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OUTCOMES OF LAPAROSCOPIC FUNDOPPLICATION

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2. Khan MA, Smythe A, Globe J, Stoddard CJ and Ackroyd R (2009), Randomized controlled trial of laparoscopic Nissen versus Lind fundoplication for gastro-oesophageal reflux disease. *Scandinavian Journal of Gastroenterology*, 44(3):269-275. doi:10.1080/00365520802495552
3. Khan M, Smythe A, Elghellal K and Ackroyd R (2010), Can intraoperative manometry during laparoscopic fundoplication predict postoperative dysphagia? *Surgical Endoscopy*, 24(9):2268-2272. doi: 10.1007/s00464-010-0949-6

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ABBREVIATIONS

BMI	Body Mass Index
CJS	Mr. Christopher J Stoddard
GORD	Gastro-oesophageal reflux disease
GI	Gastro-intestinal
HRQoL	Health Related Quality of Life
IOM	Intra-oesophageal manometry
IL-6	Interleukin 6
IL-8	Interleukin 8
LPF	Laparoscopic Partial Fundoplication
LTF	Laparoscopic Total Fundoplication
MII-pH	Multi-channel intra-luminal impedance pH
OGD	Oesophagogastroduodenoscopy
PPI	Proton Pump Inhibitor
RA	Mr. Roger Ackroyd
SD	Standard deviation
SF36	Health Related Quality of Life Inventory
SPSS	Statistical Package for the Social Sciences
TNF- α	Tumour Necrosis Factor α

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ABSTRACT

Gastro-esophageal reflux disease (GORD) is common and a variety of surgical repair techniques have been shown to be effective. This thesis contains two randomised controlled trials and a combined data analysis of both studies to establish which techniques appear the most effective in controlling reflux. It also contains a pilot study to determine whether intraoperative manometry can predict which patients are likely to suffer from postoperative dysphagia.

One hundred and three underwent partial fundoplication (Anterior or Posterior) and one hundred and twenty one patients underwent total/subtotal (Nissen or Lind) in the randomised controlled trials and 40 patients were recruited into the intraoperative manometry study. Patients were followed up for 12 months and their change in symptoms recorded.

In the partial fundoplication trial, patients who underwent posterior fundoplication had better control of symptoms compared to those who underwent anterior fundoplication at the 12 month follow up point. There was no difference between the groups who underwent Nissen and Lind fundoplication. When the studies were collated, the laparoscopic total/subtotal fundoplication appears to be superior in the control of reflux when compared to the laparoscopic partial fundoplication. Intraoperative manometry may be advantageous as the study does suggest that this investigation may be useful in predicting post-operative dysphagia.

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1. INTRODUCTION

1.1 REFLUX DISEASE

Gastro-esophageal reflux disease (GORD) is a common condition that affects approximately 10-20% of the western world although some estimates suggest that this could be as high as 40% [1]. Management of GORD is varied and there are differing consensus statements as to the optimum treatment. Historically, GORD was considered to be secondary to a hiatus hernia, however, not all patients with reflux have a hiatus hernia, and operations which were designed to correct this deformity were often ineffective at treating reflux oesophagitis [2].

Current treatment includes lifestyle modifications and the use of proton pump inhibitors (PPIs), which has revolutionised the management of reflux. However, these therapies are often ineffective in severe disease and surgery offers an alternative [3-5]. A Cochrane Collaborative meta-analysis comparing laparoscopic fundoplication and medical treatment of GORD reported that surgery was superior to medical therapy, with significantly better quality of life as measured by the SF36 questionnaire [6].

The main aim of modern surgery, the fundoplication, is to prevent gastric contents refluxing into the oesophagus by recreating the natural effect of the lower oesophageal sphincter. There are numerous indications for fundoplication, including:

- Failure of medical therapy
- Need for prolonged medical therapy and complications of long term medical therapy
- Complications of reflux disease, including Barrett's oesophagus or stricture
- Patient preference i.e. do not want long term medical therapy
- Hiatus hernia with/without volume reflux
- Recurrent symptoms and signs of reflux after surgery
- Extra-oesophageal manifestation *i.e.* respiratory complications caused by reflux, dysphonia, globus, cough, choking, post nasal drip and sore throat [7]
- Lung transplant patients

There are two main contraindications to consider when contemplating ant-reflux surgery. Patients who are unfit to have general anaesthesia should not be offered anti-reflux surgery. This is due to the unacceptably high risk of severe cardiovascular complications. The second contraindication relates to patients who have reflux-related symptoms but no clear-cut reflux. These patients tend not to have gastro-oesophageal reflux, but a different disease (*e.g.* functional heartburn), so anti-reflux surgery will not help them.

Anti-reflux surgery is in the main, performed in three distinct sets of patients. The first group represents the majority of patients who will undergo an anti-reflux operation and have established signs and symptoms of chronic reflux disease (including Barrett's oesophagus or stricture), and do not wish to continue with life-long medical therapy and request anti-reflux surgery.

The second groups of patients who undergo anti-reflux surgery are those with well-established gastro-oesophageal reflux disease who are not achieving symptomatic control with PPI therapy. This group includes patients who have volume reflux, significant regurgitation, or who regularly aspirate during the night.

The third groups of patients are those that present and have symptoms associated with extra-oesophageal manifestation of reflux disease, which include respiratory complications of reflux disease.

