further assessments.

1.2.2 Non-instrumental swallow assessments

The purpose of non-instrumental assessments is to observe for specific reported signs and symptoms of disordered swallowing in a patient (Ricci Maccarini, Filippini et al. 2007). A clinical swallowing examination is usually performed by a speech pathologist at the patient's bedside, it is divided into a preparatory examination and a swallowing examination. The preparatory examination involves gathering information based on the patient's medical status and past medical history to further understand their nutritional and respiratory requirements (Logemann 1983). Following this, the patient is examined; assessing their mental status, cranial nerves, oro-motor and laryngeal function and control, and general reaction during swallowing attempts without a bolus provided (Logemann 1983, Ricci Maccarini, Filippini et al. 2007). During the swallowing examination, boluses of varying volumes and consistencies are presented to the patient; this allows further examination into compensatory behaviours and signs of aspiration which may include coughing or a change in voice quality (Logemann 1983, Ricci Maccarini, Filippini et al. 2007). It is important to recognise that 50-60% of patients who aspirate do not cough (Logemann 1983), and therefore if a patient does not produce any visual or recognisable symptoms, aspiration may remain undiagnosed. It has been demonstrated that the clinical swallowing examination fails to identify aspiration in approximately 40% of patients (Linden and Siebens 1983, Logemann 1983, Splaingard, Hutchins et al. 1988, Leder and Espinosa 2002). These findings are further supported by a systemic review that showed that swallow tests had sensitivities and specificities as low as 27% and 63% respectively (Bours, Speyer et al. 2009). Therefore, the clinical swallowing examination is an inexpensive screening tool but it has some inaccuracies in patients that may not demonstrate symptoms, highlighting the need for instrumental and objective forms of evaluation (Logemann 1983).

1.2.3 Instrumental swallow assessments

1.2.3.1 Video-fluoroscopy

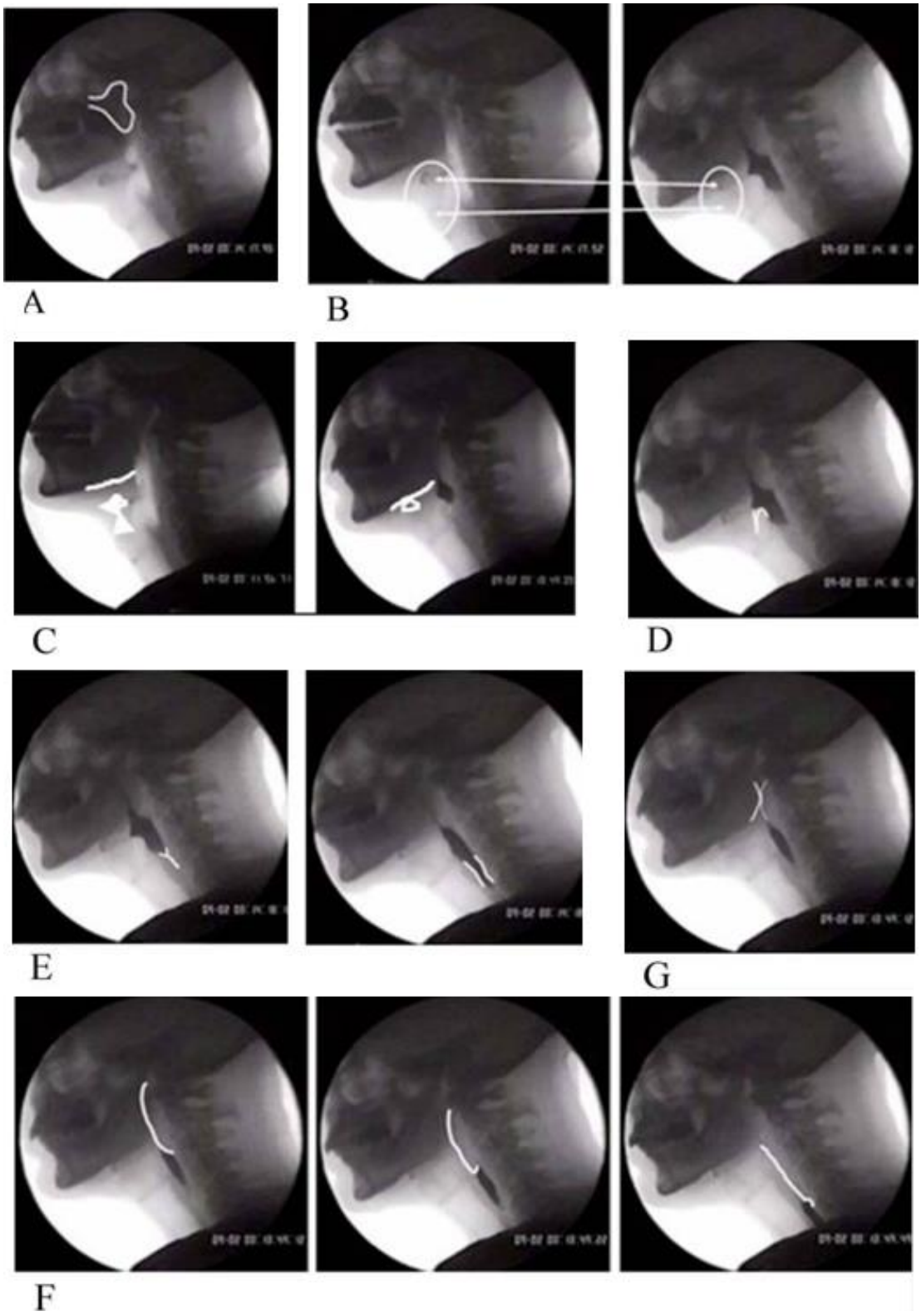
A videofluoroscopic swallow study (VFSS) is also known as a modified barium swallow (MBS) and is the gold standard for swallowing assessments. It is a recorded radiographic assessment that provides real-time visualisation of the oral cavity, oropharynx, larynx and esophagus using barium coated boluses of differing volumes and consistencies (Langmore, Schatz et al. 1991). Videofluoroscopic swallows occur in a radiology suite in the presence of a specially trained speech pathologist, radiologist and radiographer; with the patient required to be in an upright seated position. Bolus ingestion and transfer can be visualised in real-time; in the lateral and anterior-posterior view.

A VFSS is able to visualise all phases of a swallow, from the oral cavity through to the upper esophageal sphincter and esophagus (Kaye, Zorowitz et al. 1997, Martin-Harris and Jones 2008). It can radiologically demonstrate the anatomy and coordination of a swallow, which can be used to derive biomechanical measurements such as hyo-laryngeal complex elevation, base of tongue retraction and pharyngeal movements in relation to the bolus (Figure 10) (Martin-Harris and Jones 2008). Diagnostically, it can demonstrate restrictions caused by cervical osteophytes and surgical plates. Importantly, VFSS is able to identify aspiration but can also provide information about the timing of when it occurred and the subjective amount aspirated (Cook, Dodds et al. 1989, Dodds, Stewart et al. 1990, Logemann, Kahrilas et al. 1992, Martin-Harris, Logemann et al. 2000). This knowledge can be used to assess the effectiveness and influence of compensatory swallowing modifications and dietary changes (Martin-Harris, Logemann et al. 2000).

Although VFSS is the gold standard for instrumental dysphagia assessments, it has a few limitations (Martin-Harris, Logemann et al. 2000, Martin-Harris and Jones 2008). Fluoroscopic studies require screened X-ray sequences; therefore, to limit radiation exposure, only specific boluses and volumes may be tested, which may not be representative of a patient's swallow or diet. Furthermore, barium is poorly tolerated by some patients due to its unnatural taste and texture and is contraindicated in those with an allergy to it or other contrast mediums (Shapiro 2000). The need for specialised equipment, staff and a radiology suite mean that VFSS is a

costly examination that can only be provided by certain facilities. Additionally, only patients that can be safely transferred to the radiology department, that aren't pregnant and are able to tolerate sitting upright independently for a prolonged period of time can be examined using fluoroscopy (Jones 1999, Kim, Lee et al. 2018).

Figure 10 VFSS images demonstrating swallowing phases and biomechanical movements



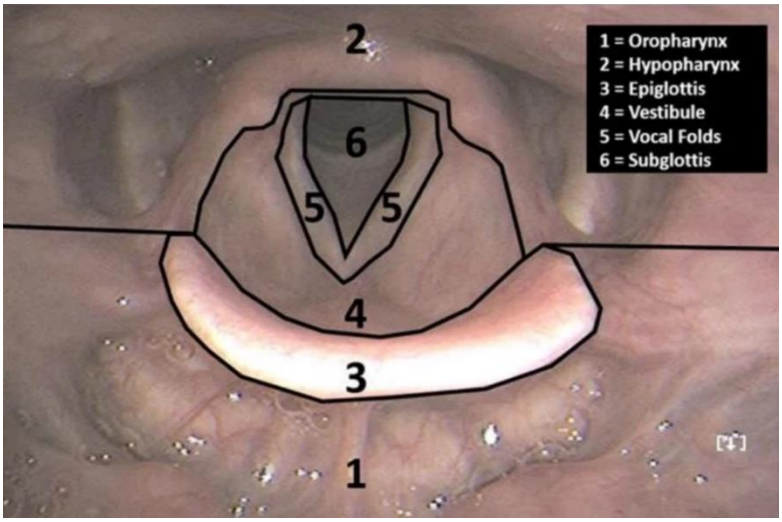
A – elevation and retraction of the soft palate, B – elevation and anterior movement of the larynx, C – hyoid bone movement, D – arytenoid apposition to epiglottic base, E – opening and distension of the pharynx, F – sequential pharyngeal contraction and G – tongue base movement against posterior pharyngeal wall

Image from "The videofluorographic swallowing study" (Martin-Harris and Jones 2008)

1.2.3.2 Fibreoptic endoscopic evaluation

The fibreoptic endoscopic evaluation of swallowing (FEES) was first published in 1988 as an alternative to VFSS to evaluate oropharyngeal dysphagia when fluoroscopic swallows could not be conducted due to patient or institutional limitations (Langmore, Schatz et al. 1988). FEES is a portable examination, usually conducted by a specially trained speech pathologist, in which a thin, flexible, nasoendoscope is passed through the nostril and used to visualise structures of the nasopharynx, oropharynx and larynx (Figure 11). The endoscope usually sits at the level of the soft palate and is used to visualise bolus and pharyngeal movement, which can be seen on a monitor.

Figure 11 Structures visualised during FEES



Oropharyngeal and laryngeal surface anatomy visualised using the fibreoptic nasoendoscope.

Image taken from "Detection of Aspiration, Penetration, and Pharyngeal Residue During Flexible Endoscopic Evaluation of Swallowing: Comparing the Effect of Color, Coating and Opacity (Curtis, Seikaly et al. 2020)

The major benefit of FEES is that it can be used at the bedside so it can be used on those patients that are critically unwell (Kaye, Zorowitz et al. 1997). Furthermore, as FEES does not require radiation, it can be performed during pregnancy and can be repeated after various interventions are implemented, to assess for improvement (Logemann 2007). FEES also provides a unique view to the surface anatomy of the pharynx and

larynx; 1) it can show mucosal abnormalities that may impact a swallow, 2) shows how a patient manages their secretions which can be indicative of aspiration, and 3) allows visualisation of velopharyngeal l closure, oropharyngeal and airway protective manoeuvres in response to the bolus (these are not possible with VFSS). As FEES is theoretically not time limited, it is more sensitive to swallowing dysfunction secondary to fatigue. Furthermore, the nasoendoscope is able to touch the laryngeal mucosa to test for sensation (Aviv, Kaplan et al. 2000, Nacci, Ursino et al. 2008, Fattori, Giusti et al. 2016).

FEES is primarily used for the assessment of oropharyngeal dysphagia as it does not allow visualisation of the oral and esophageal phase, and therefore this is inferred based on movements of the tongue base and position of the residual bolus (Langmore 2006). Furthermore, movement of the pharynx and the bolus cannot be observed 'during' the swallow due to the white-out phenomenon (Nacci, Ursino et al. 2008, Fattori, Giusti et al. 2016). The white-out is caused by the endoscope's light being reflected back from the mucosa during pharyngeal contraction, with only a brief view of tongue base retraction, lateral pharyngeal wall contraction and epiglottic retroflexion. As FEES requires a nasoendoscope to be passed through the nasopharynx, it can cause some discomfort and can induce gagging or vomiting in some patients and should be avoided in patients with facial trauma, severe epistaxis or coagulopathies (Aviv, Kaplan et al. 2000, Association 2004, Nacci, Ursino et al. 2008).

Both FEES and VFSS provide an anatomical and spatial visualisation of the pharynx, relative to the bolus (Fattori, Giusti et al. 2016). VFSS provides information about the pharyngeal phase of swallowing and is useful when the swallowing mechanism is altered in the oral and/or esophageal phase, as this cannot be visualised during FEES. On the other hand, FEES provides a unique view into the position of post-swallow residues and the oropharyngeal and laryngeal anatomy. Both assessments can reliably identify penetration (entry into the laryngeal vestibule but not past the vocal cords) and aspiration (entry of bolus past the vocal cords) (Aviv 2000, Kelly, Drinnan et al. 2007, Curtis, Seikaly et al. 2020). However, clinical interpretation of the swallow using VFSS and FEES beyond identifying penetration and aspiration is subjective and qualitative, resulting in poor intra- and interrater reliability (McCullough, Wertz et al. 2001, Stoeckli, Huisman et al. 2003, Knigge, Thibeault

et al. 2014). Therefore, due to their qualitative nature, interpretation of complex or multi-segment dysphagia using FEES or VFSS is often difficult; highlighting the need for a quantitative and instrumental method of assessment (Knigge, Thibeault et al. 2014).

1.2.3.3 High-resolution pharyngeal manometry

High-resolution pharyngeal manometry (HRPM) involves a solid-state manometric catheter, with multiple sensors to record the bolus flow and pressures generated by pharyngeal musculature during swallowing. This allows quantitative analysis which is not possible with FEES or VFSS.

1.2.3.3.1 Hardware

Manometry is currently the instrumental method of choice for the evaluation of esophageal disorders. The first manometry system was developed in 1970 by Jerry Dodds and Ron Arndorfer (Hani, Leguízamo et al. 2015). This system used hydrostatic pressures with limited sensors (usually three) to assess pressures within the esophagus, and patients could only be evaluated in the supine position. The development and introduction of high-resolution manometry has facilitated use in the sitting position and has been adapted from its esophageal application, for use in the pharynx (Carlson and Pandolfino 2015, Ryu, Park et al. 2015).

High-resolution manometry systems consist of a manometric catheter with multiple pressure transducers interfaced and integrated with various circuitry allowing digitization, display and recording of the data collected (Bredenoord and Hebbard 2012). In solid-state catheters, these pressure transducers are built within the catheter and therefore act as the point of reference. Pressures generated by contractility are converted into an electrical signal by the transducer, which is amplified and digitalized by the system. Pressure sensors can be unidirectional or circumferential; unidirectional sensors report pressures from a specific direction whilst circumferential sensors record a mean pressure around that segment (Guiu Hernandez, Gozdzikowska et al. 2018). It is thought that circumferential sensors may record data more reproducibly in asymmetric structures like the UES and the pharynx; although this has not been fully explored (Bredenoord and Hebbard

2012). HRPM allows data to be collected at more frequent intervals of time and space, compared to conventional manometry.

Newer solid-state catheters also have impedance sensors, which measures the resistance encountered between monitoring segments during the passage of a bolus. Impedance is inversely proportional to the luminal cross-sectional area and bolus conductivity (therefore impedance data will vary when differing boluses are used) (Nguyen, Domingues et al. 2006). A measuring segment surrounded by a bolus or reduction in luminal circumference will consequently have higher impedance values due to increased conductivity, compared to a segment surrounded by air. This relationship provides information about bolus presence, clearance and flow through the lumen during swallowing.

1.2.3.3.2 Preparation and testing

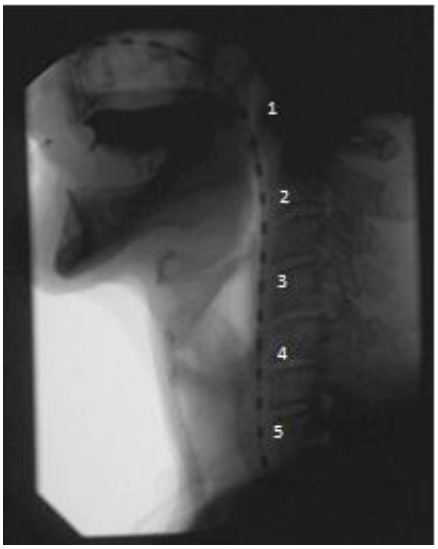
Solid-state manometry systems are simple to prepare and involve connecting the catheter to a recording system. Calibration differs across systems but are based on manufactures recommendations, it usually involves zero-referencing sensors based on the patient's position or a conductive medium like saline (Bredenoord and Hebbard 2012). There is minimal patient preparation, however, patients are to remain fasted prior to the study to minimise vomiting and aspiration during catheter insertion.

HRPM can be conducted at the bedside or in the outpatient setting. Testing usually takes approximately 30 minutes and the patient is assessed in the sitting position with their head in neutral. Lubrication and/or topical anaesthetic spray is used to introduce the catheter through the nostril. The catheter is secured to the patient's nose, for the duration of the examination, with sensors overlying parts of the nasopharynx and the entire length of the oropharynx, hypopharynx, UES and parts of the esophagus (Figure 12) (Knigge, Thibeault et al. 2014)

Based on a recent HRPM International Working Group's recommendation, a 5-minute accommodation period should occur prior to administrating boluses (Omari, Ciucci et al. 2020). A standardised saline concentrate is recommended due to its availability and a standardised ionic concentration which provides better impedance changes (Liu, Liao et al. 2018). Patients are usually verbally cued to swallow boluses of varying consistencies

(International Dysphagia Diet Standardization Initiative (IDDSI)) and volumes using a standardised saline concentrate, in order to test or challenge the structural and compensatory mechanisms of the swallowing pathway.

Figure 12 High-resolution pharyngeal manometry catheter positioning



Lateral fluoroscopic image demonstrating the HRPM catheter positioned across the 1) nasopharynx, 2) oropharynx 3) hypopharynx 4) UES and 5) esophagus

Image derived from "Implementation of high-resolution manometry in the clinical practice of speech and language pathology" (Knigge, Thibeault et al. 2014)

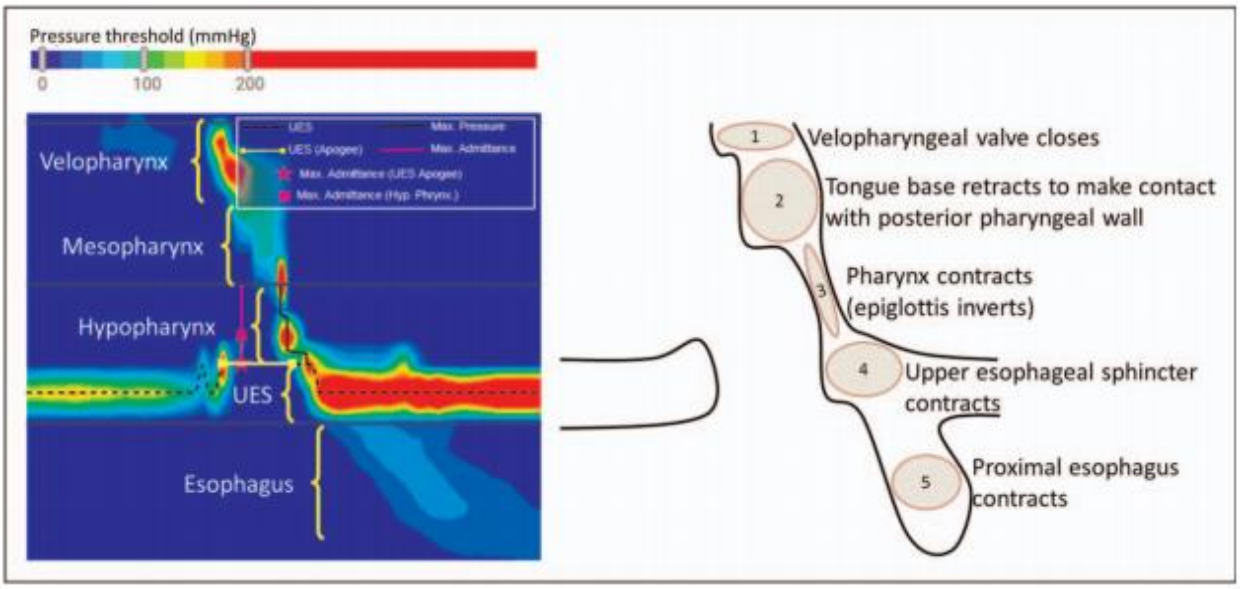
1.2.3.3.3 Safety of HRPM

HRPM has been demonstrated to be a safe and tolerable trans-nasal procedure; particularly with the use of topical anaesthesia (Knigge, Marvin et al. 2019, Hernandez, Leverson et al. 2020). Adverse events are similar to other trans-nasal procedures which include gagging, vomiting and epistaxis; however, these usually occur during insertion of the catheter and resolve once it is appropriately placed. Additionally, due to the blind technique used, difficulty in advancing the catheter including it 'looping' back into the pharynx has been reported in up to 3% of patients with no further complications (Knigge, Marvin et al. 2019).

1.2.3.3.4 Swallowing metrics

Purpose-written software such as Swallow Gateway™ is used to edit, display and subsequently analyse data recorded by the manometry system (Bredenoord and Hebbard 2012). Contractility and subsequent propulsion are recorded as a "time-linked ballistic pressure" wave with data presented as a spatiotemporal-pressure topography plot (Figure 13) (Jones, Meisner et al. 2018, Omari and Schar 2018). Data analysed includes pressures generated within the pharyngeal segments (velum, mesopharynx, hypopharynx and the UES) at rest and during a swallow, bolus flow and presence and timing. Variations in the timings or pressure generated during contractility or during bolus flow would allow precise identification of areas of weakness or impaired coordination; highlighting a disordered swallow (Jones, Meisner et al. 2018).

Figure 13 Spatiotemporal pressure topography plot



Pressure topography plot generated using purpose-build software on the left, correlated with biomechanical movements across the pharynx on the right. Brighter colours on the plot demonstrate regions where higher pressures are generated during contraction, compared to cooler colours.

Image from "High-resolution manometry: what about the pharynx?" (Omari and Schar 2018).

1.2.3.3.5 Validity of HRPM with other swallow assessments

The wide spread availability of high-resolution manometry equipment for pressure flow analysis and automated impedance manometry, has resulted in an increasing amount of interest in the clinical utility of

HRPM as an adjunct or alternate method of assessment for oropharyngeal dysphagia. Due to the use of a solid-state catheter and multiple, closely spaced pressure sensors, high-resolution manometry compared to conventional manometry, has been demonstrated to be more sensitive, reliable and accurate (Mielens, Hoffman et al. 2011, Geng, Hoffman et al. 2013, Park, Oh et al. 2016). Furthermore, it was observed that abnormal HRPM swallow parameters correlated to abnormal findings in video-fluoroscopic studies (Park, Oh et al. 2016); and importantly HRPM was demonstrated to have high intra- and inter-rater agreement, compared to video-fluoroscopy (Yoon, Park et al. 2014, Szczesniak, Maclean et al. 2015, Omari, Savilampi et al. 2016). Despite this, the test-retest reliability of HRPM differed for pharyngeal contractile variables (thought to be due to anatomical asymmetry), however was more consistent for measures of bolus flow, IBP and the Swallow Risk Index (Omari, Savilampi et al. 2016). Using several, reliable and reproducible HRPM metrics, a composite measure for global swallow function, known as the Swallow Risk Index (SRI) was developed and found to be a predictive marker for disordered swallowing and aspiration, highlighted on concurrent videofluoroscopic studies (Omari, Dejaeger et al. 2011, Cock and Omari 2017).

1.2.3.4 Role of instrumental assessments

Instrumental methods for assessing swallowing function have been demonstrated to be more reliable than patient-reported and clinical methods (Logemann 1983, Bours, Speyer et al. 2009). However, instrumental assessments require additional patient cooperation; therefore, its use is limited in patients with impaired or altered consciousness. Table 4 summarises the advantages and disadvantages of each instrumental method of assessment.

Table 4 Instrumental methods for swallowing assessment

	Advantage	Disadvantages
VFSS	▪ Can assess all phases of a swallow ▪ Assessment of the airway before, after and during a swallow ▪ Can measure hyolaryngeal elevation ▪ Can demonstrate vertebral pathology that may impact a swallow	▪ Exposure to radiation, although limited ▪ Costly due to resources and personnel required ▪ Need for a contrast medium ▪ Weight limitation ▪ Patients need to be able to remain upright unassisted ▪ Requires qualitative interpretation
FEES	▪ Ability to visualize mucosa, pharyngeal and laryngeal structures ▪ Longer duration of examination – can test for fatigue ▪ Able to use real food ▪ No radiation exposure ▪ Portable and bedside examination ▪ Visualisation of secretion management and ability to test laryngeal sensation	▪ 'White-out' period ▪ Unable to assess oral and esophageal phases of swallowing ▪ Discomfort and risk of epistaxis ▪ Can induce gagging or vomiting ▪ Special training needed ▪ Requires qualitative interpretation
HRPM	▪ Pressure and flow data are quantitative ▪ No radiation exposure ▪ Portable and bedside examination ▪ Can act as an adjunct to VFSS	▪ Unable to visualize structures ▪ Costly to set-up ▪ Discomfort and risk of epistaxis ▪ Can induce gagging or vomiting ▪ Requires training for interpretation ▪ Use of a conductive medium limits testing bolus used ▪ Time consuming analysis

1.3 TRACHEOSTOMY

Artificial means to secure an airway were depicted by the Ancient Egyptians in their artefacts and paintings as early as 3600 BC (Frost 1976). However, a surgical tracheostomy was first described in 1909 by Chevalier Jackson, with Ciaglia describing the first percutaneous tracheostomy in 1985 (Ciaglia, Firsching et al. 1985, Engels, Bagshaw et al. 2009). A tracheostomy is performed in 10-15% of critically ill patients admitted to the Intensive and Critical Care Unit (ICCU) (Whitmore, Townsend et al. 2020). The incidence of tracheostomy's performed is increasing due to advances in medicine allowing life-prolonging interventions in complex medical patients (Adhikari and Rubenfeld 2011).

1.3.1 Indications for a tracheostomy

Tracheostomies are performed electively or as an emergency to establish an artificial airway for various indications. In the ICCU, a tracheostomy is commonly performed electively in patients requiring prolonged ventilation or to facilitate weaning from respiratory support (Raimonde, Westhoven et al. 2020). Approximately 10% of patients undergo a tracheostomy, with the median time from ICCU admission to insertion approximately 9 days (Freeman and Morris 2012, Cheung and Napolitano 2014). An emergency tracheostomy is performed due to acute upper airway obstruction, in which an endotracheal tube (ETT) cannot be inserted or attempts have failed due to distorted anatomy. This usually occurs in the setting of severe facial or cervical trauma, head and neck cancers, or infections (Rashid and Islam 2017). General indications for a tracheostomy are 1) prolonged endotracheal intubation and mechanical ventilation, 2) upper airway obstruction secondary to infection, trauma or malignancy, 3) pulmonary toileting and airway protection (Engels, Bagshaw et al. 2009, Cheung and Napolitano 2014, Raimonde, Westhoven et al. 2020).

1.3.2 Tracheostomy technique

1.3.2.1 Surgical tracheostomy

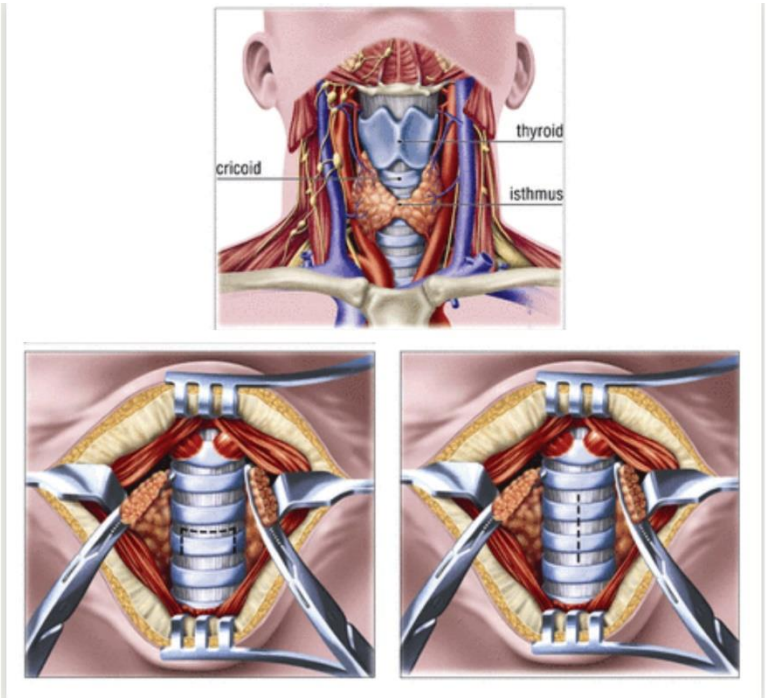
A surgical tracheostomy is performed in an operating theatre usually with a general anaesthetic, but, if necessary, can be performed under local anaesthetic (Figure 14). Firstly, a horizontal incision is made through

the skin between the cricoid cartilage and sternal notch. The surgeon dissects through the subcutaneous fat, platysma, infrahyoid muscles and thyroid isthmus, using a combination of monopolar and bipolar diathermy (Cheung and Napolitano 2014). The trachea is usually entered between the second and third tracheal rings. After confirmation of adequate ventilation and haemostasis, the tracheostomy is secured by suturing it to the skin around the tracheostomy (Zollinger and Ellison 2011).

1.3.2.2 Percutaneous tracheostomy

Percutaneous tracheostomies usually occur in ICU at the patient's bedside. The patient is sedated and positioned with their neck extended, if possible. Using a modified Seldinger technique, the trachea is punctured and sequentially dilated under bronchoscopic visualisation and guidance (Figure 15 and 16) (Seldinger 1953, Ciaglia, Firsching et al. 1985, Rashid and Islam 2017). The tracheostomy is inserted through the tract, confirmed with direct visualisation and adequate ventilation and secured with a tie.

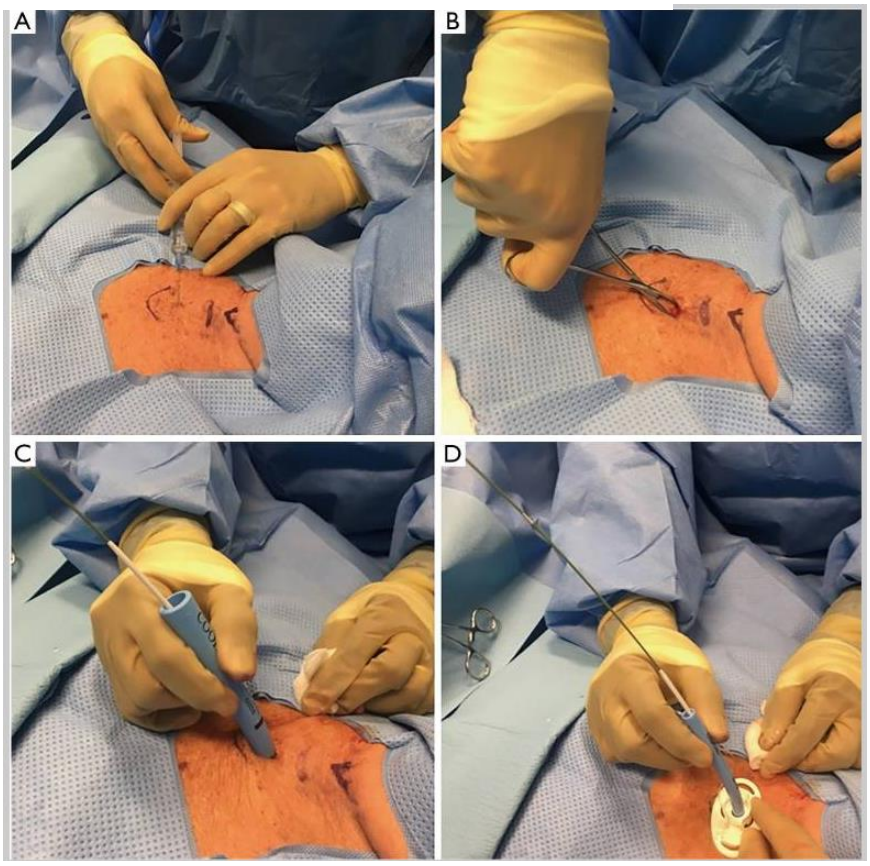
Figure 14 Surgical tracheostomy



A surgical tracheostomy in which a linear incision is made along the anterior neck. The thyroid, cricoid and sternal notch are used as surface markers. The strap muscles are retracted laterally and the isthmus is divided to expose the trachea. An incision or window is made through the tracheal rings, as demonstrated by the lower images and the tracheostomy is placed into the trachea.

