

ANATOMICAL FACTORS CONTRIBUTING TO TROUBLESOME DYSPHAGIA AFTER ANTI- REFLUX SURGERY

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THESIS ABSTRACT

Laparoscopic anti-reflux surgery, which involves hiatal repair and fundoplication, is an effective treatment for gastro-oesophageal reflux disease. Hiatal repair refers to closure of the diaphragmatic hiatus with repair of hiatal hernia where present, whereas fundoplication entails wrapping of the fundus of the stomach around the distal oesophagus and securing it within the abdominal cavity. However, some patients develop new-onset or worsening dysphagia post-operatively. The cause of troublesome post-operative dysphagia remains unclear, especially in the setting of an intact fundoplication. In this thesis, I propose that objective measurements of post-fundoplication anatomy hold the key to understanding troublesome dysphagia after fundoplication. My aim is to determine if barium swallow, through objective measurements of post-fundoplication gastro-oesophageal junction anatomy, can be used to identify factors contributing to dysphagia after anti-reflux surgery.

A review of anatomical factors previously evaluated or proposed as contributory to dysphagia was performed. Following this, novel objective measurements of select anatomical features on barium swallow studies were devised for the gastro-oesophageal junction in patients after fundoplication. Post-operative structured barium swallow studies with fluoroscopy along with pre- and post-operative dysphagia assessments obtained approximately 6-12 months after fundoplication were utilised. Over two scientific exploratory studies, I first sought to determine the level of inter- and intra-observer reproducibility of these objective measurements, followed by a second study determining if these anatomical features correlated with post-operative dysphagia.

In the first study (Chapter 2), there was overall good inter- and high intra-observer reproducibility of objective measurements of gastro-oesophageal junction (GOJ) anatomy

after fundoplication. Inter-observer reproducibility, using intra-class coefficient correlations, was good or excellent in 71% of all measurements. High agreement was found for measures of diameter, posterior distal oesophageal angle, displacement of the distal oesophagus anteriorly, and degree of angulation of the GOJ relative to the distal oesophagus, whereas measures of fundal wrap length were more variable.

Greater anterior displacement and angulation of the distal oesophagus were subsequently found to be associated with troublesome dysphagia after a complete (360°) wrap of the fundus around the distal oesophagus (Chapter 3), the likely mechanism of which is through increasing oesophageal outflow resistance. After partial anterior (90°) fundoplication, patients with or without troublesome dysphagia had no significant difference in the extent of anterior displacement and angulation of the distal oesophagus. A small reduction in maximal distal oesophageal luminal diameter relative to wrap opening luminal diameter was associated with worsening dysphagia after partial fundoplication.

In conclusion, barium swallow studies recorded with fluoroscopy show potential for detecting objective but subtle changes of post-fundoplication anatomy. Anatomical measurements were reproducible, increasing the validity of the measurements for use in further studies. Future studies need to confirm the association between troublesome dysphagia and greater anterior displacement and angulation, to inform a review of technical steps requiring care or modification during fundoplication and hiatal repair to further reduce post-surgical dysphagia.

THESIS DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree.

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CHAPTER 1

INTRODUCTION

1.1 OVERVIEW OF FUNDOPLICATION FOR GASTRO-OESOPHAGEAL REFLUX DISEASE

In Western countries, gastro-oesophageal reflux disease (GORD) is a highly prevalent disorder, which affects 10-20% of the population at least weekly (El-Serag *et al.* 2014). The Montreal consensus statement defines GORD as “troublesome or persistent symptoms and/or complications resulting from the reflux of gastro-duodenal contents” (Vakil *et al.* 2006). Typical symptoms of GORD include heartburn and regurgitation, whereas atypical symptoms are non-cardiac chest pain and extra-oesophageal syndromes (Frazzoni *et al.* 2014).

The mainstay of medical treatment of GORD is proton-pump inhibitor (PPI) therapy (Kahrilas *et al.* 2008), which provides relief of typical symptoms by reducing the acidity of reflux contents from the stomach into the oesophagus (Frazzoni *et al.* 2009). However, symptoms frequently recur rapidly on withdrawal of PPI, with some studies demonstrating a recurrence rate of 80% within 6 months (Pilotto *et al.* 2003). Long-term PPI use may not be preferred or tolerated due to the risk of infection, drug interactions, dementia and chronic kidney disease (Jaynes & Kumar 2019). In addition, up to one third of patients have partial or no response to acid suppression therapy (El-Serag *et al.* 2010). Laparoscopic fundoplication is currently the only surgical therapy recommended for overcoming failures of PPI therapy (Katz *et al.* 2013; Stefanidis *et al.* 2010).

Since its introduction in 1991, the use of laparoscopic fundoplication has increased significantly. The attractiveness of minimally invasive anti-reflux surgery relates to short post-operative recovery time, a low post-operative mortality rate (Stefanidis *et al.* 2010),

and good outcomes with sustained control of reflux symptoms in 90% of patients up to 12 years after surgery (Dallemaigne *et al.* 2006; Morgenthal *et al.* 2007; Roks *et al.* 2017a).

Despite overall symptom improvement, dysphagia is a common unwanted effect of anti-reflux surgery, although troublesome dysphagia less so (Kapadia *et al.* 2018). Dysphagia is a symptom recognised as difficulty swallowing or the unpleasant sensation of food sticking in the oesophagus after swallowing (Kapadia *et al.* 2018). Dysphagia is measured by patient reports in various scoring systems: a binary scale of presence/absence of dysphagia to solids, liquids, or both, a 4-point or 6-point scale from 0-3 or 0-5 respectively with verbal descriptors (*e.g.* 0=no dysphagia and 5=incapacitating dysphagia) and a visual analogue scale score where 0=no dysphagia and 10=total dysphagia (Kapadia *et al.* 2018; Watson *et al.* 2001; Yamamoto *et al.* 2016). In addition, of validated scoring systems, one particular validated composite dysphagia score assesses severity and frequency of difficulty swallowing a range of food consistencies (0=severe dysphagia, 45=no dysphagia) (Dakkak & Bennett 1992). A modified Dakkak & Bennett score is used in some studies with reversal of scores (0=no dysphagia, 45=severe dysphagia) as a greater score is intuitively associated with more severe dysphagia (Watson *et al.* 2001). Troublesome dysphagia is loosely defined in the Montreal consensus statement as being present when patients need to alter eating patterns or report food obstruction (Vakil *et al.* 2006). Troublesome dysphagia is the focus of this research because it significantly affects a patient's quality of life and satisfaction with surgery (Humphries *et al.* 2013). Moreover, it necessitates costly and burdensome follow-up such as medical consultations, investigations with endoscopy, manometry and barium swallow and interventions, including dilatation or re-operation (Gronnier *et al.* 2018).

Investigations undertaken to evaluate persistent dysphagia after anti-reflux surgery include upper gastrointestinal endoscopy, manometry and barium swallow. Barium swallow consists of serial x-rays or a video recording of bolus flow through the oesophagus, lower oesophageal sphincter (LOS) and stomach upon swallowing a barium meal. It has greater utility in evaluating post-operative anatomical changes compared to endoscopy and manometry (Baker & Einstein 2014). Readily identifiable causes of dysphagia, which may relate to technical errors during fundal wrap construction, include excessive fundal wrap length or tightness, wrap disruption, intra-thoracic migration of the wrap, recurrent hiatal hernia, or telescoping of the LOS through the wrap (Furnee *et al.* 2009). Nevertheless, the majority of these gross anatomical failures occur in patients who underwent fundoplication during the learning curve period for this operation (Soper & Dunnegan 1999), and occur less frequently in the hands of experienced surgeons. Therefore, surgeons are frequently perplexed as to why some patients experience troublesome dysphagia despite normal post-fundoplication appearances, while others have abnormal post-fundoplication anatomy without any symptoms (Furnee *et al.* 2009). In one systematic review evaluating 118 patients undergoing surgical re-operation for dysphagia, no intra-operative cause of failure was identified in almost half of the patients (Furnee *et al.* 2009).

Manometry studies measure the pressure in the oesophagus and LOS via a catheter containing solid-state internal or water-perfused external transducers passed through the mouth into the gastrointestinal tract. Manometry studies have been used extensively to evaluate oesophageal body motility and function of the gastro-oesophageal junction (GOJ). Much of the literature to date has focused on the risk of developing post-operative dysphagia based on patients' pre-operative oesophageal motility status and impaired bolus transport. However, a large number of studies have not demonstrated any association

between pre-operative oesophageal dysmotility and post-operative dysphagia (Montenovo *et al.* 2009; Strate *et al.* 2008; Tsuboi *et al.* 2011). In recent years, oesophageal outflow resistance at the GOJ, as measured on manometry by raised intrabolus pressure (a measurement that demonstrates the compartmentalised force exerted on a bolus during oesophageal peristalsis) and impaired swallow-induced GOJ relaxation has been linked with troublesome post-operative dysphagia (Ayazi *et al.* 2019; Myers *et al.* 2012; Wilshire *et al.* 2012). This lends credence to the theory that anatomical changes of surgery, no matter how subtle, may contribute to post-operative dysphagia by restricting flow through the GOJ. In the setting of an apparently technically successful anti-reflux surgery, the significance of anatomical features after surgery, not routinely measured, with regard to dysphagia are explored in this clinical research.

1.2 DYSPHAGIA AND ANTI-REFLUX SURGERY

1.2.1 Dysphagia before anti-reflux surgery

This research focuses on identifying causes of troublesome dysphagia after anti-reflux surgery. A confounding factor is that pre-operative dysphagia is experienced by up to 50% of patients with GORD (Anvari & Allen 1998). Mechanisms of pre-operative dysphagia related to GORD include peptic stricture, hiatal hernia, oesophageal dysmotility, oesophageal inflammation and acid hypersensitivity (Montenovo *et al.* 2009). Pre-operative dysphagia resolves after surgery in many, but not all patients (Kapadia *et al.* 2018). For example, in a retrospective study of 146 patients who underwent a complete 360° wrap of the fundus around the distal oesophagus (Nissen fundoplication) with an average of 34 months follow-up, for a subset of 23 patients with pre-operative dysphagia it was found that dysphagia resolved completely in 60% of patients, was stable or improved in a third of patients, and 10% reported worsening dysphagia (Kapadia *et al.* 2018). In the study presented in Chapter 3, a baseline assessment of dysphagia prior to surgery was conducted for all patients in order to identify patients with persistent, worsening or new-onset dysphagia after fundoplication.

1.2.2 Early post-operative dysphagia

Dysphagia experienced after fundoplication for up to six weeks is arbitrarily defined as early post-operative dysphagia (Hunter *et al.* 1996; Watson *et al.* 1999). Wills & Hunt noted early dysphagia affects between 4 to 100% of patients (Wills & Hunt 2001). The

marked variation in the number of patients affected is likely due in part to the difficulty in defining and measuring dysphagia, and the use of different scoring systems (Wills & Hunt 2001). Early dysphagia is usually mild (Contini & Scarpignato 2002) and gradually improves over a 3-6 month period following surgery (Wills & Hunt 2001). In the early post-operative period, almost all patients experience dysphagia in the initial first few days (Funch-Jensen & Jacobsen 2007) up to 3 weeks after surgery (Anvari & Allen 2003). However, dysphagia symptoms diminish substantially after 6 weeks without any intervention for most patients (Anvari & Allen 2003), when as few as 8% of patients experience dysphagia (Funch-Jensen & Jacobsen 2007).

Early dysphagia is usually related to surgery-induced oedema and inflammation, which resolves with time (Funch-Jensen & Jacobsen 2007). Another causative factor may be transient oesophageal ileus in the early post-operative period after fundoplication (Myers *et al.* 2007). The observed severe oesophageal dysmotility in the immediate post-operative period returns to baseline motility pattern by the time of 3 month post-operative testing (Myers *et al.* 2007). In rare instances, severe and acute early dysphagia may be due to slipping or rupture of the wrap (Hasak *et al.* 2019). Any nausea or vomiting should be investigated with barium swallow as these symptoms may indicate wrap disruption, early wrap herniation or an unusually tight or long fundoplication wrap (Zarzour *et al.* 2018).

In general, early post-operative dysphagia can be monitored while providing reassurance that most cases resolve over time and do not require any intervention (Hasak *et al.* 2019). Early dysphagia is mitigated by following a graduated diet initially, building up to a soft diet in the immediate post-operative period (DeMeester 2020). Thereafter, the patient

can resume a normal diet, but is advised to have small and regular meals in order to minimise dysphagia (DeMeester 2020).

1.2.3 Late post-operative dysphagia

Post-fundoplication dysphagia persisting beyond 6 weeks after surgery is known as late, persistent or troublesome dysphagia. Some authors also report persistent dysphagia as that lasting beyond 3 months (Mickevicius *et al.* 2008; Sato *et al.* 2002). Clinically significant (moderate to severe) persistent dysphagia occurs in 2% - 25% of patients (Hasak *et al.* 2019; Nikolic *et al.* 2019; Pessaux *et al.* 2005; Tsuboi *et al.* 2011; Walle *et al.* 2019) and affects patients' ability to eat normally. Investigation with barium swallow and upper gastrointestinal endoscopy is warranted. While most early dysphagia tends to resolve spontaneously, persistent dysphagia suggests a more sustained problem whereby endoscopic dilatation of the fundoplication or revisional surgery might be indicated. Sometimes persistent dysphagia is due to technical errors associated with the fundoplication as described earlier; or an incorrect primary diagnosis or missed oesophageal motility disorder (*i.e.* achalasia, oesophageal spasm, scleroderma and oesophageal carcinoma) (Furnee *et al.* 2009).

As hiatal hernia repair and crural closure (discussed in next section) are performed concomitantly with fundoplication, anatomical changes of surgery contributing to dysphagia may relate to either the hiatus or GOJ. Increased length of the narrowed segment due to fundoplication, increased angulation of the GOJ compared with distal oesophagus and anterior displacement of the GOJ are possible factors contributing to persistent dysphagia.

1.3 ANTI-REFLUX SURGERY

1.3.1 Principles of anti-reflux surgery

The goal of anti-reflux surgery is to create a functional anti-reflux barrier. This consists of three essential components *i.e.* appropriate intra-abdominal length of the oesophagus, hiatal repair or closure, and construction of the fundoplication (Fuchs *et al.* 2014). Hiatal repair refers to closure of the diaphragmatic hiatus with repair of hiatal hernia where present. It is most commonly performed with sutures posterior to the oesophagus. Fundoplication involves wrapping of the fundus of the stomach around the distal oesophagus and securing it within the abdominal cavity.

1.3.2 Evolution of fundoplication

Fundoplication for GORD began in 1956 following Rudolph Nissen's original description of a 360° wrap of fundus around the distal oesophagus (Nissen 1956). The 'Nissen fundoplication' involved an open intra-thoracic approach, creation of a 5cm-long and fairly tight wrap using both the anterior and posterior gastric fundus, and the short gastric vessels were not divided. This procedure resulted in good control of reflux symptoms, but often led to troublesome adverse effects such dysphagia, inability to belch, and gas-bloat (Thor & Silander 1989).

In the ensuing years, efforts were made with various modifications to the Nissen fundoplication to reduce its side-effect profile. In 1977, Rossetti and Hell described a

technique of fundoplication using only the anterior fundal wall, in order to preserve the vagal nerves as well as construct a tension-free fundoplication (Rossetti & Hell 1977). In the 1980s, Donahue *et al.* proposed division of the short gastric vessels (Donahue *et al.* 1985), while DeMeester *et al.* progressively introduced several modifications in a series of 100 consecutive patients. These included calibration of the fundoplication with a larger intra-oesophageal bougie, shortening the fundoplication length from 4 to 3 to 1cm, and mobilisation of the gastric fundus via division of the short gastric vessels (DeMeester *et al.* 1986). The proponents of each of the above reported good outcomes following the above technical modifications. However, until the 1990s most of the published evidence for the above technical modifications arose from retrospective case series or uncontrolled prospective studies.

Introduced in 1991, laparoscopic Nissen fundoplication involves the division of the short gastric vessels, posterior closure of the diaphragmatic hiatus and creation of a 1-2cm 360° fundoplication, calibrated by at least a 52 French (Fr) intra-oesophageal bougie (Dallempagne *et al.* 1991). Reducing the extent of fundal wrap from a total (360°) to a partial fundoplication was developed from the view that this would result in less overcorrection of the anti-reflux mechanisms in the GOJ. Various partial fundoplication techniques now exist which include:

1. Toupet (posterior 270°) fundoplication (Cuschieri *et al.* 1993)
2. Anterior 180° fundoplication (Watson *et al.* 1999)
3. Anterior 120° fundoplication (Watson *et al.* 1991)
4. Anatomical (anterior 90°) fundoplication (Yau *et al.* 2000)

There is ongoing debate regarding the best fundoplication procedure, with regional practices differing according to local preference and experience. The laparoscopic Nissen fundoplication is the most common procedure in the United States, whereas a partial fundoplication is favoured in Europe (Moore *et al.* 2016). The following subsections consist of a review of recent studies of the various technical modifications of laparoscopic fundoplication with regard to reducing persistent post-operative dysphagia.

1.3.3 Nissen vs Toupet fundoplication

The first partial fundoplication and most widely studied in the literature is the Toupet (270°) posterior partial fundoplication as described by André Toupet in 1963 (Katkhouda *et al.* 2002). It consists of intra-abdominal fixation of the gastric fundus to the diaphragm, and a wrap of the fundus posteriorly around the oesophagus.