Yet there is still no consensus as to which fundoplication provides optimum symptom control with minimal side effects. Advocates of partial fundoplication argue that it gives satisfactory symptom control with a reduced incidence of post-operative dysphagia and bloating [8]. Others believe that total/subtotal fundoplication provides superior control of reflux symptoms, and that the slightly higher incidence of post-operative dysphagia resolves by three months[9].

This thesis compares the outcomes from three studies; two comparing different forms of fundoplication: total (Nissen) *versus* subtotal (Lind) fundoplication, the other comparing posterior *versus* anterior hemi-fundoplication [10, 11], and one determining whether intraoperative manometry can help predict which patients will suffer from postoperative dysphagia [12].

The main aim of this thesis is to determine if there are any pre or intra-operative indicators (*i.e.* Pre-operative symptoms, diagnostic tests, *etc.*) that will identify if

there is going to be a successful outcome as seen by high satisfaction scores, decreased acid exposure in post-operative pH/Manometry testing, *etc.*

1.2 FACTORS AFFECTING OUTCOMES OF REFLUX SURGERY

1.2.1 PRE-OPERATIVE SYMPTOMS

There are spectrums of symptoms which GORD can present with, ranging from characteristic heartburn to the uncommon respiratory complications. Initial treatment invariably involves PPI therapy, with symptoms typically being controlled with medication. For patients who do not wish to have life-long medical therapy or who have PPI refractory disease, then fundoplication can offer a surgical treatment to alleviate these symptoms [13] with care being taken to comprehensively counsel the patient on potential post-operative effects of fundoplication (*i.e.* dysphagia, bloating, flatulence, *etc.*) [14]. There are many studies in the literature, which have addressed the issue of symptomatic control post fundoplication. The vast majority of these are long-term studies, with good follow-up[5, 9, 15, 16].

It must be stressed to patients who undergo surgery after failure of medical therapy, that they can expect an improved quality of life, although they may not return to normal levels. Pre-operative symptoms should be carefully recorded and patients should be counselled for realistic expectations [17].

Amato *et al* [18] analysed a series of 102 fundoplications, and highlighted a dramatic improvement in symptomatic relief post fundoplication; regurgitation, heartburn and epigastric pain were all alleviated and this was a statistically significant finding ($p=0.001$). As demonstrated in many other studies, there was a corresponding increase in post-operative dysphagia compared to pre-operative values ($p=0.001$).

During the same time period, a similar study [19], which followed up 145 patients over a period of 6 years, undertook physiological studies four months after operative intervention. Post-operative sphincter pressures directly correlated with heartburn (low pressure) and dysphagia (high pressures), leading the authors to conclude that post-operative adverse symptoms should be assessed with physiological studies, especially manometry, and may help determine long term symptoms following laparoscopic Nissen fundoplication.

Patients who present with extra-oesophageal manifestation of reflux disease should be adequately counselled with regards to post-operative expectations. Iqbal *et al* [20] reviewed 51 patients who had undergone laparoscopic fundoplication for extra-oesophageal reflux. Thirty-nine patients responded to the post-operative questionnaire, with 6 patients stating that they would tolerate pre-operative symptoms (rhinorhoea, cough, voice problems, *etc.*) rather than suffer the post-operative problems (gas bloating, inability to belch, dysphagia, *etc.*). This reinforces the requirement for good preoperative counselling with regards to patient expectations and post-operative outcomes and satisfaction.

As well as measurable outcomes (*i.e.* manometry studies), it is also important to note patient satisfaction with laparoscopic fundoplication. The majorities of patients are satisfied with operative intervention, and cease the use of PPI therapy. There are a small group of patients who will continue to take PPIs, but this in the main will not be for reflux symptoms [21]. Dissatisfaction mainly occurs due to dysphagia and gas bloating symptoms regardless of control of reflux symptoms. The causes of dissatisfaction usually settle after time, with dysphagia and gas bloating symptoms

alleviating [22].

A very small number of patients will have persistent symptoms of GORD after fundoplication with normal 24-hour pH studies. A recent study has demonstrated that there is a positive correlation between recurrent heartburn and functional/psychiatric co-morbidities [23].

1.2.2 BARRETT'S OESOPHAGUS

There are some patients who are asymptomatic with regards to symptoms of reflux and are only found to have signs as an incidental finding on endoscopy [24]. Persistent long-term reflux and ‘silent’ reflux can lead to the development of Barrett’s metaplasia of the squamous epithelium into columnar, more gastric mucosa like epithelium. Historically, Barrett’s was occasionally mistaken for a congenitally short oesophagus. If left untreated, and even after some forms of treatment, dysplastic change can occur, predisposing to subsequent malignant change [25].

Recent studies have suggested that pH study control of reflux disease will eliminate the risk of progression of the Barrett’s oesophagus [26, 27] (with or without mild dysplasia) towards dysplasia and subsequent cancer, with some authors advocating radiofrequency ablation of the residual Barrett’s oesophagus to eliminate the cancer risk in this subset of patients [28]. A small number of patients who have refractory disease and develop progression of the Barrett’s oesophagus may benefit from mucosectomy or radio frequency ablation [29]

The length of the Barrett’s segment also affects outcome [30, 31]. A study by

Miholic *et al* [32], which reviewed 271 patients, who had fundoplication for Barrett's oesophagus, determined that the commonest causes for recurrence of the Barrett's post-operative were the presence of a long segment Barrett's oesophagus and a hiatus hernia greater than 3cm in size.