Image from "Tracheostomy: Epidemiology, Indications, Timing, Technique, and Outcomes" (De Leyn, Bedert et al. 2007, Cheung and Napolitano 2014).

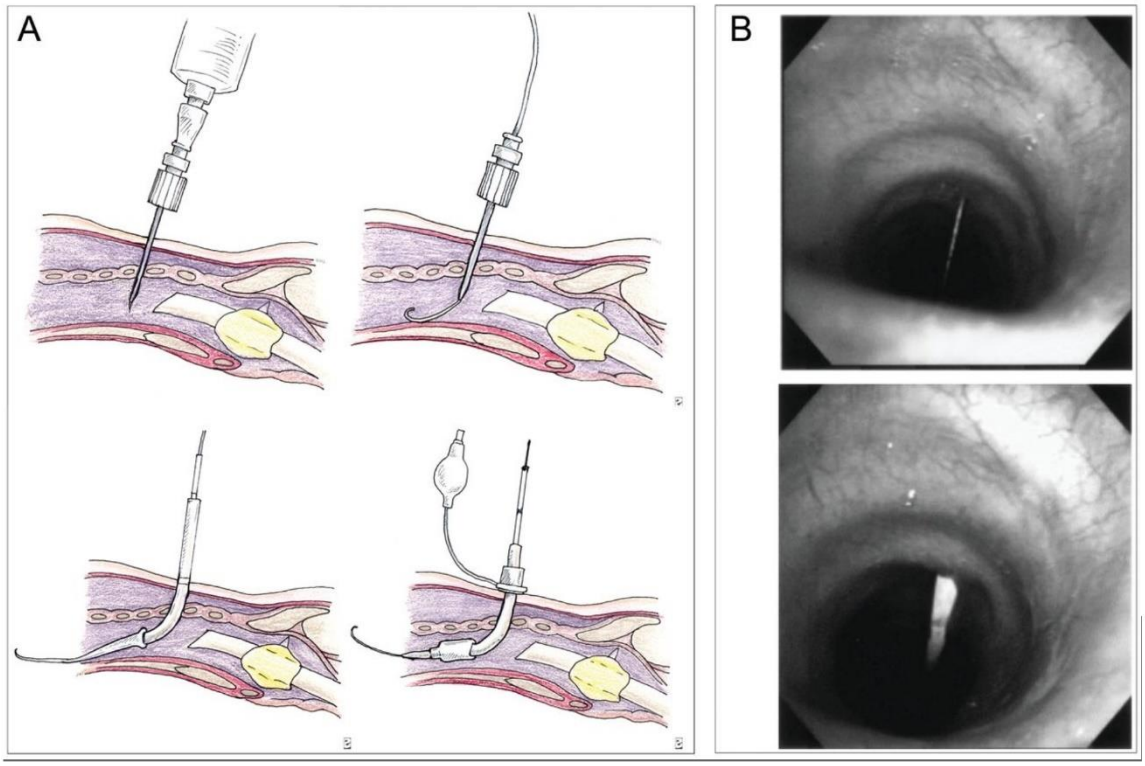
Figure 15 Percutaneous tracheostomy



Surface markings are made over the skin to identify the thyroid and cricoid cartilage and the sternal notch. Local anaesthetic is then infiltrated into the skin and along the planned percutaneous tracheostomy tract (Figure A). A puncture with a scalpel and then sequential dilatation with forceps and tapered dilators (Figure B and C). A tracheostomy is inserted into the trachea over a guidewire (Figure D)

Image sourced from “Percutaneous tracheostomy: a comprehensive review” (Rashid and Islam 2017).

Figure 16 Percutaneous tracheostomy (bronchoscopic view)



Diagrammatic image (A) demonstrating a midline puncture through the skin into the trachea which is made with a needle. This is conducted under bronchoscopic guidance (B) to avoid trauma to the posterior tracheal wall. Once in an appropriate position, a guide wire is advanced through the needle into the tracheal lumen. Dilators are sequentially inserted to dilate the tract prior to insertion of the tracheostomy.

Image sourced from "Percutaneous tracheostomy treatment and management" (Brietzke and Meyers , Durbin 2005).

The method in which a tracheostomy is performed is based on institutional preference and expertise. Surgical tracheostomies are usually performed as an adjunct in head and neck procedures but are also preferred in emergencies or in certain patient populations where insertion of a percutaneous tracheostomy maybe challenging or higher risk due to altered anatomy. This includes paediatric patients due to their smaller and conical airway, obese patients with increased anterior neck adiposity and those with cervical spine instability due to their limited neck movement (Higgins 2009, Ng, Hamrang-Yousefi et al. 2020).

1.3.3 Advantages of a tracheostomy

A tracheostomy provides several advantages over an ETT. 1) It is thought that a tracheostomy reduces the anatomical dead space and airway resistance resulting in reduced work of breathing and improved respiratory mechanics (Davis, Campbell et al. 1999, Diehl, El Atrous et al. 1999). 2) It has been demonstrated that the presence of an ETT is associated with oropharyngeal and laryngeal trauma; with the duration of intubation being directly correlated with the severity of injury, this can be minimised with a tracheostomy (Loh and Irish 2002, Rangachari, I et al. 2006, Brodsky, Levy et al. 2018). 3) Due to improved respiratory mechanics, reduced laryngeal trauma and easier pulmonary toileting; tracheostomy patients require a shorter duration of mechanical ventilation and therefore sedation resulting in improved patient comfort and mobility (Nieszkowska, Combes et al. 2005, Barquist, Amortegui et al. 2006, De Leyn, Bedert et al. 2007, Engels, Bagshaw et al. 2009). 4) Furthermore, it is thought that placement of a tracheostomy preserves individual swallow function; the absence of the ETT across the oropharynx and larynx, results in improved communication and the ability (or option) to be fed orally (Sasaki, Suzuki et al. 1977, Elpern, Scott et al. 1994, Nieszkowska, Combes et al. 2005).

1.3.4 Complications associated with a tracheostomy

Early complications (less than 7 days from insertion) of a tracheostomy are usually procedure-related. Bleeding is an early complication and is reported in around 5% of tracheostomies, but is noted to be more frequent in percutaneous tracheostomies. Early complications such as a wound infection or subcutaneous emphysema require observation whilst the formation of a false tract, accidental displacement of a tracheostomy tube or inner cannula obstruction require prompt management to re-establish a secure airway (Grillo 2004, De Leyn, Bedert et al. 2007, Engels, Bagshaw et al. 2009).

Late complications (after 7 days from insertion) are difficult to quantify and categorise as many of the patients are unwell or are lost to follow up. Tracheal stenosis is seen in 1% of patients and results from devascularisation and ischaemia due to the position of the cuff or the tube itself (Epstein 2005). Similarly, the incidence of tracheomalacia is around 8% and is related to cartilaginous disruption and weakness secondary to tracheostomy placement. Tracheoesophageal and tracheoarterial fistulas (<1%) are uncommon, although

have significant morbidity and associated health care costs (Sue and Susanto 2003, Epstein 2005, De Leyn, Bedert et al. 2007, Engels, Bagshaw et al. 2009).

Following decannulation (removal of the tracheostomy), delayed stomal closure (up to 40%) and a poor cosmetic scar (20%) are common complications (Sue and Susanto 2003, Epstein 2005, De Leyn, Bedert et al. 2007, Engels, Bagshaw et al. 2009).

1.3.5 Tracheostomy tubes

There a many different types of tracheostomy tubes with different lengths, luminal diameters and curvature. The material used to construct the tracheostomy vary from PVC, silicone or even metal (De Leyn, Bedert et al. 2007, Ng, Hamrang-Yousefi et al. 2020). A tracheostomy can also be cuffed or uncuffed (Figure 17).

1.3.5.1 Components of a tracheostomy tube

A tracheostomy has an outer cannula and usually an inner cannula that can be removed and exchanged in the case of tube obstruction or maintenance. The tracheostomy has a flange or collar which sits on the anterior aspect of the patient's neck and is usually secured with sutures or foam ties. It has a universal 15 mm connector for attachment to the ventilatory circuit (Figure 17) (Hess and Altobelli 2014, Ng, Hamrang-Yousefi et al. 2020).

In the ICU, cuffed tracheostomies are primarily used. The cuff, is an air-filled balloon that forms a seal around the tracheostomy and the tracheal wall when inflated. Cuff pressures are normally maintained between 20-30 cm H_2O to avoid mucosal necrosis (Sole, Su et al. 2011). Cuff inflation allows effective positive-pressure ventilation by preventing volume loss and leak (Ng, Hamrang-Yousefi et al. 2020). Additionally, it offers some protection from secretions being aspirated. Cuff-less or deflated cuffed tracheostomies are usually used in patients who are alert and have adequate ventilatory effort; as it provides an airway but no protection from aspiration (Han, Shin et al. 2016, Ng, Hamrang-Yousefi et al. 2020).

Figure 17 Components of a cuffed tracheostomy tube

An image of a tracheostomy tube demonstrating the universal 15 mm connector that is attached to the ventilatory circuit, the flange which sits across the patients neck and secured using foam ties or silk sutures, the shaft and distal tip which lie within the tract and trachea respectively. A cuffed tracheostomy has an air-filled balloon near the distal tip; whilst a cuff-less tube does not.

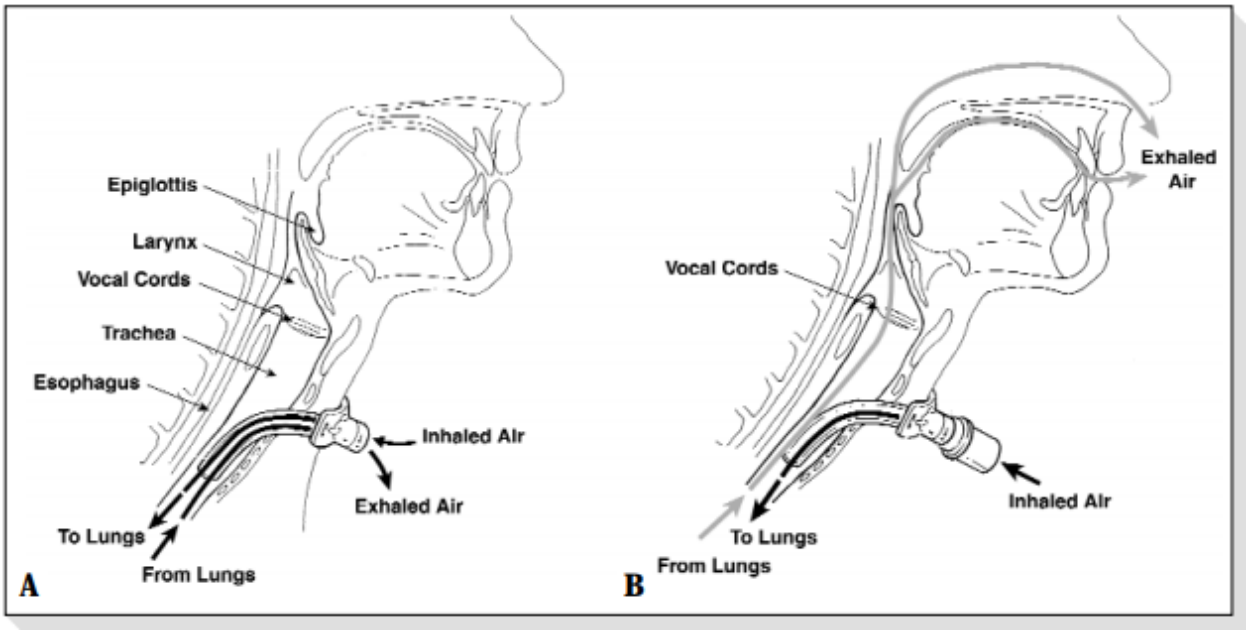
Image sourced from "Tracheostomy tubes"(Hess and Altobelli 2014)

1.3.6 Tracheostomy occlusion methods

Occlusion methods are used to assess whether a patient is suitable for weaning from their tracheostomy. 'Capping' or 'corking' completely blocks the tracheostomy lumen, therefore forcing the patient to inhale and exhale through their upper airway; this can be achieved simply with a finger over the lumen or with standardised 'cork or cap' over the outer cannula. It is vital that the tracheostomy's cuff is deflated prior to this being attempted (Engels, Bagshaw et al. 2009, Rashid and Islam 2017).

A Passy-Muir speaking valve (PMSV) (Passy-Muir Inc., Irvine, California) is a biased, closed valve that attaches to the 15 mm universal outer cannula of any tracheostomy. A PMSV remains open during inspiration, however it closes immediately after without the need for positive pressure (Dettelbach, Gross et al. 1995). Once closed, it forces expired air around the tube, trachea and larynx; enabling normal respiration and near-normal phonation (Figure 18) (Elpern, Borkgren Okonek et al. 2000).

Figure 18 Inspiration and expiration with a tracheostomy



Diagrammatic representation demonstrating inspired and expired air with a cuffed tracheostomy (cuff not visualised) (A) and a Passy-Muir speaking valve (B). With the cuffed tracheostomy, inspired and expired air flows through the tracheostomy; however, with a Passy-Muir speaking valve inspiratory flow occurs through the tracheostomy, but expired air (grey) travels around the tracheostomy, through the vocal cords into the mouth due to the deflated cuff and closed valve.

Image sourced from "Effect of the Passy-Muir tracheostomy speaking valve on pulmonary aspiration in adults" (Elpern, Borkgren Okonek et al. 2000)

1.3.7 Timing of tracheostomy insertion

Despite the benefits of a tracheostomy, the optimal timing to perform a tracheostomy has remained unclear as it requires an accurate prediction of patients who will require prolonged ventilation (Cheung and Napolitano 2014). This is important, as patients who undergo an 'earlier' tracheostomy may have it performed unnecessarily and are exposed to potential complications; conversely delayed 'late' tracheostomies will result in patients being mechanically ventilated for a prolonged period (Cheung and Napolitano 2014). The TracMan randomized trial, demonstrated the difficulty that clinicians had in predicting which patients required prolonged ventilation; as 45% of patients in the late group (after 10 days of ventilation) required a tracheostomy compared to 92% of the early group (within 4 days of ventilation) (Young, Harrison et al. 2013). These results, in addition to a Cochrane review have led most institutions to generally "wait at least 10 days to be certain a patient has an ongoing need for mechanical

ventilation…before consideration of a tracheostomy" (Cheung and Napolitano 2014, Andriolo, Andriolo et al. 2015, Bice, Nelson et al. 2015).

1.3.8 Decannulation protocol

Decannulation involves removal of the tracheostomy tube; the transition to decannulation is usually institution and clinician dependent (Engels, Bagshaw et al. 2009, Rashid and Islam 2017, Singh, Saran et al. 2017). With short-term tracheostomies, most patient's initially have their cuff-inflated or 'up' until they have medically and physically improved. Patients who are 'ready' for the decannulation process will usually have their cuff-deflated or 'down' and/or the tracheostomy down-sized; allowing further assessment of a patient's secretion management, swallowing and respiratory function. If this is tolerated by the patient, the tracheostomy is usually occluded using a speaking-valve or cork for a period of time prior to the tracheostomy removal (St John and Malen 2004, Engels, Bagshaw et al. 2009, Rashid and Islam 2017). Timing for decannulation is determined on whether the indication that necessitated the need for a tracheostomy has been resolved (Connor and White 2010, Cheung and Napolitano 2014). A Consensus statement by the American Academy of Otolaryngology highlighted, that in order for a patient to be ready for decannulation, an appropriate level of consciousness, respiratory function and effective cough is required (Mitchell, Hussey et al. 2013). Therefore, for decannulation to be successful, airway patency, respiratory protective mechanisms and management of oropharyngeal secretions and swallowing must be intact (Garuti, Reverberi et al. 2014). Once decannulated, the tracheostomy stoma is dressed and heals spontaneously over time (De Leyn, Bedert et al. 2007).

1.4 DYSPHAGIA

Eating is an enjoyable, social activity which plays a significant role in a person's quality of life (Li, Minagi et al. 2017). Dysphagia or disordered swallowing occurs when an individual experiences difficulty in swallowing (Tews and Robinson 2007). Dysphagia is a symptom; it highlights an impairment to the anatomical and/or physiology processes and pathways of swallowing (Matsuo and Palmer 2008). Dysphagia can be caused by

severe neurologic impairments affecting either the central or peripheral nervous system (CNS), structural impairments, side-effects from various medications or therapies and aging (Zuercher, Moret et al. 2019). Dysphagia can result in delayed transit or spillage of a bolus into the airway; the consequence includes malnutrition, dehydration and aspiration pneumonia which are associated with increased morbidity, mortality and health care costs (Jaradeh 1994, Matsuo and Palmer 2008).

1.4.1 Dysphagia within ICCU

The incidence of dysphagia within critically ill patients in ICCU vary from 3 to 62% (Skoretz, Flowers et al. 2010). ICCU-acquired swallowing disorders including post-extubation dysphagia are thought to be iatrogenic and multifactorial (Brodsky, Levy et al. 2018, Zuercher, Moret et al. 2019). It is thought that ICCU-acquired swallowing disorders are due to either a combination of direct trauma caused by endotracheal and tracheostomy tubes, diminished laryngeal sensory function, desynchrony between swallowing and breathing, impaired consciousness or generalised muscular weakness (Zuercher, Moret et al. 2019).

Screening for post-extubation dysphagia is not routine within the ICCU, but is of concern, as more than 60% of patients reported impaired swallowing after discharge from ICCU (Brodsky, Gonzalez-Fernandez et al. 2014, Schefold, Berger et al. 2017). Dysphagia has a significant burden on the public health system with prolonged ICU and hospital admissions; with the presence of post-extubation dysphagia associated with increased morbidity and mortality with an excess 90-day all-cause mortality rate of 9.2% (Macht, King et al. 2013, Schefold, Berger et al. 2017, Zuercher, Moret et al. 2019).

Tracheostomies are common procedures in critically unwell patients and it has been noted that tracheostomised patients have a higher incidence of aspiration and dysphagia (Elpern, Scott et al. 1994, Skoretz, Riopelle et al. 2020).

1.4.2 Disordered swallowing in patients with a tracheostomy

The reported incidence of dysphagia in patients with a tracheostomy varies significantly, from 11-93% (Skoretz, Riopelle et al. 2020). This broad range is due to diverse cohorts being assessed, with the inclusion of comorbidities known to be associated with an increased incidence of aspiration (traumatic brain injuries, head

and neck malignancies and cerebrovascular accidents), differing instrumental and clinical methods of assessments, without a standardised and comparable outcome measure. Therefore, identifying and understanding the biomechanical impact of a tracheostomy on swallowing is difficult.

1.4.2.1 Prevalence of aspiration in tracheostomy patients in the ICCU

ICCU patients with a tracheostomy are often critically unwell and therefore understanding the relationship between a tracheostomy and disordered swallowing is important, due to the life-threatening implications of aspiration in this population. Hafner et al. performed FEES prospectively over four years in 553 ICCU patients who were symptomatically thought to be aspirating; of these, 258 patients had a tracheostomy *in situ*. Aspiration was identified in 86% of tracheostomy patients on initial FESS, with 37% of these patients aspirating silently (Hafner, Neuhuber et al. 2008). Fiorelli et al. assessed 57 ICU patients with a tracheostomy using FEES and a Modified Evans Blue Dye Test (a variation of a clinical swallow examination) and found that 82% of tracheostomy patients were aspirating. Similarly, Warnecke et al. looked at 100 neurological ICU patients with a tracheostomy using FEES and a Modified Evans Blue Dye Test; 46% of patients aspirated, with the majority aspirating silently (95%). These studies highlight the prevalence of aspiration in critically ill tracheostomised patients, in particular, the frequency of silent aspiration (Warnecke, Suntrup et al. 2013, Garuti, Reverberi et al. 2014, Fiorelli, Ferraro et al. 2017). To further understand the increased incidence of disordered swallowing in this population, the biomechanics of swallowing in the presence of a tracheostomy needs to be further explored.

1.4.2.2 Swallowing biomechanics in the presence of a tracheostomy

1.4.2.2.1 Mechanisms of aspiration in a tracheostomised patient

Mechanisms for aspiration in tracheostomised patients have been proposed and include: 1) impaired glottic reflexes and laryngeal desensitisation due to diverted airflow (Feldman, Deal et al. 1966, Hafner, Neuhuber et al. 2008), 2) esophageal compression by an inflated tracheostomy cuff (Betts 1965), 3) inability to generate subglottic pressures due to an 'open' aerodigestive system (Muz, Mathog et al. 1989, Dettelbach, Gross et al. 1995, Eibling and Gross 1996) and 4) reduced hyo-laryngeal movements caused by the tracheostomy being secured to the anterior neck (Bonanno 1971).

Surprisingly, there is currently no consensus on how, or if, a tracheostomy alters the biomechanics of swallowing (Leder and Ross 2000, Ding and Logemann 2005). It has been suggested that the presence of a tracheostomy was irrelevant to impaired swallowing, as dysphagia was rather a consequence of the medical, surgical or neurological condition that necessitated the need for a tracheostomy (Leder and Ross 2000, Leder and Ross 2010). Using FEES, 45 patients were examined before and after tracheostomy insertion. It was demonstrated that in over 90% of patients their aspiration status did not change; patients who were found to aspirate 'pre-tracheostomy' also aspirated 'post' tracheostomy removal. Improvement in a patient's aspiration status was associated with positive clinical change whilst, negative changes in a patient's aspiration status (did not aspirate pre-tracheostomy but aspirated post) were associated with medical deterioration (Leder and Ross 2000, Leder and Ross 2010). This highlights that a patient's swallow maybe a representation of their overall clinical picture rather than localised dysfunction at the pharyngo-esophageal segment.

In order to further investigate the biomechanical effect of a tracheostomy on swallowing, Terk et al. examined 7 patients with a reported 'normal swallow' using VFSS. Predominantly focusing on hyolaryngeal excursion under three randomised conditions (cuff up with 5 mL of air, capped and decannulated), they demonstrated there was no significant difference in hyolaryngeal movement between the conditions, with no aspiration occurring in the cohort. Interestingly, although not statistically significant, hyo-laryngeal movements were comparatively reduced in the decannulated condition; which is contradictory to conventional views of tracheostomies. It is important to note that a standard amount of air was used to inflate the tracheostomy cuff, rather than measuring cuff pressures which is standard practice. Air required for standard cuff pressures vary based on the individual and size and type of tracheostomy used. Varying cuff pressures has been shown to influence the swallowing reflex (Amathieu, Sauvat et al. 2012). Using electromyography (EMG) and acceleromyography of submental muscles, 12 patients were tested with nine different tracheostomy cuff pressures of up to 60 cm H_2O, which is beyond the usual 20-30 cm H_2O used clinically (Sole, Su et al. 2011, Amathieu, Sauvat et al. 2012). It was demonstrated that swallowing was difficult to elicit, in addition to reduced laryngeal acceleration with cuff pressures of more than 30 cm H_2O. Laryngeal acceleration has been documented to correlate with the magnitude laryngeal elevation, therefore it would seem that cuff inflation

would influence laryngeal elevation; thereby associated with reduced laryngeal closure resulting in potential aspiration (Shaker, Milbrath et al. 1995, Reddy, Katakam et al. 2000). As a result, Terk's equivocal findings of hyolaryngeal movement may have been associated with the potentially lower pressures used in the cuff. Although both studies were conflicting, it does highlight the importance of monitoring cuff pressures in tracheostomised patients and the potential impact this may have on swallowing physiology.

1.4.2.2.2 Role of occlusion in swallowing

Occlusion of the tracheostomy lumen with capping, a one-way speaking valve or decannulation allows further evaluation into the biomechanics of swallowing; as the closed aerodigestive tract system is 'restored' allowing expired air to pass up through the glottis. Some studies have demonstrated that occlusion of the tracheostomy or decannulation did not reduce the incidence of aspiration (Leder, Tarro et al. 1996, Leder, Ross et al. 1998, Donzelli, Brady et al. 2005, Leder, Joe et al. 2005). Conversely, other studies have shown that a PMSV reduced the incidence of aspiration (Dettelbach, Gross et al. 1995, Stachler, Hamlet et al. 1996, Elpern, Borkgren Okonek et al. 2000, Suiter, McCullough et al. 2003). Although these studies mostly used VFSS in a heterogenous cohort, there is no consensus on the biomechanical impact of occlusion on swallowing. Srinet used VFSS to test swallowing parameters in various conditions including two types of one-way speaking valves and an 'open' tracheostomy without the inner cannula (Srinet, Van Daele et al. 2015). Similar to Terk, they found that there were no significant changes to hyolaryngeal displacement or the aspiration status of their patients (Terk, Leder et al. 2007, Srinet, Van Daele et al. 2015). In contrast, Suiter et al. demonstrated with VFSS, that a PMSV reduced the incidence and severity of aspiration in 80% of patients for thin liquid boluses (Suiter, McCullough et al. 2003). This change however could not be explained with any of the recorded swallowing parameters; but was thought to be due to the restoration of subglottic pressures (Suiter, McCullough et al. 2003). Logemann et al. examined eight patients who had undergone treatment for head and neck cancer; although equivocal for aspiration, they found that light digital occlusion altered four biomechanical parameters; 1) reduced tongue base contact with the posterior pharyngeal wall, 2) increased maximum laryngeal elevation, 3) increased hyolaryngeal elevation at the time of cricopharyngeal relaxation, and 4) delayed posteriorly pharyngeal wall movement in relation to cricopharyngeal relaxation (Logemann,

Pauloski et al. 1998). Although these findings varied between patients; improved hyolaryngeal excursion was observed with occlusion, an anatomical finding associated with improved, coordinated swallows. Interestingly, tongue and posterior pharyngeal wall movement was reduced with occlusion, a finding associated with poorer pharyngeal clearance; however, it did not seem to clinically impact pharyngeal bolus residue clearance. Once more, these studies were incongruent on the mechanistic impact of 'restoring' the closed aerodigestive tract; yet a PMSV may represent a simple and inexpensive option for reducing aspiration in certain patients following a review by a speech pathologist. More importantly, the difficulty in using subjective methods of evaluation (such as VFSS or FEES) to derive a numerical biomechanical metric, highlights the need for an instrumental assessment tool that is quantitative in nature to further delineate this complex interaction between a tracheostomy and disordered swallowing.

1.4.2.3 Use of manometry for swallowing assessments in tracheostomy patients

The advent of manometry has allowed further evaluation of swallowing using quantitative metrics that are potentially comparable between studies. Leder et al. once again looked at the role of tracheostomy occlusion in eleven patients, who had no history of oropharyngeal cancer or cerebrovascular events using conventional solid-state manometry. They found based on recorded pharyngeal and upper esophageal pressures, there was no statistical difference of occlusion (light digital occlusion or open tracheostomy) on aspiration status (Leder, Joe et al. 2001). Ledl et al., similarly using conventional manometry and FEES, assessed twenty patients with neurogenic dysphagia secondary to a monohemispheric lesion. They found that patients with an 'open' tracheostomy had higher penetration-aspiration scores in comparison to patients with a 'closed' tracheostomy. Although there were no significant differences in pressures, overall neurological patients with an open tracheostomy had higher oro- and hypopharyngeal pressures comparatively (Ledl and Ullrich 2017). These studies used conventional manometry, which at the time only had 3 pressure sensors; therefore, due to the limited data that could be collected, accurate analysis of rapid fluctuations in pressures across the pharyngo-esophageal segment was difficult (Ryu, Park et al. 2016).

High-resolution manometry overcomes this limitation by the use of up to 36 pressure sensors; with some catheters able to record impedance, which allows the analysis of bolus flow relative to contractility within the

pharynx. Although there are no tracheostomy studies currently using HRPM, Schar et al. recently looked at the role of high-resolution manometry in patients with post-extubation dysphagia at Flinders Medical Centre's ICCU (South Australia). 19 critically ill were recruited and examined within 24 hours of extubation; of which, 8 were recently decannulated tracheostomy patients (Schar, Omari et al. 2020). It was found that critically unwell patients demonstrated impaired swallowing when compared to age-matched controls as reflected by their Swallow Risk Index score. Interestingly, their pharyngeal contractility was comparable to controls, suggesting that their swallowing dysfunction was unlikely to be due to pharyngeal weakness as hypothesised with critically illness myopathy (Zuercher, Moret et al. 2019, Schar, Omari et al. 2020). Although patients with a tracheostomy *in situ* were not examined, this study did highlight the feasibility, safety and detailed analysis that high-resolution pharyngeal manometry can provide in a critically ill cohort.

1.4.2.4 Justification for further studies

Medical and technological advances have facilitated more medically complex and unwell patients to be stabilised, treated and subsequently discharged from the ICCU. Due to the likely complex admission often requiring prolonged intubation; tracheostomies are a common life-prolonging procedure, performed in up to 15% of critically unwell patients (Whitmore, Townsend et al. 2020). The incidence of dysphagia in critically ill patients with a tracheostomy has been reported to be up to 90%, with a significant proportion of patients aspirating silently. The risk of an aspiration pneumonia and its sequela is of serious concern in this population due to their reduced physiological reserve resulting in a higher rate of morbidity, mortality and length of stay (Hafner, Neuhuber et al. 2008).

Due to the incidence of aspiration and dysphagia in those with a tracheostomy; historically many clinicians are hesitant in starting a patient with a tracheostomy on an oral diet. In a cohort already at risk of malnutrition, this highlights the need to understand whether a tracheostomy has a biomechanical impact on the swallowing pathway (Mullender, Wheatley et al. 2014).

Historically, studies have used qualitative assessments such as VFSS and FEES, in order to understand the complex relationship between the presence of a tracheostomy and a disordered swallowing pathway (Leder

and Ross 2000, Leder and Ross 2010, Warnecke, Suntrup et al. 2013). Furthermore, some studies have derived a quantitative scoring system using subjective methods of assessment (Logemann, Pauloski et al. 1998, Suiter, McCullough et al. 2003, Leder, Joe et al. 2005, Terk, Leder et al. 2007, Srinet, Van Daele et al. 2015). Systematic reviews published within the last two years looking at the impact of tracheal modifications and cuff inflation on swallowing have highlighted the difficulty in analysing the current literature due to the varying outcome measures, assessment tools and interpretations methods used (Goff and Patterson 2019, Skoretz, Anger et al. 2020, Skoretz, Riopelle et al. 2020). There is currently no consensus on the biomechanical impact a tracheostomy has on swallowing. Therefore, the aim of this pilot study is to objectively assess the impact of a tracheostomy on swallowing biomechanics in critically unwell patients.