A number of randomised controlled trials (RCT) report lower rates of post-operative dysphagia following a posterior 270° fundoplication compared to 360° fundoplication, with similar heartburn control, with follow-up times typically ranging from one to five years (Koch *et al.* 2013; Strate *et al.* 2008; Wang *et al.* 2015). One study reported equalisation of dysphagia rates between the two procedures after 1 year (Chrysos *et al.* 2003), while another reported that dysphagia remained more common after total fundoplication over a few years of follow-up (Hakanson *et al.* 2019).

A meta-analysis of seven eligible RCTs found that patients after Nissen fundoplication were 1.61 times more likely to have post-operative dysphagia (relative risk (RR) 1.61, 95% confidence interval (CI) [1.06, 2.44]; P = 0.02) and were more likely to undergo dilatation of the GOJ for dysphagia (RR 2.45, 95% CI [1.06, 5.68]; P = 0.04) than patients after Toupet

fundoplication (Broeders *et al.* 2010). In another meta-analysis using a subgroup analysis of two trials which reported dysphagia severity, there was a higher rate of patients experiencing moderate to severe dysphagia following Nissen compared to Toupet fundoplication (8.86% vs 3.85%, RR 2.28, 95% CI [0.63, 8.30]; P = 0.21) (Tian *et al.* 2015). Limitations of the RCTs to date are their small sample size, heterogeneity of dysphagia definitions, varying timepoints of symptom assessment and a lack of detail in operative technique included.

In contrast, two large case-control studies involving experienced surgeons demonstrated a low rate of post-operative side-effects and similar re-operation rate between the Nissen and Toupet procedures, with equal control of reflux symptoms (Dalleymagne *et al.* 2006; Fein *et al.* 2008).

Due to the conflicting evidence described above, the European Association of Endoscopic Surgery (EAES) guidelines recommend that “experienced surgeons in high-volume centres may decide between total and partial posterior fundoplication according to their own experience and outcome” (Fuchs *et al.* 2014).

Differences exist between centres for each procedure with regard to the length of the fundoplication, method of fixation to the crura and oesophagus, whether the anterior fundus or both anterior and posterior fundal walls are used in constructing the wrap, and whether it is performed with or without the use of an intra-oesophageal bougie, short gastric vessels division, or routine hiatal repair. These variations likely have a subtle impact on the shape and structure of the GOJ after surgery, which are not routinely measured.

1.3.4 Posterior vs anterior partial fundoplication

In anterior partial fundoplication, the angle of His (the normally acute angle between the abdominal oesophagus and fundus of the stomach at the GOJ) is accentuated, the hiatus repaired, the distal 3-5cm of the oesophagus anchored within the abdomen to prevent proximal wrap migration, and a partial fundoplication over the anterior oesophagus sutured to the oesophagus and hiatal ring (Watson *et al.* 1999). Anterior 180° fundoplication is the most widely used anterior fundoplication procedure. A meta-analysis evaluating five RCTs found a lower prevalence (15% vs 27%; RR 0.56; 95% CI [0.38, 0.81]; P = 0.002) and severity (modified Dakkak & Bennett composite dysphagia score (range 0-45, 0=no dysphagia): 2.8 vs 4.8; weighted mean difference: -2.25; 95% CI [-2.6, -1.83]; P < 0.001) of dysphagia at 1 year after anterior 180° fundoplication than after Nissen fundoplication, while heartburn scores were similar (Broeders *et al.* 2013). In most RCTs there was routine hiatal repair and the short gastric vessels were not divided for both groups, but there was considerable variation between RCTs in the use of an intra-oesophageal bougie (ranging in size from 42 Fr to 56 Fr, if used) and fixation to the right crus and/or oesophagus for either or both the 180° or 360° fundoplication) (Broeders *et al.* 2013).

Given that patients experienced less dysphagia after the anterior 180° compared to Nissen fundoplication, the anterior 90° fundoplication was developed with the hypothesis that an even lesser extent of fundal wrap circumference would further reduce the risk of post-fundoplication dysphagia. However, the anti-reflux effects of the anterior 90° fundoplication appear to be less durable in the long-term. A study combining the 10-year outcomes of two RCTs for a total of 191 patients found that anterior 90° fundoplication was associated with less severe dysphagia to solids (modified Dakkak & Bennett composite score

2.03 vs 3.18; $P = 0.037$) but greater heartburn (visual analogue scale score 2.83 vs 1.90; $P = 0.035$) compared to Nissen fundoplication (Hopkins *et al.* 2020).

In the two studies presented in this thesis (Chapters 2 and 3), subjects underwent either a total 360° fundoplication or partial anterior 90° fundoplication for GORD. The choice of procedure was by informed patient preference. The anterior 90° fundal wrap will have the least impact on anatomical changes and is known to have lower dysphagia rates. Therefore, to contrast anatomical changes of total 360° and partial anterior 90° fundoplication would be useful to inform anatomical features warranting closer examination with regards to dysphagia.

Randomised trials comparing anterior 180° and posterior 270° fundoplication report that posterior 270° was superior for heartburn control but led to greater inability to belch (Daud *et al.* 2015) and early post-operative dysphagia (Khan *et al.* 2010), while a more recent study demonstrated no difference in reflux control and dysphagia symptoms between the two procedures at 12 months follow-up (Roks *et al.* 2017b).

1.3.5 Division of short gastric vessels

As described earlier, division of the short gastric vessels was one of the modifications deemed a requisite to fully mobilise the gastric fundus from the spleen, in order to create a sufficiently loose and tension-free fundoplication. The technique involved dividing the short gastric vessels starting from the level of inferior pole of the spleen, progressing upwards along the greater curvature of the stomach until the left hiatal crus was reached (Watson *et al.* 1997). If not divided, these vessels would tether the fundus to the posterior abdominal wall (DeMeester *et al.* 1986).

Other authors found that creation of a floppy fundal wrap was possible without division of the short gastric vessels, by using only the anterior wall of the fundus to create the fundoplication (Geagea 1994; Jamieson *et al.* 1994). The anterior fundic wall, which is mobile and not fixed, could be slid up on itself allowing sufficient length of stomach to pass behind the oesophagus to create a tension-free 360° fundoplication (Geagea 1994; Jamieson *et al.* 1994).

All six single-centre RCTs published to date have not shown any benefit of short gastric vessels division in reducing post-operative dysphagia rates in up to 20 years' follow-up (Chrysos *et al.* 2001; Farah *et al.* 2007; Kinsey-Trotman *et al.* 2018; Kosek *et al.* 2009; Luostarinen & Isolauri 1999; Mardani *et al.* 2009). Interestingly, division of the short gastric vessels was associated with more gas-bloat symptoms in one study (50% vs 26%; $P = 0.046$) (Kinsey-Trotman *et al.* 2018). While routine division of the short gastric vessels is not required, it may be necessary to divide the uppermost and posterior short gastric vessels in some patients in order to ensure construction of a floppy fundal wrap.

1.3.6 Use of intra-oesophageal bougie

An intra-oesophageal bougie is traditionally used to calibrate the hiatus and fundoplication, to prevent tight crural closure or tight wrap, thereby reducing the risk of post-operative dysphagia. In the original Nissen fundoplication, a 32Fr bougie was used, while DeMeester proposed that increasing the bougie size from 36Fr to 60Fr decreased the rate of early post-operative dysphagia (83% to 39%, $p < 0.01$) (DeMeester *et al.* 1986). In this study, dysphagia was defined as 'any discomfort in swallowing' that was temporary

(resolved within 3 months) or persistent. There was no clarification as to whether patients were reporting dysphagia to solids, liquids, or both.

A single prospective blinded RCT published in the literature (n=171) demonstrated a significantly lower incidence of post-operative dysphagia following the use of a 56Fr bougie in patients undergoing Nissen fundoplication compared to no bougie, at mean follow-up of 11 months (17% vs 31%; P = 0.047) (Patterson *et al.* 2000). One oesophageal injury occurred in the bougie group (1.2% of patients) with no instances of oesophageal perforation. Therefore, guidelines and a consensus of 40 experienced surgeons recommend the use of an intra-oesophageal bougie (Attwood *et al.* 2008; Stefanidis *et al.* 2010).

While a bougie is used for laparoscopic Nissen and most partial posterior fundoplications, it is not routinely used in partial anterior fundoplication procedures (Fein & Seyfried 2010). This likely relates to the lower radial extent of fundal wrap enabling a sufficiently loose wrap. In addition, placing the fundal wrap anteriorly is likely to place less compression on and distortion of the distal oesophagus and GOJ than a posterior fundal wrap.

1.3.7 Hiatal repair

There have been no randomised controlled trials comparing fundoplication with or without hiatal repair or closure. Hiatal repair was initially reserved for patients with a wide hiatus or hiatal hernia. Individual reports stress the importance of routine hiatal repair (discussed in next section) in reducing the rate of intra-thoracic wrap migration, recurrence of hiatal hernia and para-oesophageal hernia, all of which may lead to post-operative dysphagia with a need for re-operation (Watson *et al.* 1995a; Wu *et al.* 1996). Many

surgeons now include routine posterior hiatal repair as an essential step (Attwood *et al.* 2008). However, many variations exist for the technique of hiatal repair, and their contribution to post-operative dysphagia remains unclear. These include the method of hiatal dissection (blunt dissection vs diathermy), hiatal repair from the anterior or posterior aspect (discussed in next section), extent of hiatal narrowing and whether this is assisted by an intra-oesophageal bougie, and the use of prosthetic mesh. Using a mesh at the hiatus can lead to significant complications including post-operative dysphagia and pain, mesh dislocation and penetration sometimes requiring major resections (Parker *et al.* 2010; Tatum *et al.* 2008). Therefore, the use of a mesh is generally reserved for patients with weak crura and large hiatal defect (Fuchs *et al.* 2014).

1.4 ANATOMICAL FEATURES OF POST-FUNDOPLICATION GASTRO-OESOPHAGEAL JUNCTION CONTRIBUTING TO DYSPHAGIA

The following sections review the literature for the anatomical features of the GOJ studied as they relate to post-fundoplication dysphagia, which informs the basis for the objective anatomical features evaluated in this research.

1.4.1 Normal anatomical structures of the GOJ

The GOJ, located between the distal oesophagus and stomach, is a complex anatomical region which allows daily functions such as regulating oesophageal emptying for effective swallowing, permitting venting of air to belch or regurgitation to vomit, and preventing unwanted regurgitation of gastric contents (Miller *et al.* 2016). The GOJ comprises the intrinsic smooth muscle lower oesophageal sphincter (LOS) and the extrinsic diaphragmatic crura which surround the oesophagus as it passes through the diaphragm (Miller *et al.* 2016). Just distal to the lower oesophageal smooth muscle are the gastric sling and clasp muscles within the gastric cardia (Liebermann-Meffert *et al.* 1979). The gastric sling muscle fibres arise from greater curvature side of the stomach, while the gastric clasp muscle fibres originate from the lesser curvature side of the stomach. The gastric sling and clasp fibres crosslink in the left postero-lateral aspect of the LOS forming the angle of His (Raphael *et al.* 2020). The gastric sling fibres have lower spontaneous tension but generate significantly greater contraction in response to cholinergic stimulation than gastric clasp fibres (Preiksaitis & Diamant 1997). Using subtraction studies to inhibit the crural diaphragm skeletal muscle and ascertain the relative contribution of smooth muscle to GOJ pressure,

Brasseur *et al.* found that there are two high-pressure zones within the GOJ. The proximal high-pressure zone likely reflects the contribution of the lower oesophageal smooth muscle while the distal high-pressure zone represents the gastric sling and clasp fibre component (Brasseur *et al.* 2007). All four of these components work in tandem to form the high-pressure zone anti-reflux barrier that acts as a sphincter (Miller *et al.* 2016). In addition, the flap valve is a musculomucosal fold opposite the lesser curvature of the stomach made up of the intraluminal extension of the angle of His (Hill *et al.* 1996; Thor *et al.* 1987). During gastric filling, the fundus expands and the flap valve approximates the lesser curvature of the stomach, enhancing the anti-reflux barrier strength.

The main mechanisms of development of GORD are through an abnormally low resting LOS pressure which permits gastro-oesophageal reflux whenever the stomach pressure exceeds the LOS pressure, transient LOS relaxations, and the presence of hiatal hernia (De Giorgi *et al.* 2006). Factors which contribute to decreased resting LOS pressure and increased transient LOS relaxations include high-fat meals and alcohol, caffeine and smoking (De Giorgi *et al.* 2006). In one study comparing patients with GORD and healthy subjects, the distal component of the dual high-pressure zone of the GOJ was found to be absent in patients with GORD, leading the authors to conclude that the distal muscarinic smooth muscle pressure component (gastric sling/clasp fibre component) is defective in GORD patients (Miller *et al.* 2009). Hiatal hernia is a frequent finding in patients with GORD and the term was used almost synonymously with GORD in the past (Hyun & Bak 2011). Most studies report that a hiatal hernia is present when the proximal stomach is displaced proximally through the hiatus into the chest resulting in at least a 2cm axial separation between the LOS and crural diaphragm (Cameron 1999; van Herwaarden *et al.* 2004). The LOS and crural diaphragm are misaligned, resulting in a less effective anti-reflux barrier and

more abnormal reflux episodes via a lower resting LOS pressure and more frequent transient LOS relaxations (De Giorgi *et al.* 2006). The hernia sac may also act as a reservoir for acidic substances, which are then regurgitated into the distal oesophagus during swallowing-induced LOS relaxation (De Giorgi *et al.* 2006), leading to impaired acid clearance in GORD.

Fundoplication aims to restore the anti-reflux barrier by reducing the hiatal hernia if present, realigning the intrinsic and extrinsic GOJ sphincter, removing the hernia sac, closing the crural diaphragm with sutures to prevent recurrent hiatal herniation, and wrapping the stomach fundus around the distal oesophagus to enhance the resting LOS tone and reduce transient LOS relaxations.

1.4.2 Length of fundoplication

Originally, Nissen performed the fundoplication with a long 5cm wrap of the fundus around the intra-abdominal oesophagus (Nissen 1956). The average expected fundoplication length now is about 2cm, ranging from 1.5cm to 3cm, estimated intra-operatively by placing three sutures close together along the anterior portion of the fundoplication (Mickevicius *et al.* 2013; Tian *et al.* 2015).

A too-long fundoplication may cause increased resistance to bolus flow through the GOJ, experienced symptomatically as dysphagia. DeMeester *et al.* reported a significant reduction of dysphagia rates with a shorter fundal wrap length of a 1cm compared to 4cm Nissen fundoplication (21% vs 3%, $p < 0.01$) (DeMeester *et al.* 1986). Flaws of this study include being non-blinded, non-randomised, introducing a number of different technical modifications across four different timepoints over a series of consecutive patients, and it did not eliminate learning curve bias (Myers 2016). Following this study, objective

assessment of fundoplication length and its association with persistent dysphagia has surprisingly not been widely studied in well-designed trials.

A single randomised controlled trial comparing the construction of a fundal wrap of 3.0cm and 1.5cm-long Nissen fundoplication (n=38 and n=38 in each arm respectively) found a higher rate of significant dysphagia (grade 2 and above) in the 3.0cm compared to 1.5cm group (25.8% vs 9.1%) at 1 year, but that this difference equalised at the 5-year follow up (Mickevicius *et al.* 2008; Mickevicius *et al.* 2013). In this study, dysphagia was assessed using a 6-point Likert scale where 0=no symptoms and 5=very severe. No patients underwent dilatation of the GOJ nor re-operation for dysphagia (Mickevicius *et al.* 2013).

In a non-randomised study, the length of the Nissen fundoplication as measured on post-operative barium swallow (> 3cm, n=20 vs ≤ 3cm, n=19) did not result in a difference in post-operative dysphagia scores at 1 month (Altun *et al.* 2012). Interestingly, a wrap of approximately 3cm was created intra-operatively without the use of a ruler, but the narrowed segment length measured post-operatively ranged between a mean of 2.5cm in the ≤ 3cm group and 4.0cm in the > 3cm group. Dysphagia was graded on a 5-point scale between 0 (continuously) and 5 (none). This study only evaluated the frequency of dysphagia symptoms, and did not account for severity of dysphagia and whether dysphagia to solids was experienced. Assessing dysphagia and the narrowed segment length at 1-month after surgery may be too early, as patients in both groups had a worsening of dysphagia grade at 1-month compared to pre-operatively. This is likely due to post-surgical oedema and inflammation in the early post-operative period. Thus, this study may have missed an association between narrowed segment length and troublesome dysphagia rates by assessing dysphagia and narrowed segment length too early.

Scheffer *et al.* reported that construction of a floppy 3.0-3.5cm 360° fundoplication resulted in an increase in the manometric GOJ length post-operatively compared to pre-operatively (mean \pm standard error of mean (SEM): 36.6 ± 1.7 mm vs 26.8 ± 1.6 ; $P < 0.01$) (Scheffer *et al.* 2005). In this study, the length of fundoplication constructed intra-operatively would appear to correspond with the high-pressure zone (HPZ) on manometry. However, the relationship between manometric length of fundoplication and post-operative dysphagia was not evaluated in this study.