An important point to note is that patients with Barrett's oesophagus, even after fundoplication and radio frequency ablation must be followed up with surveillance endoscopies at regular intervals, especially if there is evidence of long segment Barrett's oesophagus to help detect early cancerous change [33].

1.2.3 CO-MORBIDITIES

There is limited literature on the effect of medical co-morbidities on the outcomes of laparoscopic fundoplication. Golkar *et al* [34] reviewed a series of 696 patients, of which 158 had one or more medical co-morbidity. The five commonest co-morbidities were vascular (29%), pulmonary (15%), psychiatric (17%), endocrine (11%) and cardiac (8%). With the exception of the co-morbidity group being older (58 *versus* 53 years, p<0.001) and having a longer hospital stay (2 *versus* 1 day, p=0.009), there were no differences in outcomes for symptomatic control of GORD compared with the non-co-morbidity group when a laparoscopic Nissen fundoplication was undertaken.

Varban *et al* [35] compared patients being treated at high and low volume centres in terms of the number of laparoscopic Nissen fundoplications. They deemed a high volume centre as an institution, which undertook greater than 10 procedures a year. They noticed that low volume centres, when the numbers were combined, between

them undertook a significant proportion of funduplications, however, there was a distinct difference in patient demographics. High volume centres had a tendency to operate on older patients with co-morbidities.

Low volume centres had also, a threefold increase in the number of oesophageal perforations; however, there was no difference in either post-operative morbidity or mortality when compared to high volume centres. There was no data available on how patients were managed, but the authors did suggest that laparoscopic Nissen fundoplication operations should be regionalised into high volume centres[35].

1.2.4 BODY MASS INDEX (BMI)

There is a relatively high incidence of GORD in obesity [36]. These patients are highly likely to have decreased lower oesophageal sphincter pressures and abnormal oesophageal acid exposure. A recent study has demonstrated that obese and morbidly obese patients had significantly higher incidence of recurrent hiatal hernia than non-obese patients (88.7 vs. 65.6 %, p<0.05). Morbidly obese patients also demonstrated significantly higher incidence of disrupted fundoplication than non-obese patients (41.7 vs. 19.4 %, p<0.05)[37].

The ideal patient should have a BMI less than 30Kg/m². For obese patients, especially those with very high BMIs, the preferred operation with the highest rate of success for controlling reflux symptoms is the laparoscopic Roux-en-Y gastric bypass[38]. It must be noted, however, that they are susceptible to the same symptoms as fundoplication problems, including dumping and oesophageal motility disorders [38].

1.3 INVESTIGATIONS

1.3.1 OESOPHAGEAL DYSMOTILITY

A number of patients who undergo investigation with manometric studies pre-operatively have abnormal oesophageal motility. This is, in some cases thought to be due as a direct result of GORD, causing acidic irritation, thereby impairing muscle contractility. Although, some sources state that impaired distal oesophageal clearance causes the symptoms of reflux.

Dysmotility can be determined by manometric or impedance testing via a catheter probe inserted through the nostril into the stomach. The probe is then slowly withdrawn to help determine the location of the gastro-oesophageal junction as demonstrated by the potential high-pressure zone on the manometric read out. The patient then takes a mouthful of water and swallows. The bolus propagation pressures and the resting pressures within the oesophagus and the gastro-oesophageal junction can then be measured.

A normal swallow of 5 mL of fluid is initiated by the contraction of the pharynx which propels the bolus towards the upper oesophageal sphincter, which quickly relaxes. A propagated peristaltic wave helps the bolus progress down the oesophagus and the relaxation of the lower oesophageal sphincter permits the bolus to successfully pass through the sphincter and into the stomach. The duration of contraction is usually up to 6 seconds and is measured from the onset of the major upstroke to the end of the pressure wave. The velocity of the peristaltic wave is normally approximately 5 cm/s in the body of the oesophagus. Normal values for successful propagation of the bolus are 7 or greater out of 10 complete swallows of

water [39].

The presence of pre-operative oesophageal dysmotility, therefore, has been linked with the development of post-operative dysphagia, leading some surgeons to tailor their wraps to accommodate the degree of dysmotility. Broeders *et al* [40] demonstrated that there was an increase in short term scores for dysphagia as the degree of wrap increased, and there was a subsequent increase in the number of dilatations and re-operations for dysphagia. Current literature demonstrates that in the long term, there appears to no impact on post-operative dysphagia by tailoring the degree of fundoplication wrap according to pre-operative manometry[41], however, there is yet no real consensus as to the ‘gold standard’ fundoplication.

Prior findings have been reinforced by similar studies, with Simic *et al* [42] demonstrating that immediate post-operative oesophageal dysmotility can cause dysphagia. However, this appears to be self-limiting, with successful relief of symptoms on long term follow up. A recent retrospective study [43] has demonstrated that regardless of baseline oesophageal motility, a Nissen fundoplication has low rates of post-operative dysphagia; leading the authors to conclude that oesophageal dysmotility does not preclude a Nissen fundoplication from being performed. Herbella *et al* [44] have even suggested that undertaking a Nissen fundoplication, by virtue of increasing the lower oesophageal pressure, may actually increase the strength of oesophageal peristalsis in patients with abnormal pre-operative oesophageal motility, resulting in normalisation of peristalsis in the majority of patients.