1.5 RESEARCH QUESTION AND AIMS

Research Hypotheses

1) HRPM can demonstrate disordered biomechanical swallowing in critically unwell patients with a tracheostomy.
2) HRPM can elucidate the biomechanical improvement in swallowing with the insertion of a PMSV onto a tracheostomy.

Research Aims

1) To assess biomechanical swallow metrics using HRPM in those with a tracheostomy compared to healthy age-matched controls.
2) To assess the change in biomechanical swallow metrics using HRPM across three tracheostomy conditions (cuff up, cuff down and a PMSV).

2 MATERIALS AND METHODS

2.1 Ethics

Ethical approval was been obtained from the Southern Adelaide Clinical Human Research Ethics Committee (Office for Research project number is 202.15, Appendix 1). Written consent was obtained from all participants in the tracheostomy cohort. Control data from healthy-age matched individuals was obtained from a previous prospective study at Flinders Medical Centre (SAC HREC EC00188) (Ferris, Doeltgen et al. 2020).

2.2 Study design

This is a prospective cohort study conducted at Flinders Medical Centre ICCU between February 2020 to November 2020. This is a 34-bed level III ICCU with medical, surgical, trauma and obstetric patients. Patients were recruited through the Department of Intensive and Critical Care. Control data was available from the Swallow Gateway™ normative database of 50 healthy participants investigated in our department using the same catheter and manometry system (Ferris, Doeltgen et al. 2020). Controls were consecutively matched for age and gender of patients included to ensure an equivalent distribution for comparison with tracheostomy patients.

2.3 Study population

Inclusion criteria:

i. 18 years or above
ii. Mechanically ventilated for more than 48 hours with a tracheostomy tube
iii. Patients who have capacity to consent and are able to swallow on command
iv. Patients who are able to swallow thin and semi-thick fluids

Exclusion criteria:

i. Pregnancy

ii. Pre-existing history of dysphagia

iii. Taking medications that are known to affected esophageal motility

iv. A history of upper gastrointestinal tract surgery including a myotomy

v. Allergy to lignocaine (local anaesthetic)

vi. History of a laryngectomy

vii. Neurological disorders

viii. Severe coagulopathy

ix. Base of skull fractures

x. Patients that the ICCU team deemed not medically appropriate

Patients undergoing mechanical ventilation with a tracheostomy tube (surgical or percutaneous), inserted at the discretion of the treatment Intensivist, were invited to participate in this study. Patients who met the inclusion were identified by the intensive care and research team and were only recruited once they were medically stable and suitable for decannulation (tolerating cuff deflation and/or having a PMSV over their tracheostomy for prolonged periods). Informed consent was obtained prior to enrolment in the study.

At Flinders Medical Centre, as part of standard care, the cuff of the tracheostomy tube is checked every 8 hours (when inflated) to ensure the pressure is between 20-30 cmH_20. Suctioning was performed as required by the bedside nurse with a flexible Y-suction catheter if required.

2.4 Study protocol

The following demographic, medical and treatment data were collected from the patient's medical records:

i. Patient demographics: age and gender

ii. Physical characteristics: height and weight to calculate body mass index

iii. Significant medical history: relevant medical co-morbidities and current medications, smoking history, use of a proton pump inhibitor, use of steroids or opiates, acute physiology and chronic health evaluation (APACHE II and III), the Charlson comorbidity index (CCI) and Clinical Frailty Scale

iv. Indications for ICCU admission

v. Endotracheal intubation information: date of intubation, number of attempts, airway grade, size of the endotracheal tube, duration of intubation and maximum positive end-expiratory pressure

vi. Tracheostomy information: date of tracheostomy insertion, technique (surgical or percutaneous), size of tracheostomy tube, duration of ventilation with tracheostomy tube prior to study

vii. Nutritional intake information: presence of NGT, duration at the time of the study and functional oral intake scale (FOIS) score

2.4.1 HRPM Swallow Assessment

Insertion of the HRPM catheter followed standardised protocols recommended by an International Working Group (Omari, Ciucci et al. 2020). Patients were fasted for a minimum of 4 hours prior to the swallow study to avoid aspiration of gastric contents. Any nasogastric or nasoenteric tube was removed and topical anaesthesia Co-Phenylcaine Forte (5% lignocaine, 0.5% phenylephrine) and 2% lignocaine gel was applied to the nostril. Prior to its use, the HRPM catheter was submerged in a bowl with warm water (37^{o}C) for one minute to ensure all the electrodes were uniformly warmed and calibrated.

The HRPM swallow study was conducted at the patient's bedside, with the patient positioned on a standard intensive care bed, upright, with their head in the neutral position. During HRPM catheter insertion, the patient was requested to take sips of water or stimulate a swallowing action when the catheter was at approximately 15 cm depth to guide passage through the upper esophageal sphincter; it was advanced to approximately 35-40 cm in depth from the nostril.

Following a five-minute accommodation period (Omari, Ciucci et al. 2020), the patient was instructed to swallow a standardised bolus (refer to Section 2.4.3) consisting of 5 and 10 mL of thin and extremely thick

liquids; this was repeated three times in a standardised manner for each volume, viscosity and tracheostomy conditions (cuff inflated, cuff deflated and PMSV) as tolerated. The bolus was administered using a syringe and during the assessment, a total of 36 swallows were recorded, resulting in a total of 270 mL oral intake. An ICCU nurse and doctor were present throughout the assessment, and patients were able to refuse at any stage with the study ceasing early if there were any clinical concerns. Following completion of the standardised protocol, the catheter was removed and the patient resumed their diet as directed by the ICCU team and speech pathologist.

2.4.2 Tracheostomy conditions

There were three tracheostomy conditions tested, the cuff inflated, cuff deflated or having a PMSV placed on the outer cannula (with the cuff deflated). The order of the conditions tested was randomised to reduce treatment order effect and fatigue related swallowing changes (https://www.randomizer.org/).

If the cuff was inflated, the pressure inside the balloon would be checked with a handheld cuff pressure gauge aiming for 20 to 30 cmH_2O.

2.4.3 Standardised Bolus Medium

The liquid bolus used in the assessments was prepared from a Standardised HRPM Bolus Medium (SBMkit™, supplied by Trisco Pty Ltd, Brisbane, Australia). The SBMkit™ is an apple flavoured, sodium chloride (NaCl) concentrate solution (also known as a saline concentrate) (and pump administration set) that was formulated for HRPM, as it allows uniform electrical conductivity through the bolus in various consistencies; resulting in consistent impedance-derived measurements (Ferris, Doeltgen et al. 2020). A separate vegetable gum-based concentrate thickener (Precise Thick-N INSTANT, supplied by Trisco Pty Ltd, Brisbane, Australia) was added to the bolus solution to conform with the International Dysphagia Diet Standardization Initiative standards (IDDSI) (Steele, Namasivayam-MacDonald et al. 2018).

The standardised bolus was prepared by adding 6 pump administrations of the saline concentrate into a beaker; this was then filled to 200 mL's with tap water and stirred until even in consistency. The bolus solution without thickener conformed to a thin liquid solution (IDDSI 0). A thickened standardised bolus (IDDSI 4) was

prepared by adding 6 pump administrations of the thickener concentrate to the 200 mL bolus solution, which was stirred for 30 seconds and allowed to rest for 5 minutes.

2.5 Sterilisation

Immediately after each assessment, the manometry catheter was sterilised using the Tristel Trio wipe system (Tristel, Snailwell, UK). It is a three-step, sequential, disinfection process that firstly uses a cleaning wipe (containing deionised water, cationic surfactant and enzyme solutions), sporicidal wipe and activating foam (containing chlorine dioxide 0.0175-0.0225%) and a rinsing wipe (containing deionised water, surface conditioner and antioxidants) to decontaminate non-luminal medical devices (Tzanidakis, Choudhury et al. 2012).

2.6 High-resolution pharyngeal manometry system

A solid-state combined manometry and impedance 8-French catheter (3.2 mm diameter) which incorporates 32 unidirectional pressures sensors (at 1 cm spacing intervals) and 16 adjoining impedance segments (2 cm in length) (Unisensor AG catheter, Attikon, Switzerland) was used. The recording segment of the catheter was positioned from the velopharynx to the proximal esophagus; this allows the sensors and electrodes to simultaneously detect, capture and record pressure and bolus presence changes along the swallowing pathway. Data acquisition occurred at 20 Hertz using the Solar GI High-Resolution Impedance Manometry (HRIM) System (Medical Measurement Systems (MMS); Enschede, the Netherlands).

Following each study, pressure-impedance data were exported from MMS in a single ASCII file format (.asc) without any patient-identifying details and uploaded to the Swallow Gateway™ web application for analysis.

2.7 Swallow Gateway™ outcome measures

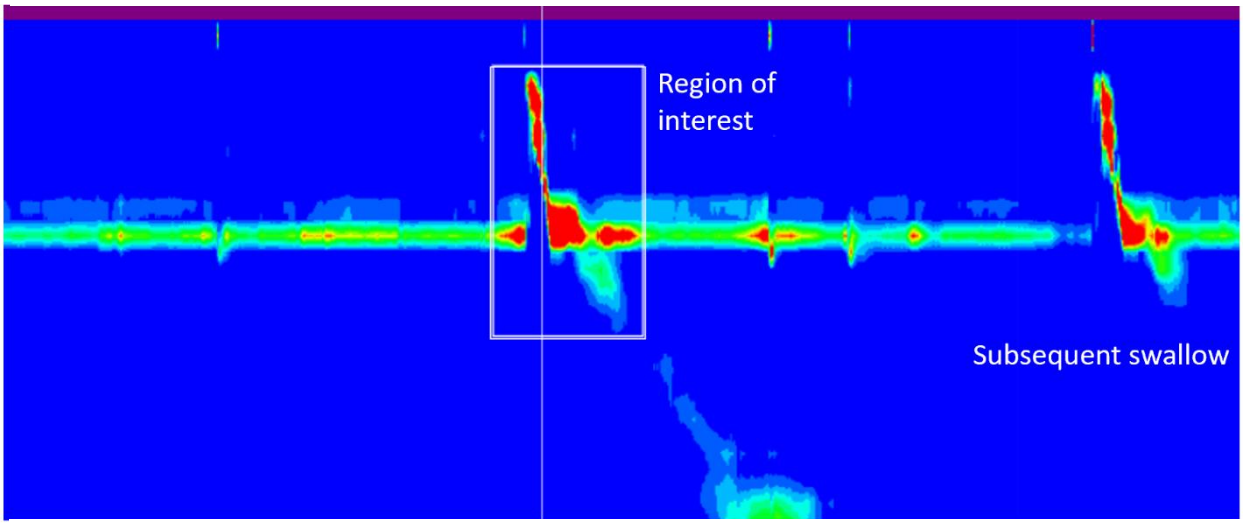
De-identified pressure and impedance data were exported and uploaded onto Swallow Gateway™. Swallow Gateway™ is an open-access cloud-based analysis portal (www.swallowgateway.com) owned by Flinders

University (Adelaide, South Australia, Australia). The data uploaded and analysis is encrypted using Microsoft Azure Cloud services.

Individual patient swallowing events (for each bolus and tracheostomy condition) were selected by highlighting a *region of interest* (ROI) from the pressure topography plot on Swallow Gateway™. The ROI box encompassed an area spanning from the velopharynx to the inferior aspect of the proximal esophagus (Figure 19). For each swallow, six spatiotemporal boundaries are defined (four anatomical and two duration markers) for automatic analysis. The anatomical markers include the proximal position of the velo-/hypopharynx, the upper esophageal sphincter apogee and the distal margin of the UES. Timing markers include the onset of UES relaxation and contraction (Figure 20). Swallows were analysed and cross-checked by an expert in HRPM analysis (Professor Taher Omari) for quality control.

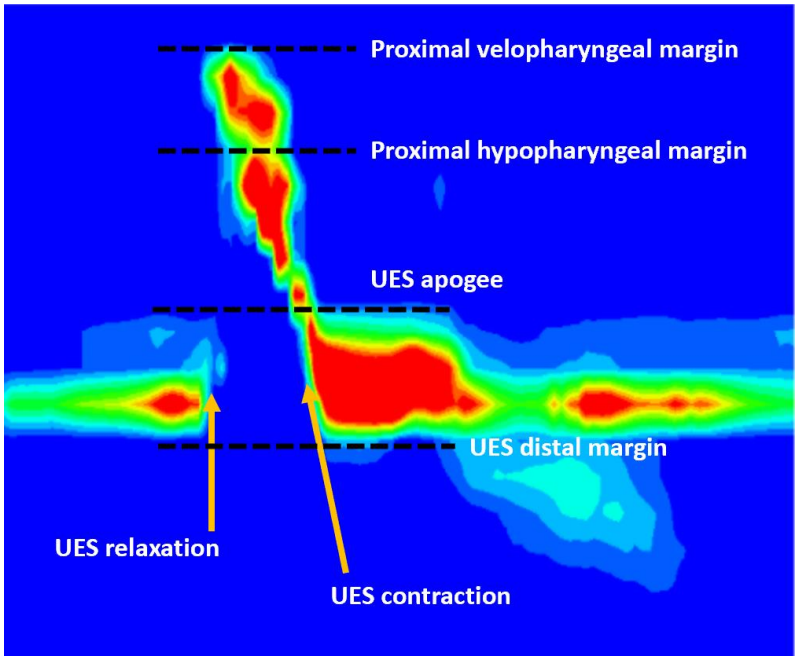
Biomechanical swallowing metrics were automatically generated and derived from pressure-flow and impedance data; using algorithms consistent with the International HRPM Working Group (Omari, Ciucci et al. 2020). This method of analysis using Swallow Gateway™ has been demonstrated to be reliable (Singendonk, Cock et al. 2019).

Figure 19 Initial pressure topography plot



An example of a pressure topography plot, with the white box highlighting the *region of interest* to be analysed

Figure 20 Spatiotemporal markers



Pressure-topography plot of a selected ROI; demonstrating the 6 spatiotemporal markers used to define a swallow for further analysis

Metrics generated by Swallow Gateway™ are described and defined in detail in Table 5, 6 and Figure 21. In general, these metrics are based or derived from the pressures generated during luminal occlusion or distension, UES contraction and relaxation and the bolus flow during these periods. The 'core' outcome set are the recommended metrics from the International HRPM Working Group that allow diagnostic characterisation of a swallow (Omari, Ciucci et al. 2020).

It is important to understand two metrics that are generated – contractile integral and admittance. Luminal occlusive pressures are described as contractile integrals (CI) which is the mean pressure generated during contraction (mmHg) of a particular region, across a certain length of space (cm) and time (s) (*mean pressure x length x duration)*. Contractile integrals describe the 'vigor' of a contraction within a particular space-time box on the pressure topography plot (Figure 21) (Omari and Schar 2018, Omari, Ciucci et al. 2020). Impedance describes the resistance that a bolus encounters during 'flow' secondary to luminal cross-sectional area; its reciprocal, *admittance* can be used to derive bolus size and 'extent of opening' of the upper esophageal sphincter (Nguyen, Domingues et al. 2006, Omari, Ciucci et al. 2020).

Table 5 HRPM Core outcome set metrics

HRPM Core Outcome Set Metrics (Omari, Ciucci et al. 2020)			
Metric class	**Metric**	**Unit**	**Definition**
Pharyngeal Luminal Occlusive Pressures	Pharyngeal Contractile Integral **PhCI**	mmHg.cm.s	A measure of overall pharyngeal contractile vigor from the velopharynx superiorly to the upper margin of the UES
	Velopharyngeal Contractile Integral **VCI**	mmHg.cm.s	A measure of contractile vigor spanning the velopharynx only
	Mesopharyngeal Contractile Integral **MCI**	mmHg.cm.s	A measure of contractile vigor spanning the mesopharynx only
	Hypopharyngeal Contractile Integral **HPCI**	mmHg.cm.s	A measure of contractile vigor spanning the hypopharynx only
Hypopharyngeal Distension Pressure	Hypopharyngeal Intra-Bolus Pressure **IBP**	mmHg	The pressure at 1 cm superior to the UES apogee, at the time of maximum hypopharyngeal distension (highlighted by impedance); the pressure gradient across the pharyngo-esophageal junction
UES relaxation and opening	UES Maximum Admittance **UES Max Adm**	millisiemens (mS)	The 'extent' of UES opening; demonstrated by the highest admittance value recorded during trans-sphincteric bolus flow
	UES Integrated Relaxation Pressure **UES IRP**	mmHg	A pressure measure of the extent of UES relaxation; derived from the median of the lowest pressure in a non-consecutive 0.20-0.25 second window
	UES Relaxation Time **UES RT**	s	A measure of the duration of UES relaxation, determined by a pressure interval below 50% of baseline or 35 mmHg

Replicated and derived from the International HRPM Working Group (Omari, Ciucci et al. 2020)

Derived from "Modulation of Pharyngeal Swallowing by Bolus Volume and Viscosity" (Ferris, Doeltgen et al. 2020)

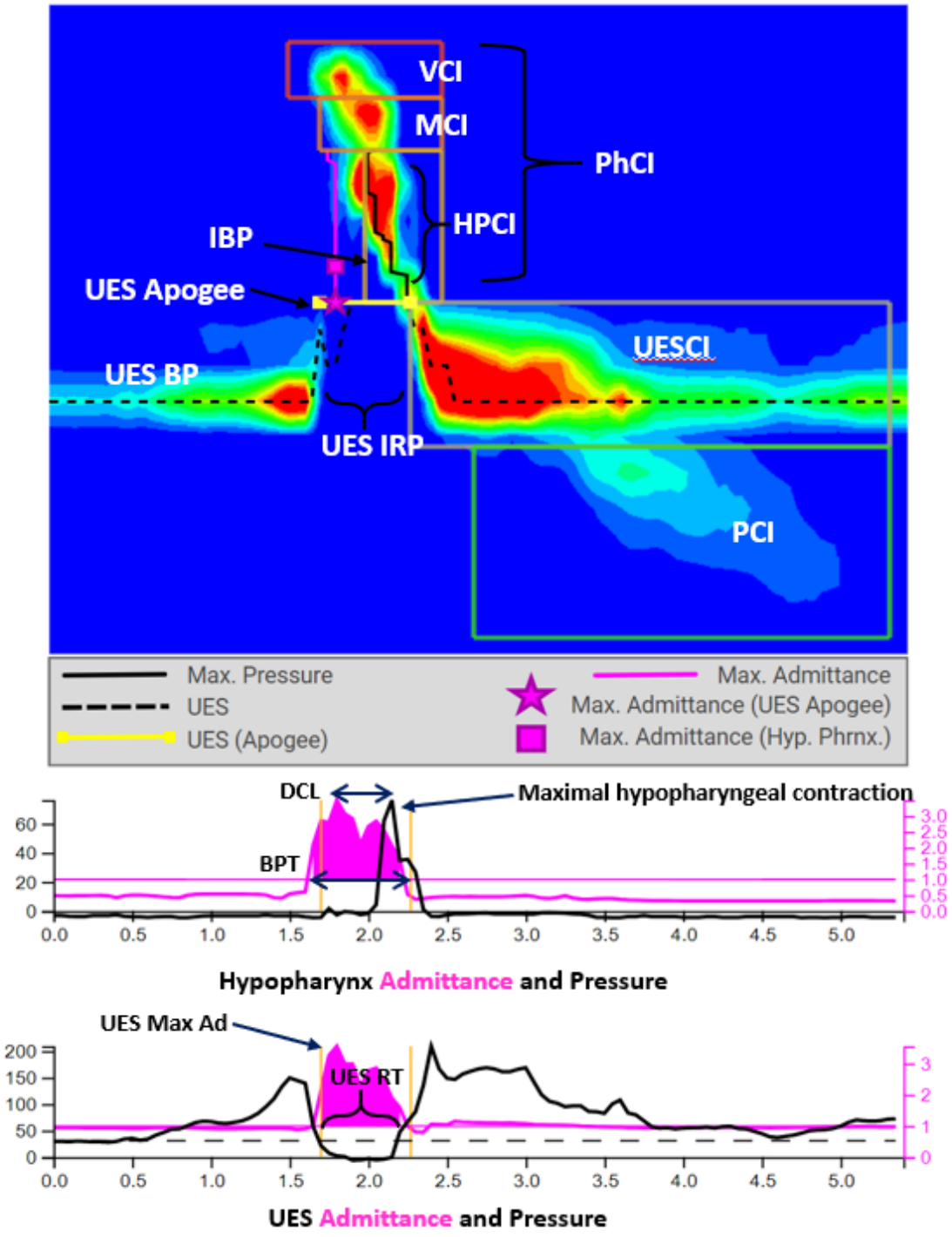
Table 6 Additional HRPM outcome set metrics

Additional HRPM Swallow Gateway™ Metrics			
Metric class	**Metric**	**Unit**	**Definition**
Global Swallowing Function	Swallow Risk Index **SRI**	-	A composite measure generated from IBP, DCL, BPT and Peak P to determine global swallowing dysfunction and aspiration risk (Omari, Dejaeger et al. 2011, Omari and Schar 2018)
Flow Timing variable	Bolus Presence Time **BPT**	s	The duration that a bolus resides within the pharynx before and after swallowing (derived from impedance)
	Distension to Contraction Latency **DCL**	s	The duration between maximum hypopharyngeal distension to maximum hypopharyngeal contraction
Hypopharyngeal Contractility	Hypopharyngeal Peak Pressure **Peak P**	mmHg	The maximum pressure generated during hypopharyngeal contraction
UES Contractility	Upper Esophageal Sphincter Contractile Integral **UESCI**	mmHg.cm.s	A measure of contractile vigor of the UES, post-swallow
	UES Peak Pressure **UES Peak P**	mmHg	The maximum pressure generated at the UES, immediately after pharyngeal contraction
	UES Basal Pressure **UES BP**	mmHg	The tonically generated resting pressure of the UES, pre-swallow
Proximal Esophageal Contractility	Proximal Esophageal Contractile Integral **PCI**	mmHg.cm.s	A measure of contractile vigor of the proximal esophagus

Replicated and derived from the International HRPM Working Group (Omari, Ciucci et al. 2020)

Derived from “Modulation of Pharyngeal Swallowing by Bolus Volume and Viscosity” (Ferris, Doeltgen et al. 2020)

Figure 21 Correlation of Swallow Gateway™ metrics on the pressure topography plot



A diagrammatic representation of the derived Swallow Gateway™ metrics; labelled to correspond with definitions used in Table 5 and 6

2.8 Statistical Analysis

Statistical analysis was performed using IBM SPSS statistics version 25.0 (IBM Corp. Statistical Package for the Social Sciences; Statistics for Windows, Armonk, NY, USA). The average of each swallowing parameter for each volume, consistency and tracheostomy condition (12 swallows for each tracheostomy condition) was calculated and tabulated on an Excel spreadsheet. Data from tracheostomy patients were compared to healthy age-matched controls. Due to the sample size, non-parametric tests were performed – 1) an Independent Samples Mann Whitney U test to compare swallowing parameters between tracheostomy patients and age-matched controls, 2) an Independent-Samples Kruskal-Wall Test to test the effect of opiates, tracheostomy duration (more than or less than two weeks duration), decannulation status (whether the patient was decannulated on the day of the study or the day after) and cuff status (cuff being down continuously for more than 24 hours prior to the study vs. intermittent inflation) on swallowing and 3) Related Samples Friedman's Two-Way Analysis of Variance to compare swallowing parameters between the three tracheostomy cuff conditions. Age-matched controls were compared with tracheostomy swallowing data with the cuff down; this is because it is the most common tracheostomy cuff condition prior to decannulation. Data is presented as a median (IQR). Statistical significance was inferred when $p<0.05$. Due to the exploratory nature and the sample size of this pilot study, correction for multiple comparisons was not applied.

2.9 Sample size estimation and the Coronavirus Pandemic

This pilot study was part of a larger project, aiming to understand and assess swallow dysfunction in the critically ill using HRPM. In planning for this pilot study, a sample size of 12 to 20 patients was estimated as adequate. This number was derived pragmatically, based on the throughput of patients likely to meet enrolment criteria over the allowed timeframe. A sample size of approximately 20 was previously found sufficient to establish swallowing dysfunction in relation to endo-trachael intubation (Schar, Omari et al. 2020). Approximately 5-6 tracheostomies are performed each month at Flinders Medical Centre's ICCU (Bihari, Prakash et al. 2018). Due to the mortality rate of 20% and an APACHE II score of 20, highlighting significant

burden of disease, it was assumed that only 1-2 of these patients per month, would be suitable for recruitment. Unfortunately, recruitment was disrupted by the Coronavirus pandemic, thus it should be acknowledged that cautious interpretation of the results of the pilot study is necessary due to the smaller sample size.

Coronavirus disease 2019 (COVID-19) is a global pandemic infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus (Lotfi, Hamblin et al. 2020). COVID-19 can be spread through direct (human-to-human transmission and aerosols) and indirect contact (airborne droplets and contaminated objects). Preventative methods to reduce transmission included social distancing, frequent sanitisation and in particular to hospitals; limiting aerosol-generation through cessation of elective operating theatres and non-essential procedures. Additionally, the use of personal protective equipment (PPE) and particulate-filtering respirators such as an N95 were critical in protecting and limiting transmission in health care workers. Due to its contagious nature, concerns about PPE shortages and limiting aerosol-generating procedures this study was suspended from the end of March 2020 and recommenced on the 11th of May 2020, once the above issues were addressed. Furthermore, all non-urgent elective surgery was postponed and only gradually returned in July 2020; this also impacted the number of tracheostomies performed during this period. Adjournment of the study and reduction of theatre activity, therefore, resulted in lower patient recruitment than initially anticipated, but in the context of the COVID-19 pandemic, this was necessary.

3 RESULTS

56 ICCU patients were screened for eligibility of which 45 patients did not fulfil the eligibility criteria (Figure 22). 11 patients were eligible; 10 gave informed consent to participate in this study. 1 patient was subsequently excluded due to inability of passing the manometry catheter into the esophagus; resulting in a total of 9 participants with swallow data available for analysis.

3.1 Patient characteristics

Demographics of the included study participants are presented in Table 7. Table 8 demonstrates general patient characteristics of those admitted to Adult Australian ICCU's, for comparison. 33% were admitted to the ICCU following a motor vehicle accident. Patients were mechanically ventilated for a median duration of 15 days (8-35). The median total hospital length of stay was 37 days, with approximately 28 days spent in the ICCU. No patient died during their ICCU or hospital admission.

7 tracheostomies were percutaneous and performed on day 10 of ICCU admission and remained *in situ* for a median of 12 days before study assessment. The median time from admission to study assessment was 27 days. All patients required NGT feeding (FOIS 1) and only 1 patient had attempted oral intake prior to investigation. 4 patients were decannulated within 12 hours of their HRPM swallow study with the remainder decannulated the following day. 6 patients progressed to a normal ward-based diet by time of discharge, with the remaining 3 patients on a soft diet and thin fluids on discharge.

Tracheostomy patients were tested using two different bolus volumes (5 and 10 mL) and viscosities (IDDSI 0 and IDDSI 4) across three tracheostomy conditions (cuff inflated, deflated and with a PMSV). The bedside HRPM procedure was well-tolerated with 6 patients able to complete the protocol of 36 swallows. 3 patients had incomplete swallows due to fatigue and abdominal fullness (Table 9). There were no other complications.

Figure 22 Flow-chart of patient selection and participation

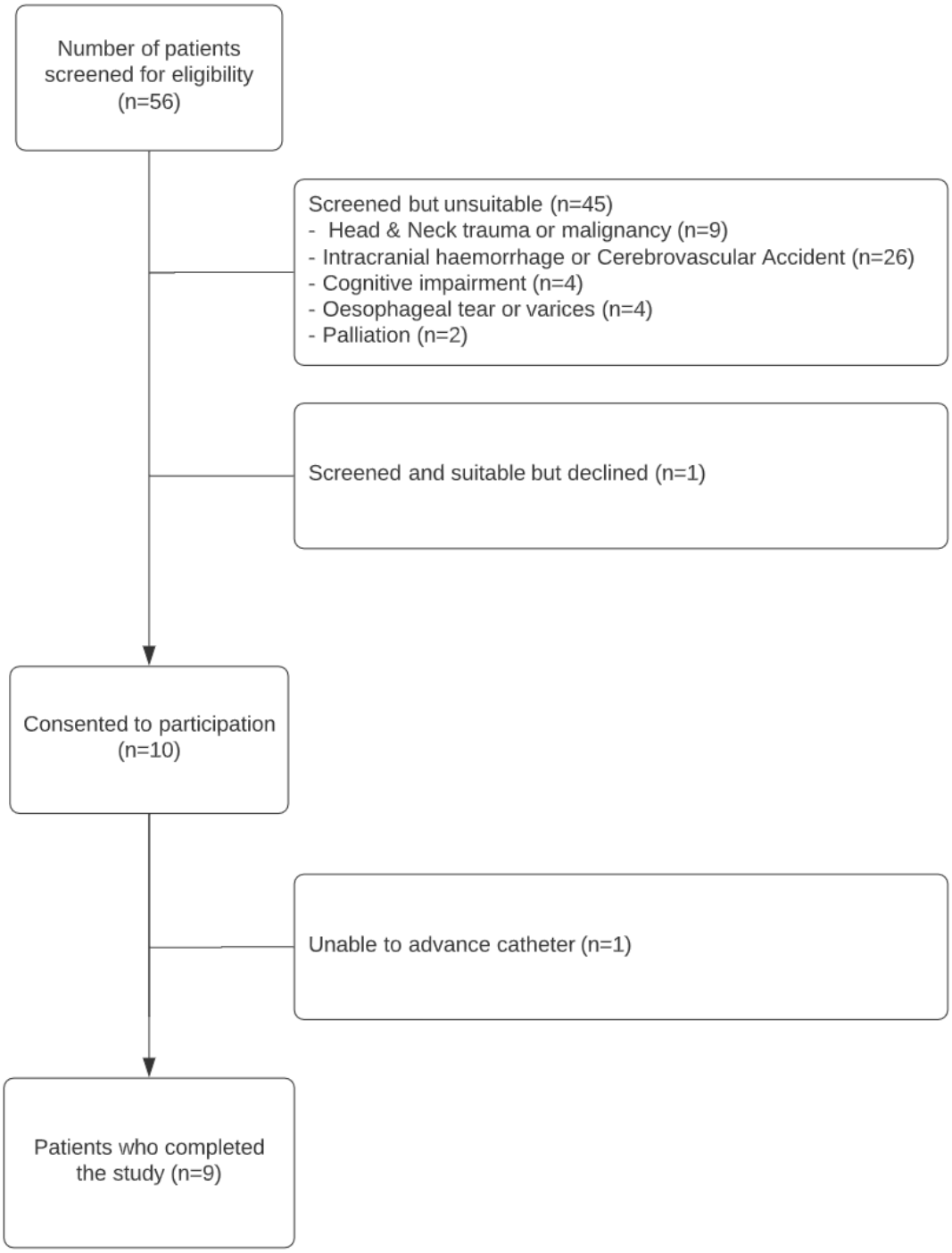


Table 7 Patient demographic and characteristics

Study cohort characteristics (n=9) (Median)(range)		
Demographics	Age (years)	64 [45-74]
	Gender (male/female)	Male 55%; Female 45%
	Body mass index (kg/m^2)	26.82 [16.98 – 30.47]
	APACHE II score	22 [11 – 25]
	CCI	4 [2 – 6]
Endotracheal and Tracheostomy Data	Total duration of mechanical ventilation (days)	15 [8 – 35]
	Duration of ETT (days)	10 [7 – 16]
	Duration of tracheostomy in-situ (days)	12 [6 – 21]
	Time from admission to study (days)	27 [14 – 35]
	Decannulated within 24 hours of participation	44% within 24 hours, 56% within 48 hours
	Duration of NGT at time of study (days)	25 [10 – 35]
Length of stay (LOS)	Total hospital LOS (days)	37 [21-53]
	ICCU LOS (days)	28 [15 – 39]

APACHE: Acute Physiology and Chronic Health Evaluation II, CCI: Charlson Comorbidity Index, ETT: Endotracheal tube, ICCU: Intensive and Critical Care Unit, NGT: Nasogastric tube and LOS: Length of Stay

Table 8 Patient characteristics for Adult Australian ICCU admissions compared to Flinders Medical Centre

	Characteristics (Median)	
Demographics	Age (years)	66 [51-75]
	Gender (male/female)	Male 56.3%; Female 43.7%
	APACHE II score	14 [10 – 19]
Endotracheal and Tracheostomy Data	Total duration of invasive mechanical ventilation (days)	2.6 [0.3 – 2.4]
	% of patient's tracheostomised	1.2%
Length of stay (LOS)	ICCU LOS (days)	1.7 [0.9 – 3.2]

Data obtained from the Australian and New Zealand Intensive Care Society Adult Patient Database (APD) activity 2019 report

Table 9 Number of swallows completed by individual patients

Swallows completed				
Patient	**Cuff UP**	**Cuff DOWN**	**PMSV**	**Total**
1	12	12	0	24
2	12	12	12	36
3	12	12	4	28
4	12	12	12	36
5	12	12	0	24
6	12	12	12	36
7	12	12	12	36
8	12	12	12	36
9	12	12	12	36

Patient 3 only completed 3, 5 mL IDDSI 0 swallows and one 5mL IDDSI 4 swallow

3.2 Patient-reported swallowing outcome measures

All patients reported 'normal' swallowing prior to their admission (Dakkak Dysphagia Score of 0).