Yamamoto *et al.* found that patients with post-operative dysphagia had a significantly longer HPZ length (3.17 ± 0.66 cm vs 2.57 ± 0.85 cm; $P = 0.020$) compared to patients without dysphagia (Yamamoto *et al.* 2016). A longer HPZ length (≥ 4 cm) also correlated with more severe dysphagia compared to a shorter HPZ (≤ 2 cm) ($P=0.01$). Unfortunately, operation details of the length of fundoplication created was not available.

Based on the above, the relationship between length of fundoplication and dysphagia is inadequately explored, and warrants closer examination in further clinical studies.

1.4.3 Anterior displacement and angulation of distal oesophagus

Several authors undertaking barium studies, observed that the distal oesophagus is displaced anteriorly after fundoplication, and propose that this may relate to post-operative dysphagia (Herbella *et al.* 2009; Watson *et al.* 2001). A representative image on barium swallow of normal post-operative findings are shown in Figure 1. In addition to anterior displacement (Figure 2), there may also be more acute angulation (anteriorly) of the posterior distal oesophageal wall (Figure 3) leading to a change in axis of the GOJ relative to the distal oesophagus (Figure 4). Anterior angulation may occur from either passage of the

fundal wrap posteriorly around the distal oesophagus, or may be due to the posterior hiatal repair pushing the distal oesophagus anteriorly at the level of the hiatus, and is thus a potential cause of dysphagia.

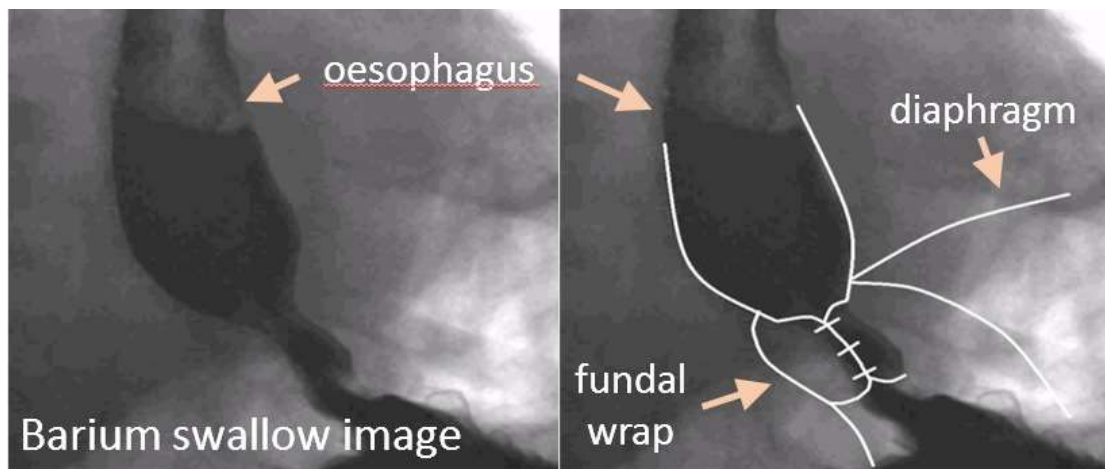


Figure 1: Representative image of GOJ on barium swallow (left) with artistic overlay (right)

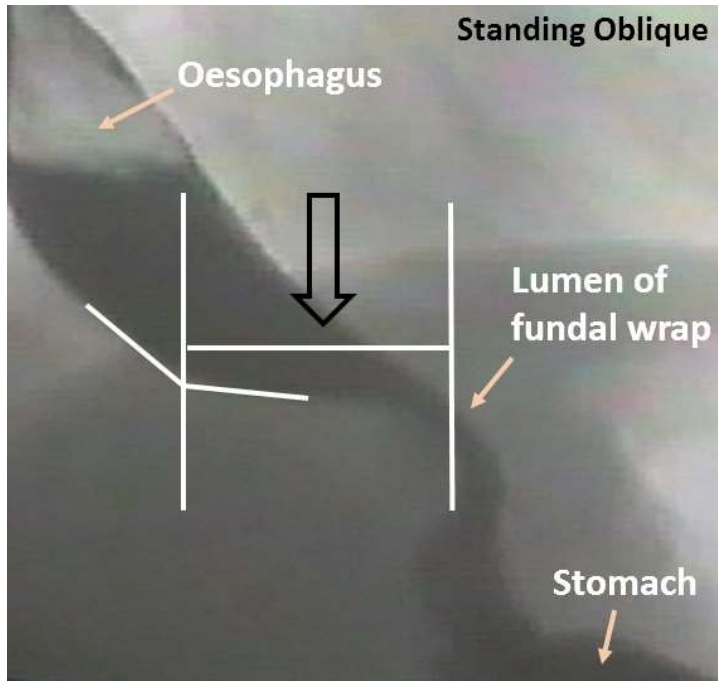


Figure 2: Illustration of anterior displacement of distal oesophagus (black arrow)

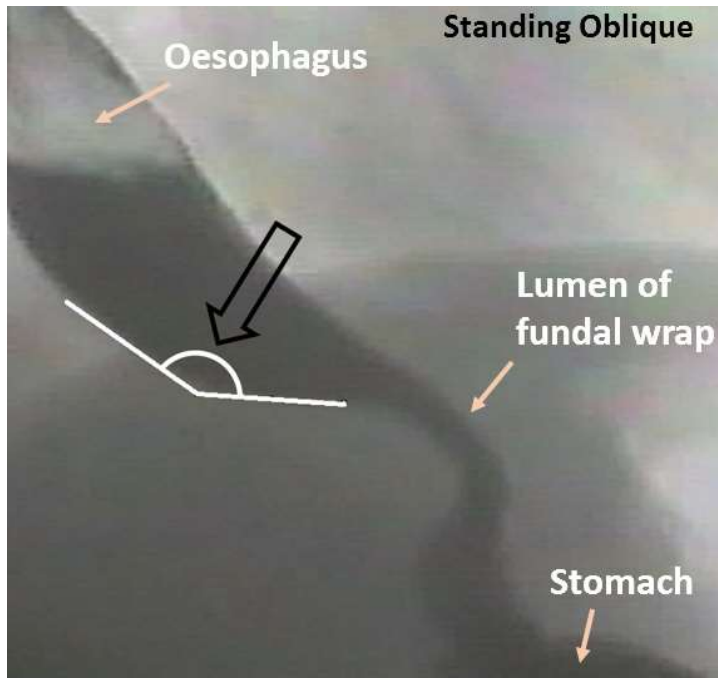


Figure 3: Illustration of anterior angulation of the posterior distal oesophageal wall (black arrow)

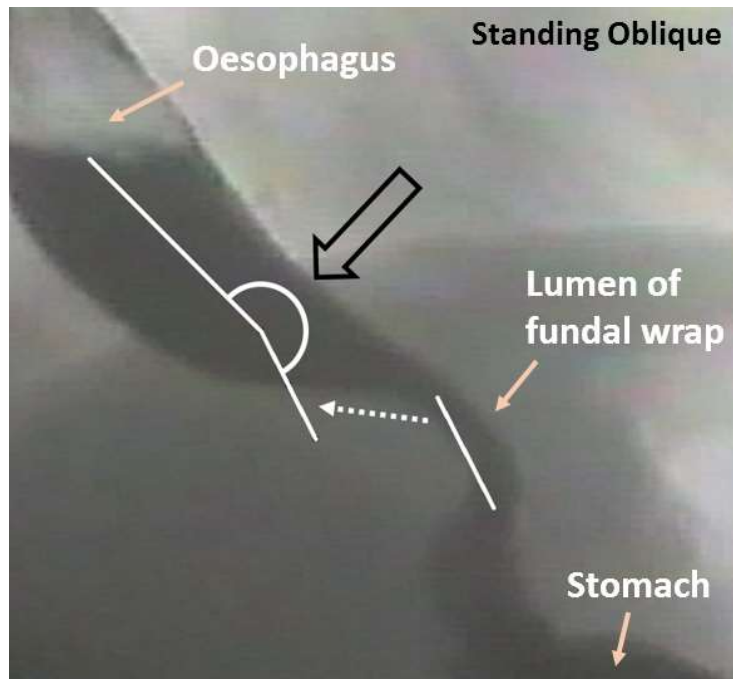


Figure 4: Axis change of gastro-oesophageal junction relative to distal oesophagus (block arrow). White dotted arrow shows translocation of distal axis to easily demonstrate axis change.

In a prospective double-blind study of 108 patients randomised to anterior vs posterior hiatal repair with a total fundoplication (n=47 and n=55 respectively), the incidence and severity of dysphagia between both groups were similar at up to 5 years' follow-up (Watson *et al.* 2001; Wijnhoven *et al.* 2008). Dysphagia was assessed by several methods including the presence or absence of dysphagia for lumpy solids, soft solids and liquids, visual analogue scale (0=no dysphagia, 10=total dysphagia) for solids and liquids, and a modified Dakkak & Bennett score (0=no dysphagia, 45=severe dysphagia) (Watson *et al.* 2001). At 10 years, dysphagia for lumpy solids was more common in the posterior hiatal repair group (39.5% vs 14.0%; $P = 0.01$) while the other 6 dysphagia assessment scores were not found to be different (Chew *et al.* 2011). However, the posterior hiatal repair group required significantly more surgical re-operations for dysphagia than the anterior hiatal

repair group (11% vs 0%; $P = 0.03$) in order to achieve the similar dysphagia rate with the anterior hiatal repair group at 6 months (Watson *et al.* 2001). This was much higher than the usually reported re-operation rate associated with posterior hiatal repair of 1% (Watson *et al.* 2001). This study found that anterior hiatal repair was not inferior to posterior hiatal repair with regard to heartburn control or incidence of para-oesophageal hernia. Therefore, additional studies are required to confirm if anterior hiatal repair provides any advantage in reducing post-operative dysphagia.

In the literature, the rate of re-operation for dysphagia after laparoscopic anti-reflux surgery ranges from 1.8% to 10.8% (Stefanidis *et al.* 2010). Lamb *et al.* studied long-term outcomes of 109 patients after re-operation surgery following laparoscopic fundoplication. (Lamb *et al.* 2009). The primary procedure consisted of either Nissen 360° fundoplication (83 patients), posterior 270° fundoplication (four patients), anterior 180° fundoplication (16 patients) and anterior 90° fundoplication (six patients) (Lamb *et al.* 2009). Out of 52 patients undergoing late re-operation for dysphagia after fundoplication, 26 were found intra-operatively to have a tight hiatus as the cause of dysphagia (Lamb *et al.* 2009), requiring hiatal-widening surgery with or without conversion to a partial wrap. Of the 26 patients, eight had dense hiatal fibrosis following 360° fundoplication. In contrast, 12 out of 52 patients undergoing re-operation for dysphagia were found to have a tight wrap as the cause for dysphagia (Lamb *et al.* 2009). The mechanism of hiatal fibrosis resulting in hiatal stenosis remains poorly understood and may be associated with diathermy dissection of the oesophagus during laparoscopic fundoplication (Watson *et al.* 1995b). The study by Lamb *et al.* highlights the importance of research into operative technique of hiatal repair during primary fundoplication, including methods to avoid an excessively tight hiatus or to prevent hiatal fibrosis.

A study by Herbella *et al.* set out to explore whether posterior hiatal repair of an enlarged hiatal defect, which could lead to anterior displacement of the oesophagus, may contribute to dysphagia after surgery. Herbella *et al.* measured the oesophageal antero-posterior angulation in the lateral view in order to establish 'normal' values in 100 patients undergoing barium swallow for various reasons (not described) and compared this to 32 patients who underwent either a total or partial posterior fundoplication with routine hiatal repair (Herbella *et al.* 2009). Results of this study were not differentiated according to fundoplication type and details regarding the number total or partial posterior fundoplications performed were not provided. There was no significant difference in the antero-posterior angulation of the mid-oesophagus between the 'normal' group and post-fundoplication group ($150.4^{\circ} \pm 10.7^{\circ}$ vs $146.6^{\circ} \pm 11.7^{\circ}$; $P = 0.1$). Among post-operative patients with and without new-onset dysphagia ($n=10$ vs $n=19$), the authors found similar degrees of angulation of the oesophagus for both groups ($P = 0.2$, data values not reported) (Herbella *et al.* 2009). It appears dysphagia of any severity was included (without characterisation of dysphagia for solids or liquids), and the oesophageal angulation in the dysphagia group may be heterogenous with less angulation in patients with mild dysphagia. Thus, the authors may have missed an association between oesophageal angulation and new-onset dysphagia. Another limitation of this study is that only 12 patients underwent a pre-operative barium swallow that allowed comparison with post-operative studies, making it difficult to conclude that surgery does not cause an increase in antero-posterior angulation of the mid-oesophagus.

In the above study, the number of sutures used for posterior hiatal repair correlated with the degree of anterior angulation of the oesophageal body (Herbella *et al.* 2009). Using this methodology *i.e.* the number of posterior hiatal sutures as a proxy for degree of anterior

angulation, Stiven *et al.* found no association between the number of sutures and severity of dysphagia using the Dakkak & Bennett dysphagia score at 1 year after primary para-oesophageal hernia repair with partial posterior fundoplication (Stiven *et al.* 2013). In this non-randomised study, calibration of fundoplication and hiatal repair with a 56 Fr intra-oesophageal bougie was omitted partway through the study, which may have affected the degree of hiatal narrowing. However, the authors did not provide a subgroup analysis showing the numbers or outcomes for the patients who underwent surgery with or without use of a bougie. The number of sutures may be an unreliable measure due to varying size of the hiatal defect, differing inter-suture depth and differing spacing of sutures by individual surgeons. Directly measuring the oesophageal body angulation or the distal oesophagus adjacent to the GOJ may be a more accurate measurement method.

In summary, only one study objectively measured anterior angulation of the oesophageal body using barium swallow in relation to post-fundoplication dysphagia. It remains unclear if anterior as opposed to posterior hiatal repair reduces the rate of post-fundoplication dysphagia. In addition, the impact of posterior vs anterior fundoplication on distal oesophageal anterior displacement and angulation has not been evaluated thus far. Further studies are required to ascertain proof of concept that measurement of anterior displacement and angulation of the distal oesophagus near the GOJ are feasible, reliable and bear a statistically significant relationship with clinically significant post-operative dysphagia. Following this, alterations in surgical technique may be explored.

1.4.4 Fundoplication luminal opening diameter

One physiological mechanism for the efficacy of fundoplication is that it reduces the distensibility of the GOJ, compared to non-surgically treated patients with GORD (Kessing *et al.* 2015). The GOJ luminal opening diameter, as measured using concurrent manometry and barium swallow, is reduced after both Nissen and anterior 180° fundoplication (Anderson *et al.* 1998; Kahrilas *et al.* 1998). In a sub-study of a RCT, for a small number of patients (n=32), patients after Nissen fundoplication had a significantly smaller radiologically measured GOJ opening diameter compared to patients after anterior 180° fundoplication (9mm vs 12mm; $P = 0.003$) (Anderson *et al.* 1998). However, this was not associated with a difference in dysphagia for liquids or solids between the two groups at 3 months after surgery (Anderson *et al.* 1998). Kahrilas *et al.* compared the hiatal opening and axial movement of the GOJ among normal subjects, patients with hiatal hernia and patients after laparoscopic Nissen fundoplication (Kahrilas *et al.* 1998). The authors found that in all groups, the constriction limiting flow to the stomach was at the hiatus and this was substantially narrowed after fundoplication. There was reduced axial GOJ movement in patients with hiatal hernia and patients after fundoplication (Kahrilas *et al.* 1998).

Further studies using barium swallow with a larger cohort are required to examine any association between the GOJ luminal opening diameter and post-operative dysphagia.

1.4.5 Hiatal opening

It is now increasingly recognised that hiatal closure is an important aspect of fundoplication surgery, yet may be associated with troublesome dysphagia. Granderath *et al.* evaluated 50 patients referred for recurrent, persistent, or new-onset dysphagia after

laparoscopic anti-reflux surgery to identify the morphologic cause of post-operative dysphagia (Granderath *et al.* 2005). Following barium swallow and subsequent examination during pneumatic dilatation or re-operation, it was confirmed that a too-tight hiatus was the cause of dysphagia in 36% of patients, whereas a tight wrap accounted for only 10% of patients with post-operative dysphagia (Granderath *et al.* 2005). In the remaining patients, partial or complete intra-thoracic wrap migration as a result of a too-loose wrap was the cause of dysphagia. Intra-thoracic wrap migration was suspected on upper gastrointestinal endoscopy, observed on barium swallow studies then confirmed by intra-operative inspection during re-operation surgery (Granderath *et al.* 2005)

In order to prevent a too-tight or too-loose hiatal closure, measuring the hiatal defect would be useful to accurately compare crural closure techniques. Koch *et al.* described a method to measure the hiatal defect size intra-operatively using an endoscopic ruler brought intra-abdominally during laparoscopic Toupet 270° fundoplication with simple sutured crura and posterior onlay of mesh prosthesis (Koch *et al.* 2011). The subjects of this study included 54 patients with large hiatal hernia. To measure the hiatal defect size, the right and left crus and crural commissure were first dissected exactly. The crural length was measured from the crural commissure up to the edge where the pars flaccida began. After this, the circuit between both crural edges was measured. These two measurements allowed the hiatal surface area (HSA) to be calculated. Using this method, following primary fundoplication, patients with recurrent hiatal herniation (diagnosed on post-operative barium swallow) had a larger HSA than patients without recurrent hiatal herniation after fundoplication (mean HSA for patients without recurrent hernia (n=19) = 7.50cm²; mean HSA for asymptomatic patients with recurrent hernia (n=4) = 9.50cm²; mean HSA for symptomatic patients with recurrent hernia (n=1) = 16.09cm² (Koch *et al.* 2011). This study

highlights that a larger hiatal defect size is associated with a higher risk of recurrent hernia, especially symptomatic recurrent hernia.