There are some authors [45, 46] who have suggested that partial funduplications are the operation of choice in individuals with oesophageal dysmotility, offering adequate reflux control without affecting oesophageal dysmotility and resulting in a low rate of post-operative dysphagia.

An incidental finding [47], described in a recent case report has also demonstrated the potential of erythromycin, a macrolide antibiotic has demonstrated motilin like activity, a potential therapeutic agent to alleviate dysmotility and increase lower oesophageal pressures in patients who suffer post-fundoplication dysphagia related to pre-operative dysmotility. It must be noted that this finding requires further study, preferable in a randomised controlled trial to determine whether this has evidence based therapeutic use.

1.3.2 OESOPHAGEAL PHYSIOLOGY AND pH STUDIES

Oesophageal physiological studies play a fundamental role in the modern day management of GORD in determining which patients will benefit from anti-reflux surgery. They are also extremely useful in the post-operative period in determining quantifiable reflux in patients who suffer from recurrence of reflux symptoms post-fundoplication [48].

In determining which patients may be suitable for anti-reflux surgery, diagnostic criteria should include symptom associated probability and symptom index alongside oesophageal acid exposure time [49]. Patients who experience atypical/no symptoms at all during 24-hour pH monitoring may still obtain a good result from anti-reflux surgery. However, care must be taken to satisfactorily counsel patients

that their outcomes may not be as good as those with typical symptoms [50].

pH studies are undertaken by placing a probe located at the end of a catheter or a wireless capsule, via the nostril to sit just above the gastro-oesophageal junction. It is then connected to a monitor, which will measure the number and duration of episodes of pH exposure of that region of the oesophagus over a 24-hour period. The patient also has a button that they need to press every time they experience their symptoms of heartburn to help establish correlation between their symptoms and quantifiable reflux measure, allowing for the determination of the Symptom Index.

Through the evolution of technology, the Bravo device is a small capsule, about the size of a gel cap, is temporarily attached to the wall of the esophagus during an upper endoscopy. The capsule measures pH levels in the oesophagus and transmits readings by radio telecommunications to a receiver worn on the patients' belt or waistband. The receiver has several buttons on it that will be pressed by the patient to record symptoms of GORD, such as heartburn [51-57].

Although these studies are extremely useful in predicting who will benefit from anti-reflux surgery, there is no single marker, including number of acid/non-acid reflux events, even multi-channel intra-luminal impedance pH monitoring (MII-pH) which can help determine the outcome post-fundoplication [58]. Similar to the other physiological studies, in MII-pH, a tube is passed via a nostril, with the tip of a catheter resting just above the gastro-oesophageal junction.

Impedance testing is then undertaken by measuring the change in resistance that occurs in a pair of metallic rings mounted on the catheter, which are supplied by an alternating current as a bolus passes by the rings. Usually, in an empty oesophagus, there is very little laying between the catheter and the mucosal surface, hence, relatively few ions present. If a liquid bolus passes by, this has a higher concentration of ions, thereby higher conductivity, resulting in a change in resistance. When the oesophagus contracts this causes a momentary decrease in the luminal diameter of the oesophagus and therefore an increase in impedance. When MII-pH is combined with pH or manometry, it allows demonstration of cephalad-gastric reflux or bolus propagation.

Patients who have had a partial fundoplication are likely to have more acid exposure compared to total fundoplication, although the numerical values remain within normal limits [59]. As mentioned previously, oesophageal physiological studies play an invaluable role in assessing patients who suffer from post-fundoplication recurrent reflux. Recurrent symptoms after fundoplication with a negative pH study have been shown to have an association with pre-existing psychiatric/functional disorders [60].

There is very limited data on the usage of intra-operative manometry on predicting patients who will develop post-operative adverse effects or using manometry to tailor the degree of fundoplication to patients' requirements. The only determinant of post-operative dysphagia appears to be the presence of pre-operative dysphagia [61]. Both the paper submitted as a part of this thesis [12] and Del Genio *et al*'s study from 2007 [62] demonstrate that intra-operative manometry can help provide good

outcomes and show potential in helping predict those patients that will suffer from potential adverse outcomes *i.e.* post-operative dysphagia.

1.4 ANTI-REFLUX SURGERY

1.4.1 OPEN *VERSUS* LAPAROSCOPIC ANTI-REFLUX SURGERY

The initial operative interventions up until the turn of the millennia were historically undertaken using the open operative approach. The main aim of the operation is thought to be:

- The creation of a floppy valve by maintaining close apposition between the abdominal oesophagus and the gastric fundus. As intra-gastric pressure rises, the intra abdominal oesophagus is compressed by the adjacent fundus.
- Exaggeration of the flap valve at the angle of His.
- Increase in the baseline pressure generated by the lower oesophageal sphincter.
- Reduction in the triggering of transient lower oesophageal sphincter relaxations.
- Reduction in the capacity of the gastric fundus, thereby speeding proximal and total gastric emptying [63].

However, with the advent and evolution of laparoscopic surgery, the ‘gold standard’ approach rapidly became the laparoscopic fundoplication.

Even though laparoscopic fundoplication has been adopted as the preferred approach, there are still numerous studies being undertaken, especially in the last decade to determine whether it is actually superior in terms of outcomes to the open fundoplication approach.