3.3 TRACHEOSTOMY VS. AGE-MATCHED CONTROLS

For this initial comparison of general swallowing function, (median) patient data for the cuff down condition (this was the most common tracheostomy condition prior to decannulation) was compared against age-matched controls and 10 mL IDDSI 0 bolus is used as the reference test bolus condition.

3.3.1 High-Resolution Pharyngeal Manometry Core Outcome Metrics

3.3.1.1 Hypopharyngeal Intra-Bolus Distension Pressure

Hypopharyngeal intrabolus distension pressure (IBP) was significantly elevated in the tracheostomy group compared with age-matched healthy controls (p=0.024). The control group demonstrated sub-atmospheric pressures (Table 10).

3.3.1.2 UES Relaxation Pressure, relaxation duration and UES opening diameter

UES relaxation pressure (UES IRP) was statistically elevated in the tracheostomy group compared with age-matched healthy controls (p=0.003). The control group demonstrated sub-atmospheric pressures; with IRP

increasing with large bolus volumes and viscosity. In the tracheostomy group, UES relaxation pressures were elevated across all volume and bolus conditions (Table 10).

Relaxation duration (UES RT) was statistically shorter in the tracheostomy group compared with age-matched healthy controls (p=0.038). A shorter resting duration was demonstrated in the tracheostomy group across all bolus conditions; however, it was not significant in the 10 mL thick condition (Table 11). UES opening diameter, as measured using UES maximum admittance (UES Max Adm) was similar in the tracheostomy group compared with age-matched healthy controls (p=0.965). This was demonstrated across all bolus conditions (Table 10).

3.3.1.3 Pharyngeal, Velo-, Meso- and Hypopharyngeal Contractility

Luminal occlusive pressures across the pharynx (PhCI) were elevated in tracheostomy patients when compared to healthy controls; although this was only statistically significant in the 10 mL thin condition (p=0.031). Similarly, luminal occlusive pressure across the velopharynx (VCI), mesopharynx (MCI) and hypopharynx (HPCI) were elevated in tracheostomy patients when compared to healthy controls (rather than reduced, as would be expected with disuse atrophy); however, this was not statistically significant for any volume or viscosity condition (Table 10).

3.3.2 High-Resolution Pharyngeal Manometry Additional Metrics

3.3.2.1 Swallow Risk Index

The Swallow Risk Index (SRI) was elevated in the tracheostomy group when compared to healthy controls; this was significant in all volume and viscosity conditions (p=0.040) apart from the 10 mL thin condition. The median SRI *across all bolus conditions* ranged from 2-3; although the SRI was sometimes elevated to more than 15 (threshold indicating aspiration) with specific boluses (Table 11).

3.3.2.2 Bolus Presence and Pharyngeal Flow Metrics

Bolus presence duration within the hypopharynx (BPT) did not significantly differ between the tracheostomy group and healthy controls (p=0.289) across any volume or viscosity conditions. In general bolus presence duration was prolonged with larger volumes and shortened with more viscous boluses (Table 11)

Distension to contraction latency (DCL) did not differ between the tracheostomy group and healthy controls (p=0.354) across any volume or viscosity conditions. In general, DCL was demonstrated to be lengthened by volume and shortened by viscosity (Table 11).

3.3.2.3 Hypopharyngeal Peak Pressures

Peak pressures generated within the hypopharynx during swallowing (Peak P) did not differ statistically between the tracheostomy group and healthy controls (p=0.825) across any volume or viscosity condition (Table 11).

3.3.2.4 UES Tonicity and Contractility

Upper esophageal sphincter basal pressures (UES BP) were generally lower in the tracheostomy cohort when compared to healthy controls, however, this was not significant (p=0.070) (Table 11).

Upper esophageal contractile integral (UES CI) similarly, was generally lower in the tracheostomy group when compared to healthy controls, however, this was not significant (p=0.070) (Table 11).

UES peak pressures (UES Peak P) were also generally lower in the tracheostomy group when compared to healthy controls, but only statistically significant in the 5 mL thick condition (p=0.024).

3.3.2.5 Proximal esophageal contractility

Proximal esophageal contractility (PCI) did not differ between the tracheostomy group and healthy controls (p=0.402) across all bolus conditions (Table 11).

Table 10 HRPM Core Outcome Metrics

Metric	Bolus condition	Control group n=9 median [IQR]	Tracheostomy n=9 median [IQR]	p=
Pharyngeal Contractile Integral PhCI (mmHg.cm.s)	1	183.4 [120.7, 216.8]	242.1 [139.6, 487.7]	0.113
	2	131.4 [135.7, 224.7]	244.9 [173.4, 513.6]	0.031
	3	168.5 [127.8, 271.7]	249.6 [130.0, 450.6]	0.436
	4	210.7 [135.8, 256.7]	283.9 [143.5, 449.1]	0.190
Velopharyngeal Contractile Integral VCI (mmHg.cm.s)	1	55.4 [22.3, 81.3]	62.2 [31.3, 170.4]	0.387
	2	53.1 [25.1, 58.8]	87.0 [45.4, 224.1]	0.058
	3	41.6 [24.4, 78.4]	66.4 [29.2, 164.9]	0.258
	4	44.5 [28.2, 79.7]	64.6 [37.3, 186.0]	0.222
Mesopharyngeal Contractile Integral MCI (mmHg.cm.s)	1	66.2 [58.3, 88.2]	108.2 [50.7, 131.2]	0.297
	2	66.1 [44.7, 84.6]	90.3 [55.8, 128.6]	0.200
	3	64.7 [46.9, 122.0]	112.9 [45.7, 119.0]	0.546
	4	72.3 [45.8, 107.2]	105.1 [52.4, 137.4]	0.222
Hypopharyngeal Contractile Integral HPCI (mmHg.cm.s)	1	47.2 [22.3, 69.8]	53.1 [41.8, 130.9]	0.222
	2	65.8 [31.5, 87.4]	69.5 [47.7, 90.9]	0.453
	3	56.5 [38.7, 81.7]	76.5 [37.8, 117.4]	0.666
	4	64.5 [34.4, 83.6]	74.5 [46.1, 114.9]	0.730
Hypopharyngeal Intra-Bolus Pressure IBP (mmHg)	1	-2.18 [-5.12, 0.70]	7.62 [4.94, 14.7]	0.001
	2	-0.07 [-1.78, 3.68]	3.78 [1.57, 11.4]	0.024
	3	2.60 [-5.81, 7.10]	11.4 [4.3, 15.5]	0.011
	4	3.41 [-3.24, 6.23]	9.02 [5.68, 18.9]	0.050
UES Maximum Admittance UES Max Adm (mS)	1	3.98 [3.48, 4.29]	4.01 [3.69, 4.61]	0.666
	2	4.78 [4.20, 5.53]	4.98 [4.05, 5.41]	0.965
	3	4.76 [4.41, 5.21]	3.6 [3.3, 5.3]	0.605
	4	5.69 [5.34, 6.16]	4.55 [4.19, 5.81]	0.113
UES Integrated Relaxation Pressure UES IRP (mmHg)	1	-5.13 [-8.35, -1.93]	12.0 [-1.29, 21.5]	0.002
	2	-5.56 [-8.41, -0.93]	9.47 [-1.60, 15.3]	0.003
	3	-3.49 [-8.56, 2.75]	14.2 [1.1, 20.5]	0.006
	4	-3.23 [-5.41, 1.43]	19.2 [3.97, 22.7]	0.006
UES Relaxation Time UES RT (s)	1	0.52 [0.45, 0.53]	0.34 [0.31, 0.45]	0.014
	2	0.59 [0.46, 0.64]	0.37 [0.35, 0.51]	0.038
	3	0.50 [0.42, 0.54]	0.38 [0.29, 0.46]	0.024
	4	0.57 [0.45, 0.62]	0.42 [0.31, 0.56]	0.113

Colours: Orange – IDDSI 0, Blue – IDDSI 4

Bolus conditions: (1) 5 mL thin, (2) 10 mL thin, (3) 5 mL thick and (4) 10 mL thick

Yellow highlights a value of statistical significance $p<0.05$

Table 11 HRPM Additional Metrics

Metric	Bolus Condition	Control group n=9 median [IQR]	Tracheostomy n=9 median [IQR]	p=
Swallow Risk Index SRI	1	0.45 [0.34, 1.77]	2.28 [1.28, 8.87]	0.040
	2	0.68 [0.32, 3.17]	2.95 [0.64, 4.96]	0.270
	3	0.86 [0.35, 2.15]	3.35 [1.65, 4.38]	0.031
	4	0.89 [0.59, 1.95]	2.13 [1.62, 6.98]	0.031
Bolus Presence Time BPT (s)	1	0.55 [0.50, 0.88]	0.53 [0.46, 0.70]	0.605
	2	0.63 [0.61, 0.98]	0.55 [0.53, 0.80]	0.289
	3	0.52 [0.46, 0.65]	0.43 [0.35, 0.82]	0.436
	4	0.60 [0.47, 0.80]	0.55 [0.43, 0.67]	0.489
Distension-Contraction Latency DCL (s)	1	0.42 [0.40, 0.46]	0.45 [0.36, 0.49]	0.546
	2	0.52 [0.45, 0.56]	0.48 [0.43, 0.55]	0.354
	3	0.41 [0.37, 0.43]	0.44 [0.37, 0.47]	0.190
	4	0.44 [0.40, 0.47]	0.46 [0.36, 0.50]	0.796
UES Basal Pressure UES BP (mmHg)	1	52.7 [36.3, 80.8]	35.2 [24.4, 58.6]	0.161
	2	64.9 [37.3, 104.0]	33.5 [31.5, 47.6]	0.070
	3	39.7 [32.3, 70.9]	32.7 [20.7, 52.2]	0.161
	4	40.3 [31.7, 101.4]	36.6 [19.4, 49.7]	0.161
UES Contractile Integral UESCI (mmHg.cm.s)	1	396.4 [274.2, 596.6]	228.0 [190.7, 381.3]	0.077
	2	368.6 [277.6, 669.7]	296.0 [197.5, 326.1]	0.070
	3	489.4 [298.4, 654.6]	267.9 [188.9, 385.6]	0.077
	4	402.4 [255.6, 642.5]	270.5 [163.4, 372.3]	0.136
Proximal Esophageal Contractile Integral PCI (mmHg.cm.s)	1	207.6 [133.3, 416.1]	270.8 [64.8, 319.8]	0.605
	2	243.1 [167.4, 463.4]	244.5 [102.2, 340.9]	0.402
	3	340.4 [132.8, 412.9]	235.6 [57.7, 492.5]	0.436
	4	280.8 [222.1, 408.4]	260.8 [53.3, 493.4]	0.546
Hypopharyngeal Peak Pressures Peak P (mmHg)	1	117.8 [58.3, 133.8]	118.3 [72.5, 214.1]	0.546
	2	139.9 [74.5, 167.8]	137.5 [98.4, 146.8]	0.825
	3	145.3 [79.7, 189.9]	119.7 [89.0, 170.6]	0.863
	4	154.9 [72.2, 210.1]	134.5 [90.4, 192.4]	0.863
UES Peak Pressures UES PeakP (mmHg)	1	204.5 [161.2, 359.4]	199.6 [137.7, 381.5]	0.796
	2	223.6 [177.2, 341.3]	185.6 [121.9, 302.2]	0.310
	3	233.4 [218.2, 377.0]	172.1 [150.0, 238.4]	0.024
	4	267.0 [213.7, 371.9]	181.9 [136.1, 268.5]	0.094

Colours: Orange – IDDSI 0, Blue – IDDSI 4

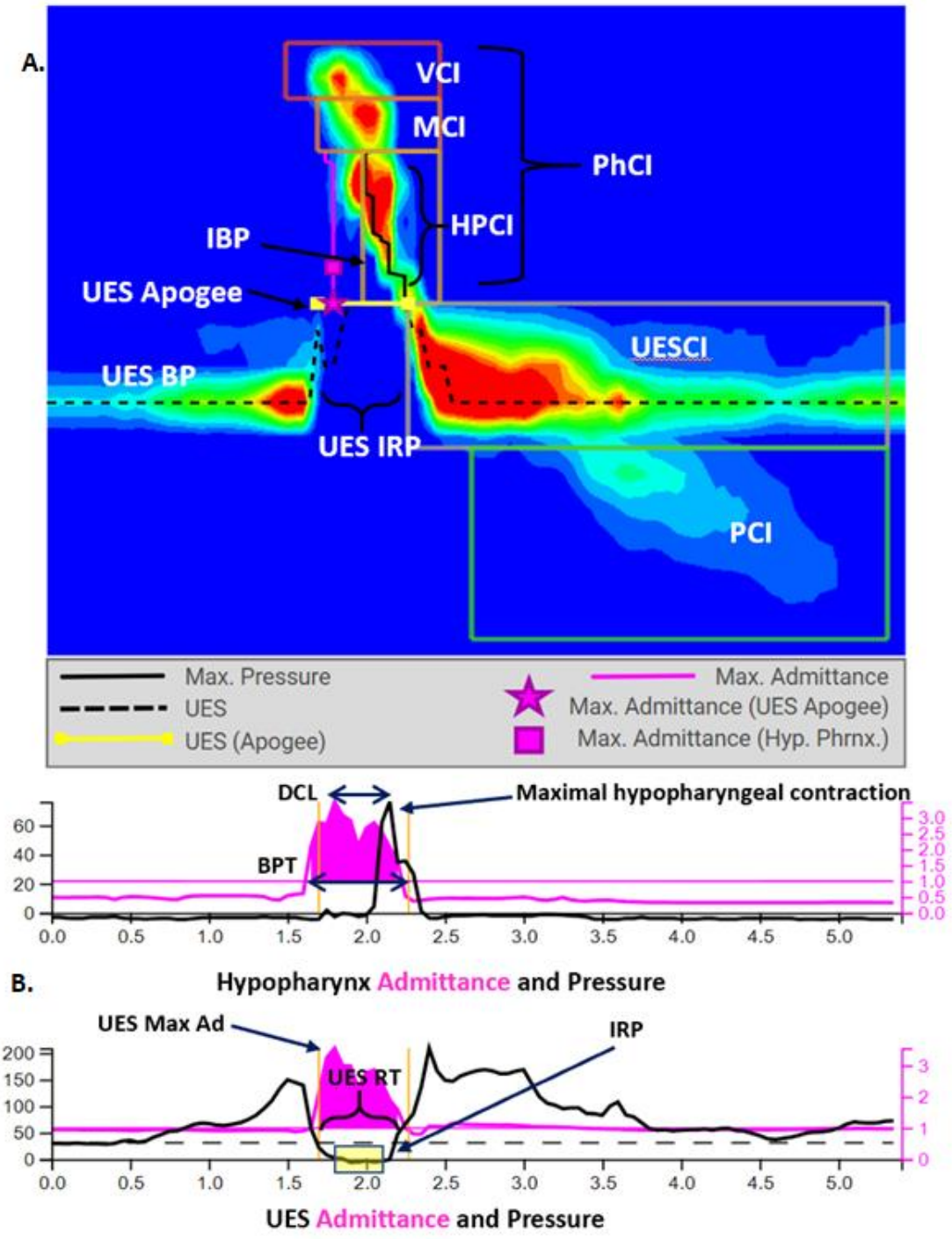
Bolus conditions: (1) 5 mL thin, (2) 10 mL thin, (3) 5 mL thick and (4) 10 mL thick

Yellow highlights a value of statistical significance $p<0.05$

3.3.3 Qualitative examples of disordered swallowing in critically ill patients with a tracheostomy using SwallowGateway™

Qualitative swallowing anomalies observed in patients are illustrated by comparing Figure 23 (control) with Figures 24-26 (patients). For each case, the interpretation provided is based on the pressure topography plot and objective data for the core-swallowing metrics.

Figure 23 Control "normal" swallow



(A) HRPM Colour pressure topography plot in a healthy individual. Cooler colours such as blue demonstrate 'lower' pressures whilst warmer colours such as red demonstrate 'higher' pressures. The Y-axis is distance (in cm) relative to the UES apogee and the X-axis is time (seconds). (B) Admittance & Pressure graph at the hypopharynx and UES from the above topography plot with the Y-axis being pressure (in mmHg) and X-axis being time (second).

- Pharynx is divided into the velo-, meso, hypopharyngeal regions with their own contractile integral (VCI, MCI and HPCI) and an overall pharyngeal contractile integral (PhCI). It demonstrates segments of higher pressures exhibiting contraction to push the bolus inferiorly with surrounding lower pressures for relaxation

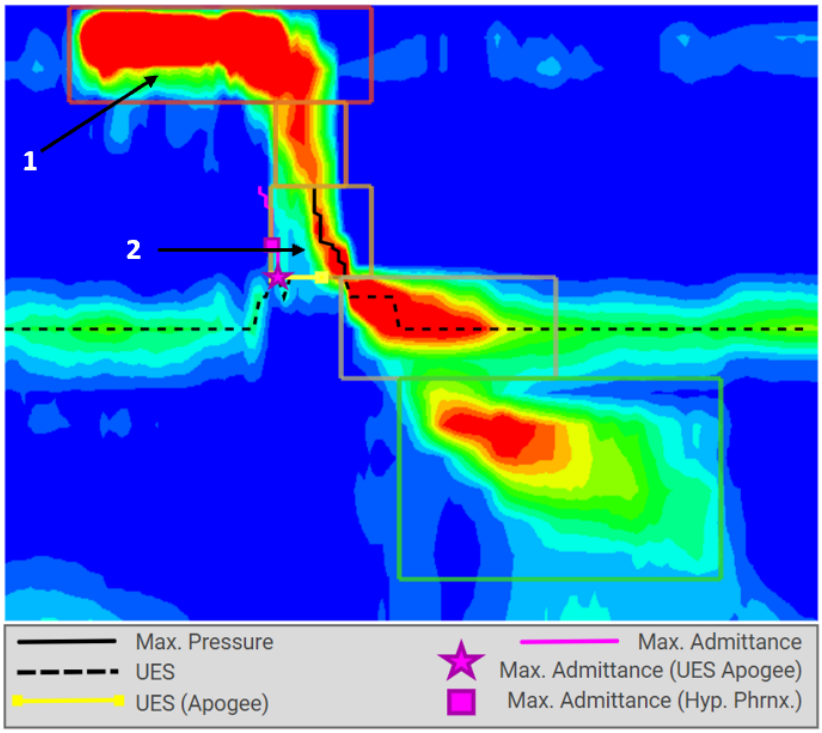
- Inferior aspect of the hypopharynx, note relatively lower pressures (IBP) highlighting ease of flow through the UES

- UES resting pressure (UES BP) with a pre-swallow rise in UES pressures (seen by the red segment), followed by UES relaxation (blue region following) and subsequently UES contraction and return to baseline resting tone. This is clearly appreciated in the UES admittance and pressure plot with the UES pressures being highlighted in black.

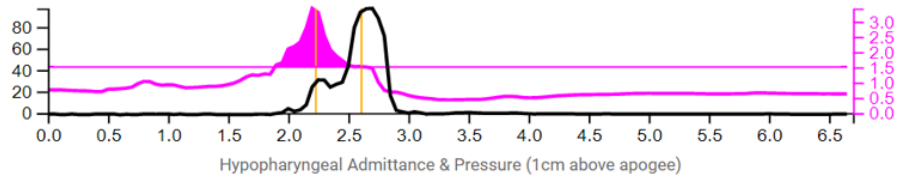
- Hypopharyngeal Admittance and Pressure waveform demonstrating hypopharyngeal distension, derived from admittance (pink), with an upstroke pressure waveform (black) highlighting hypopharyngeal contraction to propel the bolus towards the UES

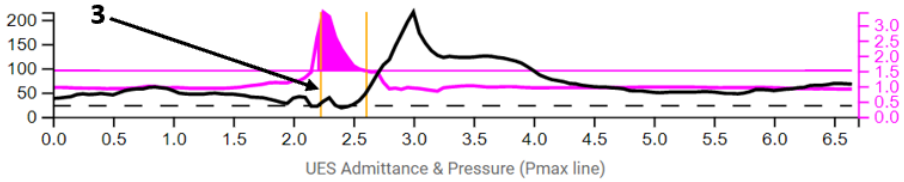
- UES Admittance and Pressure waveform demonstrating the UES pressures in black. To note, the resting UES pressure, followed by the pre-swallow upstroke with subsequent relaxation, post-swallow contraction and return to baseline. Only at time of UES relaxation, is there bolus admittance (flow) through it.

Figure 24 Abnormal swallow 1



Swallow Properties		
PhCI	1008.48	mmHg.s.cm
VCI	800.19	mmHg.s.cm
MCI	107.04	mmHg.s.cm
HPCI	101.26	mmHg.s.cm
UES IRP	23.77	mmHg
UES RT	0.38	s
UES Max Adm	3.43	mS
IBP	24.27	mmHg
Swallow Risk Index	12.16	
BPT	0.80	s



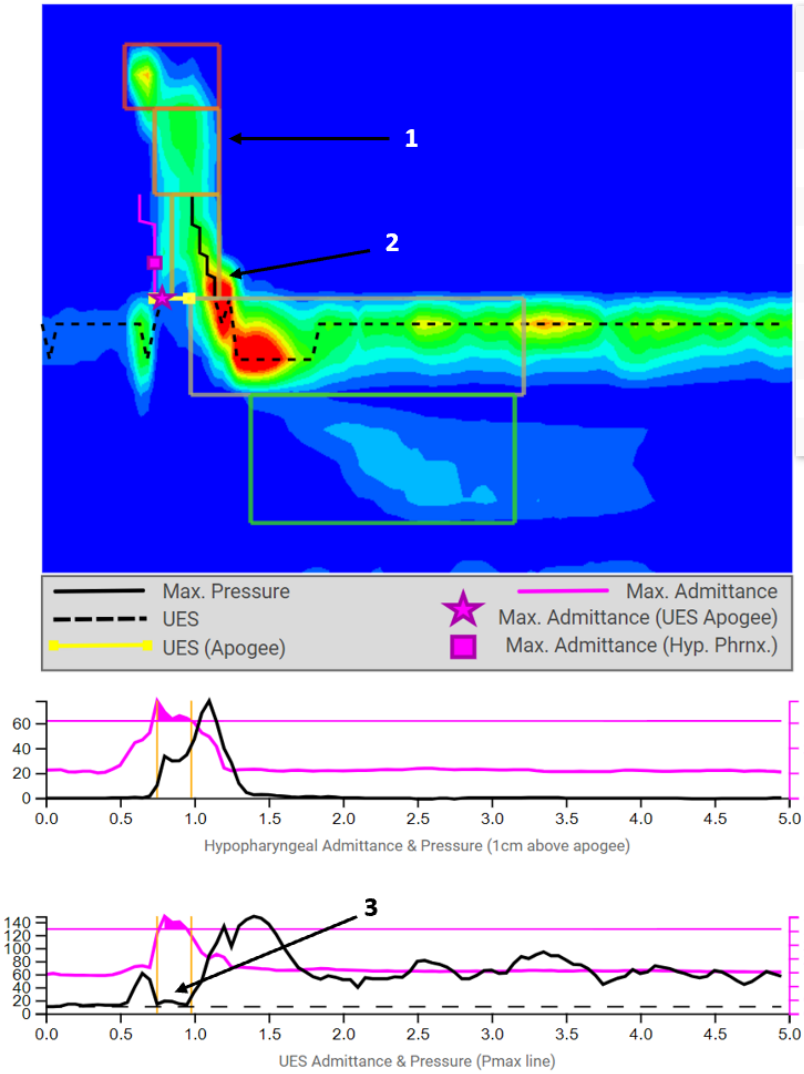


68-year-old female requiring a tracheostomy following a motor vehicle accident; who prior to the accident was fit and healthy. Findings in this 'abnormal' SwallowGateway™ analysis:

1. Extremely higher pharyngeal pressures, particularly in the velopharynx (800 mmHg.s.cm)
2. Elevated IBP, demonstrated by higher pressures above the UES apogee, highlighting restricted flow through the UES
3. Elevated UES basal pressures and higher than normal UES relaxation pressures (UES IRP)

Interpretation: This swallow demonstrates a patient with restricted flow through the UES and altered UES resting and relaxation pressures with elevated upstream pharyngeal contraction pressures particularly in the velopharynx. This resulted in an SRI of 12; consistent with a disordered swallow.

Figure 25 Abnormal swallow 2



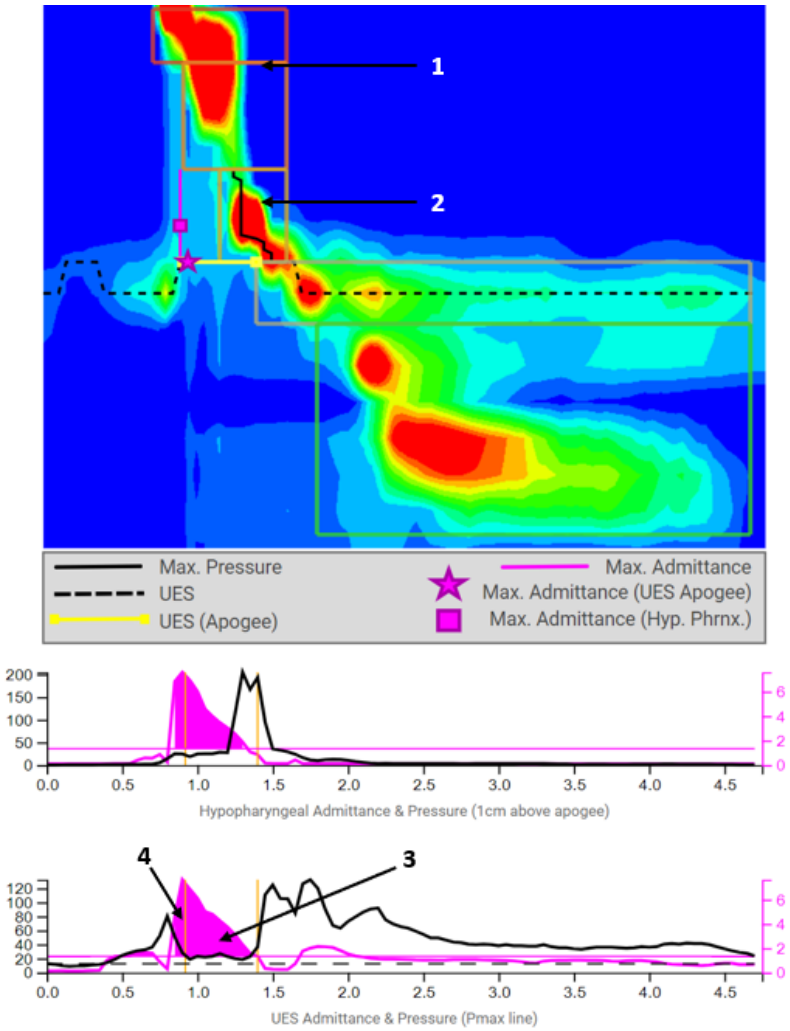
Swallow Properties		
PhCI	108.60	mmHg.s.cm
VCI	26.43	mmHg.s.cm
MCI	40.01	mmHg.s.cm
HPCI	42.16	mmHg.s.cm
UES IRP	15.54	mmHg
UES RT	0.23	s
UES Max Adm	3.52	mS
IBP	10.15	mmHg
Swallow Risk Index	2.65	
BPT	0.25	s

64-year-old male requiring a tracheostomy following a motor vehicle accident, with a background of cardiac disease. Findings in this 'abnormal' SwallowGateway™ analysis:

1. Very low pressures throughout the pharynx
2. Elevated IBP
3. Slightly elevated UES BP with higher-than-normal UES relaxation pressures and short UES resting relaxation time.

Interpretation: This swallow demonstrates a patient that was unable to generate adequate upstream pharyngeal pressures; there was restricted flow through the UES with altered UES resting and relaxation pressures.

Figure 26 Abnormal swallow 3



Swallow Properties		
PhCI	250.74	mmHg.s.cm
VCI	82.94	mmHg.s.cm
MCI	96.57	mmHg.s.cm
HPCI	71.22	mmHg.s.cm
UES IRP	20.31	mmHg
UES RT	0.48	s
UES Max Adm	6.86	mS
IBP	24.05	mmHg
Swallow Risk Index	6.29	
BPT	0.50	s

45-year-old female requiring a tracheostomy for respiratory failure, with a background of COPD and alcoholic liver disease. Findings in this 'abnormal' SwallowGateway™ analysis:

1. Elevated pharyngeal pressures
2. Elevated IBP
3. Elevated UES basal pressures and relaxation pressures
4. Bolus flow through the UES prior to complete UES relaxation, potentially due to delayed UES opening

Interpretation: This swallow demonstrates elevated pressures upstream with altered UES pressures and timings; however, this swallow highlights pressure flow through the UES despite incomplete relaxation

3.3.4 Summary of swallowing parameters in tracheostomy patients

It has been demonstrated that this cohort of patients with a tracheostomy, qualitatively and quantitatively have a more disordered swallow compared to healthy age-matched controls. The following HRPM swallow metrics were altered: 1) an elevated hypopharyngeal intrabolus pressure, 2) elevated UES relaxation pressures, 3) reduced UES relaxation duration, 4) higher than normal upstream pharyngeal contractile integrals; overall resulting in 5) a higher swallow risk index.

3.3.5 Assessing the impact of treatment factors on swallowing

Critically unwell tracheostomy patients are often mechanically ventilated and have a tracheostomy *in situ* for varying periods of time based on their medical needs and support required; furthermore, patients are often on various medications including opiates to assist with pain and comfort. These factors were evaluated in order to assess their potential impact on swallowing with a tracheostomy *in situ*. Variables tested include 1) opiate use within 24 hours of the study and 2) tracheostomy duration at the time of the study (less than or more than 2 weeks) (Table 12).

10 mL thin was used as the reference bolus condition with cuff down being the reference tracheostomy condition.