In an innovative technique of calibrating crural closure, Mandovra *et al.* described inserting through a laparoscopic port, a 7 French Fogarty catheter after crural closure, and inflating it with 1 cc of air at the repaired hiatus (Mandovra *et al.* 2020). This allowed quantitative assessment of the adequacy of crural closure while assessing adequate space to allow food bolus passage through the GOJ without causing mechanical obstruction at the level of the repaired hiatus (Mandovra *et al.* 2020). None of the 102 patients in this study developed long-term dysphagia.

Hiatal closure has a significant impact on post-operative dysphagia. Quantitative measurement of hiatal closure shows promise and further studies in well-designed trials are required to assess if this technique results in a reduction of post-operative dysphagia.

1.5 AIMS

To date, efforts to reduce the risk of post-operative dysphagia mainly included modifying technical aspects of surgery based on reasonable assumptions, not on objective data informing the anatomical causes of dysphagia. Despite advances over almost 30 years of laparoscopic fundoplication, there remains a low risk of persistent post-operative dysphagia. The overarching aim of this thesis is to define and quantify subtle anatomical features after surgery which may relate to dysphagia, in the presence of an apparently technically successful operation. This would provide a framework for further studies to evaluate these anatomical features, with a view to identifying crucial technical steps requiring care, calibration or modification during fundoplication with hiatal repair surgery.

The clinical research presented in this thesis was undertaken to address the following specific aims:

1. To evaluate the inter- and intra-observer reliability of novel objective measurements on barium swallow studies of anatomical features of the GOJ after fundoplication with hiatal repair.
2. To determine the relationship between novel objective measurements and post-operative dysphagia.

CHAPTER 2

QUANTIFICATION OF FLUOROSCOPIC FUNDOPLICATION ANATOMY: INTER- AND INTRA-OBSERVER RELIABILITY

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Principal Author

Name of Principal Author (Candidate)	Siang Wei Gan
Contribution to the Paper	Co-conceived and designed the study, performed literature search, conceived novel approach for data analysis, undertook novel analysis for data, performed statistical analysis and interpreted the study findings, drafted the manuscript including critical revision for submission for publication.
Overall percentage (%)	70%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 25/11/20

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

- i. the candidate's stated contribution to the publication is accurate (as detailed above);
- ii. permission is granted for the candidate to include the publication in the thesis; and
- iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Name of Co-Author	Jennifer C Myers		
Contribution to the Paper	Co-conceived and designed the study, supervised the data analysis phase of the study, contributed to interpretation of findings, contributed to drafting the manuscript, including critical revision and approval of final manuscript.		
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2.2 ABSTRACT

Background: Ascertaining the cause of troublesome post-fundoplication dysphagia remains challenging. Subtle changes of gastro-esophageal junction (GEJ) anatomy may be contributory. We aim to assess inter- and intra-observer reliability of fluoroscopic measurements of post-fundoplication anatomy.

Methods: At 6-12 months after laparoscopic fundoplication, 31 patients underwent structured barium swallow with video-fluoroscopic recording of views: standing antero-posterior; standing oblique (x2); prone oblique (x2); and prone oblique with continuous free drinking. A primary observer recorded 11 variables of GEJ anatomy for each view, repeated 3-months later, forming two datasets to assess intra-observer consistency. Inter-observer reliability was determined using a dataset each from the primary observer, and two medical students (after training). Intra-class correlation coefficients (ICC) were based on a two-way mixed-effects model (ICC agreement: 0.40-0.59 'fair'; 0.60-0.74 'good'; 0.75-1.00 'excellent').

Results: Inter-observer reliability was good to excellent for 47 of a total 66 measurements. Measures of maximal esophageal diameter *cf.* wrap opening diameter and posterior esophageal angle showed high inter-observer reproducibility for all views (ICC range 0.84-0.91; 0.68-0.80 respectively). Inter-observer agreement was good to excellent for 5/6 views when measuring anterior GEJ displacement and axis deviation (ICC range 0.56-0.79; 0.41-0.77 respectively). Measures of fundoplication wrap length showed lower reproducibility. Of all views, prone oblique measurements showed highest reproducibility (good to excellent agreement in 19/22 measurements). Intra-observer consistency was excellent for 98% of measurements (ICC range 0.74-0.99).

Conclusions: Objective fluoroscopic measurements of post-fundoplication gastro-esophageal junction anatomy are reproducible and may prove useful in future studies for interrogation of anatomical features contributing to post-fundoplication dysphagia.

2.3 INTRODUCTION

Laparoscopic fundoplication is commonly used to treat gastro-esophageal reflux disease (GERD) (Fuchs *et al.* 2014). Persistent and troublesome dysphagia is an uncommon but feared adverse effect of surgery (Blom *et al.* 2002). Technical modifications such as partial fundal wraps, reduce but do not eliminate the risk of dysphagia (Ma *et al.* 2012). While routine division of the short gastric vessels has not shown a benefit for lower dysphagia rates after fundoplication (Kinsey-Trotman *et al.* 2018).

Troublesome dysphagia often leads to a range of diagnostic investigations. Barium swallow is usually the first employed for visualization of both morphology and function of the gastro-esophageal junction (GEJ) (Baker & Einstein 2014; Carbo *et al.* 2014). Many structural causes of dysphagia can be revealed on barium swallow, including a too-long or too-tight wrap, para-esophageal herniation, disrupted wrap, recurrent hiatal hernia, intra-thoracic migration of the wrap, and slippage of the proximal stomach through an intact wrap (Baker & Einstein 2014; Carbo *et al.* 2014). In many patients however, no cause is found for troublesome dysphagia using current available diagnostic procedures. Moreover, a systematic review found that in 43% of patients undergoing re-do surgery because of troublesome dysphagia, no anatomical abnormality was found during inspection of the GEJ and fundoplication at re-operation (Furnee *et al.* 2009).

In the search of further modifications of primary surgery that may prevent or reduce post-operative dysphagia, it would be useful to have diagnostic criteria for anatomical causes using a widely available and inexpensive modality, such as barium swallow. Barium swallow findings are highly dependent on the accuracy of the observer (Raeside *et al.* 2012).

Nevertheless, studies evaluating video-fluoroscopy of swallowing found that accuracy can be increased using observer training and improved definitions of measures (Baijens *et al.* 2013).

Anterior displacement and angulation of the distal esophagus, as observed empirically on barium swallows, may relate to dysphagia (Herbella *et al.* 2009; Watson *et al.* 2001). However, this has not been definitively demonstrated in the few objective studies published to date (Herbella *et al.* 2009; Stiven *et al.* 2013). We propose that these features, in addition to other anatomical measures of length and diameter, could be utilized to explore correlations with dysphagia if standardized objective measurements are performed using a structured protocol for barium swallows. Therefore, we undertook a study to evaluate inter- and intra-observer reliability of objective measurements of post-fundoplication anatomical features, using structured barium swallows with video-fluoroscopy.

2.4 METHODS

Consecutive patients presenting for primary fundoplication due to GERD were invited to participate in this prospective cohort study. Exclusion criteria included atypical GERD symptoms, large hiatal hernia >5cm, or a primary motility disorder such as scleroderma or achalasia. The inter- and intra-observer reliability of anatomical GEJ measurements were evaluated on structured barium swallow studies conducted approximately six months after fundoplication surgery. The Human Research Ethics Committee, Royal Adelaide Hospital approved the protocol (#990614a). All participants gave written informed consent.

Patients were recruited over a six-year period, prior to undergoing fundoplication at either the Royal Adelaide Hospital, a tertiary referral center and teaching hospital of the University of Adelaide, or one of three private hospitals in Adelaide, Australia. Thirty-one patients underwent a total or partial anterior 90° laparoscopic fundoplication by three experienced upper gastrointestinal surgeons at the aforementioned centers. The choice of extent of fundal wrap was determined by informed patient preference.

At 6-12 months after fundoplication, a structured barium swallow protocol with video-fluoroscopy was used to record 20mL upright or 15mL prone bolus swallows (Liquid Polibar® barium sulphate suspension [100% w/v; 56% w/w], E-Z-EM Inc. Westbury, New York USA) for these acquisition views: standing antero-posterior (SAP), 2x standing oblique (SOB), 2x prone oblique (POB), and prone oblique with continuous free drinking (PCont, 150mL cup of 50% Polibar/water). The studies were recorded at 25 frames per second and stored in digital format using digital imaging and communications in medicine (DICOM). Included in the radiological field of vision was swallow onset and fluoroscopic chase of barium head-of-

bolus passing through the esophagus, with a focus on the GEJ and distal half of the esophagus.

The digital fluoroscopic images were extracted from the hospital's picture archiving and communication system (PACS) in DICOM file format. VLC media player (VideoLAN) and digital image analysis software (ImageJ1, W Rasband, National Institute of Health, University of Wisconsin, USA) were utilized for data analysis. The primary observer reviewed the digital video files for each patient's six acquisition views several times, before taking a screenshot that best represented optimal flow and GEJ anatomy in each view. Eleven specific measurements that characterized GEJ features were recorded for each screenshot (Figure 1 and Table 1) to evaluate GEJ anterior displacement, angulation and deviation of the axis, luminal diameter of the distal esophagus and fundal wrap canal, and fundal wrap length. Two separate datasets, collected for intra-observer consistency analysis, were generated three months apart to reduce recall bias by the primary observer.

Two senior medical students, with no prior experience in interpreting barium swallows, were enlisted and trained by the primary observer in two 2-hour sessions conducted 2-weeks apart. Training included interpretation of fluoroscopy images, demonstration of the method of recording measurements, assessment and correction of the students' practice measurements. The students then independently generated a set of measurements each. Inter-observer reliability was evaluated using these two datasets and one dataset from the primary observer.

To determine measurements on a metric scale, adjustment for magnification was guided by known distances between radio-opaque tantalum markers within an esophageal catheter placed transnasally at the time of fluoroscopy. Pixel units obtained by digital

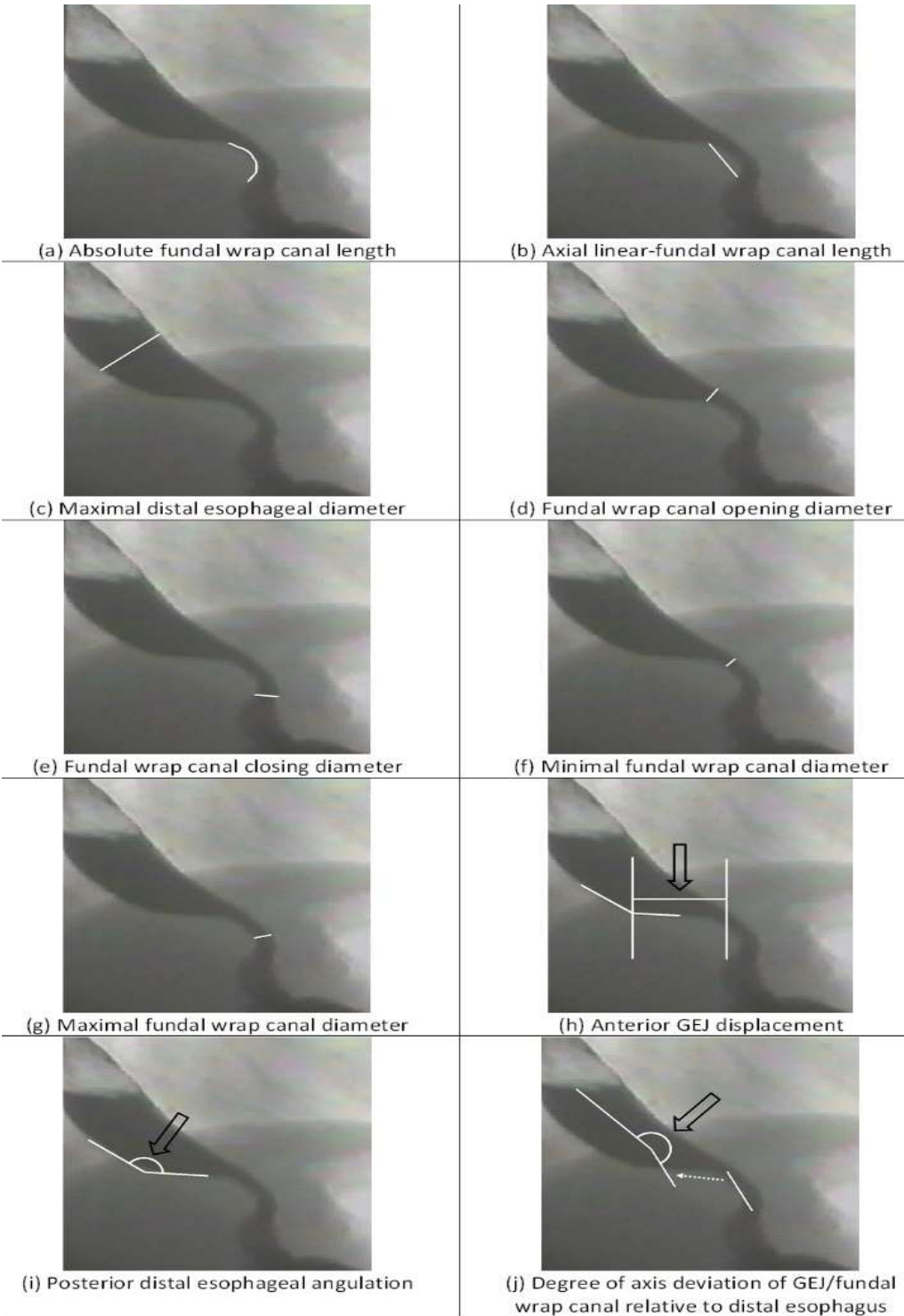
software were converted to centimeters (cm) by obtaining the ratio of pixels to cm for the known distance between markers observed in each fluoroscopic view.

Statistical Analysis

Statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Reproducibility of measurements was undertaken irrespective of operative procedure. To this end, intra-class correlation coefficients (ICCs) were calculated for inter- and intra-observer reliability using a consistency of agreement, two-way mixed-effects model with a confidence interval of 95%. ICC values were interpreted as 'excellent' through to 'poor' agreement as per Cicchetti (Table 2) (Cicchetti 1994). Data are presented as mean \pm standard error, number, n (%) or ICC (95% confidence interval).

Figure 1: Measurements of anatomical features of the post-fundoplication GEJ



White line in 1a-1g and black arrow in 1h-1j show the length or angle measured; White arrow in 1j depicts translocation of the axis of GEJ/fundal wrap canal, for calculation of degree of axis deviation.

Table 1: Description of objective measurements methodology

Anatomical feature	Measurement methodology
Absolute wrap length	Free-hand measurement from proximal to distal end of the fundal wrap canal, along the posterior border. Proximal wrap endpoint defined as narrowed region at the top of the fundal wrap canal; Distal wrap endpoint defined as the point where the fundal canal begins to widen (Figure 1a).
Axial linear-wrap length	Linear measurement from proximal to distal endpoint of the fundal wrap canal, as defined above (Figure 1b).
Maximal distal esophageal diameter	Measurement of greatest distal esophageal diameter perpendicular to direction of bolus flow, proximal to 'esophageal tapering' of contrast above the GEJ (Figure 1c).
Wrap opening diameter	Diameter at proximal endpoint of the fundal wrap canal (Figure 1d).
Wrap closing diameter	Diameter at distal endpoint of the fundal wrap canal (Figure 1e).
Maximal distal esophageal diameter <i>cf.</i> wrap opening diameter	Absolute difference between maximal distal esophageal diameter and wrap opening diameter.
Minimal wrap diameter	Smallest diameter within the fundal wrap canal (Figure 1f).
Maximal wrap diameter	Largest diameter within the fundal wrap canal (Figure 1g).
Anterior GEJ displacement	Linear horizontal distance between the posterior aspect of distal endpoint of fundal wrap canal (vertical line) and the point of change in angle of contrast flow in the distal esophagus (Figure 1h; Figure 1i).
Posterior distal esophageal angulation	The point of greatest angulation at the intersection of the posterior esophageal body wall and 'point of esophageal tapering' of contrast (Figure 1i).
Axis deviation of GEJ/fundal wrap canal <i>cf.</i> esophagus	The axis lines of the distal esophagus and fundal wrap were identified. The axis line of the fundal wrap is translocated to intersect the axis line of the distal esophagus, then the angle between the two axes measured clockwise. For views with inferior angulation, the angle would be >180° (Figure 1j).

Table 2: Intra-class correlation coefficient interpretation

ICC Value	Interpretation
0.75 - 1.00	Excellent
0.60 - 0.74	Good
0.40 - 0.59	Fair
0.00 - 0.39	Poor

Reference: Cicchetti *et al.* (Cicchetti 1994)

2.5 RESULTS

All thirty-one subjects enrolled (19M: 12F, mean age 47.0 ± 2.6 years) underwent structured fluoroscopy after fundoplication (mean 9.3 ± 0.7 months). Approximately 16% of acquisition views were not available for measurements, in the first few patients' fluoroscopic studies due to technical error, or due to patients being unable to tolerate multiple barium swallows. Data measurements by all observers were completed on all the available views.