One of the original studies undertaken in this field was by Ackroyd *et al* [64], and they performed a randomised controlled trial to determine whether there was a

significant difference in both in the logistics and outcomes of open compared to laparoscopic Nissen fundoplication. Both groups of patients were selected so that they did not have the presence of pre-operative oesophageal dysmotility and were followed for 1-year post operatively.

The authors noted an increased operating time between the two groups of patients; with laparoscopic fundoplication having a mean duration of 82 minutes compared the open operation requiring 46 minutes. However, recovery time, post-operative control of pain and time to solid food intake was better in the laparoscopic intervention group. There was no calculable difference in post-operative dysphagia and satisfactory outcomes between either group of patients. There were equally good outcomes in both groups at the 1-year follow up point.

A similar study was undertaken a few years later [65], which utilised a different form of fundoplication, known as the posterior fundoplication. This randomised controlled trial demonstrated that patients who underwent an open procedure had higher rates of complication, increased length of hospital stay and increased time off work compared with the laparoscopic group. However, they did note that there was an increased incidence of post-operative recurrent reflux in the laparoscopic group. There was no difference in the outcomes between the groups at either the 1 or the 3-year follow up appointment.

At this point, it appears that the main differences between the open and laparoscopic groups are occurring in the short-term with no long-term differences in outcome measures. Another collection of studies that reinforce this claim [66, 67] also

demonstrate that the only significant difference in the immediate peri-operative period is that laparoscopic fundoplication is longer in duration compared to the open procedure, and there is no evidence that one technique is superior compared to the other in the long-term.

Further studies have demonstrated a decrease in hospital stay and subsequent healthcare costs in patients who have preferentially undergone a laparoscopic repair compared to patients who have had an open procedure. A recent study [68] undertaken on patients who were being admitted for re-do fundoplication demonstrated the median cost was cheaper for a laparoscopic procedure compared to an open procedure, \$13,303 compared to \$22,487. The average length of stay for a laparoscopic fundoplication was 4 days, compared to 10 days for an open procedure. It must be noted that although the overall stay in the laparoscopic group was shorter, the cost per day was higher in the laparoscopic group, \$3224 *versus* \$2721. The study also found that patients who underwent a laparoscopic procedure were less likely to get infective and other post-operative complications. It must be noted that this study was undertaken on patients who already had a laparotomy, but does suggest that patients who have a laparoscopic intervention have a shorter hospital stay than patients who have open surgery.

Studies have also been undertaken to evaluate whether there are significant differences in the inflammatory response between open and laparoscopic interventions, which could potentially affect the outcomes of fundoplication. A recent study by Knatten *et al* [69], has demonstrated no significant differences between either group according to measurements of Tumour Necrosis Factor Alpha

(TNF- α), Interleukin 6 (IL-6) and Interleukin 8 (IL-8).

Therefore, current evidence suggests that although there are no differences in outcomes of reflux control in the long term, in the short term, laparoscopic intervention is superior compared to open fundoplication with regards to decreased post operative complications, decreased hospital stay and decreased hospital costs.

1.4.2 HIATAL REPAIR

A number of intra-operative factors have been implicated in the development of unwanted outcomes after laparoscopic fundoplication. Mechanical obstruction due to narrowing of the oesophageal hiatus is constantly being discussed as the causative factor and in some circumstances re-operation is required to alleviate this stenosis/constriction when it occurs. Different techniques of hiatal repair have been trialed to determine whether this affects outcome. Watson et al [70] endeavoured to clarify this point by undertaking a 102 patient randomised controlled study to determine whether there was a difference between anterior and posterior hiatal repair. They excluded all patients with pre-operative dysmotility and found no difference in outcomes in either group of patients.

A subsequent 5-year follow up study undertaken by the same group [71] did find a statistically significant difference in the actual number of re-operations between the groups: two after anterior hiatal repair *versus* 11 after posterior hiatal repair. There were no statistically significant differences in satisfaction outcome scores at the 5-year follow up point.

The 10-year follow up of this group of patients [72] reported that patients who have had an anterior repair of the hiatus were less likely to report dysphagia to lumpy solids compared to those patients who had a posterior hiatal repair (14.0% *versus* 39.5%, p=0.01).

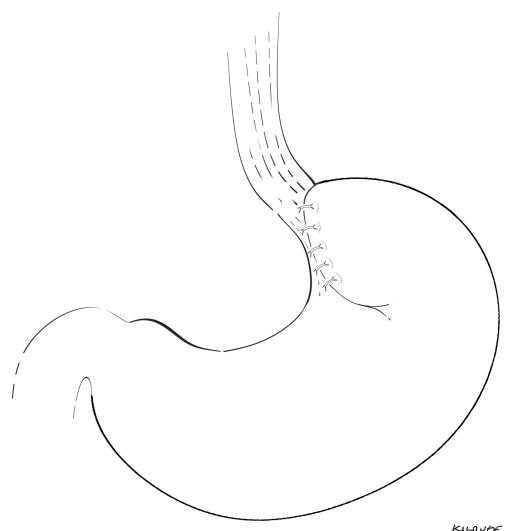
1.4.3 FUNDOPPLICATION VARIANTS

Numerous types of fundoplication exist. Dr. Rudolf Nissen (1896-1981), first described the fundoplication procedure in the 1950s for treatment of severe reflux oesophagitis [73]. The classic Nissen fundoplication involves a full 360⁰ wrap of the fundus around the lower oesophagus. Other operations include a sub-total wrap, such as the Lind fundoplication (a 270-300⁰ wrap), or a partial (180⁰) wrap, which can be performed anterior or posterior to the lower oesophagus.