Table 12 Patient medical, opiate and tracheostomy data

Patient	Reason for Admission	Medical History	Type of tracheostomy	Brand and size of tracheostomy (with outer diameter)	Duration of tracheostomy (days)	Cuff down for 24 hours before study	Medications of note
1	MVA	Asthma	Percutaneous	Size 8 Portex™ (11.9 mm)	12	Intermittent	TCA and opiate on day of study
2	Respiratory failure	COPD	Percutaneous	Size 8 Portex™ (11.9 mm)	11	Intermittent	PPI, corticosteroid and Quetiapine
3	Respiratory failure	COPD, pulmonary hypertension, alcoholic liver cirrhosis and Child's B cirrhosis	Percutaneous	Size 7 Portex™ (10.5 mm)	6	Intermittent	PPI, Pregabalin, MAOI anti-depressant and Prednisolone
4	CABG with cardiogenic shock	HTN, COPD and IHD	Percutaneous	Size 8 Portex™ (11.9 mm)	21	Intermittent	PPI and Quetiapine
5	MVA	Nil	Percutaneous	Size 7 Portex™ (10.5 mm)	11	Continuous	Oxycodone, Quetiapine and Metoclopramide
6	AAA dissection	HTN, COPD and hypothyroidism	Surgical	Size 7 Shiley™ (11.4 mm)	7	Continuous	PPI
7	Perforated peptic ulcer and sepsis	T2DM on Insulin and smoker	Percutaneous	Size 8 Portex™ (11.9 mm)	18	Intermittent	Oxycodone, Quetiapine, SSRI, PPI and Metoclopramide
8	MVA	IHD with stents, PVD, HTN	Surgical	Size 8 Shiley™ (12.2 mm)	17	Continuous	PPI, Oxycodone and Olanzapine
9	Urosepsis	T2DM, gastric sleeve	Percutaneous	Size 7 Portex™ (10.5 mm)	15	Continuous	PPI, SSRI, Risperidone and Temazepam

MVA – motor vehicle accident, COPD – chronic obstructive pulmonary disease, T2DM – type-2 diabetes mellitus, HTN – hypertension, PVD – peripheral vascular disease, MAOI – monoamine oxidase inhibitors, PPI – proton pump inhibitor, TCA – tricyclic antidepressant, SSRI – selective serotonin reuptake inhibitor

3.3.5.2 Opiate Use within 24 hours

Tracheostomy patients were divided into two groups based on the opiate usage within the 24 hours prior to the study being conducted; 4 patients had used opioids (oxycodone) within 24 hours, whilst 5 patients did not use any opioid analgesia in the 24 hours leading to the study (Table 12). Opioid use in the tracheostomy cohort resulted in a significantly reduced UES Max Admittance (Table 13 and Figure 27) and trending elevation in UES IRP, IBP and SRI (Figure 28-30).

Table 13 Swallowing metrics in tracheostomy patients that had used opiates within 24 hours of the study

Swallow Parameter	No opioids used median [IQR]	Opioids used median [IQR]	P-value
PhCI	244.9 [229, 437.2]	245.3 [165.2, 625.1]	0.806
VCI	87.0 [40.2, 187.4]	101.9 [57.7, 457.8]	0.624
MCI	90.3 [78.5, 122.8]	81.0 [47.0, 121.7]	0.462
HPCI	86.2 [63.5, 95.6]	56.3 [32.4, 73.7]	0.142
IRP	2.8 [-0.66, 9.47]	14.6 [4.02, 18.9]	0.221
UES RT	0.37 [0.37, 0.47]	0.43 [0.35, 0.66]	1.000
UES Max Ad	5.1 [4.98, 5.70]	4.1 [3.18, 4.59]	0.027
UES IBP	3.78 [1.57, 7.26]	7.47 [1.58, 15.4]	0.624
SRI	2.22 [0.64, 2.95]	6.21 [2.53, 11.3]	0.221
UESCI	296.0 [197.5, 326.1]	298.3 [223.8, 332.0]	1.000
PeakP	143.5 [137.5, 146.8]	87.4 [72.4, 138.3]	0.142
BPT	0.55 [0.53, 0.60]	1.05 [0.42, 1.78]	0.539
DCL	0.48 [0.43, 0.55]	0.49 [0.40, 0.54]	1.000
UES BP	47.6 [20.6, 72.5]	33.2 [32.3, 34.9]	0.624
UES PeakP	215.4 [185.6, 302.2]	152.8 [119.4, 245.8]	0.462
PCI	244.5 [102.2, 483.8]	228.0 [96.0, 332.2]	0.806

10 mL thin is the referenced condition
Yellow highlights a value of statistical significance $p<0.05$

Figure 27 Boxplot demonstrating the UES Max Adm between controls and tracheostomy patients based on opiates use within 24 hours (using 10 mL thin bolus)

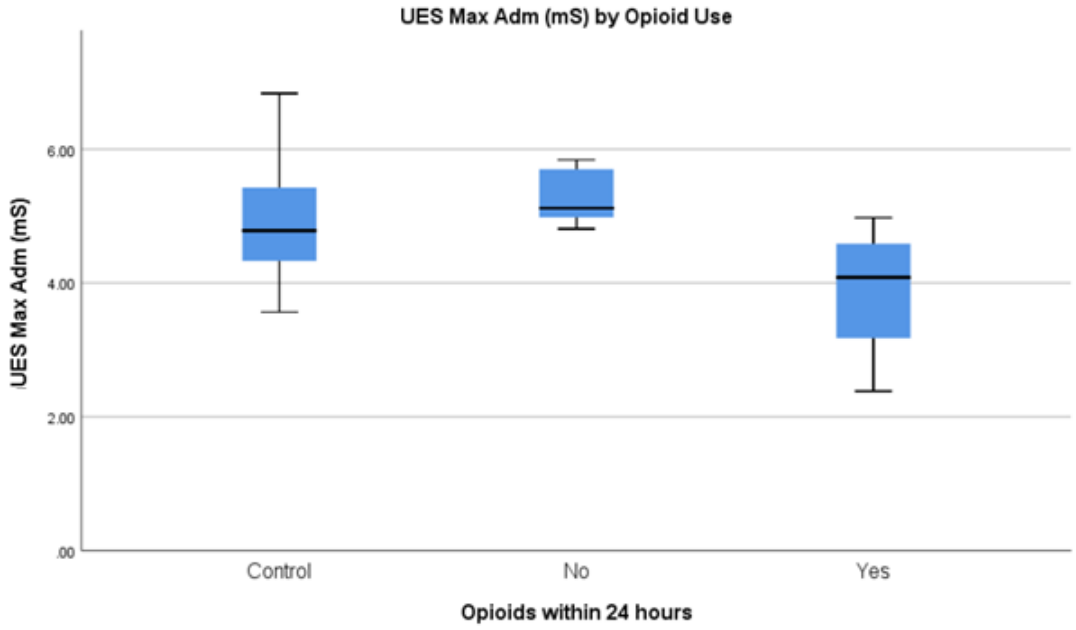


Figure 28 Boxplot demonstrating the UES IRP Adm between controls and tracheostomy patients based on opiates use within 24 hours (using 10 mL thin bolus)

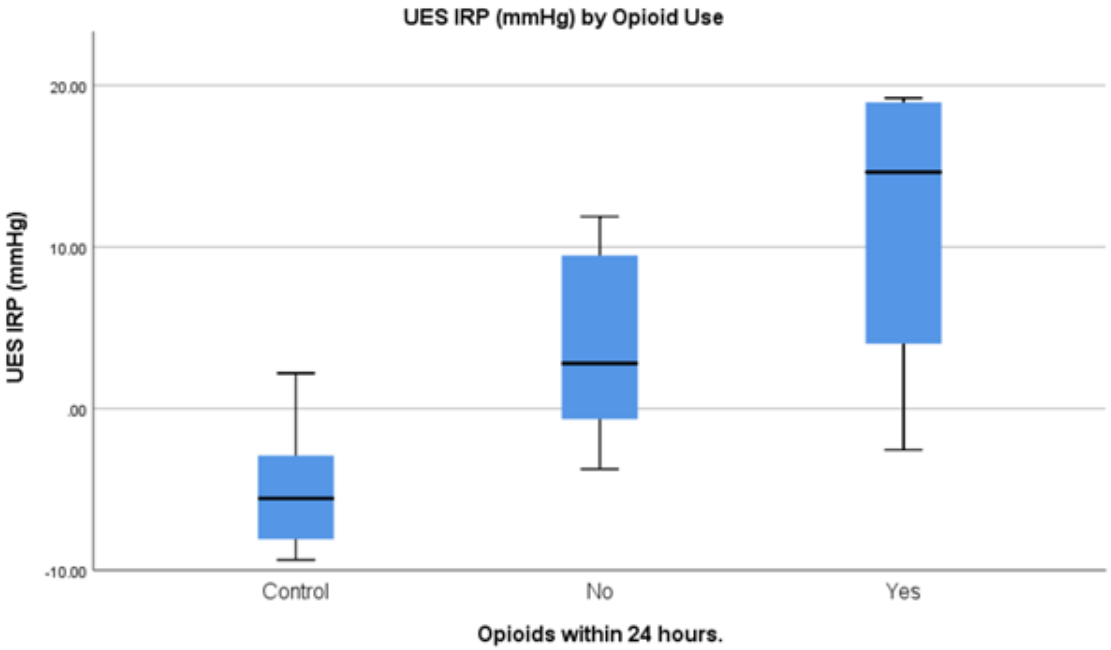


Figure 29 Boxplot demonstrating the IBP between controls and tracheostomy patients based on opiates use within 24 hours (using 10 mL thin bolus)

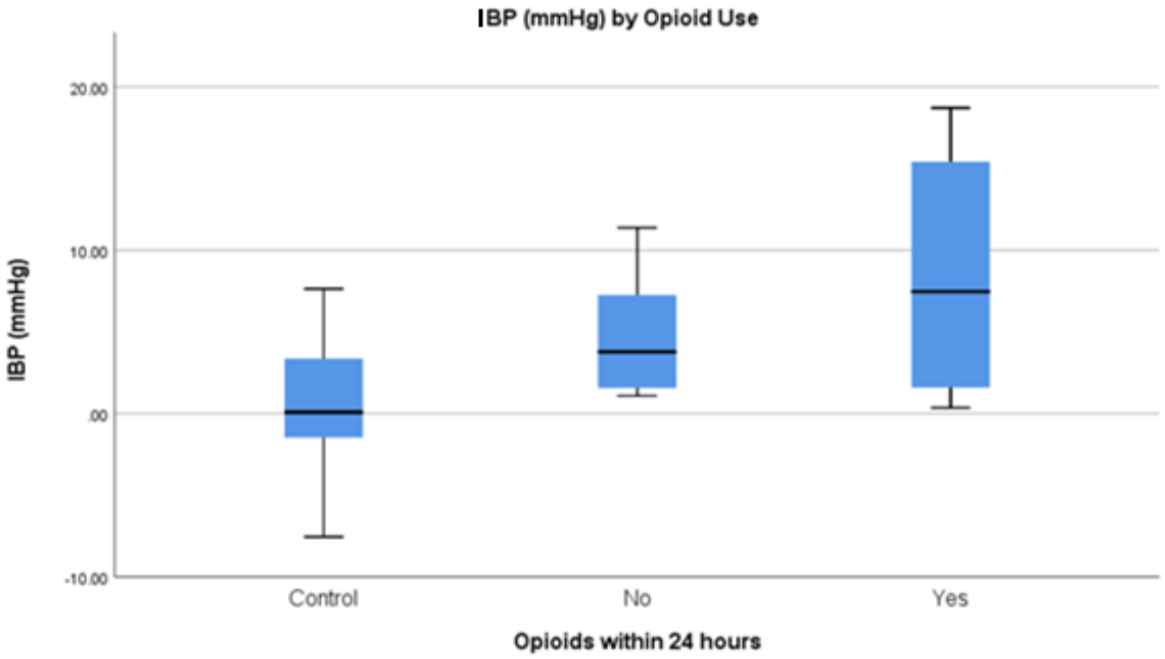
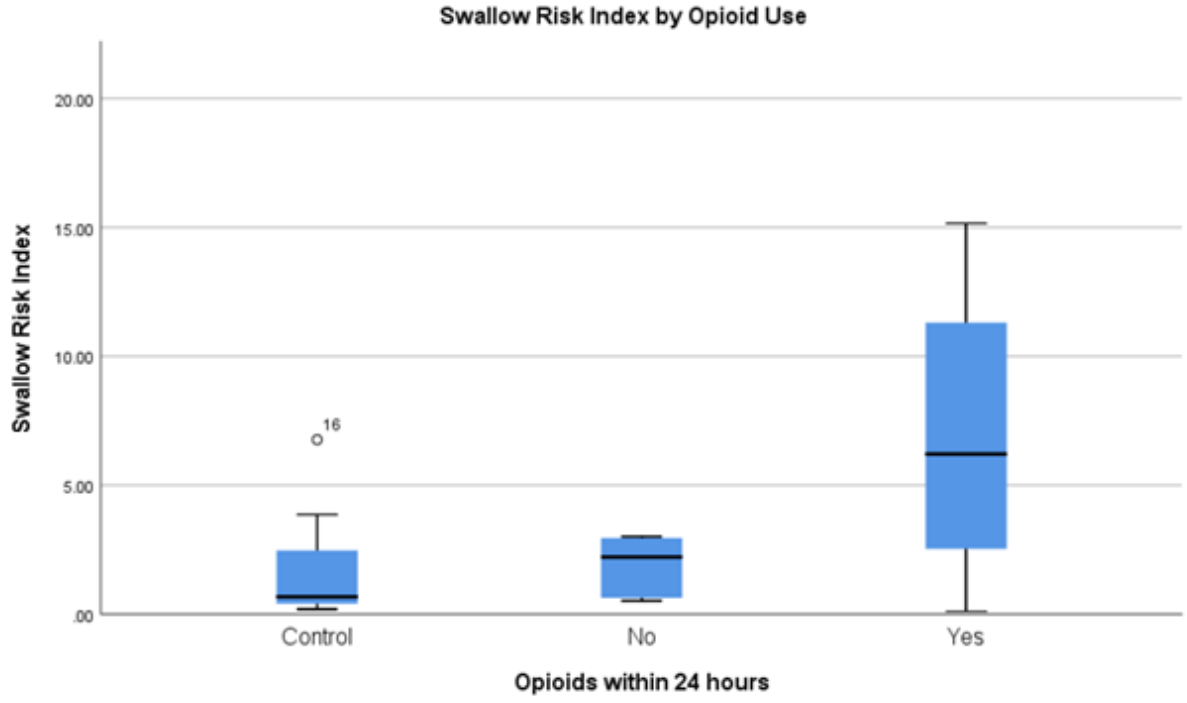


Figure 30 Boxplot demonstrating the SRI between controls and tracheostomy patients based on opiates use within 24 hours (using 10 mL thin bolus)



3.3.5.3 Tracheostomy duration (less than or more than 2 weeks)

Tracheostomy patients were split into two groups, based on tracheostomy duration. 4 patients had a tracheostomy for less than 2 weeks and 5 patients had a tracheostomy for more than 2 weeks; with a maximum duration of 21 days (Table 12). In this cohort of patients, swallowing metrics were not significantly altered, however, trends were observed in those with a tracheostomy for more than 2 weeks. It was observed that these patients had a lower HPCI, Peak P and PCI, compared to patients who had a tracheostomy for less than 2 weeks (Table 14).

Table 14 Swallowing metrics in tracheostomy patients based on tracheostomy duration

Swallow Parameter	Less than 2 weeks median [IQR]	More than 2 weeks median [IQR]	P-value
PhCI	244.9 [229.0, 589.9]	223.1 [143.0, 366.1]	0.327
VCI	87.0 [64.8, 187.4]	94.8 [45.4, 199.9]	0.806
MCI	109.1 [78.5, 122.8]	74.5 [49.9, 112.4]	0.462
HPCI	77.9 [69.5, 95.6]	47.7 [32.4, 69.3]	0.086
IRP	11.9 [9.47, 18.7]	1.07 [1.6, 6.69]	0.221
UES RT	0.47 [0.36, 0.51]	0.37 [0.35, 0.59]	0.806
UES Max Ad	4.98 [4.81, 5.12]	4.48 [3.18, 5.34]	0.463
UES IBP	1.57 [1.08, 11.4]	5.52 [3.30, 9.68]	0.462
SRI	0.64 [0.52, 3.00]	3.95 [2.58, 6.21]	0.327
UESCI	296.0 [197.5, 305.8]	308.5 [201.3, 342.1]	1.000
PeakP	146.8 [137.5, 178.3]	95.8 [72.4, 129.3]	0.086
BPT	0.53 [0.50, 0.60]	0.68 [0.55, 1.40]	0.219
DCL	0.53 [0.45, 0.55]	0.41 [0.33, 0.51]	0.327
UES BP	36.1 [33.0, 47.6]	32.5 [22.1, 57.7]	0.624
UES PeakP	185.6 [183.6, 302.2]	168.6 [115.6, 261.7]	0.624
PCI	340.9 [323.6, 483.8]	96.0 [32.3, 188.5]	0.050

3.3.5.4 Summary of the role of treatment factors on swallowing parameters

As differences in swallow metrics between tracheostomy patients and age-matched controls were evident, treatment factors were explored to ensure that the differences observed were due to the placement of the tracheostomy itself rather than external factors. The use of opiates 24 hours prior to the study had an impact on swallowing parameters with a significant reduction in UES Max Admittance and trending elevation in UES Relaxation and Intrabolus pressures and Swallow Risk Index. Placement of the tracheostomy for more 2 weeks,

trended to reduce Hypopharyngeal and Proximal Esophageal Contractile Integrals and Hypopharyngeal Peak Pressures.

3.4 COMPARING SWALLOWING METRICS ACROSS CUFF CONDITIONS

Tracheostomy patients were assessed across the three tracheostomy conditions (cuff deflated, inflated and with a Passy-Muir speaking valve with the cuff deflated), the patient was used as their own reference.

Quantitatively, the differences between the three tracheostomy cuff conditions were not significant. There were however some important trends that were observed, that can be demonstrated quantitatively and qualitatively using the SwallowGateway™ pressure-topography plot.

3.4.1 High-Resolution Pharyngeal Manometry Core Outcome Metrics

3.4.1.1 Hypopharyngeal Intra-Bolus Distension Pressure

A tracheostomy with the cuff inflated trended to higher median IBPs across all bolus conditions (Table 15). This finding was also demonstrated qualitatively in some patients on a pressure-topography plot, in which transient pressurisation occurred across the pharynx and this resolved with cuff deflation (Figure 31).

3.4.1.2 UES Relaxation Pressure, relaxation duration and UES opening diameter

UES relaxation pressures trended to be higher in tracheostomy patients with the cuff inflated, however, patients with a PMSV had lower median relaxation pressures across all bolus conditions. Quantitatively, UES relaxation pressures approached normal values with the placement of the PMSV (Table 15).

UES relaxation duration (UES RT) was varied across the tracheostomy cuff conditions; with no obvious trend observed (Table 15).

UES opening, derived from UES Max Admittance varied across tracheostomy cuff conditions, with no obvious trend observed (Table 15).

3.4.1.3 Pharyngeal, Velo-, Meso- and Hypopharyngeal Contractility

Luminal occlusive pressures across the pharyngeal segment varied across the tracheostomy cuff conditions. Inflation of the cuff however resulted in higher median PhCI's in the 10 mL thin and 5 mL thick bolus condition. Similarly, insertion of the PMSV resulted in a higher median mesopharyngeal pressures in all bolus conditions excluding 5 mL thin; it conversely had the lowest median pressures in the hypopharynx (Table 15).

3.4.2 High-Resolution Pharyngeal Manometry Additional Metrics

3.4.2.1 Swallow Risk Index

Inflation of the tracheostomy cuff, compared to other cuff conditions, trended to higher median Swallow Risk Index scores across all bolus conditions (with the exclusion of 5 mLs thick); however, this was not significant (Table 16).

3.4.2.2 Bolus Presence and Pharyngeal Flow Metrics

Placement of the PMSV trended to prolong the BPT within the hypopharynx; with a higher median time particularly in the thin and 5 mL thick bolus condition (Table 16).

Deflation of the cuff trended to prolong the DCL timing, as patients with the tracheostomy cuff down had a higher median DCL across all bolus conditions (Table 16).

3.4.2.3 Hypopharyngeal Peak Pressures

Inflation of the cuff resulted in higher peak pressures generated within the hypopharynx during swallowing, compared to the other tracheostomy cuff conditions. It was demonstrated that inflation of the cuff resulted in higher median peak pressures across the thin boluses and the 5 mL thick bolus, of which it was significant ($p=0.006$) (Table 16).

3.4.2.4 UES Contractility

In tracheostomy patients with a PMSV, UES BP trended to be higher compared to other tracheostomy conditions (and were closer to standard control values). This trend was demonstrated with both the thick and the 10 mL thin bolus condition. (Table 16).

Upper esophageal contractile integral (UES CI), was inconsistent across the tracheostomy and bolus conditions (Table 6).

In tracheostomy patients with a PMSV, UES Peak P trended to be generally higher compared to other tracheostomy conditions (and were closer to standard control values). This trend was demonstrated with the 5 mL thin and both thick bolus conditions (Table 16).

3.4.2.5 Proximal esophageal contractility

Proximal esophageal contractility (PCI) was consistently lower in tracheostomy patients with the PMSV across all bolus conditions, however, it was only significant for the 5 mL thick condition (p=0.018) (Table 16).

Table 15 HRPM Core Outcome Metrics between cuff conditions

Metric	Bolus condition	Control median [IQR]	Down median [IQR]	PMSV median [IQR]	Up median [IQR]	p=
PhCI (mmHg.cm.s)	1	183.4 [120.7, 216.8]	242.1 [139.6, 487.7]	199.4 [164.4, 329.2]	220.5 [158.5, 412.6]	0.651
	2	131.4 [135.7, 224.7]	244.9 [173.4, 513.6]	234.5 [170.4, 467.9]	324.2 [170.1, 455.3]	0.607
	3	168.5 [127.8, 271.7]	249.6 [130.0, 450.6]	206.8 [129.3, 309.6]	272.3 [136.5, 385.6]	0.156
	4	210.7 [135.8, 256.7]	283.9 [143.5, 449.1]	299.9 [133.7, 409.4]	266.0 [139.5, 430.0]	0.607
VCI (mmHg.cm.s)	1	55.4 [22.3, 81.3]	62.2 [31.3, 170.4]	53.1 [33.0, 162.3]	66.2 [42.5, 125.7]	0.368
	2	53.1 [25.1, 58.8]	87.0 [45.4, 224.1]	75.6 [43.0, 173.1]	68.6 [45.7, 148.9]	0.846
	3	41.6 [24.4, 78.4]	66.4 [29.2, 164.9]	61.8 [28.9, 101.1]	62.2 [33.4, 138.7]	0.180
	4	44.5 [28.2, 79.7]	64.6 [37.3, 186.0]	80.6 [34.0, 124.3]	74.6 [35.8, 159.6]	0.846
MCI (mmHg.cm.s)	1	66.2 [58.3, 88.2]	108.2 [50.7, 131.2]	84.1 [52.3, 120.]	78.1 [58.6, 147.5]	0.368
	2	66.1 [44.7, 84.6]	90.3 [55.8, 128.6]	125.0 [65.5, 138.0]	101.8 [72.1, 124.4]	0.846
	3	64.7 [46.9, 122.0]	112.9 [45.7, 119.0]	121.4 [45.0, 143.6]	92.1 [61.5, 144.8]	0.368
	4	72.3 [45.8, 107.2]	105.1 [52.4, 137.4]	129.9 [50.0, 155.7]	107.8 [61.1, 154.3]	0.846
HPCI (mmHg.cm.s)	1	47.2 [22.3, 69.8]	53.1 [41.8, 130.9]	53.3 [34.5, 82.8]	60.3 [46.4, 87.0]	0.368
	2	65.8 [31.5, 87.4]	69.5 [47.7, 90.9]	51.4 [39.8, 104.2]	65.1 [50.2, 103.3]	0.846
	3	56.5 [38.7, 81.7]	76.5 [37.8, 117.4]	62.9 [36.8, 104.2]	67.3 [38.9, 101.8]	0.276
	4	64.5 [34.4, 83.6]	74.5 [46.1, 114.9]	66.1 [30.5, 160.6]	48.1 [32.0, 81.3]	0.846
IBP (mmHg)	1	-2.18 [-5.12, 0.70]	7.62 [4.94, 14.7]	5.1 [2.21, 12.1]	8.12 [4.01, 15.86]	0.565
	2	-0.07 [-1.78, 3.68]	3.78 [1.57, 11.4]	4.83 [2.92, 7.67]	8.75 [1.81, 12.1]	0.607
	3	2.60 [-5.81, 7.10]	11.4 [4.3, 15.5]	7.89 [0.05, 16.5]	14.5 [2.62, 19.7]	0.156
	4	3.41 [-3.24, 6.23]	9.02 [5.68, 18.9]	10.1 [3.00, 16.7]	15.2 [4.47, 16.6]	0.311
UES Max Adm (mS)	1	3.98 [3.48, 4.29]	4.01 [3.69, 4.61]	3.98 [3.77, 4.65]	3.71 [3.51, 4.79]	0.867
	2	4.78 [4.20, 5.53]	4.98 [4.05, 5.41]	4.55 [4.14, 5.04]	4.47 [4.23, 4.95]	0.607
	3	4.76 [4.41, 5.21]	3.6 [3.3, 5.3]	3.91 [3.34, 5.22]	3.87 [3.38, 5.00]	0.368
	4	5.69 [5.34, 6.16]	4.55 [4.19, 5.81]	4.92 [4.49, 5.97]	4.95 [4.53, 5.82]	0.311
UES IRP (mmHg)	1	-5.13 [-8.35, -1.93]	12.0 [-1.29, 21.5]	7.22 [-1.76, 14.3]	10.2 [3.25, 21.3]	0.066
	2	-5.56 [-8.41, -0.93]	9.47 [-1.60, 15.3]	5.4 [-2.63, 12.5]	14.0 [-0.81, 17.4]	0.135
	3	-3.49 [-8.56, 2.75]	14.2 [1.1, 20.5]	13.3 [2.1, 20.3]	18.0 [4.1, 19.2]	0.368
	4	-3.23 [-5.41, 1.43]	19.2 [3.97, 22.7]	8.77 [0.39, 18.6]	11.0 [5.10, 20.3]	1.000
UES RT (s)	1	0.52 [0.45, 0.53]	0.34 [0.31, 0.45]	0.41 [0.31, 0.60]	0.36 [0.29, 0.56]	0.618
	2	0.59 [0.46, 0.64]	0.37 [0.35, 0.51]	0.35 [0.34, 0.51]	0.37 [0.36, 0.54]	0.422
	3	0.50 [0.42, 0.54]	0.38 [0.29, 0.46]	0.40 [0.30, 0.42]	0.38 [0.31, 0.45]	0.964
	4	0.57 [0.45, 0.62]	0.42 [0.31, 0.56]	0.39 [0.33, 0.50]	0.46 [0.34, 0.53]	0.438

Colours: Orange – IDDSI 0, Blue – IDDSI 4

Bolus conditions: (1) 5 mL thin, (2) 10 mL thin, (3) 5 mL thick and (4) 10 mL thick

Table 16 HRPM Additional Outcome Metrics between cuff conditions

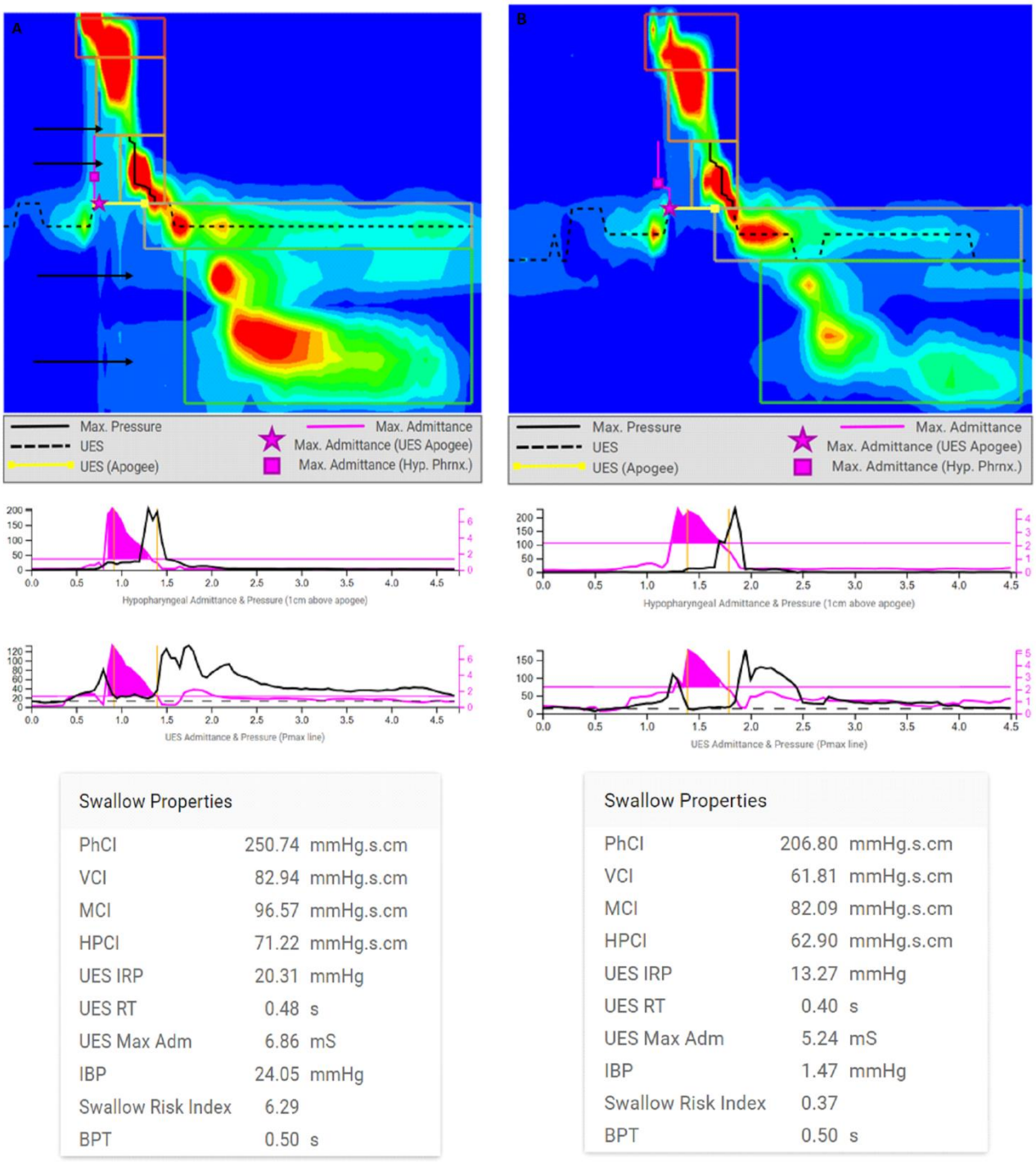
Metric	Bolus condition	Control median [IQR]	Down median [IQR]	PMSV median [IQR]	Up median [IQR]	p=
SRI	1	0.45 [0.34, 1.77]	2.28 [1.28, 8.87]	2.56 [1.69, 3.87]	3.22 [0.61, 5.51]	1.000
	2	0.68 [0.32, 3.17]	2.95 [0.64, 4.96]	2.82 [2.17, 3.51]	3.48 [1.13, 4.12]	0.311
	3	0.86 [0.35, 2.15]	3.35 [1.65, 4.38]	3.6 [0.37, 5.72]	2.74 [1.19, 7.08]	0.651
	4	0.89 [0.59, 1.95]	2.13 [1.62, 6.98]	2.83 [1.37, 6.71]	3.58 [1.55, 8.56]	0.846
BPT (s)	1	0.55 [0.50, 0.88]	0.53 [0.46, 0.70]	0.57 [0.48, 0.75]	0.50 [0.43, 0.66]	0.772
	2	0.63 [0.61, 0.98]	0.55 [0.53, 0.80]	0.73 [0.53, 0.90]	0.66 [0.48, 0.93]	1.000
	3	0.52 [0.46, 0.65]	0.43 [0.35, 0.82]	0.55 [0.47, 0.65]	0.53 [0.35, 0.74]	0.156
	4	0.60 [0.47, 0.80]	0.55 [0.43, 0.67]	0.53 [0.44, 0.75]	0.50 [0.39, 0.73]	0.568
DCL (s)	1	0.42 [0.40, 0.46]	0.45 [0.36, 0.49]	0.43 [0.37, 0.49]	0.42 [0.38, 0.46]	0.276
	2	0.52 [0.45, 0.56]	0.48 [0.43, 0.55]	0.47 [0.38, 0.59]	0.47 [0.42, 0.55]	0.607
	3	0.41 [0.37, 0.43]	0.44 [0.37, 0.47]	0.44 [0.37, 0.50]	0.41 [0.35, 0.44]	0.050 Valve > Cuff Up
	4	0.44 [0.40, 0.47]	0.46 [0.36, 0.50]	0.44 [0.33, 0.52]	0.42 [0.37, 0.48]	0.568
UES BP (mmHg)	1	52.7 [36.3, 80.8]	35.2 [24.4, 58.6]	35.2 [29.9, 142.0]	38.8 [28.4, 61.8]	0.565
	2	64.9 [37.3, 104.0]	33.5 [31.5, 47.6]	57.8 [25.1, 121.8]	43.1 [40.0, 47.3]	0.513
	3	39.7 [32.3, 70.9]	32.7 [20.7, 52.2]	46.9 [25.5, 63.3]	35.0 [29.6, 59.3]	0.651
	4	40.3 [31.7, 101.4]	36.6 [19.4, 49.7]	46.1 [23.5, 72.5]	35.8 [27.6, 50.7]	0.115
UESCI (mmHg.cm.s)	1	396.4 [274.2, 596.6]	228.0 [190.7, 381.3]	299.2 [210.6, 443.1]	296.3 [215.2, 447.2]	0.066
	2	368.6 [277.6, 669.7]	296.0 [197.5, 326.1]	307.0 [176.0, 498.0]	283.3 [208.6, 346.4]	0.311
	3	489.4 [298.4, 654.6]	267.9 [188.9, 385.6]	250.1 [172.0, 468.0]	306.0 [186.9, 414.5]	0.651
	4	402.4 [255.6, 642.5]	270.5 [163.4, 372.3]	316.4 [166.2, 518.6]	324.7 [165.3, 440.2]	0.846
PCI (mmHg.cm.s)	1	207.6 [133.3, 416.1]	270.8 [64.8, 319.8]	118.8 [21.1, 378.4]	258.0 [82.1, 335.3]	0.651
	2	243.1 [167.4, 463.4]	244.5 [102.2, 340.9]	108.3 [7.88, 289.0]	232.5 [94.2, 289.7]	0.846
	3	340.4 [132.8, 412.9]	235.6 [57.7, 492.5]	126.1 [35.2, 317.9]	275.9 [105.0, 374.9]	0.018 Valve > Cuff Down
	4	280.8 [222.1, 408.4]	260.8 [53.3, 493.4]	113.6 [33.1, 334.9]	303.1 [113.1, 468.205]	0.006
Peak P (mmHg)	1	117.8 [58.3, 133.8]	118.3 [72.5, 214.1]	116.3 [70.2, 151.4]	149.8 [85.6, 165.9]	0.867
	2	139.9 [74.5, 167.8]	137.5 [98.4, 146.8]	108.8 [83.4, 159.1]	143.6 [88.5, 182.0]	0.223
	3	145.3 [79.7, 189.9]	119.7 [89.0, 170.6]	130.7 [65.6, 161.5]	135.2 [98.1, 214.6]	0.006 Valve < Cuff Up
	4	154.9 [72.2, 210.1]	134.5 [90.4, 192.4]	115.3 [74.1, 213.1]	131.9 [74.6, 165.6]	0.607
UES PeakP (mmHg)	1	204.5 [161.2, 359.4]	199.6 [137.7, 381.5]	230.9 [150.2, 323.2]	210.4 [156.8, 315.2]	0.651
	2	223.6 [177.2, 341.3]	185.6 [121.9, 302.2]	57.8 [25.1, 121.8]	177.0 [145.9, 201.7]	0.223
	3	233.4 [218.2, 377.0]	172.1 [150.0, 238.4]	322.2 [142.0, 418.4]	203.3 [135.8, 293.8]	0.368
	4	267.0 [213.7, 371.9]	181.9 [136.1, 268.5]	212.7 [125.2, 370.7]	183.4 [132.6, 249.8]	0.311