Inter-observer reliability

For the eleven parameters assessed in six fluoroscopic views, the overall inter-observer reliability ICCs demonstrated excellent and good agreement for 24/66 (36%) and 23/66 (35%) measurements respectively (Table 3). Thus, for three observers, measurements were considered reliable for a total of 47/66 views (71%). Three parameters demonstrated consistently high reproducibility in all views (ICC good/excellent agreement), namely maximal distal esophageal diameter; maximal distal esophageal diameter *cf.* wrap opening diameter; and posterior distal esophageal angulation (ICC range 0.74-0.78; 0.84-0.91; 0.68-0.80 respectively). In 5/6 views, ICCs demonstrated good/excellent agreement for wrap closing diameter; minimal wrap diameter; anterior GEJ displacement and axis deviation of GEJ *cf.* esophagus (ICC range 0.50-0.85; 0.58-0.93; 0.56-0.79; 0.41-0.77 respectively).

Both absolute and axial linear-wrap length measurements were poorly reproducible, with good ICCs in 2/6 (33%) and 1/6 (17%) views respectively. Measures of diameter showed better agreement amongst observers, with ICCs demonstrating good/excellent agreement for 22/30 (73%) measurements.

The greatest inter-observer reproducibility was found for measurements in the prone oblique view, with ICCs showing good/excellent agreement in 19/22 (86%) measurements (Table 4). The measurements that were less reliable in this fluoroscopic view were the absolute and axial linear-wrap length measurements.

Intra-observer reliability

All parameters for each fluoroscopic view demonstrated high intra-observer consistency, with ICCs showing excellent agreement for all measurements except one (Table 5). ICCs ranged from 0.79-0.93 for absolute and axial linear-wrap length measurements, and from 0.80-0.99 for all measurements of diameter. The highest ICC of 0.99 was found for measurements of maximal distal esophageal diameter and minimal wrap diameter. The lowest ICC was found for anterior GEJ displacement (standing oblique view).

Table 3: Inter-observer reliability of anatomical measurements of the post-fundoplication GEJ

Anatomical feature	Fluoroscopic acquisition view					
	SAP	SOB1	SOB2	POB1	POB2	PCont
Absolute wrap length	0.30 (-0.28-0.64)	0.43 (-0.05-0.71)	0.23 (-0.43-0.61)	0.61 (0.27-0.80)‡	0.43 (-0.04-0.72)	0.66 (0.25-0.86)‡
Axial linear-wrap length	0.43 (-0.04-0.70)	0.40 (-0.12-0.70)	0.24 (-0.42-0.62)	0.38 (0.15-0.61)	0.44 (-0.03-0.72)	0.69 (0.31-0.87)‡
Maximal distal esophageal diameter	0.78 (0.60-0.89)†	0.76 (0.55-0.88)†	0.78 (0.59-0.89)†	0.77 (0.58-0.89)†	0.77 (0.57-0.88)†	0.74 (0.43-0.90)‡
Wrap opening diameter	0.61 (0.29-0.80)‡	0.27 (-0.35-0.63)	0.30 (-0.29-0.65)	0.68 (0.41-0.84)‡	0.63 (0.32-0.82)‡	0.49 (-0.12-0.79)
Maximal distal esophageal diameter <i>cf.</i> wrap opening diameter	0.84 (0.72, 0.92)†	0.90 (0.81-0.95)†	0.84 (0.70-0.92)†	0.89 (0.80-0.95)†	0.91 (0.84-0.96)†	0.86 (0.70-0.94)†
Wrap closing diameter	0.50 (0.09-0.74)	0.64 (0.33-0.82)‡	0.63 (0.31-0.81)‡	0.85 (0.72-0.92)†	0.85 (0.73-0.93)†	0.84 (0.64-0.93)†
Minimal wrap diameter	0.76 (0.56-0.87)†	0.58 (0.22-0.79)	0.84 (0.71-0.92)†	0.92 (0.85-0.96)†	0.93 (0.86-0.96)†	0.65 (0.23-0.86)‡
Maximal wrap diameter	0.62 (0.31-0.81)‡	0.26 (-0.38-0.63)	0.09 (-0.69-0.54)	0.82 (0.67-0.91)†	0.68 (0.41-0.84)‡	0.55 (0.01-0.82)
Anterior GEJ displacement	0.63 (0.33-0.81)‡	0.73 (0.50-0.86)‡	0.56 (0.18-0.78)	0.69 (0.42-0.84)‡	0.66 (0.36-0.83)‡	0.79 (0.53-0.91)†
Posterior distal esophageal angulation	0.68 (0.42-0.84)‡	0.79 (0.62-0.90)†	0.80 (0.63-0.90)†	0.70 (0.45-0.85)‡	0.72 (0.49-0.86)‡	0.70 (0.34-0.88)‡

Axis deviation of GEJ <i>cf.</i> esophagus	0.72 (0.48-0.85)‡	0.72 (0.48-0.86)‡	0.77 (0.57-0.88)†	0.67 (0.39-0.84)‡	0.76 (0.55-0.88)†	0.41 (-0.30-0.76)
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Table 3 legend:

SAP, standing antero-posterior; SOb1, standing oblique first; SOb2, standing oblique second; POB1, prone oblique first; POB2, prone oblique second; PCont, prone oblique with continuous free drinking. Data are ICC (95% confidence interval); †ICC 'excellent', ‡ICC 'good'.

Table 4: Inter-observer reproducibility of measurements by view type

Acquisition view	ICC 'Excellent'	ICC 'Good'	ICC 'Fair'	ICC 'Poor'	Total number measurements†
Standing antero-posterior	3 (27%)	5 (46%)	2 (18%)	1 (9%)	11
Standing oblique	8 (36%)	4 (18%)	4 (18%)	6 (27%)	22
Prone oblique	10 (46%)	9 (41%)	2 (9%)	1 (4%)	22
Prone oblique with continuous free drinking	3 (27%)	5 (46%)	3 (27%)	0 (0%)	11
TOTAL	24 (36%)	23 (35%)	11 (17%)	8 (12%)	66

†For 6 views, 11 measurements for each view.

Table 5: Intra-observer reproducibility of anatomical measurements of the post-fundoplication GEJ.

Anatomical feature	Fluoroscopic acquisition view			
	SAP	SOB	POB	PCont
Absolute wrap length	0.92 (0.83-0.96)	0.79 (0.55-0.90)	0.87 (0.72-0.94)	0.87 (0.65-0.95)
Axial linear-wrap length	0.93 (0.84-0.96)	0.80 (0.58-0.91)	0.86 (0.70-0.93)	0.87 (0.66-0.95)
Maximal distal esophageal diameter	0.95 (0.89-0.97)	0.99 (0.97-0.99)	0.97 (0.94-0.99)	0.99 (0.97-1.00)
Wrap opening diameter	0.92 (0.83-0.96)	0.94 (0.87-0.97)	0.89 (0.77-0.95)	0.93 (0.83-0.97)
Maximal distal esophageal diameter <i>cf.</i> wrap opening diameter	0.93 (0.86-0.97)	0.97 (0.94-0.99)	0.95 (0.99-0.98)	0.95 (0.88-0.98)
Wrap closing diameter	0.94 (0.89-0.97)	0.80 (0.57-0.91)	0.96 (0.92-0.98)	0.92 (0.78-0.97)
Minimal wrap diameter	0.91 (0.81-0.95)	0.96 (0.91-0.98)	0.99 (0.98-0.99)	0.92 (0.79-0.97)
Maximal wrap diameter	0.89 (0.78-0.95)	0.85 (0.67-0.93)	0.96 (0.91-0.98)	0.93 (0.82-0.97)
Anterior GEJ displacement	0.90 (0.79-0.95)	0.74 (0.44-0.88)	0.96 (0.92-0.98)	0.93 (0.81-0.97)
Posterior distal esophageal angulation	0.80 (0.58-0.90)	0.83 (0.63-0.92)	0.82 (0.63-0.92)	0.94 (0.85-0.98)
Axis deviation of GEJ <i>cf.</i> esophagus	0.96 (0.92-0.98)	0.94 (0.87-0.97)	0.88 (0.75-0.94)	0.90 (0.73-0.96)

Data are ICC (95% confidence interval); Data in bold refers to ICC interpreted as good (*cf.* 'excellent' for all other ICCs).

2.6 DISCUSSION

There are limited studies in the literature that explore objective measures of fundoplication anatomy. In this study, we present data to demonstrate good inter- and high intra-observer reliability for objective fluoroscopic measurements of the post-fundoplication GEJ anatomy. Reliable quantification of post-fundoplication anatomy will inform future exploratory studies to determine whether dysphagia is associated with certain anatomical features.

Dysphagia after fundoplication may relate to esophageal outflow resistance at the GEJ, exacerbated by low distal esophageal contractile vigour (*i.e.* peristaltic pressure) and high residual GEJ pressure on swallow-induced relaxation (Myers *et al.* 2012). Possibly contributing to impaired esophageal outflow are anterior displacement and angulation of the distal esophagus (proximal to the GEJ), occurring due to either posterior hiatal repair undertaken during anti-reflux surgery (Watson *et al.* 2001) or posterior fundoplication elevating the abdominal segment of the esophagus (Lundell 2010). Herbella *et al.* found no difference between the pre- and post-fundoplication distal esophageal antero-posterior angle, nor any correlation of esophageal angle with post-operative dysphagia (Herbella *et al.* 2009). However, their study was limited by small size (12 patients with pre- and post-operative esophagrams) and evaluated only one measure of dysphagia (new dysphagia lasting >10 weeks). Stiven *et al.* used the number of posterior sutures for posterior hiatal repair as a proxy for anterior esophageal angulation, in patients undergoing para-esophageal hernia repair with fundoplication, and found no correlation between the number of posterior sutures and post-operative dysphagia (Stiven *et al.* 2013). Directly measuring

anterior GEJ displacement and angulation on imaging is likely to be a more accurate method, and these measures were found to have good reproducibility in our study.

A too-long or too-tight fundoplication may also cause post-fundoplication dysphagia (Sobrino-Cossio *et al.* 2017). We found that measures of absolute and axial linear-wrap length were poorly reproducible among observers. This may be due to difficulty determining with consistency the proximal and distal endpoints of the fundal wrap on fluoroscopic images. Altun *et al.* measured the 'narrowed segment length' on barium esophagram (classed as $\leq 30\text{mm}$ or $>30\text{mm}$) in patients one month after laparoscopic Nissen fundoplication and found similar post-operative dysphagia scores between the two groups (Altun *et al.* 2012). However, we believe their measurement overestimates the length of fundoplication, as the point where the fundal canal lumen first begins to widen likely marks the distal endpoint of the wrap (Figure 1a). By contrast, in the present study measurements of diameter of the wrap and esophagus were more reliable among observers. We propose that this could be due to better imaging contrast between the wall of the esophagus/fundal wrap and the surrounding thoracic and abdominal cavity.

To our knowledge, no previous study has evaluated reliability of objective anatomical measurements using contrast studies in patients deemed to have an intact fundoplication. There are two published studies that evaluated inter-observer agreement for qualitative interpretation of barium swallows for gross abnormalities of fundoplication failure. Hainaux *et al.* showed good agreement between two radiologists to distinguish between partial and total intra-thoracic wrap migration on fluoroscopy (*kappa* statistic for observer agreement, $\kappa = 0.84$) (Hainaux *et al.* 2002). Another study revealed surgeons are better able to identify normal wrap position on barium studies than radiologists (specificity 91.6% vs 78.9%), and

with greater inter-observer reliability than radiologists ($\kappa = 0.65$, 95% CI 0.59–0.71 vs $\kappa = 0.54$, 95% CI 0.49–0.59) (Raeside *et al.* 2012).

Overall, we found 71% of measurements had good/excellent agreement among all observers. This is comparable to the study by Raeside *et al.* whereby 50% of measures had moderate/good agreement between observers (Raeside *et al.* 2012), and better than studies of video-fluoroscopy of swallowing, where inter-observer agreement was poor for most measures, even among experienced observers (McCullough *et al.* 2001). These studies utilized subjective visual ratings of oropharyngeal function, presence of penetration-aspiration and residue, and timed bolus transit.

Measurements for fluoroscopic views in the prone oblique position had the greatest inter-observer reliability. Prior to the study, we hypothesized that the oblique views would best demonstrate anatomy of the region, due to the orientation of curvatures of the post-fundoplication GEJ. The inconsistency among observers for standing oblique view measurements compared to prone oblique may be due to slower bolus transit in the latter gravity-neutral position, allowing all observers to adequately visualize the GEJ and take the screenshot that best depicted GEJ anatomy. Measurements from the prone oblique view with continuous free drinking were likely less reproducible due to each observer selecting a different screenshot during the prolonged bolus flow time recording. In other published fluoroscopic studies, the right anterior prone oblique position is commonly used to assess esophageal motility and the presence of para-esophageal hernias (Baker & Einstein 2014; Contini & Scarpignato 2002; Watson *et al.* 1997). The findings of the present study indicate that the prone oblique view may have greater clinical utility and it is worth using in future studies exploring anatomical features and dysphagia.

As expected, intra-observer reliability was greater than inter-observer reliability, even with a 3-month interval between collection of duplicate datasets. This may be due to the primary observer being more experienced and consistent in interpreting relevant surgical anatomy across patients and time. This view is supported by McCullough *et al.* who demonstrated higher intra-observer reliability than inter-observer reliability for commonly used video-fluoroscopic swallowing evaluation measures (McCullough *et al.* 2001).

There are several strengths of this study. All observers were blinded to each other's measurements including independently selecting a fluoroscopic image/timepoint from the contrast study to perform anatomical measurements, raising the value of the current study methodology and findings. Greater observer experience is known to increase inter-rater agreement in interpretation of various imaging modalities (Ekberg *et al.* 1988; Erly *et al.* 2002; Moga *et al.* 2018). We assessed inter-observer reliability using a primary observer and two medical students, demonstrating that if inexperienced observers with a little training can achieve good inter-observer agreement, then the same or better can be expected with more experienced clinicians in day-to-day practice. This study evaluated GEJ anatomy through objective measurements, whereas most studies to date have relied upon qualitative visual assessment of fluoroscopy images (Contini & Scarpignato 2002; Hainaux *et al.* 2002; Raeside *et al.* 2012).

A limitation of this study is the relatively small sample size and the use of liquid barium swallows rather than solid bolus swallows such as bread, marshmallow or barium tablet. While adequate training for recording measurements was provided, it is feasible that not all observers followed the recommendation to apply slow-motion playback when selecting the best screenshot image for analysis. In addition, intra-observer reproducibility

was based on measurements from one observer. Further evaluation of intra-observer consistency with a larger sample of observers is needed.

2.7 CONCLUSION

Objective fluoroscopic measurements of the GEJ anatomy after fundoplication demonstrate good reproducibility and are best obtained using prone oblique fluoroscopic views. Measures of diameter, posterior distal esophageal angulation, anterior GEJ displacement and axis deviation showed high levels of agreement, while measures of wrap length were more variable. These novel objective fluoroscopic measurements have potential to be used in future studies to explore correlations of GEJ post-surgical anatomy with dysphagia, with a view to identifying technical steps requiring care or modification during fundoplication surgery.

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CHAPTER 3

IMPACT OF ANATOMICAL CHANGES OF TOTAL AND PARTIAL ANTERIOR FUNDOPLICATION ON TROUBLESOME DYSPHAGIA

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3.2 ABSTRACT

Purpose: To determine if a barium study, via measurements of gastro-esophageal junction (GEJ) anatomy, identifies anatomical features correlating with troublesome dysphagia (TDysph) after laparoscopic fundoplication.

Methods: Thirty-one patients underwent total (TotLF) or partial anterior 90° (PAntLF) fundoplication. After 6-12 months, structured barium studies with fluoroscopy recorded bolus transport during these views: standing AP (SAP), standing oblique (SOB), prone oblique (POB) and prone oblique with continuous free drinking (PCont). Objective measurements on still images of fluoroscopy views included anterior GEJ displacement, axis deviation of GEJ cf. esophagus, posterior distal esophageal angle, and maximal esophageal diameter cf. GEJ opening diameter. Pre- and post-operative dysphagia composite score (range: 0-45, 0=no dysphagia, ≥ 12 =TDysph) was recorded. Associations between dysphagia and fluoroscopic measurements by operation type were assessed with linear regression analysis and linear mixed-effects models.

Results: TDysph was reported by 5/18 TotLF and 4/13 PAntLF patients. After TotLF, patients with TDysph had greater anterior GEJ displacement (SOB, 2.92cm vs 2.31cm, $p=0.04$) and greater magnitude of axis deviation (PCont, 12.3° vs -6.6° , $p<0.003$) than patients with no/mild dysphagia. For patients with worsening post-operative dysphagia (compared to pre-operative) after PAntLF, for every unit increase in the dysphagia score there was a 0.03cm decrease in GEJ opening diameter cf. maximal esophageal diameter (SAP, $p<0.01$).

Conclusion: Anatomical features such as anterior GEJ displacement and axis deviation are associated with troublesome post-fundoplication dysphagia. A small reduction in maximal esophageal diameter cf. GEJ opening diameter associated with worsening dysphagia requires evaluation to determine if bolus flow is limited by GEJ diameter/length.