The laparoscopic operation begins with dissection of the hiatal pillars, followed by full oesophageal mobilisation and posterior hiatal repair using a median of 2 non-absorbable sutures. A tape is placed around the oesophagus to assist with oesophageal retraction and the short gastric vessels are not divided. Then the differing types of fundoplication are performed:

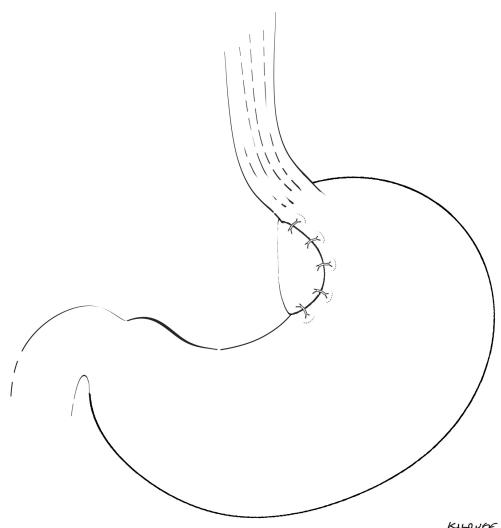
Anterior fundoplication: the fundus of the stomach is brought across the front of the lower oesophagus and is sutured to the right side of the oesophagus using 2 nylon sutures and then to the right crus with a further 2 nylon sutures. If necessary, the fundus is sutured to the apex of the crura (Figure 1.4.3.1).

Figure 1.4.3.1: Anterior fundoplication



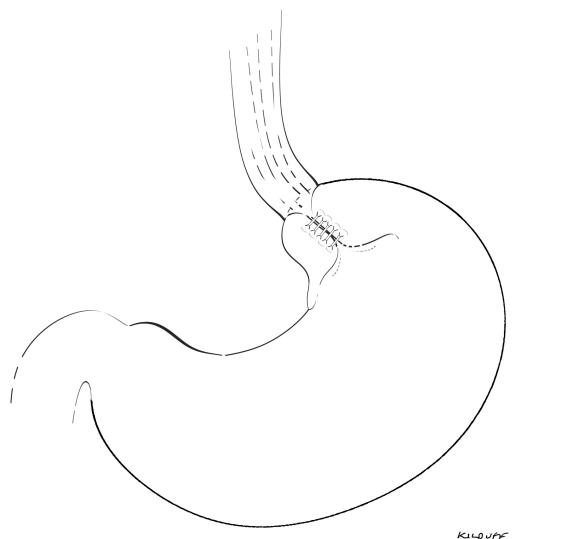
Posterior fundoplication: the fundus of the stomach is wrapped behind the lower oesophagus and is again anchored to the right side of the oesophagus and the right crus (Figure 1.4.3.2).

Figure 1.4.3.2: Posterior fundoplication



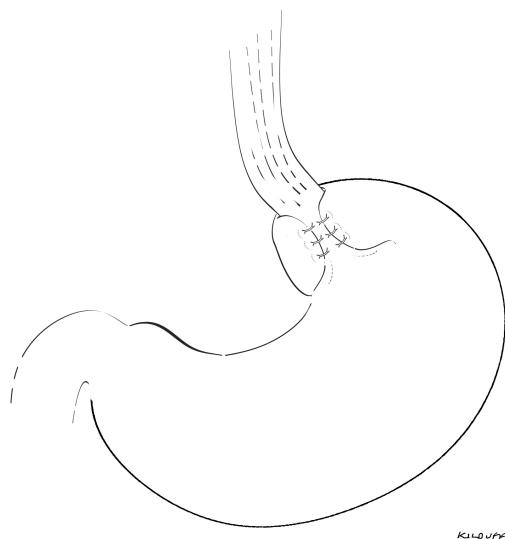
Nissen fundoplication: a bougie is used in all cases. Then the posterior fundus of the stomach is wrapped behind the lower oesophagus and the anterior fundus of the stomach is brought across the front of the lower oesophagus and 3 sutures are placed fundus to fundus (one suture incorporating the oesophagus)(Figure 1.4.3.3).

Figure 1.4.3.3: Nissen fundoplication



Lind fundoplication, no bougie is used: A similar operation to the Nissen is undertaken, however, a 'bare' area is left between the anterior and posterior fundal wraps resulting in a 270-300° wrap being formed using six sutures (3 on each side)(Figure 1.4.3.4).

Figure 1.4.3.4: Lind fundoplication



1.5 CRITICAL OVERVIEW

At the time of undertaking these trials and publishing the manuscripts there was limited literature on the long-term outcomes of these procedures. The initial available literature that was reviewed and the points raised demonstrated that there was no real consensus as to which anti-reflux procedure can be deemed the ‘gold standard’. There are many factors, which can determine the outcome, ranging from pre-existing conditions to the operative technique. Given such varied approaches and published materials, it was deemed prudent to undertake randomised controlled trials of the four commonest anti-reflux procedures to establish which one offered the best outcome as determined by quantitative and qualitative reflux.