Colours: Orange – IDDSI 0, Blue – IDDSI 4

Bolus conditions: (1) 5 mL thin, (2) 10 mL thin, (3) 5 mL thick and (4) 10 mL thick

Yellow highlights a value of statistical significance $p<0.05$

Figure 31 Transient pressurisation across the pharynx



Pressure-topography plot previously described in Figure 26. (A) the patient was asked to swallow a 5 mL thin bolus with the cuff inflated, (B) the same patient is asked to swallow the same bolus with the cuff deflated. The black arrows highlight the transient pressurisation throughout the pharyngeal chamber demonstrating a build-up in pressure; which is reflected with the elevated IBP. As the patient's cuff is deflated (B), this pressurisation phenomena disappears with improvement in UES swallowing metrics – IBP, IRP and SRI.

3.4.3 Summary of swallowing parameters between tracheostomy cuff conditions

This study demonstrates that patients with a tracheostomy have a more disordered swallow than age-matched controls; however, there were no demonstrable significant differences between the three tested tracheostomy cuff conditions. Interesting trends were however observed, these included 1) patients with the cuff inflated had higher median IBP's and in general had an elevated SRI and PhCI, and 2) the PMSV improved UES relaxation and basal pressures. Qualitatively, in some patients, it was observed that inflation of the cuff resulted in a transient build-up of pressure across the pharynx during swallowing, this resolved upon deflation of the cuff with an improvement of UES metrics (IBP, IRP and SRI).

3.5 RESULTS SUMMARY

This study demonstrates that tracheostomy patients have a more disordered swallow than age-matched controls, with altered biomechanical metrics consisting of an elevated IBP, UES relaxation and pharyngeal pressures (trending), shortened UES relaxation time, overall resulting in an elevated SRI. The use of opiates 24 hours prior to the study was shown to potentially negatively impact a swallow with reduced UES Max Admittance, elevated SRI, IBP and IRP. It was also observed that patients with a tracheotomy for more than 2 weeks trended to have reduced hypopharyngeal and proximal esophageal contractile and peak pressures. Swallowing parameters between tracheostomy cuff conditions had interesting observable trends (cuff inflation resulted in an elevated IBP and SRI and PMSV placement improved UES relaxation and basal pressures) however there was no significant differences demonstrated.

4 DISCUSSION

Patients with a tracheostomy are known to have a high frequency of dysphagia and aspiration, resulting in increased morbidity, mortality and healthcare costs (Zuercher, Moret et al. 2019, Skoretz, Riopelle et al. 2020). In this pilot study, patients with a tracheostomy and in the ICCU were investigated with HRPM to non-radiologically assess their swallowing function prior to decannulation. Importantly, the HRPM swallow assessment was well tolerated and feasible at the bedside of these critically ill patients with a tracheostomy *in situ*. Furthermore, the HRPM swallow assessment demonstrated that tracheostomised patients had measurable swallowing impairments when compared to healthy age-matched controls. Upper esophageal sphincter dysfunction, evidenced by high intrabolus pressure and restricted UES relaxation was the most prevalent biomechanical feature associated with the tracheostomy, and therefore considered likely to contribute to swallowing disorders in this population. Cuff inflation, hypothesised to worsen swallowing (Amathieu, Sauvat et al. 2012), did not significantly alter swallowing parameters. However, some individuals did demonstrate features of worsening swallowing function with increased bolus flow resistance when the cuff was inflated. Placement of a PMSV resulted in reduced UES relaxation pressures, potentially attributed to improved glottic airflow. Of medical-related factors investigated to likely impair swallowing function, opioid use and duration of tracheostomy placement is potentially relevant

4.1 FEASIBILITY OF HRPM IN THE CRITICALLY ILL

The assessment of swallowing in critically ill patients is challenging, particularly due to the impact of the medical and surgical pathologies that necessitated the ICCU admission, reduced patient mobility and at times impaired cognitive function. Instrumental swallowing assessments are preferable over clinical assessments as they are consistently and objectively able to identify patients who are silently aspirating, a common feature in those with a tracheostomy (Logemann 1983, Warnecke, Suntrup et al. 2013, Garuti, Reverberi et al. 2014, Fiorelli, Ferraro et al. 2017). The utility of videofluoroscopic swallow studies is limited in the critical care environment as patients are required to be medically stable for transportation to the radiology suite and be able to sit unassisted for the duration of the study (usually 15 minutes) which is sometimes not possible due

to spinal or abdominal injuries (Jones 1999, Kim, Lee et al. 2018). Furthermore, specially trained staff are required to safely transport and observe the patient, which can impact ICCU staffing. Alternatively, FEES is a 15-minute bedside swallowing evaluation that uses a flexible fibre-optic nasoendoscope to visualise bolus movement and pharyngeal anatomy; therefore it does not encounter the limitations seen with VFSS. However, due to the nature of the FEES study and the white-out phenomenon, it has a limited utility in the assessment of the biomechanics of swallowing (Chapter 1.2.3.2) (Nacci, Ursino et al. 2008, Fattori, Giusti et al. 2016). Due to these limitations, an alternative instrumental swallow assessment is required to facilitate a quantitative, bedside evaluation of the entire swallowing pathway.

HRPM is an assessment tool that incorporates the advantages of a bedside evaluation whilst being non-radiological and quantitative in nature. Swallowing is a pressure-driven process, therefore the use of highly sensitive and pressure-responsive sensors that are capable of detecting contractile pressures (Ryu, Park et al. 2015) allows a quantitative and accurate assessment of muscular weakness and incoordination resulting in dysphagia. HRPM has been demonstrated to have high patient tolerability in healthy individuals, with similar rates of complications as those reported for other transnasal procedures (Knigge, Marvin et al. 2019). Importantly, the procedure was well tolerated in this current study of critically ill tracheostomised patients, with each patient swallow assessment lasting approximately 30 minutes (for a total of 36 swallows) and no complications observed in any patient. With HRPM demonstrating high patient tolerability in tracheostomised ICCU patients, in addition to having high sensitivity for characterising dysphagia (Omari, Dejaeger et al. 2011), HRPM and the development of the Swallow Risk Index (a global overview of swallowing function) may be useful for the development of predictive algorithms to inform clinicians of safe strategies for feeding (oral vs. enteral). This is particularly of benefit in the critical care setting as often patients lack the ability to reliably describe their symptoms. HRPM would assist speech pathologists and clinicians as an adjunct to other instrumental swallow evaluation methods and to guide treatments for swallowing related issues. As HRPM is able to provide a detailed analysis of pressure generation and bolus clearance along the swallow pathway, it allows for targeted and individualised interventions towards the affected or deficient region(s). Such interventions (Mittal, Mishra et al. 2015) could include 1) compensatory strategies to improve or re-direct the

bolus (Logemann 1999), 2) modifications to bolus viscosity, volume or texture, 3) rehabilitative exercises and swallow manoeuvres to strengthen or change oro-motor bolus control, protective mechanisms and oro-sensory awareness, 4) using HRPM as a biofeedback tool and to assess treatment effect (Davidson and O'Rourke 2019) or alternatively 5) highlighting the need for enteral feeding due to significant aspiration despite the above measures. Similar algorithms have been proposed in progressive pathologies such as amyotrophic lateral sclerosis (Suh, Park et al. 2019). A potential algorithm for tracheostomised patients, would involve the use of PhCI (and it's subsites) to assess whether sufficient pressures are generated to push the bolus towards the UES, UES IRP and IBP to assess UES relaxation and bolus flow restriction, DCL and BPT to assess bolus clearance and residue and SRI as a quantitative global marker of aspiration risk. This algorithm would allow an assessment with subsequent individualised interventions; resulting in 3 generalised options – the patient could return to oral intake immediately, or can resume oral intake with certain modifications to the bolus and/or swallow technique, or the patient would remain nil orally due to significant aspiration risk. Overall, this pilot study, together with a similar-sized study (Schar, Omari et al. 2020), highlights the potential utility of HRPM within the critical care setting as a safe, reliable and quantitative bedside swallow assessment tool.

4.2 SWALLOWING WITH A TRACHEOSTOMY

In a cohort of patients already at risk of malnutrition and aspiration pneumonia, it is imperative to understand whether a tracheostomy has a biomechanical impact on swallowing as this would allow earlier oral intake or facilitate the implementation of targeted interventions to reduce dysphagia and aspiration. In this study, patients with a tracheostomy (cuff-deflated) were observed to have a dysfunctional swallow, highlighted by elevated intra-bolus and UES relaxation pressures with a shorter relaxation duration, demonstrating that the UES is the primary region affected in the presence of a tracheostomy. Compared to age-matched healthy controls, tracheostomy patients also had elevated pharyngeal contractile pressures and this is hypothesised to be compensatory in nature due to restricted downstream flow associated with the dysfunctional UES.

The tracheostomy cohort was observed to have elevated IBPs, with pressures of up to 25 mmHg recorded in some individual's swallows (normal control IBPs are close to 0 mmHg). IBP is the mechanical result of pressures generated by lingual propulsion and pharyngeal contraction to push the bolus through the upper esophageal sphincter (Cook, Dodds et al. 1989, Cock and Omari 2017). Therefore, when pharyngeal function is sufficient to propel the bolus inferiorly, an elevated IBP is highly predictive of UES flow restriction (Cook, Gabb et al. 1992, Williams, Wallace et al. 2002, Cock and Omari 2017). The elevated IBP in this tracheostomy cohort together with elevated UES relaxation pressures is suggestive of UES outflow obstruction, due to failed or incomplete UES relaxation.

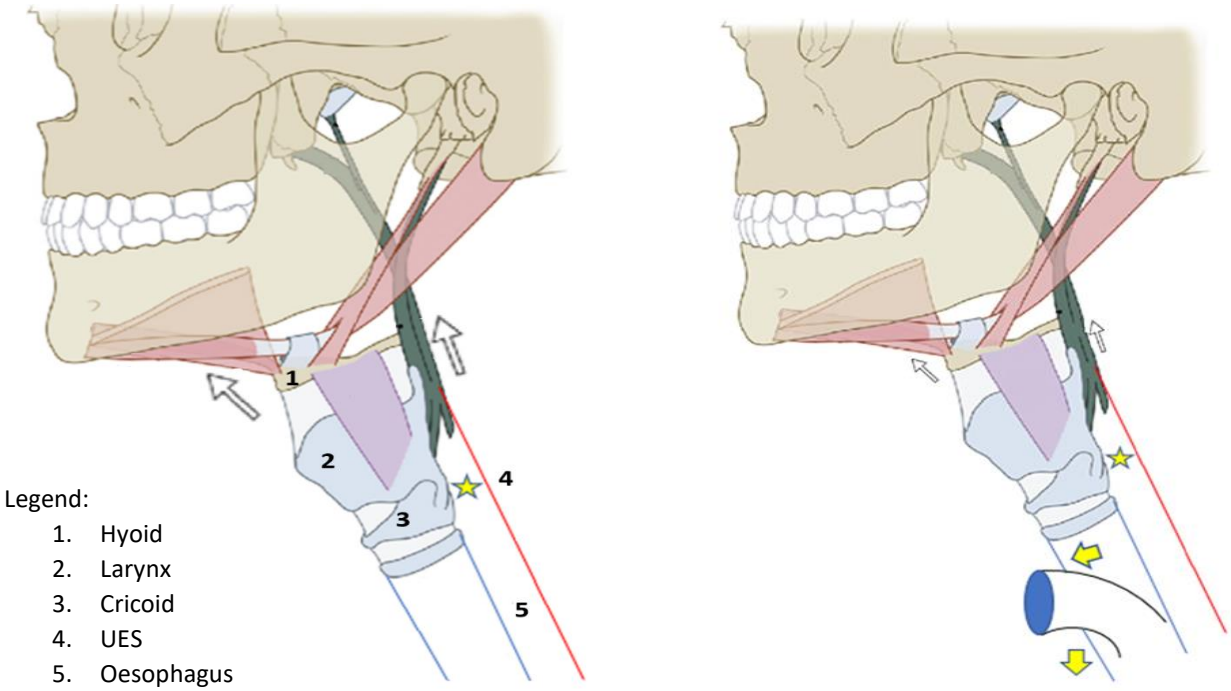
Incomplete UES relaxation in those with a tracheostomy is hypothesised to be a consequence of the tracheostomy being inserted and secured to the anterior neck, thereby anchoring the hyolaryngeal complex and thus limiting its excursion, resulting in a dysfunctional UES (Figure 31). The biomechanical effect of restricted hyolaryngeal excursion through external pressure directed towards the thyroid and cricoid cartilage has been explored in healthy volunteers using HRPM (Jiao, Mei et al. 2016, Shaker, Sanvanson et al. 2016). External pressure applied onto the thyroid cartilage resulted in a significant reduction in superior and anterior hyoid excursion, reduced UES opening and slightly elevated pharyngeal pressures (Shaker, Sanvanson et al. 2016). Perpendicular pressure on the cricoid cartilage resulted in elevated intrabolus and UES relaxation pressures (Jiao, Mei et al. 2016). These two studies demonstrate that external pressure onto the laryngeal framework, subsequently reducing hyolaryngeal excursion, results in unfavourable changes to UES opening (as represented by the HRPM metrics of IBP, UES IRP and UES Max Adm). This supports the findings in this current study, that a tracheostomy mechanically impedes UES function.

Incomplete UES relaxation due to anchorage of the hyolaryngeal complex by the tracheostomy would logically result in reduced UES opening and therefore reduced bolus transfer. However surprisingly, this cohort was observed to have a normal UES opening extent (derived from UES Max Adm) indicating that functional bolus passage occurred. Interestingly in the tracheostomy cohort, pharyngeal (PhCI), velopharyngeal (VCI) and mesopharyngeal (MCI) contractile integrals were all trending higher than age-

matched controls, implying that compensatory pharyngeal recruitment occurred to generate higher propulsive pressure onto the tail-end of the bolus to assist it in forcing the UES open. Compensatory pharyngeal mechanisms have not been described in recent literature related to tracheostomy patients; however, they have been observed in various other cohorts (Kunieda, Fujishima et al. 2021, Schar, Omari et al. 2021) including those patients who had external pressure applied to the thyroid cartilage (Jiao, Mei et al. 2016). Patients with moderate-severe obstructive sleep apnoea manometrically had impaired UES relaxation, with an associated elevation in pharyngeal contractile pressures and was hypothesised to represent a compensatory mechanism (Schar, Omari et al. 2021). Additionally, this phenomenon was also observed in dysphagic, non-tracheostomised patients with Parkinson's disease or medullary lesions; the magnitude of UES opening in an incompletely relaxing sphincter (using simultaneous videofluoroscopy and conventional pharyngeal manometry) was found to directly correlate with the degree of preserved pharyngeal function and external traction placed onto the UES (Ali, Wallace et al. 1996, Williams, Wallace et al. 2002). The importance of compensation (due to its absence) is highlighted in patients with head and neck cancers who are known to have multifactorial dysphagia as a result of structural or treatment changes, neuropathies, scarring and oedema (Hutcheson and Lewin , Son, Choi et al. 2015, Szczesniak, Maclean et al. 2015, Lippert, Hoffman et al. 2016, Schaen-Heacock, Jones et al. 2020). A key mechanism observed leading to dysphagia in this population is the generation of lower pharyngeal pressures resulting in the inability to compensate and/or the inability to propel the bolus through the UES (Schaen-Heacock, Jones et al. 2020). Interestingly, it was also observed that in individuals with a failed UES relaxation, their perception of dysphagia severity directly correlated to their inability to compensate rather than the inadequacy of UES relaxation (Williams, Wallace et al. 2002). As this current cohort of tracheostomy patients were planned for decannulation at the time of the HRPM swallow assessment, it is important to acknowledge that these patients had mostly recovered from the illness that necessitated the need for a tracheostomy, and in addition, patients did not have any pre-existing structural or neurological pathologies to exacerbate their swallow function; thereby they could compensate and generate sufficient propulsive pharyngeal pressures to overcome the dysfunctional UES, resulting in a functional swallow, albeit still a disordered one.

Mechanical disruption to hyolaryngeal excursion is likely the main contributor to a dysfunctional swallow in tracheostomised patients, however, there are other possibilities. The duration of UES relaxation was significantly shorter in the tracheostomy cohort, this could be a mechanical consequence of the tracheostomy, alternatively, this could be due to distorted neurosensory pathways within the pharynx as a result of reduced glottic airflow and mucosal trauma (Elpern, Scott et al. 1994, Elpern, Borkgren Okonek et al. 2000). The role of sensory stimulation on swallowing has been investigated in healthy participants using HRPM; cold, sour and carbonated boluses were observed to induce changes in UES relaxation duration and the magnitude of UES opening (Regan 2020). Similarly, the use of capsaicin has been found to be beneficial in modulating the swallowing pathway due to an increase in pharyngeal contractility and improved duration of UES relaxation (Suntrup-Krueger, Muhle et al. 2021). Therefore, some aspects of UES dysfunction demonstrated with HRPM in patients with a tracheostomy could be due to altered peripheral sensory pathways, related to reduced glottic airflow or mucosal trauma (this was partially explored with manipulation of the tracheostomy cuff). This possibility requires further research.

Figure 32 Diagrammatic representation of the proposed anchoring effect of a tracheostomy



Legend:

1. Hyoid
2. Larynx
3. Cricoid
4. UES
5. Oesophagus

A modified image demonstrating the proposed anchoring effect of the tracheostomy. On the left, a normal swallow (with superior and anterior hyolaryngeal excursion represented by the white arrows) and on the right, swallowing in the presence of a tracheostomy. The yellow arrows illustrate the traction created by the tracheostomy being secured to the anterior neck, resulting in anchorage of the hyo-larynx resulting in reduced hyolaryngeal excursion (as demonstrated by the smaller white arrows) and overall altered UES metrics.

Edited image sourced from "Evaluating the structural properties of suprahyoid muscles and their potential for moving the hyoid" (Pearson, Langmore et al. 2011)

A tracheostomy is a life-saving procedure, however, its insertion results in a disordered swallow as demonstrated by the altered HRPM metrics of IBP, IRP, SRI and UES RT, identifying UES dysfunction as the key mechanism modified in the swallowing pathway. This current cohort demonstrated that a functional swallow is possible with a tracheostomy *in situ* if sufficient compensatory pharyngeal pressures are generated to overcome the dysfunctional UES. However, this may not be possible in all tracheostomised patients due to poor recovery from the medical condition that necessitated the need for a tracheostomy, or exacerbating structural and/or neurological pathologies, thereby placing these patients at a higher risk of aspiration. Therefore the identification and implementation of an appropriate intervention is essential for improving

swallowing function in these patients, resulting in a faster return to oral intake, reduced risk of aspiration and an improved quality of life (Bonvento, Wallace et al. 2017).

There are a variety of pathologies that necessitate the need for a tracheostomy; therefore, by nature, this is a diverse population with a variety of variables that could impact one's swallowing. The following section will discuss the treatment-related factors that potentially have an effect on swallowing in a patient with a tracheostomy.

4.3 EXTRINSIC FACTORS AFFECTING SWALLOWING WITH A TRACHEOSTOMY

Due to the differences demonstrated between tracheostomy patients (with the cuff down) and healthy age-matched controls, the role of opiates, tracheostomy duration and disuse atrophy were explored to understand their contribution to a disordered swallow.

4.3.1 The potential impact of opiates on swallowing

Patients admitted into hospital, and in particular the ICCU often receive opioids for pain management and/or sedation, with up to 48% of patients receiving opioids for almost 70% of their hospital stay (Ordonez Gallego, Gonzalez Baron et al. 2007). In this study, tracheostomised patients who had used opioids within 24 hours of their swallowing assessment had significantly reduced UES opening extent, with a trending increase in SRI, IBP and IRP indicating worsening swallow function, compared to those patients who had not recently used opioids. The effect of opioids (remifentanil and morphine) on swallowing has been demonstrated in healthy non-tracheostomised volunteers with HRPM and characterised as reduced pharyngeal contractile strength, increased UES resistance (IBP) and elevated residual UES pressures (IRP), therefore resulting in an elevated SRI (Savilampi 2015, Doeltgen, Omari et al. 2016, Savilampi, Omari et al. 2016, Cajander, Omari et al. 2021). The deterioration in swallow function of the opioid group is therefore in line with the changes observed in healthy volunteers and attributable to altered centrally mediated neuroregulatory mechanisms (Doeltgen, Omari et al. 2016, Cajander, Omari et al. 2021). Clinically, these findings highlight the need for judicious

prescribing of opioids in tracheostomised patients, balancing the analgesic requirements of the patient, with the increased risk of swallow dysfunction.

4.3.2 Duration of tracheostomy placement

Laryngeal injuries due to intubation are common and can occur within hours of intubation. The length of endotracheal intubation correlates with the severity of laryngeal and tracheal injuries (Loh and Irish 2002, Rangachari, I et al. 2006, Brodsky, Levy et al. 2018) and therefore it was hypothesised that patients who required a tracheostomy for more than two weeks would have a poorer swallow due to more severe pharyngeal injuries, altered sensation and disuse atrophy; compared to those who had been tracheostomised for a shorter period of time. This study found that there were no significant differences in HRPM metrics in patients who had a tracheostomy *in situ* for more than two weeks, compared to those who had been tracheostomised for a shorter period of time, however, certain trends were observed. Patients with a tracheostomy for more than two weeks were observed to have a lower hypopharyngeal and proximal esophageal contractile integral and hypopharyngeal peak pressure. The importance of these findings is of uncertain significance, particularly due to the results in Chapter 3.4 (cuff inflation did not affect Peak P, HPCI or PCI). It should be recognised that patients in this study had sufficiently recovered from the medical condition (that necessitated the tracheostomy's insertion) and were planned to be decannulated at the time of the HRPM swallow assessment, therefore they had likely achieved a similar medical baseline necessary for decannulation (Chapter 1.3.8), which was irrespective of the duration of tracheostomy insertion. Further research with a larger cohort of patients with tracheostomies of varying durations would allow clarification into the relevance of these findings.

4.3.3 Critical illness myopathy

Dysphagia in critically ill patients in the ICCU, is hypothesised to be associated with disuse atrophy and neuromyopathy resulting in muscular weakness, an entity known as critical illness myopathy (Macht, Wimbish et al. 2013, Zuercher, Moret et al. 2019). In this pilot study, tracheostomised patients did not demonstrate reduced pharyngeal contractile integrals, thereby disputing this hypothesis. These results are supported by a similar study of recently extubated or decannulated patients (Schar, Omari et al. 2020). Additionally, this

current cohort of tracheostomy patients were observed to have higher pharyngeal contractile pressures compared to age-matched controls, suggestive of a compensatory mechanism. It is then likely that impaired swallowing in tracheostomised patients due to the loss of upstream pharyngeal muscular compensation is associated with various neuromuscular or structural pathologies often present in patients admitted to the ICCU rather than disuse atrophy.

Historically tracheostomy cuff modifications and the insertion of a PMSV have been used to manipulate a tracheostomised patients swallow, however, its utility has been disputed (Dettelbach, Gross et al. 1995, Leder, Tarro et al. 1996, Leder, Ross et al. 1998, Elpern, Borkgren Okonek et al. 2000, Suiter, McCullough et al. 2003, Donzelli, Brady et al. 2005, Leder, Joe et al. 2005). The following section will discuss the potential role of tracheostomy cuff manipulation on optimising a swallow.

4.4 COMPARING SWALLOWING METRICS ACROSS CUFF CONDITIONS

To determine whether manipulation of the tracheostomy cuff could act as a simple adjunct to improving swallow function, this study also evaluated swallowing biomechanics across different cuff conditions (cuff inflated, cuff deflated and placement of a PMSV). Historically, the cuff was thought to protect the patient from aspiration and therefore patients were often started on oral intake with the cuff inflated (Amathieu, Sauvat et al. 2012). The findings from this pilot HRPM study suggest otherwise, as IBP and SRI trended to increase with cuff inflation, compared to the two cuff-deflated conditions, thereby indicating further flow restriction through the UES. This is likely due to additional traction exerted by the inflated cuff within the trachea further impeding laryngeal excursion. The worsened swallowing function observed by HRPM with cuff inflation is supported by fluoroscopic studies where aspiration rates were three-fold higher in patients that were enterally fed with the tracheostomy cuff-inflated, compared with it deflated (Davis, Bears et al. 2002, Ding and Logemann 2005). The effect of cuff inflation was visualised on the HRPM pressure-topography plot across the pharynx as ‘transient pressurisation’ (Figure 29), signalling the build-up of pressures within the sealed pharyngeal chamber with cuff inflation, which was immediately reversed upon deflation. Furthermore, cuff

inflation is also hypothesised to alter swallowing biomechanics through compression of the esophagus (Betts 1965). Findings from this pilot study do not support this theory as there was no significant alteration in PCI, UESCI or UES Peak P, which would occur if cervical esophageal contractility was impeded by the cuff. However, additional videomanometry analysis may be required to elucidate this mechanism further. In a system already stressed by the presence of a tracheostomy, cuff inflation likely worsens a patient's swallow and therefore should be avoided when trialling oral intake.

Placement of a PMSV is a relatively simple and quick manoeuvre that allows expired airflow through the upper airway in those with a tracheostomy. Its use within this cohort resulted in an reduction in UES IRP, signalling an improvement in UES relaxation pressures which would theoretically improve swallow function, although in this current pilot study there was no significant change in IBP or SRI, potentially due to the limited cohort size. The improvement in UES IRP is however in-line with a similar sized videomanometry study of acquired brain injury tracheostomised patients (Han, Dou et al. 2018), who were observed to have improved UES residual pressures when using the PMSV with no observable changes in hyolaryngeal excursion (which was expected as the tracheostomy still remained secured to the neck). Nasal and tracheal flow recordings have demonstrated that the use of PMSV results in improved glottic airflow (Prigent, Lejaille et al. 2012), supporting the notion that distorted neurosensory pathways may be a contributory factor to the dysfunctional swallow in those with a tracheostomy, in addition to mechanically impeded hyolaryngeal excursion (Dettelbach, Gross et al. 1995, Stachler, Hamlet et al. 1996, Elpern, Borkgren Okonek et al. 2000, Suiter, McCullough et al. 2003). Restoration of glottic airflow and sensory pathways through the use of a PMSV, likely led to the improvement in UES IRP and therefore reducing the degree of underlying UES dysfunction. Larger studies are required to investigate this observed phenomenon, as it advocates for the use of a PMSV for making a swallow more functional.

4.5 STRENGTHS AND LIMITATIONS

This is the first pilot study to assess the biomechanical impact of a tracheostomy on swallowing in critically unwell patients using HRPM. HRPM has been shown to be a safe bedside swallowing assessment tool in critically ill patients, and importantly, this study has highlighted that HRPM can objectively demonstrate disordered swallowing in patients with a tracheostomy. This pilot study was designed to address the major limitations from previous studies that have resulted in the lack of consensus on the impact of a tracheostomy on swallowing (Goff and Patterson 2019, Skoretz, Anger et al. 2020, Skoretz, Riopelle et al. 2020). The strength of this thesis is the use of HRPM and Swallow Gateway™ to provide a quantitative assessment, compared to a qualitative assessment generated by using VFSS or FEES. A need for objective quantitative measurements was identified as a significant issue in previous studies (Logemann, Pauloski et al. 1998, Suiter, McCullough et al. 2003, Leder, Joe et al. 2005, Terk, Leder et al. 2007, Srinet, Van Daele et al. 2015). The current study also employed protocols recommended by the HRPM International Working Group (Omari, Ciucci et al. 2020), to complement previous studies and provides a benchmark for further research in the area. The other strength of this thesis is the exclusion of confounders observed in previous studies which resulted in patients with significant heterogeneity (such as, co-morbidities known to have a significant incidence of baseline dysphagia, tracheostomy's that had been *in situ* for varying durations and a mixture of acute and chronic patients). This pilot study excluded such confounders allowing for easier interpretation of the impact a tracheostomy has on swallowing. Due to the heterogeneity and complexity of tracheostomised patients, it is important to acknowledge that there are several limitations and potential confounders that may impact manometric measures:

1. This is a pilot study with a small sample size, as recruitment was impacted by the COVID-19 pandemic. The small sample size may make it difficult to determine if a particular outcome is true, with potential of a Type II error (that is, the null hypothesis is incorrectly accepted, reporting no difference between groups when in fact there is). The size of this cohort is however similar to published data on swallowing evaluations in tracheostomised patients (Leder, Tarro et al. 1996, Leder and Ross 2000, Leder and Ross 2010). It does represent a homogenous cohort of critically unwell patients by excluding those with

confounding pathologies known to impact swallow function which allowed for a more objective assessment of the impact of a tracheostomy on swallowing.