3.3 INTRODUCTION

Laparoscopic fundoplication is the most reliable therapeutic option in surgical treatment of gastro-esophageal reflux disease (GERD) (Fuchs *et al.* 2014). Early post-operative dysphagia is common (Wills & Hunt 2001), and usually improves with resolution of surgery-induced edema (Funch-Jensen & Jacobsen 2007), esophageal stretching (Bessell *et al.* 2000) or transient esophageal hypomotility (Low 1994; Myers *et al.* 2007). However, troublesome dysphagia which persists into the late post-operative period, is an unwanted side effect and can mar the benefits of surgery. Modifications to the laparoscopic Nissen fundoplication with partial fundoplication techniques result in a modest reduction of dysphagia rates (Broeders *et al.* 2010; Broeders *et al.* 2013).

Troublesome dysphagia affects 2-25% of patients at least one year after fundoplication (Nikolic *et al.* 2019; Tsuboi *et al.* 2011; Walle *et al.* 2019). Easily identifiable causes identified on barium esophagram or endoscopy include hiatal hernia recurrence, intra-thoracic migration of the fundoplication and wrap disruption or slippage of the wrap onto the stomach (Furnee *et al.* 2009; Soper & Dunnegan 1999). However, these failures are uncommon and tend to occur in the hands of less experienced surgeons (Soper & Dunnegan 1999). In the remaining patients with troublesome dysphagia with normal post-operative appearances on the aforementioned investigations, its etiology remains poorly understood. Resistance to flow at the gastro-esophageal junction (GEJ) can contribute to post-fundoplication dysphagia (Myers *et al.* 2012; Wilshire *et al.* 2012), which may be caused by structural changes of fundoplication and hiatal repair imposing a restriction on GEJ opening.

Possible structural causes of troublesome dysphagia include a tight or long fundoplication wrap (Altun *et al.* 2012; Mickevicius *et al.* 2013), tight hiatus (Granderath *et*

al. 2005), or anterior displacement of the GEJ (Watson *et al.* 2001). The literature rarely contains objective evaluation of the impact of structural and anatomical changes of anti-reflux surgery on dysphagia (Sobrino-Cossio *et al.* 2017). We propose that troublesome dysphagia is caused by subtle anatomical changes after fundoplication. In this study, we aim to objectively examine post-fundoplication anatomical features via fluoroscopy to identify factors contributing to troublesome dysphagia.

3.4 METHODS

Study population

Patients with GERD referred for esophageal function tests as part of pre-operative evaluation for primary laparoscopic fundoplication were invited to participate. Exclusion criteria were a primary motility disorder such as scleroderma and achalasia, atypical reflux symptoms, or large hiatal hernia (>5 cm). Thirty-one patients underwent a laparoscopic Nissen 360° (TotLF) or partial anterior 90° fundoplication (PAntLF) between April 2004 and October 2010. The type of fundoplication performed was determined by informed patient preference. All patients gave written informed consent and the Human Research Ethics Committee of the Royal Adelaide Hospital approved the protocol.

Symptom assessment

Patients completed a standardised self-administered symptom assessment questionnaire pre- and 6-12 months post-operatively. The post-operative questionnaire was completed on the same day as fluoroscopic evaluation. In the questionnaires, the presence or absence of heartburn, regurgitation, and dysphagia was recorded. Further, visual analog scale (VAS) data of heartburn, regurgitation, and dysphagia to liquids and solids recorded the frequency of symptoms (0 none, 10 frequent). In addition, a validated dysphagia composite score (DCS) was used to assess difficulty swallowing for nine different food types of increasing viscosity (range: 0-45, 0=no dysphagia) (Dakkak & Bennett 1992). Troublesome dysphagia (TDysph) was defined as a composite score of ≥ 12 .

Surgical procedure

After hiatal mobilization, hiatal repair was routinely performed in all patients with posterior sutures. For TotLF, a loose, 2-cm 360° wrap was constructed over a 52F intra-esophageal bougie without division of the short gastric vessels (Jamieson *et al.* 1994). The PAntLF procedure included posterior esophagopexy to the right hiatal pillar, accentuation of the angle of His, and wrapping of the gastric fundus over approximately 90° of the antero-lateral intra-abdominal esophagus (Kryztopik *et al.* 2002).

Fluoroscopy

At 6-12 months after fundoplication, all patients underwent a barium swallow with video-fluoroscopy. The structured protocol used 20ml upright or 15ml prone swallows delivered with a syringe (Liquid Polibar® barium sulphate suspension [100% w/v; 56% w/w], E-Z-EM Inc. Westbury, New York USA) and sequentially recorded six acquisition views: standing antero-posterior (SAP), standing oblique (SOB1 and SOB2), prone oblique (POB1 and POB2) and prone oblique with continuous free drinking (PCont). Fluoroscopy images were recorded with image intensifiers at 25 frames per second on either Super VHS magnetic-tape (Panasonic NV-FS 90 Super VHS recorder, Japan) or directly in digital format using digital imaging and communications in medicine (DICOM). The radiological field of vision included swallow onset, fluoroscopic chase of the barium head-of-bolus passing through the esophagus, with a focus on the GEJ and the distal half of the esophagus.

Data analysis

The video-fluoroscopy images recorded on VHS magnetic tapes were converted to digital data on DVD optical media using analog-to-digital adaptor software. The remaining fluoroscopy data were extracted from the hospital's picture archiving and communication

system (PACS) in DICOM file format. The expert observer (SWG) analysed all fluoroscopy data utilising VLC media player (VideoLAN) and image analysis software (ImageJ1, W Rasband, National Institute of Health, University of Wisconsin, USA). After observing each fluoroscopic view for each patient several times, the expert observer selected a screenshot of the view with optimal bolus flow through the GEJ, and performed objective measurements using image analysis software. The expert observer was blinded to the type of operative procedure or dysphagia symptoms when conducting measurements. The measurements recorded are defined as below (established previously, see Chapter 2):

1) Anterior GEJ displacement (AntDisp): Horizontal distance between posterior distal esophageal angle and posterior aspect of distal end point of fundal wrap canal.

2) Axis deviation of GEJ/fundal wrap canal relative to distal esophagus (GEJ-Es): The angle formed by intersection of the axes of the fundal wrap canal and distal esophagus was measured. Angles $>180^\circ$ indicated posterior deviation, while angles $<180^\circ$ represented anterior deviation. The magnitude of deviation from the straight axis (180°) was used in our analysis.

3) Posterior distal esophageal angle (PostAngl): Two straight lines were drawn to trace the posterior border of the distal esophagus, at the point of esophageal tapering of contrast, both before and after the point of greatest angulation. The PostAngl was measured by the intersection of these two lines.

4) Maximal distal esophageal diameter *cf.* wrap opening diameter (MEs-GEJ): Absolute difference between the measured maximal distal esophageal diameter and fundal wrap canal opening diameter.

To adjust for variations in magnification, an esophageal catheter with radio-opaque tantalum markers was placed transnasally at the time of fluoroscopy for each patient and taped in place to enable visualisation of the tantalum markers in the distal esophagus. The expert observer converted measurements recorded from digital images in pixels into centimeters, cm, by using the known distance between tantalum markers as seen in each fluoroscopic view.

Statistical methods

Discrete data are presented as absolute numbers and percentage, and continuous variables as mean \pm standard deviation. A p value of <0.05 was considered statistically significant. Associations between dysphagia both as a binary (presence or absence of TDysph) and a continuous score (range 0-45), and fluoroscopic measurements by operation type were assessed with linear regression analysis and linear mixed-effects models, adjusting for repeated measurements. All statistical calculations were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

3.5 RESULTS

Thirty-one patients participated in the study, of which 18 and 13 underwent TotLF and PAntLF respectively. Female and male patients comprised 39% and 61% respectively. In the PAntLF group, there were more females, and patients were slightly older and had a lower BMI than patients in the TotLF group (Table 1). Typical GERD symptoms of heartburn and regurgitation were experienced for an average of 12.4 ± 11.1 years. All but one patient (97%) reported ongoing use of proton pump inhibitors (PPIs) prior to surgery. Pre-operatively, patients subjectively reported the presence of heartburn (100%) and regurgitation (97%) which improved to 26% and 35% respectively after fundoplication. Symptoms according to operation type are shown in Table 2.

All patients underwent structured barium swallow with video-fluoroscopy at an average of 9.3 ± 3.8 months after laparoscopic fundoplication. An intact fundoplication located below the diaphragm was confirmed in all patients.

Dysphagia

In our study, fundoplication resolved or improved pre-existing dysphagia in 8/31 patients (26%), whilst new-onset or worsening dysphagia occurred in 13/31 patients (42%) according to their DCS. Of these 13 patients, 4 had troublesome dysphagia (TDysph, $DCS \geq 12$) while the other 9 had mild dysphagia. 9/31 patients (29%) had no dysphagia either pre- or post-operatively. New-onset dysphagia tended to be milder than post-operative dysphagia that was present prior to surgery (Table 2). The overall rate of post-operative dysphagia was 21/31 (68%) compared to 11/31 patients (36%) pre-operatively. However, only 8/31 (26%) and 9/31 (29%) of patients had TDysph before and after surgery respectively.

Measurements of anatomical features after surgery

After TotLF, there was a trend towards greater anterior GEJ displacement compared to PAntLF, and this was statistically significant in the SOb view (mean 2.49cm vs 2.00cm, $p=0.03$) (Table 3). For TotLF patients, there was minimal deviation of the GEJ axis from the axis of the distal esophagus, while PAntLF patients tended to have GEJ axis deviated anteriorly relative to the distal esophagus (SAP, mean 181.0° vs 156.7° , $p<0.001$; POB, 178.1° vs 163.9° , $p<0.001$). There was no statistical difference in posterior esophageal wall angle in patients after TotLF and PAntLF. TotLF resulted in a larger difference in maximal esophageal diameter *cf.* wrap opening diameter when compared to PAntLF, which was statistically significant in all views (Table 3).

Anterior GEJ displacement and dysphagia after surgery

Comparisons were made between patients with and without post-operative TDysph. For patients with TDysph who underwent TotLF, there was a trend towards greater anterior displacement across all acquisition views compared to patients without TDysph, and was statistically significant in the standing oblique view (2.92cm vs 2.31cm, $p=0.04$) (Table 4). PAntLF patients with TDysph post-operatively tended to have smaller anterior displacement than patients without TDysph, although this did not reach statistical significance (Table 4).

In analysis of continuous data for dysphagia severity using the DCS, for every one-unit increase in the post-operative DCS for TotLF patients, mean anterior displacement in the SOb view increased by 0.04cm ($p=0.0192$, 95% confidence interval 0.01, 0.08).

Axis deviation of GEJ cf. esophagus and dysphagia after surgery

For patients with TDysph post-operatively, there was a general trend towards having greater deviation from the straight axis (*i.e.* a greater positive or negative difference from 180°) compared to patients without TDysph for both operation types. This reached statistical significance for TotLF patients in the PCont view with a mean axis deviation of 12.3° vs -6.6° for patients with and without TDysph respectively (192.3° vs 173.4°, $p=0.0029$) (Table 5).

For every one-unit increase in the post-operative DCS for TotLF patients, mean axis deviation in the PCont view increased by 0.97° ($p=0.0272$, 95% confidence interval 0.11, 1.83).

Posterior distal esophageal angle and dysphagia after surgery

For both operation types, there was no statistical difference in posterior distal esophageal angle in patients with or without TDysph (Table 6). A greater DCS was also not significantly associated with a change in posterior distal esophageal angle.

Maximal distal esophageal diameter cf. wrap opening diameter and dysphagia after surgery

Binary or continuous DCS analysis did not reveal associations with maximal distal esophageal diameter *cf.* wrap opening diameter for both operation types (Table 7). However, in PAntLF patients, for every one-unit increase in worsening post-operative DCS compared to pre-operative DCS, in the SAP view: mean maximal distal esophageal diameter *cf.* wrap opening diameter decreased by 0.03cm ($p=0.0074$, 95% confidence interval -0.06, -0.01) (Figure 1a). In the PCont view for PAntLF patients, for every one-unit increase in worsening post-operative DCS compared to pre-operative DCS, mean maximal distal esophageal diameter *cf.*

wrap opening diameter decreased by 0.03cm ($p=0.0225$, 95% confidence interval -0.05, 0.00) (Figure 1b).

Table 1: Patient demographics

	TotLF (n=18)	PAntLF (n=13)	P value
Age, years	42.6 ± 13.4	53.2 ± 14.8	0.047
Sex ratio, M : F	17 : 1	2 : 11	<0.001
BMI, kg/m ²	30.7 ± 4.0	26.2 ± 4.3	0.006

TotLF, laparoscopic total fundoplication; PAntLF, laparoscopic partial anterior fundoplication; BMI, body mass index. Data are mean ± standard deviation. Bold text = statistical significance, P <0.05.

Table 2: Pre- and post-operative symptom assessment

	Pre-operative			Post-operative		
	TotLF (n = 18)	PAntLF (n = 13)	P value	TotLF (n = 18)	PAntLF (n = 13)	P value
Heartburn, n (%)	18 (100)	12 (92)	0.22	2 (11)	6 (46)	0.03
Heartburn VAS ^a	9.0 ± 1.3	7.5 ± 3.0	0.12	0.8 ± 2.4	2.8 ± 3.9	0.13
Regurgitation, n (%)	18 (100)	13 (100)	-	4 (22)	7 (54)	0.07
Regurgitation VAS ^a	6.2 ± 2.9	5.7 ± 3.3	0.62	0.8 ± 1.8	1.2 ± 1.5	0.49
Dysphagia, n (%)	4 (22)	8 (62)	0.02	10 (56)	9 (69)	0.46
New-onset, n (%)	-	-	-	7 (39)	3 (23)	0.35
Dysphagia VAS						
Solids ^a	0.7 ± 1.6	1.8 ± 2.0	0.12	1.4 ± 2.0	1.6 ± 2.0	0.79
Liquids ^a	0.6 ± 1.6	0.8 ± 1.5	0.71	0.7 ± 1.7	1.0 ± 1.6	0.59
DCS						
Overall ^a	2.6 ± 6.0	7.9 ± 9.1	0.08	6.1 ± 7.1	7.7 ± 8.5	0.59
Zero only, n (%)	15 (83)	5 (38)	<0.01	7 (39)	3 (23)	0.35
Pre- & post- ^a	15.5 ± 2.2	14.1 ± 8.2	0.68	14.7 ± 4.2	10.6 ± 8.9	0.35
New-onset ^a	-	-	-	8.2 ± 6.5	8.5 ± 8.9	0.96
TDysph, n (%)	3 (17)	5 (38)	0.19	5 (28)	4 (31)	0.86
TDysph ^a	15.5 ± 2.2	18.5 ± 3.8	0.21	15.7 ± 5.0	19.3 ± 3.3	0.24

VAS, visual analog scale; DCS, dysphagia composite score; TDysph, troublesome dysphagia (DCS ≥12). ^aData are mean ± standard deviation. Bold text = statistical significance, P <0.05.

Table 3: Comparison of anatomical measurements by operation type, regardless of dysphagia score

Measurement	Acquisition view	TotLF (n = 18)	PAntLF (n = 13)	P value
AntDisp, cm	SAP	2.40 ± 0.60	2.42 ± 0.93	0.90
	SOb	2.49 ± 0.82	2.00 ± 0.78	0.03
	POb	2.35 ± 0.80	1.94 ± 0.94	0.09
	PCont	2.69 ± 0.96	2.15 ± 0.98	0.12
GEJ-Es, °	SAP	181.0 ± 22.5	156.7 ± 9.1	<0.001
	SOb	179.5 ± 18.0	175.9 ± 19.7	0.48
	POb	178.1 ± 14.9	163.9 ± 12.7	<0.001
	PCont	179.2 ± 14.0	170.2 ± 12.6	0.06
PostAngl, °	SAP	137.7 ± 11.8	142.0 ± 12.1	0.17
	SOb	146.0 ± 10.4	144.5 ± 10.8	0.60
	POb	142.0 ± 9.7	147.3 ± 14.2	0.12
	PCont	141.3 ± 12.1	142.0 ± 13.0	0.86
MEs-GEJ, cm	SAP	1.93 ± 0.55	1.01 ± 0.44	<0.001
	SOb	1.54 ± 0.52	0.81 ± 0.34	<0.001
	POb	1.60 ± 0.46	0.71 ± 0.32	<0.001
	PCont	1.70 ± 0.50	0.79 ± 0.22	<0.001

AntDisp, anterior GEJ displacement; GEJ-Es, axis deviation of GEJ/fundal wrap canal relative to distal esophagus; PostAngl, posterior distal esophageal angle; MEs-GEJ, maximal distal esophageal diameter *cf.* wrap opening diameter; SAP, standing antero-posterior; SOb, standing oblique; POb, prone oblique, PCont, prone oblique with continuous free drinking. Data are mean ± standard deviation. Bold text = statistical significance, P <0.05.