Anterior and posterior fundoplication are partial wraps, encircling only around 180° of the oesophagus as compared to Nissen and Lind funduplications, which encircle 360° and $270-300^{\circ}$ respectively. This may be advantageous, as a partial wrap may decrease postoperative symptoms such as dysphagia, inability to belch, post prandial fullness, epigastric bloating and flatus [74-77].

Nissen fundoplication is a total wrap encircling the oesophagus by 360° , whereas Lind fundoplication is a subtotal wrap encircling the oesophagus by $270-300^{\circ}$. A total wrap may have disadvantages in that it may increase post-operative symptoms of dysphagia, bloating, inability to belch and increased flatus as compared to a subtotal wrap. However, conversely it may have the advantage of decreased rates of recurrent reflux when compared to subtotal wrap [78-80].

There are several trials in the literature comparing a variety of funduplications [81-83]. At the time of the studies there was limited literature comparing Anterior and Posterior fundoplication and Nissen *versus* Lind fundoplication in randomised controlled trials, as well as long-term symptom control and outcome of individuals who have undergone partial fundoplication [74].

The aim of these studies was to compare the outcome of Anterior *versus* Posterior and Nissen *versus* Lind fundoplication in individuals with gastro-oesophageal reflux disease, to determine whether one is superior in the control of gastro-oesophageal reflux disease and incidence of undesired post-operative symptoms. The primary outcome measure was the resolution of the symptoms of GORD, with secondary measures being absence of adverse post-operative symptoms, requirement for re-operation, Outcome scale and Visick grading, whereas the intra-operative manometry study analysed the difference in pressures at various stages in the operation.

The initial study was to determine the differences in outcome between Anterior and Posterior funduplications. Given the favourable outcome of the Posterior fundoplication, the natural progression was to then compare Nissen and Lind funduplications.

Given the data available from the two randomised controlled trials, the authors deemed it prudent to combine the data sets and undertake an analysis to determine whether there was a difference between the combined groups of Anterior and Posterior *versus* Nissen and Lind fundoplication group.

A major problem associated with anti-reflux surgery is the potential of post-operative dysphagia occurring. Many trials have endeavoured to establish a pattern or potential methods of identifying patients who are at risk of developing these symptoms.

Unfortunately, dysphagia is a common occurrence after fundoplication and its pathophysiology is still relatively poorly understood. Studies undertaken on individuals with pre-existing motility disorders have failed to demonstrate adverse outcomes even when a Nissen fundoplication is utilised [84] and this is re-iterated in other studies which have failed to demonstrate useful criteria by which one can anticipate post-fundoplication dysphagia [85].

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2. METHODS

2.1 PATIENT SELECTION

It was calculated that 100 patients were required to demonstrate a 20% difference in outcome measures, with a significance level of $p<0.050$ and a power of 90%. All analyses were performed on an intention-to-treat basis.

All individuals presenting for primary gastro-oesophageal reflux surgery were considered for entry into these trials, and enrolled on an intention-to-treat basis. For the fundoplication trials, similar selection criteria and methods were used, as detailed by Ackroyd *et al* (2004) [86].

Inclusion criteria were:

- Age >18 years
- Quantifiable evidence of GORD

Exclusion criteria were:

- Oesophageal motility disorder
- Requirement of a concurrent abdominal procedure
- Previous anti-reflux surgery
- Not suitable for general anaesthesia
- Not suitable for laparoscopy
- BMI greater than 30
- Inability to give informed consent
- Pregnant

All eligible patients underwent pre-operative endoscopy and oesophageal manometry, followed by 24-hour ambulatory pH investigations.

If pre-operative endoscopy and pH/manometric studies were found to be negative, and patients were still experiencing symptomatic reflux, they were sent for barium studies.

The comparison of fundoplication analysis was undertaken by combining the groups in the laparoscopic anterior *versus* posterior fundoplication randomised controlled trial and comparing that to the laparoscopic Nissen *versus* Lind fundoplication randomised controlled trial.

2.2 PATIENT RANDOMISATION

Patients were randomised to undergo either anterior or posterior fundoplication in one trial, and Nissen or Lind fundoplication in the other. Informed consent was obtained and randomisation was achieved by opening an opaque sealed envelope, after the individual was anaesthetised. At follow-up, both the patient and clinician were aware of the fundoplication they had received.

The South Sheffield Research Ethics Committee approved the study protocols and the studies were conducted in accordance with the World Medical Association declaration of Helsinki (revised 1989). Since the inception of the studies, the South Sheffield Research Ethics Committee has been amalgamated with the North Yorkshire and Humberside Research Ethics Committees. Unfortunately, this has led to the transfer of electronic data only after the 2005 date, therefore, the only Research Ethics Committee Number available from the committee is for the Intra-operative Manometry trial – 05/Q2305/105. The Anterior *versus* Posterior fundoplication trial was registered with the ISRCTN Registry (ISRCTN31024562)

2.3 PATIENT ASSESSMENT

During initial enrolment onto the trial, patients presenting with GORD were interviewed by an experienced Consultant Surgeon (RA or CJS), both of whom had extensive operative experience of performing all four variants of fundoplication. Questions were asked using a standard, structured questionnaire. Subsequent clinical appointments were undertaken by an experienced clinician (RA or CJS) at 1, 3, 6 and 12 months after the procedure using the same questionnaire format. At each visit, it was determined whether the individual was still convalescent or had returned to full activity. The presence or absence of a detailed list of symptoms was sought. Patients ranked the outcome of surgery on a modified Visick grading (Table 2.3.1), and were asked to score the outcome ranging from excellent to poor.