2. Tracheostomised patients, due to their complex nature, results in individuals with various co-morbidities. For an accurate assessment of swallowing, patients with pre-existing dysphagia were excluded; patients and their families were screened using a validated questionnaire and their medical records were reviewed (Section 2.3). A formal swallow assessment was not conducted prior to admission to the ICCU as patients were critically ill at the time and is therefore impractical.
3. Gender, due to the anatomical differences between males and females results in differing volumes across the pharynx and therefore differing pharyngeal contractile pressures (Butler, Stuart et al. 2009). Age, in particular aging, is known to worsen swallowing function (this is known as presbyphagia), with manometric studies demonstrating reduced hyolaryngeal movement, pharyngeal contractility and UES function in older patients (more than 65 years of age) (Yokoyama, Mitomi et al. 2000, Aslam and Vaezi 2013, Reginelli, D'Amora et al. 2016, Kunieda, Fujishima et al. 2021, Mancopes, Gandhi et al. 2021). The median age of a tracheostomised patient in this study was 65 years. The potential confounding effects of age and gender were minimised by using a normative dataset of age and gender matched healthy controls.
4. Critical illness and ICU status is an important recognised factor for dysphagia (raised in Section 1.4.1). A previous manometry study by our group assessing swallowing post-extubation identified that patients had normal pharyngeal pressures with an abnormal SRI, bolus flow and timing metrics and UES function (Schar, Omari et al. 2020). The inclusion of a non-tracheostomised ICCU cohort as a control group for this study was pragmatically unfeasible, as exposure to potential risks were unjustifiable given the already known effects of critical illness on swallowing (Macht, Wimbish et al. 2013, Zuercher, Moret et al. 2019, Schar, Omari et al. 2020, Skoretz, Riopelle et al. 2020).
5. Cued swallows are frequently used with HRPM, however, videofluoroscopic studies have shown that pharyngeal pressures and time-metrics differ between cued and non-cued swallows (Daniels,

Schroeder et al. 2007, Nagy, Leigh et al. 2013). The potential confounding effect of cued swallows was minimised by using control data that was collected also using cued swallows.

6. Pharyngeal musculature and the UES are formed by striated muscles which are prone to the effects of fatigue (Shaker, Sanvanson et al. 2016). Successive swallows theoretically can result in the reduction of pharyngeal contractile pressure due to this effect. To minimise treatment order effect and fatigue-related swallowing changes potentially skewing the data set, the sequence of tracheostomy cuff conditions tested was randomised.
7. The pharynx and UES are asymmetric anatomical structures, with this asymmetry being further exacerbated during swallowing (Meyer, Jones et al. 2016). It is thought that the radial asymmetry, may results in changes in swallow metrics based on the catheters position, with pressure values being potentially higher in the anteroposterior direction in unidirectional sensors (Bhatia and Shah 2013). Although circumferential sensors are thought to record data more reproducibly from asymmetric structures, there are several potential pitfalls. Firstly, as highlighted in the HRPM International Working Group the circumferential sensor generates a mean pressure from the area around it, it can be influenced by the contact of anatomical structures such as the epiglottis, resulting in inaccurate intra-bolus and hypopharyngeal pressures (Park, Lee et al. 2017, Omari, Ciucci et al. 2020). Secondly, the diameter of circumferential HRPM catheters are typically larger (usually 4.2 mm) than unidirectional catheters (3.2 mm); catheter diameter has been demonstrated to influence UES metrics with generally higher UES BP, UES Peak P and IRP recorded (Ferris, Schar et al. 2018). Finally, the mean pressures generated by a circumferential sensor are not the equivalent to multiple, separate, radially oriented readings (Rosen, Jones et al. 2017), with simultaneous multi-directional measurements only achievable with a 3D-manometry device (Nollet, Cajander et al. 2021). Despite this, a recent study (Nollet, Cajander et al. 2021) highlighted that the modulatory effects generated using unidirectional sensors were replicated with circumferential sensors (with varying bolus volumes and viscosities) in healthy participants.

4.6 CLINICAL RECOMMENDATIONS

This is the first known HRPM study conducted in tracheostomised patients, within the ICCU. The findings from this study have important clinical implications for the care of patients with a tracheostomy, and the following recommendations are suggested:

1. Patients with a tracheostomy have a disordered swallow; however, it may be functional enough to tolerate safe oral intake. The functionality of a swallow is based on the current clinical picture of the patient and their co-morbidities; therefore, the resumption of oral intake should occur in consultation with the treating medical practitioner and a trained speech pathologist.
2. Cuff-inflation worsens a tracheostomised patient's swallow; therefore, oral intake should only be attempted once the cuff can be safely deflated.
3. Placement of a PMSV may improve a tracheostomised patients swallow through the restoration of glottic airflow, however, this decision should occur after consultation and examination by a trained speech pathologist.
4. Opioids can worsen an individual's swallow. The risks and benefits of opioid analgesia in enterally fed tracheostomised patients must be considered due to the increased risk of aspiration; this could be reduced by using opioid-sparing analgesics.
5. HRPM has been demonstrated to be a feasible and safe bedside swallowing assessment tool in critically unwell patients within the ICCU. Further research into swallowing with a tracheostomy is recommended, this includes the development of an algorithm to stratify swallowing risk in critically unwell patients

4.7 FUTURE DIRECTION

This pilot study provides an understanding into the swallowing biomechanics in tracheostomised patients. Findings from this pilot study should be confirmed with a larger study, however, there are a number of aspects that follow on from our findings that would benefit from further research.

1. A future study should evaluate patients soon after decannulation and/or once the tract has healed, this would clarify whether removal of the tracheostomy reverses the proposed anchorage effect, resulting in an improvement in HRPM UES metrics.
2. The role of cuff conditions should be explored further in a larger cohort, to clarify the detrimental effect cuff inflation has on swallowing and conversely, the potential positive impact a PMSV has on swallowing. Other tracheostomy conditions that could be tested, include the role of corking/capping and/or downsizing the tracheostomy to further understand the mechanistic and neuromodulatory impact a tracheostomy has on the swallowing pathway.
3. A similar study HRPM should be extended to patients with tracheostomies of varying durations (including long-term) or the assessment of patients at multiple time points to clarify the findings seen in those patients with a tracheostomy *in situ* for more than 2 weeks (reduced HPCI, PCI and PeakP) and the compensatory mechanism observed in this pilot study.
4. Specific cohorts of tracheostomised patients (post-stroke or neuromuscular disorders) should be assessed using HRPM to understand the impact of particular pathologies on the swallowing pathway. This would potentially facilitate the implementation of targeted interventions to allow earlier safer oral intake and/or the development of an algorithm to stratify swallowing risk prior to oral intake.

5 CONCLUSION

This pilot study used HRPM as an objective swallow assessment tool in critically ill patients with a tracheostomy in the ICCU. HRPM objectively demonstrated that tracheostomised patients had a disordered swallow, as evidenced by altered metrics within the pharynx (elevated IBP and pharyngeal contractile pressures) and UES (increased IRP and reduced RT). This is potentially, primarily attributable to anchorage of the tracheostomy to the anterior neck resulting in reduced hyolaryngeal excursion, however, altered neurosensory pathways are also proposed to play a role in the resulting UES dysfunction. Importantly, a disordered swallow can remain functional if pharyngeal contractility is sufficient to compensate for the dysfunctional UES. Cuff inflation showed signs of worsening swallow metrics (IBP, Peak P and SRI) likely through further traction exerted by the inflated cuff within the trachea. Placement of the PMSV showed signs of improving UES function (UES IRP), likely through restored glottic airflow. Opioid therapy was shown to potentially worsen swallowing and therefore its use should be reconsidered in tracheostomised patients. In conclusion, this pilot study has demonstrated that HRPM is a safe instrumental swallow assessment tool in critically ill patients and demonstrates the mechanistic impact a tracheostomy has on the swallow pathway.

6 REFERENCES

Adhikari, N. K. and G. D. Rubenfeld (2011). "Worldwide demand for critical care." Curr Opin Crit Care **17**(6): 620-625.

Ali, G. N., K. L. Wallace, R. Schwartz, D. J. DeCarle, A. S. Zagami and I. J. Cook (1996). "Mechanisms of oral-pharyngeal dysphagia in patients with Parkinson's disease." Gastroenterology **110**(2): 383-392.

Amathieu, R., S. Sauvat, P. Reynaud, V. Slavov, D. Luis, A. Dinca, L. Tual, S. Bloc and G. Dhonneur (2012). "Influence of the cuff pressure on the swallowing reflex in tracheostomized intensive care unit patients." Br J Anaesth **109**(4): 578-583.

Andersen, L. I., P. V. Madsen, P. Dalgaard and G. Jensen (1987). "Validity of clinical symptoms in benign esophageal disease, assessed by questionnaire." Acta Med Scand **221**(2): 171-177.

Andriolo, B. N., R. B. Andriolo, H. Saconato, A. N. Atallah and O. Valente (2015). "Early versus late tracheostomy for critically ill patients." Cochrane Database Syst Rev **1**: CD007271.

Armstrong, W. B. and J. L. Netterville (1995). "Anatomy of the larynx, trachea, and bronchi." Otolaryngol Clin North Am **28**(4): 685-699.

Aslam, M. and M. F. Vaezi (2013). "Dysphagia in the elderly." Gastroenterol Hepatol (N Y) **9**(12): 784-795.

Asoh, R. and R. K. Goyal (1978). "Manometry and electromyography of the upper esophageal sphincter in the opossum." Gastroenterology **74**(3): 514-520.

Association, A. S.-L.-H. (2004). "Special interest division 13." Atlanta, GA. Role of the speech-language pathologist in the performance and interpretation of endoscopic evaluation of swallowing: Guidelines.

Aviv, J. E. (2000). "Prospective, randomized outcome study of endoscopy versus modified barium swallow in patients with dysphagia." Laryngoscope **110**(4): 563-574.

Aviv, J. E., S. T. Kaplan, J. E. Thomson, J. Spitzer, B. Diamond and L. G. Close (2000). "The safety of flexible endoscopic evaluation of swallowing with sensory testing (FEESST): an analysis of 500 consecutive evaluations." Dysphagia **15**(1): 39-44.

Baker, E. and F. Lui (2019). Neuroanatomy, Vagal Nerve Nuclei (Nucleus Vagus), StatPearls Publishing, Treasure Island (FL).

Barlow, S. M. (2009). "Central pattern generation involved in oral and respiratory control for feeding in the term infant." Curr Opin Otolaryngol Head Neck Surg **17**(3): 187-193.

Barquist, E. S., J. Amortegui, A. Hallal, G. Giannotti, R. Whinney, H. Alzamel and J. MacLeod (2006). "Tracheostomy in ventilator dependent trauma patients: a prospective, randomized intention-to-treat study." J Trauma **60**(1): 91-97.

Belafsky, P. C., D. A. Mouadeb, C. J. Rees, J. C. Pryor, G. N. Postma, J. Allen and R. J. Leonard (2008). "Validity and reliability of the Eating Assessment Tool (EAT-10)." Ann Otol Rhinol Laryngol **117**(12): 919-924.

Betts, J. G. D. P. J. E. J. J. E. K. O. K. D. H. P. B. W. J. A. W. M. Y. K. A. (2017). "Anatomy and physiology."

Betts, R. H. (1965). "Post-Tracheostomy Aspiration." N Engl J Med **273**: 155.

Bhatia, S. J. and C. Shah (2013). "How to perform and interpret upper esophageal sphincter manometry." J Neurogastroenterol Motil **19**(1): 99-103.

Bice, T., J. E. Nelson and S. S. Carson (2015). "To Trach or Not to Trach: Uncertainty in the Care of the Chronically Critically Ill." Semin Respir Crit Care Med **36**(6): 851-858.

Bihari, S., S. Prakash, P. Hakendorf, C. M. Horwood, S. Tarasenko, A. W. Holt, J. Ratcliffe and A. D. Bersten (2018). "Healthcare costs and outcomes for patients undergoing tracheostomy in an Australian tertiary level referral hospital." J Intensive Care Soc **19**(4): 305-312.

Bonanno, P. C. (1971). "Swallowing dysfunction after tracheostomy." Ann Surg **174**(1): 29-33.

Bonvento, B., S. Wallace, J. Lynch, B. Coe and B. A. McGrath (2017). "Role of the multidisciplinary team in the care of the tracheostomy patient." J Multidiscip Healthc **10**: 391-398.

Bours, G. J., R. Speyer, J. Lemmens, M. Limburg and R. de Wit (2009). "Bedside screening tests vs. videofluoroscopy or fibreoptic endoscopic evaluation of swallowing to detect dysphagia in patients with neurological disorders: systematic review." J Adv Nurs **65**(3): 477-493.

Bredenoord, A. J. and G. S. Hebbard (2012). "Technical aspects of clinical high-resolution manometry studies." Neurogastroenterol Motil **24 Suppl 1**: 5-10.

Brietzke, S. and A. Meyers Percutaneous tracheotomy treatment and management.

Brodsky, M. B., M. Gonzalez-Fernandez, P. A. Mendez-Tellez, C. Shanholtz, J. B. Palmer and D. M. Needham (2014). "Factors associated with swallowing assessment after oral endotracheal intubation and mechanical ventilation for acute lung injury." Ann Am Thorac Soc **11**(10): 1545-1552.
Brodsky, M. B., M. J. Levy, E. Jedlanek, V. Pandian, B. Blackford, C. Price, G. Cole, A. T. Hillel, S. R. Best and L. M. Akst (2018). "Laryngeal Injury and Upper Airway Symptoms After Oral Endotracheal Intubation With Mechanical Ventilation During Critical Care: A Systematic Review." Crit Care Med **46**(12): 2010-2017.
Butler, S. G., A. Stuart, D. Castell, G. B. Russell, K. Koch and S. Kemp (2009). "Effects of age, gender, bolus condition, viscosity, and volume on pharyngeal and upper esophageal sphincter pressure and temporal measurements during swallowing." J Speech Lang Hear Res **52**(1): 240-253.
Cajander, P., T. I. Omari, C. Cock, A. Magnuson, M. Scheinin and J. Savilampi (2021). "Effects of remifentanil on pharyngeal swallowing and esophageal motility - no impact of different bolus volumes, and partial antagonism by methylnaltrexone." Am J Physiol Gastrointest Liver Physiol.
Carlson, D. A. and J. E. Pandolfino (2015). "High-Resolution Manometry in Clinical Practice." Gastroenterol Hepatol (N Y) **11**(6): 374-384.
Carrau, R. L., T. Murry and R. J. Howell (2016). Comprehensive Management of Swallowing Disorders, Second Edition, Plural Publishing, Incorporated.
Chen, A. Y., R. Frankowski, J. Bishop-Leone, T. Hebert, S. Leyk, J. Lewin and H. Goepfert (2001). "The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the M. D. Anderson dysphagia inventory." Arch Otolaryngol Head Neck Surg **127**(7): 870-876.
Cheung, N. H. and L. M. Napolitano (2014). "Tracheostomy: epidemiology, indications, timing, technique, and outcomes." Respir Care **59**(6): 895-915; discussion 916-899.
Ciaglia, P., R. Firsching and C. Syniec (1985). "Elective percutaneous dilatational tracheostomy. A new simple bedside procedure; preliminary report." Chest **87**(6): 715-719.
Cock, C. and T. Omari (2017). "Diagnosis of Swallowing Disorders: How We Interpret Pharyngeal Manometry." Curr Gastroenterol Rep **19**(3): 11.
Connor, H. H. and A. C. White (2010). "Tracheostomy Decannulation." Respiratory Care **55**(8): 1076.
Cook, I. J., W. J. Dodds, R. O. Dantas, M. K. Kern, B. T. Massey, R. Shaker and W. J. Hogan (1989). "Timing of videofluoroscopic, manometric events, and bolus transit during the oral and pharyngeal phases of swallowing." Dysphagia **4**(1): 8-15.
Cook, I. J., W. J. Dodds, R. O. Dantas, B. Massey, M. K. Kern, I. M. Lang, J. G. Brasseur and W. J. Hogan (1989). "Opening mechanisms of the human upper esophageal sphincter." Am J Physiol **257**(5 Pt 1): G748-759.
Cook, I. J., M. Gabb, V. Panagopoulos, G. G. Jamieson, W. J. Dodds, J. Dent and D. J. Shearman (1992). "Pharyngeal (Zenker's) diverticulum is a disorder of upper esophageal sphincter opening." Gastroenterology **103**(4): 1229-1235.
Corbin-Lewis, K. and J. M. Liss (2014). Clinical Anatomy & Physiology of the Swallow Mechanism, Cengage Learning.
Curtis, J. A., Z. N. Seikaly, A. E. Dakin and M. S. Troche (2020). "Detection of Aspiration, Penetration, and Pharyngeal Residue During Flexible Endoscopic Evaluation of Swallowing (FEES): Comparing the Effects of Color, Coating, and Opacity." Dysphagia.
Daniels, S. K., M. F. Schroeder, P. C. DeGeorge, D. M. Corey and J. C. Rosenbek (2007). "Effects of verbal cue on bolus flow during swallowing." Am J Speech Lang Pathol **16**(2): 140-147.
Davidson, K. and A. O'Rourke (2019). "The Utility of High-Resolution Pharyngeal Manometry in Dysphagia Treatment." Perspectives of the ASHA Special Interest Groups **4**: 1-10.
Davis, D. G., S. Bears, J. E. Barone, P. R. Corvo and J. B. Tucker (2002). "Swallowing With a Tracheostomy Tube in Place: Does Cuff Inflation Matter?" Journal of Intensive Care Medicine **17**(3): 132-135.
Davis, K., Jr., R. S. Campbell, J. A. Johannigman, J. F. Valente and R. D. Branson (1999). "Changes in respiratory mechanics after tracheostomy." Arch Surg **134**(1): 59-62.
De la Corte-Rodriguez, H. and E. C. Rodriguez-Merchan (2016). "The ICF (International Classification of Functioning, Disability and Health) developed by the WHO for measuring function in hemophilia." Expert Rev Hematol **9**(7): 661-668.

De Leyn, P., L. Bedert, M. Delcroix, P. Depuydt, G. Lauwers, Y. Sokolov, A. Van Meerhaeghe, P. Van Schil, P. Belgian Association of and S. Belgian Association of Cardiothoracic (2007). "Tracheotomy: clinical review and guidelines." Eur J Cardiothorac Surg **32**(3): 412-421.
Dettelbach, M. A., R. D. Gross, J. Mahlmann and D. E. Eibling (1995). "Effect of the Passy-Muir Valve on aspiration in patients with tracheostomy." Head Neck **17**(4): 297-302.
Diehl, J. L., S. El Atrous, D. Touchard, F. Lemaire and L. Brochard (1999). "Changes in the work of breathing induced by tracheotomy in ventilator-dependent patients." Am J Respir Crit Care Med **159**(2): 383-388.
Ding, R. and J. A. Logemann (2005). "Swallow physiology in patients with trach cuff inflated or deflated: a retrospective study." Head Neck **27**(9): 809-813.
Dodds, W. J., E. T. Stewart and J. A. Logemann (1990). "Physiology and radiology of the normal oral and pharyngeal phases of swallowing." AJR Am J Roentgenol **154**(5): 953-963.
Doeltgen, S. H., T. I. Omari and J. Savilampi (2016). "Remifentanil alters sensory neuromodulation of swallowing in healthy volunteers: quantification by a novel pressure-impedance analysis." Am J Physiol Gastrointest Liver Physiol **310**(11): G1176-1182.
Donzelli, J., S. Brady, M. Wesling and M. Theisen (2005). "Effects of the removal of the tracheotomy tube on swallowing during the fiberoptic endoscopic exam of the swallow (FEES)." Dysphagia **20**(4): 283-289.
Dua, K. S., J. Ren, E. Bardan, P. Xie and R. Shaker (1997). "Coordination of deglutitive glottal function and pharyngeal bolus transit during normal eating." Gastroenterology **112**(1): 73-83.
Durbin, C. G., Jr. (2005). "Techniques for performing tracheostomy." Respir Care **50**(4): 488-496.
Eibling, D. E. and R. D. Gross (1996). "Subglottic air pressure: a key component of swallowing efficiency." Ann Otol Rhinol Laryngol **105**(4): 253-258.
Elpern, E. H., M. Borkgren Okonek, M. Bacon, C. Gerstung and M. Skrzynski (2000). "Effect of the Passy-Muir tracheostomy speaking valve on pulmonary aspiration in adults." Heart Lung **29**(4): 287-293.
Elpern, E. H., M. G. Scott, L. Petro and M. H. Ries (1994). "Pulmonary aspiration in mechanically ventilated patients with tracheostomies." Chest **105**(2): 563-566.
Engels, P. T., S. M. Bagshaw, M. Meier and P. G. Brindley (2009). "Tracheostomy: from insertion to decannulation." Can J Surg **52**(5): 427-433.
Epstein, S. K. (2005). "Late complications of tracheostomy." Respir Care **50**(4): 542-549.
Ertekin, C. and I. Aydogdu (2002). "Electromyography of human cricopharyngeal muscle of the upper esophageal sphincter." Muscle Nerve **26**(6): 729-739.
Fattori, B., P. Giusti, V. Mancini, M. Grosso, M. R. Barillari, L. Bastiani, S. Molinaro and A. Nacci (2016). "Comparison between videofluoroscopy, fiberoptic endoscopy and scintigraphy for diagnosis of oro-pharyngeal dysphagia." Acta Otorhinolaryngol Ital **36**(5): 395-402.
Feldman, S. A., C. W. Deal and W. Urquhart (1966). "Disturbance of swallowing after tracheostomy." Lancet **1**(7444): 954-955.
Ferris, L., S. H. Doeltgen, C. Cock, N. Rommel, M. Schar, S. Carrion, I. Scholten and T. I. Omari (2020). "Modulation of Pharyngeal Swallowing by Bolus Volume and Viscosity." Am J Physiol Gastrointest Liver Physiol.
Ferris, L., M. Schar, L. McCall, S. Doeltgen, I. Scholten, N. Rommel, C. Cock and T. Omari (2018). "Characterization of swallow modulation in response to bolus volume in healthy subjects accounting for catheter diameter." Laryngoscope **128**(6): 1328-1334.
Fiorelli, A., F. Ferraro, F. Nagar, P. Fusco, S. Mazzone, G. Costa, D. Di Natale, N. Serra and M. Santini (2017). "A New Modified Evans Blue Dye Test as Screening Test for Aspiration in Tracheostomized Patients." J Cardiothorac Vasc Anesth **31**(2): 441-445.
Freeman, B. D. and P. E. Morris (2012). "Tracheostomy practice in adults with acute respiratory failure." Crit Care Med **40**(10): 2890-2896.
Frost, E. A. (1976). "Tracing the tracheostomy." Ann Otol Rhinol Laryngol **85**(5 Pt.1): 618-624.
Garuti, G., C. Reverberi, A. Briganti, M. Massobrio, F. Lombardi and M. Lusuardi (2014). "Swallowing disorders in tracheostomised patients: a multidisciplinary/multiprofessional approach in decannulation protocols." Multidisciplinary Respiratory Medicine **9**(1): 36.

Geng, Z., M. R. Hoffman, C. A. Jones, T. M. McCulloch and J. J. Jiang (2013). "Three-dimensional analysis of pharyngeal high-resolution manometry data." Laryngoscope **123**(7): 1746-1753.
Goff, D. and J. Patterson (2019). "Eating and drinking with an inflated tracheostomy cuff: a systematic review of the aspiration risk." Int J Lang Commun Disord **54**(1): 30-40.
Grillo, H. C. (2004). Surgery of the trachea and bronchi, PMPH USA.
Guiu Hernandez, E., K. Gozdzikowska, R. Jones and M. L. Huckabee (2018). "Comparison of unidirectional and circumferential manometric measures within the pharyngoesophageal segment: an exploratory study." Eur Arch Otorhinolaryngol **275**(9): 2303-2310.
Hafner, G., A. Neuhuber, S. Hirtenfelder, B. Schmedler and H. E. Eckel (2008). "Fiberoptic endoscopic evaluation of swallowing in intensive care unit patients." Eur Arch Otorhinolaryngol **265**(4): 441-446.
Han, H., G. Shin, A. Jun, T. Park, D. Ko, E. Choi and Y. Kim (2016). "The Relation Between the Presence of Aspiration or Penetration and the Clinical Indicators of Dysphagia in Poststroke Survivors." Ann Rehabil Med **40**(1): 88-94.
Han, X., Z. Dou and X. Wei (2018). "Effect of a speaking valve on biomechanical properties of swallowing and the upper airway flow characteristics for tracheotomized patients after acquired brain damage." Annals of Physical and Rehabilitation Medicine **61**: e221.
Hani, A., A. M. Leguízamo, J. J. Carvajal, G. Mosquera-Klinger and V. A. Costa (2015). "Cómo realizar e interpretar una manometría esofágica de alta resolución." Revista Colombiana de Gastroenterologia **30**: 74-83.
Hernandez, J., G. Leverson and S. Thibeault (2020). "Effect of Lidocaine on Comfort and Swallowing Pressures During Pharyngeal High-Resolution Manometry." Dysphagia.
Hess, D. R. and N. P. Altobelli (2014). "Tracheostomy tubes." Respir Care **59**(6): 956-971; discussion 971-953.
Higgins, D. (2009). "Basic nursing principles of caring for patients with a tracheostomy." Nurs Times **105**(3): 14-15.
Hiiemae, K. M. and J. B. Palmer (1999). "Food transport and bolus formation during complete feeding sequences on foods of different initial consistency." Dysphagia **14**(1): 31-42.
Hutcheson, K. A. and J. S. Lewin Dysphagia in Patients With Head and Neck Cancer. A. Argiris, R. L. Ferris and D. I. Rosenthal. New York, Springer Publishing Company**:** 457-478.
Jacob, P., P. J. Kahrilas, J. A. Logemann, V. Shah and T. Ha (1989). "Upper esophageal sphincter opening and modulation during swallowing." Gastroenterology **97**(6): 1469-1478.
Jaradeh, S. (1994). "Neurophysiology of swallowing in the aged." Dysphagia **9**(4): 218-220.
Jiao, H., L. Mei, T. Sharma, M. Kern, P. Sanvanson and R. Shaker (2016). "A human model of restricted upper esophageal sphincter opening and its pharyngeal and UES deglutitive pressure phenomena." Am J Physiol Gastrointest Liver Physiol **311**(1): G84-90.
Jones, B. (1999). "Radiologic evaluation of the dysphagic patient." Nutrition in clinical practice **14**: S10-S12.
Jones, C. A., E. L. Meisner, C. K. Broadfoot, S. P. Rosen, C. R. Samuelsen and T. M. McCulloch (2018). "Methods for measuring swallowing pressure variability using high-resolution manometry." Front Appl Math Stat **4**.
Kaye, G. M., R. D. Zorowitz and S. Baredes (1997). "Role of flexible laryngoscopy in evaluating aspiration." Ann Otol Rhinol Laryngol **106**(8): 705-709.
Kelly, A. M., M. J. Drinnan and P. Leslie (2007). "Assessing penetration and aspiration: how do videofluoroscopy and fiberoptic endoscopic evaluation of swallowing compare?" Laryngoscope **117**(10): 1723-1727.
Kim, S. B., S. J. Lee, K. W. Lee, J. H. Lee and D. W. Kim (2018). "Usefulness of Early Videofluoroscopic Swallowing Study in Acute Stroke Patients With Dysphagia." Ann Rehabil Med **42**(1): 42-51.
Knigge, M. A., S. Marvin and S. L. Thibeault (2019). "Safety and Tolerability of Pharyngeal High-Resolution Manometry." Am J Speech Lang Pathol **28**(1): 43-52.
Knigge, M. A., S. Thibeault and T. M. McCulloch (2014). "Implementation of high-resolution manometry in the clinical practice of speech language pathology." Dysphagia **29**(1): 2-16.
Kuhlemeier, K. V. (1994). "Epidemiology and dysphagia." Dysphagia **9**(4): 209-217.

Kunieda, K., I. Fujishima, H. Wakabayashi, T. Ohno, T. Shigematsu, M. Itoda, F. Oshima, T. Mori, N. Ogawa and S. Ogawa (2021). "Relationship Between Tongue Pressure and Pharyngeal Function Assessed Using High-Resolution Manometry in Older Dysphagia Patients with Sarcopenia: A Pilot Study." Dysphagia **36**(1): 33-40.
Kupirovic, U. P., I. Elmadfa, M. A. Juillerat and P. Raspor (2017). "Effect of saliva on physical food properties in fat texture perception." Crit Rev Food Sci Nutr **57**(6): 1061-1077.
Langmore, S. (2006). "Endoscopic evaluation of oral and pharyngeal phases of swallowing." Nature.
Langmore, S. E., K. Schatz and N. Olsen (1988). "Fiberoptic endoscopic examination of swallowing safety: a new procedure." Dysphagia **2**(4): 216-219.
Langmore, S. E., K. Schatz and N. Olson (1991). "Endoscopic and videofluoroscopic evaluations of swallowing and aspiration." Ann Otol Rhinol Laryngol **100**(8): 678-681.
Last, R. J. and R. M. H. McMinn (1994). Last's anatomy, regional and applied. Edinburgh; New York, Churchill Livingstone.
Leder, S. B. and J. F. Espinosa (2002). "Aspiration risk after acute stroke: comparison of clinical examination and fiberoptic endoscopic evaluation of swallowing." Dysphagia **17**(3): 214-218.
Leder, S. B., J. K. Joe, S. E. Hill and M. Traube (2001). "Effect of tracheotomy tube occlusion on upper esophageal sphincter and pharyngeal pressures in aspirating and nonaspirating patients." Dysphagia **16**(2): 79-82.
Leder, S. B., J. K. Joe, D. A. Ross, D. H. Coelho and J. Mendes (2005). "Presence of a tracheotomy tube and aspiration status in early, postsurgical head and neck cancer patients." Head Neck **27**(9): 757-761.
Leder, S. B. and D. A. Ross (2000). "Investigation of the causal relationship between tracheotomy and aspiration in the acute care setting." Laryngoscope **110**(4): 641-644.
Leder, S. B. and D. A. Ross (2010). "Confirmation of no causal relationship between tracheotomy and aspiration status: a direct replication study." Dysphagia **25**(1): 35-39.
Leder, S. B., D. A. Ross, M. I. Burrell and C. T. Sasaki (1998). "Tracheotomy tube occlusion status and aspiration in early postsurgical head and neck cancer patients." Dysphagia **13**(3): 167-171.
Leder, S. B., J. M. Tarro and M. I. Burrell (1996). "Effect of occlusion of a tracheotomy tube on aspiration." Dysphagia **11**(4): 254-258.
Ledl, C. and Y. Y. Ullrich (2017). "Occlusion of Tracheostomy Tubes Does Not Alter Pharyngeal Phase Kinematics But Reduces Penetration by Enhancing Pharyngeal Clearance: A Prospective Study in Patients With Neurogenic Dysphagia." Am J Phys Med Rehabil **96**(4): 268-272.
Li, Q., Y. Minagi, T. Ono, Y. Chen, K. Hori, S. Fujiwara and Y. Maeda (2017). "The biomechanical coordination during oropharyngeal swallowing: an evaluation with a non-invasive sensing system." Sci Rep **7**(1): 15165.
Linden, P. and A. A. Siebens (1983). "Dysphagia: predicting laryngeal penetration." Arch Phys Med Rehabil **64**(6): 281-284.
Lippert, D., M. R. Hoffman, C. J. Britt, C. A. Jones, J. Hernandez, M. R. Ciucci and T. M. McCulloch (2016). "Preliminary Evaluation of Functional Swallow After Total Laryngectomy Using High-Resolution Manometry." Ann Otol Rhinol Laryngol **125**(7): 541-549.
Liu, Z., J. Liao, D. Tian, M. Liu, Z. Dan and Q. Yu (2018). "Assessment of Esophageal High-Resolution Impedance Manometry in Patients with Nonobstructive Dysphagia." Gastroenterol Res Pract **2018**: 6272515.
Logemann, J. (1983). Evaluation and Treatment of Swallowing Disorders.
Logemann, J. (1998). Evaluation and Treatment of Swallowing Disorders, Austin, Tex. : PRO-ED.
Logemann, J. A. (1999). "Behavioral management for oropharyngeal dysphagia." Folia Phoniatr Logop **51**(4-5): 199-212.
Logemann, J. A. (2007). "Swallowing disorders." Best Pract Res Clin Gastroenterol **21**(4): 563-573.
Logemann, J. A., P. J. Kahrilas, J. Cheng, B. R. Pauloski, P. J. Gibbons, A. W. Rademaker and S. Lin (1992). "Closure mechanisms of laryngeal vestibule during swallow." Am J Physiol **262**(2 Pt 1): G338-344.
Logemann, J. A., B. R. Pauloski and L. Colangelo (1998). "Light digital occlusion of the tracheostomy tube: a pilot study of effects on aspiration and biomechanics of the swallow." Head Neck **20**(1): 52-57.
Logemann, J. A. and L. L. Pitts (2013). "Optimal Outcomes for Oropharyngeal Dysphagia." Current Physical Medicine and Rehabilitation Reports **1**(4): 223-230.