Table 4: Anterior GEJ displacement (AntDisp) according to dysphagia status after surgery

	Acquisition view	AntDisp for patients with TDysph, cm	AntDisp for patients without TDysph, cm	P value
TotLF	SAP	2.52 ± 0.27	2.35 ± 0.69	0.45
	SOb	2.92 ± 0.94	2.31 ± 0.72	0.04
	POb	2.41 ± 0.48	2.32 ± 0.91	0.82
	PCont	2.25 ± 0.99	2.89 ± 0.91	0.23
PAntLF	SAP	2.16 ± 0.20	2.54 ± 1.10	0.49
	SOb	1.74 ± 0.90	2.13 ± 0.71	0.43
	POb	1.61 ± 1.00	2.11 ± 0.90	0.40
	PCont	1.79 ± 0.70	2.33 ± 1.09	0.50

TotLF, laparoscopic total fundoplication; PAntLF, laparoscopic partial anterior fundoplication; SAP, standing antero-posterior; SOb, standing oblique; POb, prone oblique, PCont, prone oblique with continuous free drinking. TDysph, troublesome dysphagia (dysphagia composite score ≥ 12). Data are mean ± standard deviation. Bold text = statistical significance, P < 0.05.

Table 5: Axis deviation of GEJ *cf.* esophagus (GEJ-Es) according to dysphagia status after surgery

	Acquisition view	GEJ-Es for patients with TDysph, °	GEJ-Es for patients without TDysph, °	P value
TotLF	SAP	185.8 ± 20.8	179.2 ± 23.3	0.57
	SOb	182.8 ± 20.1	178.2 ± 17.4	0.63
	POb	187.3 ± 17.6	174.3 ± 12.1	0.09
	PCont	192.3 ± 11.2	173.4 ± 11.0	0.003
PAntLF	SAP	157.0 ± 9.1	156.5 ± 9.4	0.81
	SOb	174.6 ± 21.4	176.6 ± 19.5	0.88
	POb	159.1 ± 4.2	166.3 ± 14.8	0.33
	PCont	160.8 ± 8.3	174.8 ± 12.0	0.11

TotLF, laparoscopic total fundoplication; PAntLF, laparoscopic partial anterior fundoplication; SAP, standing antero-posterior; SOb, standing oblique; POb, prone oblique, PCont, prone oblique with continuous free drinking. TDysph, troublesome dysphagia (dysphagia composite score ≥ 12). Data are mean ± standard deviation. Bold text = statistical significance, P < 0.05.

Table 6: Posterior distal esophageal angle (PostAngl) according to dysphagia status after surgery

	Acquisition view	PostAngl for patients with TDysph, °	PostAngl for patients without TDysph, °	P value
TotLF	SAP	145.4 ± 6.0	134.7 ± 12.2	0.06
	SOb	142.6 ± 9.7	147.4 ± 10.6	0.33
	POb	143.5 ± 7.2	141.4 ± 10.7	0.65
	PCont	143.6 ± 11.1	140.2 ± 12.6	0.63
PAntLF	SAP	143.1 ± 13.7	141.4 ± 11.6	0.71
	SOb	141.4 ± 11.4	146.1 ± 10.4	0.44
	POb	139.9 ± 14.7	151.0 ± 12.9	0.16
	PCont	146.0 ± 12.6	140.1 ± 13.6	0.58

TotLF, laparoscopic total fundoplication; PAntLF, laparoscopic partial anterior fundoplication; SAP, standing antero-posterior; SOb, standing oblique; POb, prone oblique, PCont, prone oblique with continuous free drinking. TDysph, troublesome dysphagia (dysphagia composite score ≥ 12). Data are mean ± standard deviation.

Table 7: Maximal distal esophageal diameter *cf.* wrap opening diameter (MEs-GEJ) according to dysphagia status after surgery

	Acquisition view	MEs-GEJ for patients with TDysph, cm	MEs-GEJ for patients without TDysph, cm	P value
TotLF	SAP	2.04 ± 0.44	1.89 ± 0.59	0.60
	SOb	1.80 ± 0.41	1.43 ± 0.53	0.18
	POb	1.47 ± 0.63	1.65 ± 0.37	0.45
	PCont	1.75 ± 0.80	1.68 ± 0.33	0.79
PAntLF	SAP	0.89 ± 0.15	1.07 ± 0.51	0.43
	SOb	0.82 ± 0.23	0.81 ± 0.40	0.97
	POb	0.77 ± 0.26	0.68 ± 0.35	0.63
	PCont	0.72 ± 0.16	0.82 ± 0.24	0.54

TotLF, laparoscopic total fundoplication; PAntLF, laparoscopic partial anterior fundoplication; SAP, standing antero-posterior; SOb, standing oblique; POb, prone oblique, PCont, prone oblique with continuous free drinking. TDysph, troublesome dysphagia (dysphagia composite score ≥ 12). Data are mean ± standard deviation.

Figure 1a: Worsening post-operative dysphagia composite score (compared to pre-operative) in relation to maximal esophageal diameter *cf.* wrap opening diameter in patients after partial anterior 90° fundoplication (standing antero-posterior view).

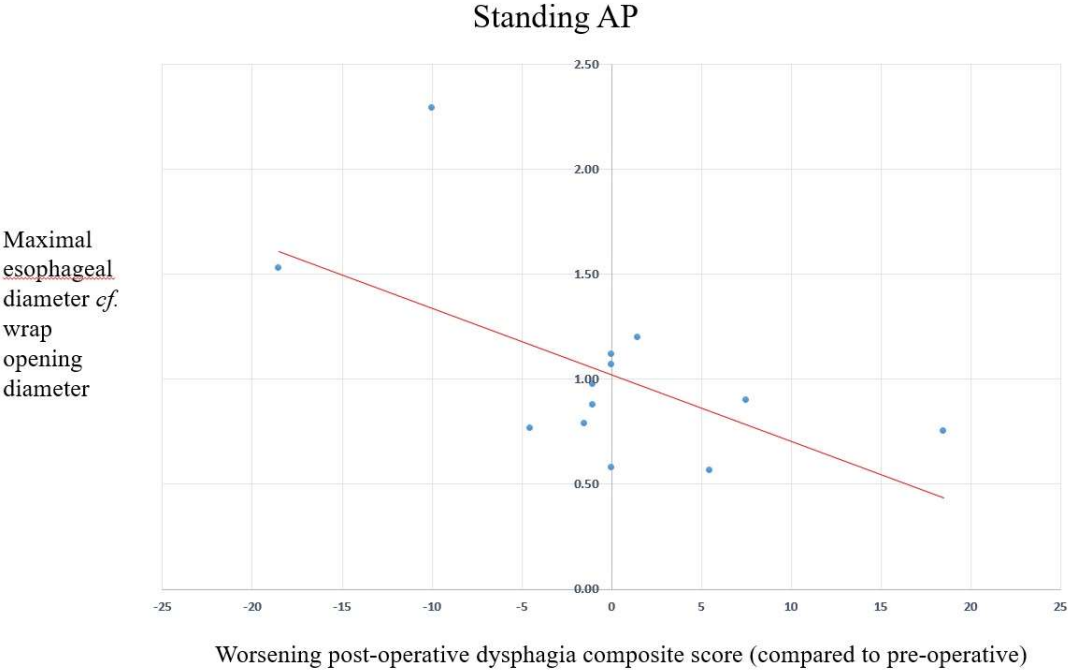
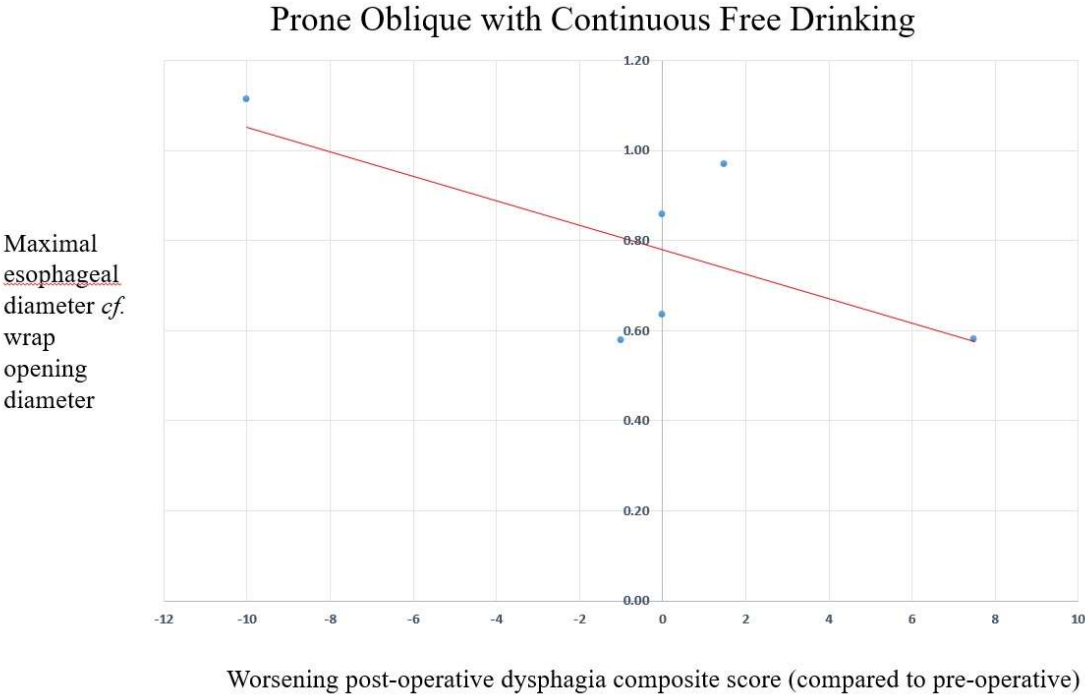


Figure 1b: Worsening post-operative dysphagia composite score (compared to pre-operative) in relation to maximal esophageal diameter *cf.* wrap opening diameter in patients after partial anterior 90° fundoplication (prone continuous with free drinking view).



3.6 DISCUSSION

The most important finding from this study is that anatomical features such as greater anterior GEJ displacement and angulation of the GEJ from the axis of the distal esophagus are associated with troublesome dysphagia after total 360° fundoplication. These associations with troublesome dysphagia are not seen in patients after partial anterior 90° fundoplication. This study also demonstrates that total fundoplication imposes greater structural changes than partial anterior fundoplication *i.e.* greater anterior GEJ displacement and restriction of fundal canal opening (as shown by the greater difference in maximal distal esophageal diameter *cf.* wrap opening diameter).

It is interesting to note that partial anterior fundoplication was associated with anterior axis deviation of the GEJ *cf.* distal esophagus, whereas the axis was mostly straight following total fundoplication. Routine posterior hiatal repair undertaken for all patients just prior to construction of the fundoplication. A recent published study highlighted the likely role of posterior hiatal repair in causing a relatively uniform elevation in GEJ pressure after partial anterior 90° fundoplication, in addition to the expected focal elevated pressure in the left antero-lateral segment of the GEJ (Myers *et al.* 2020). It is feasible that PAntLF which causes minimal compression on the GEJ, is susceptible to the effects of the hiatal repair which pushes the GEJ anteriorly causing a change in the axis. Conversely, in TotLF which gives more structural integrity to the fundoplication, the GEJ is less likely to be pushed forward by the posterior hiatal repair.

Barium esophagram is useful in identifying functional and morphological problems (Baker & Einstein 2014) and is often the first test used in investigation of post-fundoplication dysphagia. However, most previous studies included only qualitative instead of quantitative

assessments of barium esophagram, such as assessing for the presence or absence of complete or partial intra-thoracic wrap migration (Hainaux *et al.* 2002; Le Blanc-Louvry *et al.* 2000; Raeside *et al.* 2012). Barium swallow has been critiqued as a test that is highly subjective and user-dependent (Tsuboi *et al.* 2011), with greater accuracy stemming from an increased level of skill or familiarity with post-fundoplication radiological appearances (Raeside *et al.* 2012). Our study is the first to utilize a range of objective measurements on carefully selected still images on video-fluoroscopy, to explore subtle anatomical changes not seen by casual, qualitative examination. Furthermore, having a clearly defined and reproducible set of outcomes of video-fluoroscopy may eliminate or reduce variability between assessors (Baijens *et al.* 2013). A standardized video-fluoroscopy protocol was used for all patients as described above, which can be replicated in other centres to allow further larger-scale studies.

In this study, objective measurements of post-fundoplication GEJ anatomy demonstrated several statistically significant associations with post-fundoplication dysphagia. Greater anterior GEJ displacement in patients who underwent TotLF was associated with worse dysphagia scores and a higher likelihood of having TDysph, compared to TotLF patients without significant dysphagia. PAntLF patients with or without TDysph had no significant difference in anterior GEJ displacement measurements. Anterior GEJ displacement and angulation is reported by several authors as a potential cause of post-fundoplication dysphagia (Herbella *et al.* 2009; Sato *et al.* 2002; Watson *et al.* 2001). Watson *et al.* postulated that this phenomenon may be due to posterior hiatal repair during fundoplication pushing the distal esophagus anteriorly, and that the alternative of anterior hiatal repair may lead to a lower incidence of dysphagia (Watson *et al.* 2001). A randomized controlled trial comparing posterior and anterior hiatal repair found no difference in

dysphagia rates at 6 months and 5 years, although more patients who underwent posterior hiatal repair required further surgery for dysphagia to achieve the similar dysphagia rate (Watson *et al.* 2001; Wijnhoven *et al.* 2008). At the 10-year follow up, dysphagia for lumpy solid foods was less common in patients who underwent anterior compared to posterior hiatal repair (14% vs 39.5%, $p=0.01$), although dysphagia rates for six other dysphagia assessment scores were similar (Chew *et al.* 2011).

To our knowledge, no previous study has directly measured anterior GEJ displacement. The role of hiatal repair on anterior GEJ displacement is difficult to elucidate as all patients underwent posterior hiatal repair in our study. However, it is likely that TotLF contributes to anterior GEJ displacement by a combination of reinforcing the posterior aspect of the GEJ through wrapping of the gastric fundus posteriorly, and increasing the length of the GEJ. In manometry studies, there is greater radial pressure in the posterior aspect of the GEJ in patients after total fundoplication, and this difference is significantly associated with greater post-operative dysphagia (Myers *et al.* 2020).

Greater magnitude of axis deviation of the GEJ *cf.* esophagus was found to be significantly associated with TDysph as well as a worse dysphagia score in patients who underwent TotLF. There was also a general trend for PAntLF patients with TDysph to have greater axis deviation than PAntLF patients without TDysph, although statistical significance was not reached. Although the mechanism of anterior or posterior axis deviation is unclear, a greater magnitude of deviation likely contributes to greater resistance of bolus flow through the GEJ which is experienced symptomatically as dysphagia. Herbella *et al.* evaluated the esophageal antero-posterior angle in 32 patients after fundoplication, and found no correlation between the angle and the incidence of new-onset dysphagia (Herbella

et al. 2009). The different result between our findings may be due to the different method of measuring the angle. Herbella *et al.* measured the angle/axis change between the proximal thoracic and distal thoracic/abdominal esophagus, whereas in our study, we measured the axis change between the fundal wrap canal and the distal esophagus. In another study, Stiven *et al.* used the number of posterior hiatal repair sutures as a proxy for anterior esophageal angulation in patients who underwent primary large paraesophageal hernia repair with laparoscopic partial posterior fundoplication. There was no demonstrable association between the number of posterior hiatal repair sutures and post-operative dysphagia outcomes (Stiven *et al.* 2013). Although the number of posterior sutures was found to correlate with the esophageal antero-posterior angle (Herbella *et al.* 2009), we deem this a poor proxy for esophageal angle, as the inter-suture gap and number of sutures for posterior hiatal repair used may differ based on the experience and preference of individual surgeons. The impact of supplementary anterior hiatal sutures placed for some patients in addition to posterior hiatal sutures on esophageal angle and dysphagia is unclear, as these patients were included in the same analysis as patients with only posterior sutures.

Following PAntLF, patients with worsening dysphagia compared with before surgery were significantly more likely to have decreased maximal esophageal diameter *cf.* wrap opening diameter. Despite being statistically significant, the very small reduction of 0.03cm is unlikely to be meaningful in practice. In addition, it contradicts our theory that a greater differential may be related with worse dysphagia, due to increased resistance to flow from greater luminal narrowing. More studies are required to investigate if the difference between maximal esophageal diameter and wrap opening diameter is an anatomical feature related to post-fundoplication dysphagia.

Strengths of this study include its prospective design in a well-defined patient group with pre- and post-operative symptom assessments. A validated DCS in addition to VAS scores allowed for a more accurate capture of patients' symptoms. Despite the availability of objective tests, subjective symptom reporting which reflects patients' perception remains a highly suitable method of tracking outcomes of surgery (Chew *et al.* 2011). A structured video-fluoroscopy protocol was used in the same centre for all patients.

This study is an underpowered study due to the small sample size. Thus, a larger study is needed to determine if the statistical difference for findings of this study were found by chance. There may also be a bias as more females chose to undergo the partial fundoplication procedure following informed consent, likely due to concern for the greater risk of post-fundoplication dysphagia after total fundoplication. There is a tendency for females to report worse dysphagia after laparoscopic fundoplication compared to males (analog scores 2.7 ± 2.9 vs. 2.0 ± 2.5 , $p=0.0049$) (Beck *et al.* 2009).

3.7 CONCLUSION

Using objective measurements on structured video-fluoroscopy studies, this study is the first to report that greater anterior GEJ displacement and axis deviation following total fundoplication are associated with troublesome dysphagia. Following partial fundoplication, a small reduction in maximal esophageal diameter cf. wrap opening diameter associated with worsening dysphagia requires further investigation to determine if fundoplication length or diameter limit bolus flow from the esophagus into the stomach. Future studies in larger patient populations, employing standardized contrast studies are required to confirm these anatomical factors contributing to post-fundoplication dysphagia.

3.8 ACKNOWLEDGEMENTS

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3.9 REFERENCES

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CHAPTER 4

CONCLUSIONS AND FUTURE DIRECTIONS

4.1 CONCLUSIONS

4.1.1 Aim 1

- **To evaluate the inter- and intra-observer reliability of novel objective measurements on barium swallow studies of anatomical features of the gastro-oesophageal junction after fundoplication with hiatal repair**

In the first study (Chapter 2), 11 novel objective measurements on barium swallow studies of anatomical features of gastro-oesophageal junction anatomy after fundoplication were found to have good inter- and high intra-observer reliability. These findings are significant as novel objective measures were devised in the course of this research according to anecdotal anatomical factors raised in the literature.

The level of agreement for measurements between observers in this study is equal to or better than that reported in other studies. This was despite having two medical students inexperienced in barium swallow interpretation and training the students for only four hours in total. Based on this, similar or higher levels of agreement can be expected among more experienced clinicians, lending external validity to this study.

Measures of diameter, posterior distal oesophageal angulation, anterior gastro-oesophageal junction displacement and axis deviation showed high levels of agreement, while measures of wrap length were poorly reproducible. Agreement for measures of wrap length may be improved by using clearer definitions of the wrap length and/or emphasising the use of slow-motion playback in video analysis. In essence, the good level of reproducibility found demonstrates the utility of barium swallow for examination of

anatomical causes of dysphagia, and the potential for further studies to explore correlations between these objective anatomical factors and troublesome dysphagia.

Dysphagia is often attributed to an overly tight fundoplication wrap impeding bolus flow through the GEJ, seen radiologically as a narrowing and compression of the distal oesophagus by the surrounding wrap (Katzka 2018). However, diagnosing a tight wrap remains challenging due to a lack of consensus on the extent of narrowing required for the development of dysphagia (Katzka 2018). To date, a single published cohort study of 41 patients evaluating the narrowed segment length on barium swallow did not find an association between a long (>3cm) or short (\leq 3cm) narrowed segment length and post-operative dysphagia (Altun *et al.* 2012). Based on current evidence from manometry studies, the interplay of relationships between the length of fundoplication created intra-operatively, the length of the high-pressure zone (representing the GEJ) on manometry, as well as their correlation with troublesome dysphagia remains inadequately explored.

Recent studies using manometry suggest that hiatal repair may have a greater impact on structural changes following fundoplication and post-fundoplication dysphagia compared to the impact of the fundoplication itself, than is currently appreciated (Myers *et al.* 2020; Nicodeme *et al.* 2015). Structurally, hiatal repair and/or the fundal wrap may lead to anatomical changes such as increased anterior displacement of the GOJ, increased acuity of angulation at the posterior distal oesophageal wall, or a change of axis of the GOJ relative to the distal oesophagus.

Barium swallow studies of the gastro-intestinal tract are increasingly de-emphasised due to the availability of other imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) as well as upper gastro-intestinal endoscopy (Baker &

Einstein 2014; Sanchez-Carpintero de la Vega & Garcia Villar 2017). However, barium swallow remains a crucial tool in the investigation of post-fundoplication dysphagia. More studies are needed to objectively study anatomical changes of fundoplication with hiatal repair and their correlation with dysphagia. The study in Chapter 2 describes a clearly defined methodology of recording measurements using a structured barium swallow protocol which led to good inter-observer reproducibility of measurements. The current study provides a point of reference for future studies exploring the correlation of anatomical features with dysphagia.

4.1.2 Aim 2

- **To determine correlations of novel objective measurements with troublesome dysphagia after fundoplication**

In the second study (Chapter 3), greater anterior displacement and angulation of the distal oesophagus correlated with the presence of troublesome dysphagia after total fundoplication. This indicates that the incidence and severity of dysphagia may be reduced with more care during total fundoplication and hiatal repair, to minimise distortion of flow through the gastro-oesophageal junction.

This study is the first to report a correlation between greater anterior GOJ displacement and axis deviation of the GOJ relative to the distal oesophagus with dysphagia. Other authors observed this finding on barium swallow studies after fundoplication, but associations with dysphagia were not corroborated by objective data (Sato *et al.* 2002; Watson *et al.* 2001). Anterior hiatal repair instead of posterior hiatal repair was proposed as an approach to minimise displacement and angulation of the gastro-oesophageal junction,

but the displacement and angulation was not measured directly in this study, and dysphagia rates were similar for patients with either an anterior or posterior hiatal repair (Chew *et al.* 2011).

Abnormal oesophageal outflow resistance, manometrically measured as elevated intrabolus pressure and swallowing-induced GOJ relaxation pressure, may lead to post-fundoplication dysphagia (Wilshire *et al.* 2012). Greater anterior displacement and angulation of the distal oesophagus adjacent to the GOJ are likely to be the causative factors for dysphagia, and they add to the list of potential causes of oesophageal outflow resistance (other reported factors being narrowing of hiatal opening and elongation of fundoplication length) (Scheffer *et al.* 2005). In an elegantly designed study, Ayazi *et al.* quantified the increase in oesophageal outflow resistance imposed by Nissen fundoplication needed to be overcome by the distal oesophageal contraction amplitude in order to avoid persistent post-operative dysphagia (Ayazi *et al.* 2019). The 95th percentile intrabolus pressure of 20mmHg was overcome by oesophageal contraction in all patients in the validation population. The authors concluded that the fundoplication should be constructed to avoid an intrabolus pressure greater than 20mmHg, in order to avoid persistent post-operative dysphagia (Ayazi *et al.* 2019). Further studies to clarify the associations between greater anterior displacement and angulation of the distal oesophagus with oesophageal outflow resistance are awaited.

In the study presented in Chapter 3, total fundoplication was associated with greater anterior GOJ displacement than partial anterior 90° fundoplication. Patients with troublesome dysphagia after total fundoplication had greater anterior GOJ displacement than patients without troublesome dysphagia. Putting the two together, it can be derived

that a) total 360° fundoplication imparts greater structural change than partial anterior 90° fundoplication, and b) the development of greater anterior GOJ displacement in some but not all patients after total fundoplication may be either due to the lack of calibration of the posterior hiatal repair, or patient-related factors, such as the natural tortuosity of the distal oesophagus and stomach after fundoplication.

Greater magnitude of axis deviation of the GOJ relative to distal oesophagus is associated with troublesome dysphagia after total fundoplication (Chapter 3). This association was not seen in patients after partial anterior 90° fundoplication. Similarly, the mechanism of why some patients develop greater axis deviation of the GOJ-oesophagus is unclear, as all patients in this study had a routine posterior hiatal repair, no patient had a hiatal hernia larger than 5cm and for total fundoplication, and the wrap was calibrated over a 52Fr intra-oesophageal bougie. Further characterisation of the hiatal defect and calibration of hiatal repair may provide clarification.

The relatively small sample size must be considered in interpreting these findings, and it can be concluded that further larger scale studies are required to investigate the correlation between anatomical features of anti-reflux surgery and post-operative dysphagia.

4.2 FUTURE DIRECTIONS

- **Objective measurement of the anatomical changes after fundoplication and hiatal repair and their impact on troublesome dysphagia**

There is a need for current anti-reflux procedures to be informed by objective data on the anatomical changes of surgery, in order to reduce post-fundoplication dysphagia. Laparoscopic anti-reflux surgery is still under-utilised due to the perceived adverse effects of surgery, and is reserved for patients with refractory disease or large hiatal hernia (Bonavina 2020). As described in Chapters 2 and 3, barium swallow has potential for use to detect subtle anatomical changes of fundoplication via objective measurement and it remains one of the best diagnostic tools to evaluate anatomy of the GOJ. By contrast, CT imaging is mainly used to look for wrap disruption or contrast leak in suspected perforation following anti-reflux surgery (LeBedis *et al.* 2013; Zarzour *et al.* 2018). A limitation of CT is that it does not allow direct visualisation of bolus passage. An alternative is real-time MRI assessment of swallowing, a non-invasive and non-ionising modality. Real-time MRI demonstrated the cause of recurrent or persistent reflux symptoms after fundoplication (correlated with endoscopy findings) in 90% of patients, including wrap disruption, migration and recurrent gastric hernia (Seif Amir Hosseini *et al.* 2019). Real-time MRI has high diagnostic ability but is associated with significant cost compared to barium swallow studies (Zu *et al.* 2013). Upper gastrointestinal tract endoscopy is widely used to evaluate structural causes of post-fundoplication dysphagia, but its use is hindered by the absence of standardised endoscopic reporting (Abdelmoaty & Swanstrom 2017).

Careful adherence to a structured protocol of barium swallow with clear definitions of objective measurements on image analysis software can improve reliability and utility of

measurements to assess correlations with dysphagia and to further our understanding of anatomical causes of post-fundoplication dysphagia.

- **Correlation of anatomical features with troublesome dysphagia after fundoplication**

In the setting of an intact fundoplication without gross failures of surgery (*e.g.* wrap disruption, migration or recurrent hernia), the cause of troublesome dysphagia remains poorly understood and represents a challenge in further management (Nikolic *et al.* 2019). More studies are required to interrogate the association between anatomical factors such as anterior displacement and angulation of the distal oesophagus and troublesome dysphagia. In addition, the individual contribution of anterior vs posterior hiatal repair, and posterior vs anterior fundoplication towards these anatomical factors could be closely evaluated. If no clear benefit of anterior hiatal repair on dysphagia rates can be found, the role of the surgeon taking more care to avoid excessive anterior displacement and angulation of the distal oesophagus in construction of the fundoplication could be explored in order to minimise post-operative dysphagia.

- **Intra-operative quantification of hiatal repair and fundoplication**

Using Endo-FLIP (endoluminal functional luminal imaging probe), measurements performed at various stages of robotic assisted laparoscopic hiatal hernia repairs and anti-reflux procedures in 100 consecutive patients showed that hiatal closure had greater contribution towards reducing GOJ compliance, reducing the cross-sectional area and

increasing the length of the GOJ high-pressure zone compared to the contribution of either Nissen or Toupet fundoplication or magnetic sphincter augmentation (Stefanova *et al.* 2020). This is a relatively new usage of Endo-FLIP which has been primarily used to assess GOJ distensibility in patients with GOJ outlet obstruction, such as achalasia. It confirms findings from an earlier study on 18 patients randomised to either a 'hiatal repair first' or '360° fundoplication first' procedure, whereby 'hiatal repair first' resulted in a greater increase in GOJ pressure than the 'fundoplication first' group (10.2mmHg vs 3.5mmHg, P = 0.07) (Louie *et al.* 2013). Further studies could assess correlations between Endo-FLIP intra-operative measurements with outcome data on dysphagia.

In contrast to the study by Stefanova *et al.*, both crural closure and fundoplication led to a significant increase in balloon pressure and decrease in GOJ distensibility compared to initial measurements and measurements taken after hernia reduction (Su *et al.* 2020a). Patients with a lower GOJ distensibility had significantly more gas bloat and dysphagia at the 1-year and 2-year follow up compared to patients with greater GOJ distensibility (Su *et al.* 2020a).

In future studies, it would be interesting to see if there is any correlation of anatomical changes on post-operative barium swallow such as anterior GOJ displacement and angulation in patients with low GOJ distensibility with persistent dysphagia.

Calibration of the fundoplication with an intra-oesophageal bougie is well-accepted as a means to reduce post-operative dysphagia (Stefanidis *et al.* 2010). The use of the Endo-FLIP as a calibration device for fundoplication instead of a traditional bougie was trialled on the basis that the soft tip of Endo-FLIP would be less likely to cause oesophageal injury. However, patients whose fundoplication (either Nissen or Toupet) was calibrated with Endo-

FLIP had significantly higher dysphagia scores at 6 months than patients in whom a bougie was used (1.5 ± 1.0 vs 1.1 ± 0.3 , $P = .007$) (dysphagia score 1-5, 1=no dysphagia, 5=unable to swallow anything) (Su *et al.* 2020b).

In contrast to calibration of the fundoplication, calibration of the hiatal repair is less well-recognised, but could be an important step to reduce post-operative dysphagia. Mandovra *et al.* described a technique of using an air-inflated balloon catheter in the repaired hiatus to ensure adequate space for passage of food, with none of the 109 patients reporting persistent dysphagia after the 360° fundoplication (Mandovra *et al.* 2020). There is also potential for Endo-FLIP to be used intra-operatively to tailor the tightness of both the crural closure and fundoplication, by removing or adding a suture as required to avoid excessively low minimal GOJ diameter and low GOJ distensibility (Kim *et al.* 2018). There was good short-term follow up with none of the 40 patients reporting dysphagia at 1-month post-operatively (Kim *et al.* 2018).

The perfect fundoplication procedure which prevents recurrent reflux without unwanted troublesome dysphagia is yet to be determined. Objective measurements of the anatomical changes after fundoplication and hiatal repair and with greater attention paid to hiatal repair show promise for reducing troublesome dysphagia after fundoplication.

APPENDIX: PUBLISHED ABSTRACTS AND POSTERS

1. **Gan SW**, Edwards S, Kiroff G, Myers J. Assessment of Angulation and Anterior Displacement of the Gastro-oesophageal Junction in Patients with Troublesome Dysphagia after Fundoplication. Proceedings of International Society for Diseases of the Esophagus: Australasian Section Conference. Sydney 22nd-23rd February 2019.
2. **Gan SW**, Edwards S, Kiroff G, Myers J. Determination of Bolus Flow through the Anteriorly Displaced Gastro-oesophageal Junction with regard to Troublesome Post Fundoplication Dysphagia. RACS 88th Annual Scientific Congress 2019. Bangkok. ANZ J Surg 2019; 89 (suppl 1): 217.
3. **Gan SW**, Lee N, Tan SE, Edwards S, Kiroff G, Myers J. Inter- and intra-observer reliability of video-fluoroscopic measurements of oesophago-gastric junction anatomy post-fundoplication. RACS Annual Scientific Congress 2020. Melbourne (Accepted for poster, ASC was cancelled). ANZ J Surg 2020; 90 (suppl 1): 254.
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6. **Gan SW**, Lee N, Tan SE, Edwards S, Kiroff, G, Myers J. Anterior Displacement and Angulation of the Distal Oesophagus Correlate with Dysphagia after Reflux Surgery. 2020 Florey Postgraduate Research Conference. Adelaide (Poster and mini-oral format).

APPENDIX: PUBLISHED ABSTRACTS AND POSTERS (continued)

Poster presented in mini-oral format for 2020 Florey Postgraduate Research Conference: Anterior Displacement and Angulation of the Distal Oesophagus Correlate with Dysphagia after Reflux Surgery, 30th September, 2020.



Anterior Displacement and Angulation of the Distal Oesophagus Correlate with Dysphagia after Reflux Surgery


SW Gan, N Lee, SE Tan, SM Edwards, GK Kiroff, JC Myers



Background

- Anti-reflux surgery prevents gastro-oesophageal reflux.
- During surgery, the fundus (top) of the stomach is wrapped fully or partially around the end of the oesophagus.
- After surgery patients may have difficulty swallowing.

→ Barium swallows enable view of anatomy i.e. shape of the stomach entry, but formal measurements are not routine.



Methods (continued)

➤ Statistical analysis

- Inter-observer reliability calculated using intraclass correlation coefficients (ICC) two-way mixed-effects model^[1]

Agreement	ICC Value	Agreement	ICC Value
Excellent	0.75 - 1.00	Good	0.60 - 0.74
Fair	0.40 - 0.59	Poor	0.00 - 0.39

- Correlation between fluoroscopic measurements and dysphagia scores – by linear regression analysis and linear mixed-effects models.





Aim

To utilise barium swallows to:

- Evaluate reliability of measurements of stomach entry anatomy after surgery
- Determine if anatomical features correlate with troublesome dysphagia

Results

- Evaluation of fluoroscopic measurements between observers showed good to excellent agreement in 92% of measurements.
- After complete wrap, patients with troublesome dysphagia had greater anterior displacement and angulation of the distal oesophagus than patients without troublesome dysphagia.

	Patients with troublesome dysphagia	Patients without troublesome dysphagia	Significance
Anterior displacement of distal oesophagus (cm)	 2.9 cm	 2.3 cm	Oblique view: 2.9 ± 0.3 cm vs. 2.3 ± 0.2 cm p = 0.04
Angulation of GOJ cf. oesophagus (°)	 12°	 7°	Prone with free drinking view: 12 ± 4° vs. 7 ± 3° P < 0.003

Methods

- Subjects:** N = 31, 19M: 12F, mean age 47 ± 3 years
- Operation:** Complete stomach fundal wrap, N = 18
Partial stomach fundal wrap, N = 13
- After surgery: ~6 mo post op:
 - Dysphagia assessment: validated score for difficulty swallowing (range 0 - 45, troublesome ≥12)^[2]
 - Barium swallow + video-fluoroscopy
 - Focus on flow into stomach
 - Front view, 2 x oblique view, 2 x prone view, prone with free drinking view
 - 3 observers undertook training for measurements
 - Objective measurements on still-video images:

Conclusions


Barium swallows after reflux surgery show:

- Measurements of stomach entry anatomy are reproducible.
- Anatomical features: lumen diameter, anterior displacement & angulation of the distal oesophagus correlate with degree of swallowing difficulty.

→ During surgery, care is needed to minimise distortion of stomach entry anatomy to reduce post op dysphagia.

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