Loh, K. S. and J. C. Irish (2002). "Traumatic complications of intubation and other airway management procedures." Anesthesiol Clin North Am **20**(4): 953-969.
Lotfi, M., M. R. Hamblin and N. Rezaei (2020). "COVID-19: Transmission, prevention, and potential therapeutic opportunities." Clin Chim Acta **508**: 254-266.
Macht, M., C. J. King, T. Wimbish, B. J. Clark, A. B. Benson, E. L. Burnham, A. Williams and M. Moss (2013). "Post-extubation dysphagia is associated with longer hospitalization in survivors of critical illness with neurologic impairment." Crit Care **17**(3): R119.
Macht, M., T. Wimbish, C. Bodine and M. Moss (2013). "ICU-acquired swallowing disorders." Crit Care Med **41**(10): 2396-2405.
Mancopes, R., P. Gandhi, S. Smaoui and C. Steele (2021). "Which Physiological Swallowing Parameters Change with Healthy Aging?" OBM Geriatrics **5**.
Martin-Harris, B., M. B. Brodsky, Y. Michel, C. L. Ford, B. Walters and J. Heffner (2005). "Breathing and swallowing dynamics across the adult lifespan." Arch Otolaryngol Head Neck Surg **131**(9): 762-770.
Martin-Harris, B. and B. Jones (2008). "The videofluorographic swallowing study." Phys Med Rehabil Clin N Am **19**(4): 769-785, viii.
Martin-Harris, B., J. A. Logemann, S. McMahon, M. Schleicher and J. Sandidge (2000). "Clinical utility of the modified barium swallow." Dysphagia **15**(3): 136-141.
Matsuo, K. and J. B. Palmer (2008). "Anatomy and physiology of feeding and swallowing: normal and abnormal." Phys Med Rehabil Clin N Am **19**(4): 691-707, vii.
McCullough, G. H., R. T. Wertz, J. C. Rosenbek, R. H. Mills, W. G. Webb and K. B. Ross (2001). "Inter- and intrajudge reliability for videofluoroscopic swallowing evaluation measures." Dysphagia **16**(2): 110-118.
McFarland, D. H. and J. P. Lund (1995). "Modification of mastication and respiration during swallowing in the adult human." J Neurophysiol **74**(4): 1509-1517.
McHorney, C. A., D. E. Bricker, J. Robbins, A. E. Kramer, J. C. Rosenbek and K. A. Chignell (2000). "The SWAL-QOL outcomes tool for oropharyngeal dysphagia in adults: II. Item reduction and preliminary scaling." Dysphagia **15**(3): 122-133.
Medda, B. K., I. M. Lang, W. J. Dodds, M. Christl, M. Kern, W. J. Hogan and R. Shaker (1997). "Correlation of electrical and contractile activities of the cricopharyngeus muscle in the cat." Am J Physiol **273**(2 Pt 1): G470-479.
Meyer, J. P., C. A. Jones, C. C. Walczak and T. M. McCulloch (2016). "Three-dimensional manometry of the upper esophageal sphincter in swallowing and nonswallowing tasks." Laryngoscope **126**(11): 2539-2545.
Mielens, J. D., M. R. Hoffman, M. R. Ciucci, J. J. Jiang and T. M. McCulloch (2011). "Automated analysis of pharyngeal pressure data obtained with high-resolution manometry." Dysphagia **26**(1): 3-12.
Mitchell, R. B., H. M. Hussey, G. Setzen, I. N. Jacobs, B. Nussenbaum, C. Dawson, C. A. Brown, 3rd, C. Brandt, K. Deakins, C. Hartnick and A. Merati (2013). "Clinical consensus statement: tracheostomy care." Otolaryngol Head Neck Surg **148**(1): 6-20.
Mittal, R. K. (2011). Motor Function of the Pharynx, Esophagus, and its Sphincters. San Rafael (CA).
Mittal, R. R., A. K. Mishra and A. Nilakantan (2015). "Therapeutic interventions by speech language pathologist in managing adult dysphagia: An evidence based review." Journal of Laryngology and Voice **5**: 11 - 16.
Moore, K. L., A. F. Dalley and A. M. R. Agur (2013). Clinically Oriented Anatomy, Wolters Kluwer Health/Lippincott Williams & Wilkins.
Mullender, J., E. Wheatley and D. Nethercott (2014). "Oral Feed for Patients with a Tracheostomy: Balancing Risks and Benefits." Journal of the Intensive Care Society **15**: 336-339.
Murry, T., R. L. Carrau and K. Chan (2020). Clinical management of swallowing disorders, Plural Publishing.
Muz, J., R. H. Mathog, R. Nelson and L. A. Jones, Jr. (1989). "Aspiration in patients with head and neck cancer and tracheostomy." Am J Otolaryngol **10**(4): 282-286.
Nacci, A., F. Ursino, R. La Vela, F. Matteucci, V. Mallardi and B. Fattori (2008). "Fiberoptic endoscopic evaluation of swallowing (FEES): proposal for informed consent." Acta Otorhinolaryngol Ital **28**(4): 206-211.
Nagy, A., C. Leigh, S. F. Hori, S. M. Molfenter, T. Shariff and C. M. Steele (2013). "Timing differences between cued and noncued swallows in healthy young adults." Dysphagia **28**(3): 428-434.

Ng, J., S. Hamrang-Yousefi and A. Agarwal (2020). Tracheostomy Tube Change. StatPearls. Treasure Island (FL).
Nguyen, H. N., G. R. Domingues and F. Lammert (2006). "Technological insights: combined impedance manometry for esophageal motility testing-current results and further implications." World J Gastroenterol **12**(39): 6266-6273.
Nieszkowska, A., A. Combes, C. E. Luyt, H. Ksibi, J. L. Trouillet, C. Gibert and J. Chastre (2005). "Impact of tracheotomy on sedative administration, sedation level, and comfort of mechanically ventilated intensive care unit patients." Crit Care Med **33**(11): 2527-2533.
Nishino, T. and K. Hiraga (1991). "Coordination of swallowing and respiration in unconscious subjects." J Appl Physiol (1985) **70**(3): 988-993.
Nishino, T., T. Yonezawa and Y. Honda (1985). "Effects of swallowing on the pattern of continuous respiration in human adults." Am Rev Respir Dis **132**(6): 1219-1222.
Nollet, J. L., P. Cajander, L. F. Ferris, J. Ramjith, T. I. Omari and J. Savilampi (2021). "Pharyngo-Esophageal Modulatory Swallow Responses to Bolus Volume and Viscosity Across Time." Laryngoscope.
Ohmae, Y., J. A. Logemann, P. Kaiser, D. G. Hanson and P. J. Kahrilas (1995). "Timing of glottic closure during normal swallow." Head Neck **17**(5): 394-402.
Omari, T. and M. Schar (2018). "High-resolution manometry: what about the pharynx?" Curr Opin Otolaryngol Head Neck Surg **26**(6): 382-391.
Omari, T. I., M. Ciucci, K. Gozdzikowska, E. Hernandez, K. Hutcheson, C. Jones, J. Maclean, N. Nativ-Zeltzer, E. Plowman, N. Rogus-Pulia, N. Rommel and A. O'Rourke (2020). "High-Resolution Pharyngeal Manometry and Impedance: Protocols and Metrics-Recommendations of a High-Resolution Pharyngeal Manometry International Working Group." Dysphagia **35**(2): 281-295.
Omari, T. I., E. Dejaeger, D. van Beckevoort, A. Goeleven, G. P. Davidson, J. Dent, J. Tack and N. Rommel (2011). "A method to objectively assess swallow function in adults with suspected aspiration." Gastroenterology **140**(5): 1454-1463.
Omari, T. I., E. Dejaeger, D. Van Beckevoort, A. Goeleven, P. De Cock, I. Hoffman, M. H. Smet, G. P. Davidson, J. Tack and N. Rommel (2011). "A novel method for the nonradiological assessment of ineffective swallowing." Am J Gastroenterol **106**(10): 1796-1802.
Omari, T. I., J. Savilampi, K. Kokkinn, M. Schar, K. Lamvik, S. Doeltgen and C. Cock (2016). "The Reliability of Pharyngeal High Resolution Manometry with Impedance for Derivation of Measures of Swallowing Function in Healthy Volunteers." Int J Otolaryngol **2016**: 2718482.
Ordonez Gallego, A., M. Gonzalez Baron and E. Espinosa Arranz (2007). "Oxycodone: a pharmacological and clinical review." Clin Transl Oncol **9**(5): 298-307.
Palmer, J. B., N. J. Rudin, G. Lara and A. W. Crompton (1992). "Coordination of mastication and swallowing." Dysphagia **7**(4): 187-200.
Panara, K., E. Ramezanpour Ahangar and D. Padalia (2020). Physiology, Swallowing. StatPearls. Treasure Island (FL).
Park, D., H. H. Lee, S. T. Lee, Y. Oh, J. C. Lee, K. W. Nam and J. S. Ryu (2017). "Normal contractile algorithm of swallowing related muscles revealed by needle EMG and its comparison to videofluoroscopic swallowing study and high resolution manometry studies: A preliminary study." J Electromyogr Kinesiol **36**: 81-89.
Park, D., Y. Oh and J. S. Ryu (2016). "Findings of Abnormal Videofluoroscopic Swallowing Study Identified by High-Resolution Manometry Parameters." Arch Phys Med Rehabil **97**(3): 421-428.
Patel, D. A., R. Sharda, K. L. Hovis, E. E. Nichols, N. Sathe, D. F. Penson, I. D. Feurer, M. L. McPheeters, M. F. Vaezi and D. O. Francis (2017). "Patient-reported outcome measures in dysphagia: a systematic review of instrument development and validation." Dis Esophagus **30**(5): 1-23.
Pearson, W. G., Jr., S. E. Langmore and A. C. Zumwalt (2011). "Evaluating the structural properties of suprahyoid muscles and their potential for moving the hyoid." Dysphagia **26**(4): 345-351.
Pedersen, A. M., A. Bardow, S. B. Jensen and B. Nauntofte (2002). "Saliva and gastrointestinal functions of taste, mastication, swallowing and digestion." Oral Dis **8**(3): 117-129.
Plural Publishing, I. (2016). Clinical Management of Swallowing Disorders, Fourth Edition, Plural Publishing, Incorporated.

Prigent, H., M. Lejaille, N. Terzi, D. Annane, M. Figere, D. Orlikowski and F. Lofaso (2012). "Effect of a tracheostomy speaking valve on breathing-swallowing interaction." Intensive Care Med **38**(1): 85-90.
Raimonde, A. J., N. Westhoven and R. Winters (2020). Tracheostomy. StatPearls. Treasure Island (FL).
Rangachari, V., S. I, S. V and K. Kkrishna (2006). "Laryngeal sequelae following prolonged intubation: A prospective study." Indian Journal of Critical Care Medicine (ISSN: 0972-5229) Vol 10 Num 3 **10**.
Rashid, A. O. and S. Islam (2017). "Percutaneous tracheostomy: a comprehensive review." J Thorac Dis **9**(Suppl 10): S1128-S1138.
Reddy, N. P., A. Katakam, V. Gupta, R. Unnikrishnan, J. Narayanan and E. P. Canilang (2000). "Measurements of acceleration during videofluorographic evaluation of dysphagic patients." Med Eng Phys **22**(6): 405-412.
Regan, J. (2020). "Impact of Sensory Stimulation on Pharyngo-esophageal Swallowing Biomechanics in Adults with Dysphagia: A High-Resolution Manometry Study." Dysphagia **35**(5): 825-833.
Reginelli, A., M. D'Amora, L. Del Vecchio, L. Monaco, M. R. Barillari, N. Di Martino, U. Barillari, G. Motta, S. Cappabianca and R. Grassi (2016). "Videofluoroscopy and oropharyngeal manometry for evaluation of swallowing in elderly patients." Int J Surg **33 Suppl 1**: S154-158.
Ricci Maccarini, A., A. Filippini, D. Padovani, M. Limarzi, M. Loffredo and D. Casolino (2007). "Clinical non-instrumental evaluation of dysphagia." Acta Otorhinolaryngol Ital **27**(6): 299-305.
Rofes, L., V. Arreola, J. Almirall, M. Cabre, L. Campins, P. Garcia-Peris, R. Speyer and P. Clave (2011). "Diagnosis and management of oropharyngeal Dysphagia and its nutritional and respiratory complications in the elderly." Gastroenterol Res Pract **2011**.
Rosen, S. P., C. A. Jones and T. M. McCulloch (2017). "Pharyngeal swallowing pressures in the base-of-tongue and hypopharynx regions identified with three-dimensional manometry." Laryngoscope **127**(9): 1989-1995.
Ryu, J. S., D. Park, Y. Oh, S. T. Lee and J. Y. Kang (2016). "The Effects of Bolus Volume and Texture on Pharyngeal Pressure Events Using High-resolution Manometry and Its Comparison with Videofluoroscopic Swallowing Study." J Neurogastroenterol Motil **22**(2): 231-239.
Ryu, J. S., D. H. Park and J. Y. Kang (2015). "Application and Interpretation of High-resolution Manometry for Pharyngeal Dysphagia." J Neurogastroenterol Motil **21**(2): 283-287.
Sasaki, C. T., M. Suzuki, M. Horiuchi and J. A. Kirchner (1977). "The effect of tracheostomy on the laryngeal closure reflex." Laryngoscope **87**(9 Pt 1): 1428-1433.
Sasegbon, A. and S. Hamdy (2017). "The anatomy and physiology of normal and abnormal swallowing in oropharyngeal dysphagia." Neurogastroenterol Motil **29**(11).
Savilampi, J. (2015). Effects of Remifentanil on Esophageal Sphincters and Swallowing Function, Orebro University.
Savilampi, J., T. Omari, A. Magnuson and R. Ahlstrand (2016). "Effects of remifentanil on pharyngeal swallowing: A double blind randomised cross-over study in healthy volunteers." Eur J Anaesthesiol **33**(9): 622-630.
Schaen-Heacock, N. E., C. A. Jones and T. M. McCulloch (2020). "Pharyngeal Swallowing Pressures in Patients with Radiation-Associated Dysphagia." Dysphagia.
Schar, M. S., T. I. Omari, R. J. Fraser, A. D. Bersten and S. Bihari (2020). "Disordered swallowing associated with prolonged oral endotracheal intubation in critical illness." Intensive Care Med **46**(1): 140-142.
Schar, M. S., T. I. Omari, C. M. Woods, L. F. Ferris, S. H. Doeltgen, K. Lushington, A. Kontos, T. Athanasiadis, C. Cock, C. L. Chai Coetzer, D. J. Eckert and E. H. Ooi (2021). "Altered swallowing biomechanics in people with moderate-severe obstructive sleep apnea." J Clin Sleep Med.
Schefold, J. C., D. Berger, P. Zurcher, M. Lensch, A. Perren, S. M. Jakob, I. Parviainen and J. Takala (2017). "Dysphagia in Mechanically Ventilated ICU Patients (DYnAMICS): A Prospective Observational Trial." Crit Care Med **45**(12): 2061-2069.
Seldinger, S. I. (1953). "Catheter replacement of the needle in percutaneous arteriography; a new technique." Acta radiol **39**(5): 368-376.
Shaker, R., W. J. Dodds, R. O. Dantas, W. J. Hogan and R. C. Arndorfer (1990). "Coordination of deglutitive glottic closure with oropharyngeal swallowing." Gastroenterology **98**(6): 1478-1484.

Shaker, R., Q. Li, J. Ren, W. F. Townsend, W. J. Dodds, B. J. Martin, M. K. Kern and A. Rynders (1992). "Coordination of deglutition and phases of respiration: effect of aging, tachypnea, bolus volume, and chronic obstructive pulmonary disease." Am J Physiol **263**(5 Pt 1): G750-755.
Shaker, R., M. Milbrath, J. Ren, B. Campbell, R. Toohill and W. Hogan (1995). "Deglutitive aspiration in patients with tracheostomy: effect of tracheostomy on the duration of vocal cord closure." Gastroenterology **108**(5): 1357-1360.
Shaker, R., P. Sanvanson, G. Balasubramanian, M. Kern, A. Wuerl and A. Hyngstrom (2016). "Effects of laryngeal restriction on pharyngeal peristalsis and biomechanics: Clinical implications." Am J Physiol Gastrointest Liver Physiol **310**(11): G1036-1043.
Shapiro, J. (2000). "Evaluation and treatment of swallowing disorders." Compr Ther **26**(3): 203-209.
Shaw, D. W., I. J. Cook, M. Gabb, R. H. Holloway, M. E. Simula, V. Panagopoulos and J. Dent (1995). "Influence of normal aging on oral-pharyngeal and upper esophageal sphincter function during swallowing." Am J Physiol **268**(3 Pt 1): G389-396.
Singh, R. K., S. Saran and A. K. Baronia (2017). "The practice of tracheostomy decannulation-a systematic review." J Intensive Care **5**: 38.
Sivarao, D. V. and R. K. Goyal (2000). "Functional anatomy and physiology of the upper esophageal sphincter." Am J Med **108 Suppl 4a**: 27S-37S.
Skoretz, S. A., N. Anger, L. Wellman, O. Takai and A. Empey (2020). "A Systematic Review of Tracheostomy Modifications and Swallowing in Adults." Dysphagia.
Skoretz, S. A., H. L. Flowers and R. Martino (2010). "The incidence of dysphagia following endotracheal intubation: a systematic review." Chest **137**(3): 665-673.
Skoretz, S. A., S. J. Riopelle, L. Wellman and C. Dawson (2020). "Investigating Swallowing and Tracheostomy Following Critical Illness: A Scoping Review." Crit Care Med **48**(2): e141-e151.
Snyder, C. F., R. E. Jensen, J. B. Segal and A. W. Wu (2013). "Patient-reported outcomes (PROs): putting the patient perspective in patient-centered outcomes research." Med Care **51**(8 Suppl 3): S73-79.
Sole, M. L., X. Su, S. Talbert, D. A. Penoyer, S. Kalita, E. Jimenez, J. E. Ludy and M. Bennett (2011). "Evaluation of an intervention to maintain endotracheal tube cuff pressure within therapeutic range." Am J Crit Care **20**(2): 109-117; quiz 118.
Son, Y. R., K. H. Choi and T. G. Kim (2015). "Dysphagia in tongue cancer patients." Ann Rehabil Med **39**(2): 210-217.
Splaingard, M. L., B. Hutchins, L. D. Sulton and G. Chaudhuri (1988). "Aspiration in rehabilitation patients: videofluoroscopy vs bedside clinical assessment." Arch Phys Med Rehabil **69**(8): 637-640.
Srinet, P., D. J. Van Daele, S. I. Adam, M. I. Burrell, R. Aronberg and S. B. Leder (2015). "A Biomechanical Study of Hyoid Bone and Laryngeal Movements During Swallowing Comparing the Blom Low Profile Voice Inner Cannula and Passy-Muir One Way Tracheotomy Tube Speaking Valves." Dysphagia **30**(6): 723-729.
St John, R. E. and J. F. Malen (2004). "Contemporary issues in adult tracheostomy management." Crit Care Nurs Clin North Am **16**(3): 413-430, ix-x.
Stachler, R. J., S. L. Hamlet, J. Choi and S. Fleming (1996). "Scintigraphic quantification of aspiration reduction with the Passy-Muir valve." Laryngoscope **106**(2 Pt 1): 231-234.
Steele, C. M., A. M. Namasivayam-MacDonald, B. T. Guida, J. A. Cichero, J. Duivestein, B. Hanson, P. Lam and L. F. Riquelme (2018). "Creation and Initial Validation of the International Dysphagia Diet Standardisation Initiative Functional Diet Scale." Arch Phys Med Rehabil **99**(5): 934-944.
Stoeckli, S. J., T. A. Huisman, B. Seifert and B. J. Martin-Harris (2003). "Interrater reliability of videofluoroscopic swallow evaluation." Dysphagia **18**(1): 53-57.
Sue, R. D. and I. Susanto (2003). "Long-term complications of artificial airways." Clin Chest Med **24**(3): 457-471.
Suh, J. H., D. Park, I. S. Kim, H. Kim, C. M. Shin and J. S. Ryu (2019). "Feasibility of high-resolution manometry for decision of feeding methods in patients with amyotrophic lateral sclerosis." Medicine (Baltimore) **98**(23): e15781.
Suiter, D. M., G. H. McCullough and P. W. Powell (2003). "Effects of cuff deflation and one-way tracheostomy speaking valve placement on swallow physiology." Dysphagia **18**(4): 284-292.

Suntrup-Krueger, S., P. Muhle, I. Kampe, P. Egidi, T. Ruck, F. Lenze, M. Jungheim, R. Gminski, B. Labeit, I. Claus, T. Warnecke, J. Gross and R. Dziewas (2021). "Effect of Capsaicinoids on Neurophysiological, Biochemical, and Mechanical Parameters of Swallowing Function." Neurotherapeutics.
Szczesniak, M. M., J. Maclean, T. Zhang, R. Liu, C. Cock, N. Rommel, T. I. Omari and I. J. Cook (2015). "Inter-rater reliability and validity of automated impedance manometry analysis and fluoroscopy in dysphagic patients after head and neck cancer radiotherapy." Neurogastroenterol Motil **27**(8): 1183-1189.
Tarrazona, V. and J. Deslauriers (2007). "Glottis and subglottis: a thoracic surgeon's perspective." Thorac Surg Clin **17**(4): 561-570.
Terk, A. R., S. B. Leder and M. I. Burrell (2007). "Hyoid bone and laryngeal movement dependent upon presence of a tracheotomy tube." Dysphagia **22**(2): 89-93.
Tews, L. and J. Robinson (2007). "Dysphagia." 381-385.
Tzanidakis, K., N. Choudhury, S. Bhat, A. Weerasinghe and J. Marais (2012). "Evaluation of disinfection of flexible nasendoscopes using Tristel wipes: a prospective single blind study." Ann R Coll Surg Engl **94**(3): 185-188.
Wallace, K. L., S. Middleton and I. J. Cook (2000). "Development and validation of a self-report symptom inventory to assess the severity of oral-pharyngeal dysphagia." Gastroenterology **118**(4): 678-687.
Warnecke, T., S. Suntrup, I. K. Teismann, C. Hamacher, S. Oelenberg and R. Dziewas (2013). "Standardized endoscopic swallowing evaluation for tracheostomy decannulation in critically ill neurologic patients." Crit Care Med **41**(7): 1728-1732.
Whitmore, K. A., S. C. Townsend and K. B. Laupland (2020). "Management of tracheostomies in the intensive care unit: a scoping review." BMJ Open Respir Res **7**(1).
Williams, R. B., K. L. Wallace, G. N. Ali and I. J. Cook (2002). "Biomechanics of failed deglutitive upper esophageal sphincter relaxation in neurogenic dysphagia." Am J Physiol Gastrointest Liver Physiol **283**(1): G16-26.
Yokoyama, M., N. Mitomi, K. Tetsuka, N. Tayama and S. Niimi (2000). "Role of laryngeal movement and effect of aging on swallowing pressure in the pharynx and upper esophageal sphincter." Laryngoscope **110**(3 Pt 1): 434-439.
Yoon, K. J., J. H. Park, J. H. Park and I. S. Jung (2014). "Videofluoroscopic and manometric evaluation of pharyngeal and upper esophageal sphincter function during swallowing." J Neurogastroenterol Motil **20**(3): 352-361.
Young, D., D. A. Harrison, B. H. Cuthbertson, K. Rowan and C. TracMan (2013). "Effect of early vs late tracheostomy placement on survival in patients receiving mechanical ventilation: the TracMan randomized trial." JAMA **309**(20): 2121-2129.
Zollinger, R. M. and E. C. Ellison (2011). Zollinger's atlas of surgical operations, McGraw-Hill Medical.
Zraick, R. I., S. R. Atcherson and A. M. Brown (2012). "Readability of patient-reported outcome questionnaires for use with persons who stutter." J Fluency Disord **37**(1): 20-24.
Zuercher, P., C. S. Moret, R. Dziewas and J. C. Schefold (2019). "Dysphagia in the intensive care unit: epidemiology, mechanisms, and clinical management." Crit Care **23**(1): 103.

7 Appendix

Human Research Ethics Approval

Southern Adelaide Clinical Human Research Ethics Committee

Government of South Australia
Southern Adelaide Health Service

Ethics application approval

You are reminded that this letter constitutes ethical approval only. You must not commence this research project at any SA Health sites listed in the application until a Site Specific Assessment (SSA) form has been authorised by the Chief Executive or delegate of each site.

21 September 2015

Dear Dr Bihari

This is a formal correspondence from the Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC EC00188). This committee operates in accordance with the "National Statement on Ethical Conduct in Human Research (2007)." No hard copy correspondence will be issued.

Application Number: 202.15 - HREC/15/SAC/164

Title: Incidence of post extubation dysphagia in short-term and long-term stay critical care patients using high resolution pharyngoesophageal manometry and impedance.

Chief investigator: Dr Shailesh Bihari

Public health sites approved: Flinders Medical Centre

The Issue: The Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC) have reviewed and approved the above application. The approval extends to the following documents / changes:

- Minute addressing specific committee concerns dated 14 July 2015 and 08 September 2015
- SAC HREC general research application form v4 dated 08 September 2015
- NEAF: AU/1/E22028
- SA Health indemnity approval dated 28 May 2015
- Letter of support from Professor Robert Fraser, Head of Gastroenterology and Hepatology FMC dated 24 March 2015
- Participant information sheet and consent form v4 dated September 2015
- Swallowing score submitted dated 08 September 2015
- Clinical Frailty Scale – no date
- SF-36 questionnaire – no date

Noted:

- Article: A new dysphagia score with objective validation
- Article: Initial Psychometric Assessment of a Functional Oral Intake Scale for Dysphagia in Stroke Patients

Approval Period: 18 September 2015 – 18 September 2018

Please read the terms and conditions of ethical approval below, as researchers have a significant responsibility to comply with reporting requirements and the other stated conditions.

For example, the implications of not providing annual reports and requesting an extension for research prior to approval expiring could lead to the suspension of the research, and has further serious consequences.

Flinders Medical Centre
The Flats G5 – Rooms 3 and 4
Flinders Drive, Bedford Park SA 5042
T: 08 8204 6453
F: 08 8204 4586
E:Research.ethics @health.sa.gov.au

Please retain a copy of this approval for your records.

TERMS AND CONDITIONS OF ETHICAL APPROVAL
Final ethical approval is granted subject to the researcher agreeing to meet the following terms and conditions.

As part of the Institution's responsibilities in monitoring research and complying with audit requirements, it is essential that researchers adhere to the conditions below.

Researchers have a significant responsibility to comply with the *National Statement 5.5.* in providing the SAC HREC with the required information and reporting as detailed below:

1. **The approval only covers the science and ethics component of the application**. A SSA will need to be submitted and authorised before this research project can commence at any of the approved sites identified in the application.
2. **It is the policy of the SAC HREC not to provide signed hardcopy or signed electronic approval letters**, as our office is moving to electronic documentation. The SAC HREC office provides an unsigned electronic PDF version of the study approval letter to the Chief Investigator/Study Manager via email. These email approvals are generated via the email address research.ethics@health.sa.gov.au which can be linked back to the SAC HREC.
3. **If University personnel are involved in this project**, the Principal Investigator should notify the University before commencing their research to ensure compliance with University requirements including any insurance and indemnification requirements.
4. **Compliance** with the *National Statement on Ethical Conduct in Human Research* (2007) & the *Australian Code for the Responsible Conduct of Research* (2007).
5. To **immediately report to SAC HREC** anything that may change the ethical or scientific integrity of the project.
6. **Report Significant Adverse events (SAE's)** as per SAE requirements available at our website.
7. **Submit an annual report on each anniversary of the date of final approval** and in the correct template from the SAC HREC website.
8. **Confidentiality** of research participants MUST be maintained at all times.
9. A copy of the **signed consent form** must be given to the participant unless the project is an audit.
10. Any **reports or publications derived from the research** should be submitted to the Committee at the completion of the project.
11. All requests for **access to medical records** at any SALHN site must be accompanied by this approval email.
12. To **regularly review the SAC HREC website** and comply with all submission requirements, as they change from time to time.
13. The researchers agree to use **electronic format** for all correspondence with this department.

Kind Regards

Petrina Kasperski
Executive Officer, SAC HREC

On behalf of
Professor David Gordon
Chair, SAC HREC

Health:SALHN Office for Research
Wed 4/29/2020 1:44 PM
Inbox

To: Cheriyan, Sanith (Health);
Cc: Bihari, Shailesh (Health);

You forwarded this message on 6/3/2020 11:39 AM.

Action Items

Dear Sanith,

OFR reference: 202.15
Title: Incidence of post extubation dysphagia in short-term and long-term stay critical care patients using high resolution pharyngoesophageal manometry and impedance
Principal investigator: A/Prof Shailesh Bihari

The amendment to the above study has been reviewed and approved by the SAC HREC.

Approval period: 18 September 2015 – 17 December 2021

Public Health sites approved under this application:

- Flinders Medical Centre

The following documents have been reviewed and approved:

Document	Version	Date
Project amendment form	-	15 April 2020
General research application form	8	15 April 2020
Participant information sheet and consent form	7	15 April 2020

The terms and conditions of ethics and governance approval remain unchanged from the original approval. Please note a formal approval letter will not be provided. Please retain a copy of this email as evidence of approval.

Kind Regards,

Dominic How

On behalf of

Professor Bill Heddle
Chair
SAC HREC