Table 2.3.1: Modified Visick grading

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

Stationary oesophageal manometry including response to several swallows of water and ambulatory pH monitoring was undertaken prior to operative intervention, and approximately 3 months post-procedure. A standardised procedure was closely followed; patients were fasted for 6 hours prior to the pH and manometry studies. A single use antimony crystal probe (Mediplus, High Wycombe, UK) was positioned 5cm above the lower oesophageal sphincter and connected to a Flexilog™ 2000

datalogger (Oakfield Instruments, Whitney, UK) [86]. The total number of reflux episodes and the percentage of time the pH was less than 4 recorded.

Prior to manometry being performed, all individuals were asked to cease medication known to affect oesophageal motility for 48 hours prior to the test. An eight lumen water-perfused catheter was used in 4 of the lumens placed concentrically at the region of the sphincter and amplified signals recorded using a PhoenixTM recording system (Albyn Medical, Dingwall, UK). The location and resting pressure of the lower oesophageal sphincter (or high pressure zone post-fundoplication) was located by the station pull through technique. Oesophageal wave amplitude and propagation were measured by ten 10 ml water bolus swallowing 30 seconds apart.

For the intra-operative manometry study, after establishing anaesthesia, an eight-lumen water perfused catheter (Oakfield Instruments Limited, Oxford, England) was placed into the oesophagus of the patient via the nose. The catheter was attached to a flexilog 3000 datalogger (Oakfield Instruments Limited, Oxford, England) that in turn was connected to a portable pneumohydrolic pump (Oakfield Instruments Limited, Oxford, England). Gastric pressure, the location and resting pressure of the lower oesophageal sphincter (or high pressure zone post-fundoplication) and oesophageal body pressure was obtained using the station pull through technique. Manometry readings were then undertaken at pre-determined intervals *i.e.* post-anaesthetic with no pneumoperitoneum, post-anaesthetic with pneumoperitoneum, post-fundoplication with pneumoperitoneum and post-fundoplication with no pneumoperitoneum

Laparoscopic anterior and posterior funduplications were carried out as described previously [87, 88]. After introduction of the laparoscope, a brief inspection was performed to identify any hiatus hernia or the presence of adhesions; these were then subsequently graded. Intra-operative problems and the requirement to convert to open surgery were then noted. A standardised procedure was followed and any reason for variation was documented.

Operative procedures were undertaken by one of two experienced Upper GI Consultant Surgeons (RA and CJS). The operation began with dissection of the hiatal pillars, followed by full oesophageal mobilisation and posterior hiatal repair using a median of 2 nylon sutures. A tape was placed around the oesophagus to assist with oesophageal retraction and the short gastric vessels were not divided. In the anterior fundoplication, the fundus of the stomach was brought across the front of the lower oesophagus and was sutured to the right side of the oesophagus using 2 nylon sutures and then to the right crus with a further 2 nylon sutures. If necessary, the fundus was sutured to the apex of the crura. In the posterior fundoplication, the fundus of the stomach was wrapped behind the lower oesophagus and was again anchored to the right side of the oesophagus and the right crus.

Laparoscopic Nissen and Lind funduplications were performed as described previously [89] by one of two experienced Consultant Upper Gastro-Intestinal Surgeons (RA and CJS). After introduction of the laparoscope, a brief inspection was performed to identify any hiatus hernia or the presence of adhesions; these were then subsequently graded. Intra-operative problems and the requirement to convert

to open surgery were then noted. A standardised procedure was followed and any reason for variation was documented.

Both procedures began with dissection of the hiatal pillars, followed by full oesophageal mobilisation and posterior hiatal repair. A tape was placed around the oesophagus to assist with oesophageal retraction and the short gastric vessels were not divided. In the Nissen fundoplication, a bougie was used in all cases, with the size used depending on the observed diameter of the oesophagus. Then the posterior fundus of the stomach was wrapped behind the lower oesophagus and the anterior fundus of the stomach was brought across the front of the lower oesophagus and 3 sutures were placed fundus to fundus (one suture incorporating the oesophagus).

In the Lind fundoplication, no bougie was used. A similar operation to the Nissen was undertaken, however, a ‘bare’ area was left between the anterior and posterior fundal wraps resulting in a 270-300^o wrap being formed using six sutures (3 on each side). The operation was given a difficulty grading of 1-10 (1=easy; 10=difficult). This was an analogue qualitative assessment, with a value of 1 correlating with an operation that was undertaken with no difficulty, and a value of 10 correlating with a near impossible operation with extensive adhesions. The length of post-operative hospital stay and symptoms at discharge were noted.

2.4 POST-OPERATIVE CARE

Oral fluids were commenced on the evening of surgery, and subsequently, if tolerated, a soft diet was allowed the next day and a dietary advice sheet provided to the patient to adhere to for the next six weeks. This included instructions not to eat bread or lumpy foods for the first four weeks. Discharge from hospital was allowed when the patient was stable and able to manage at home. Ant-reflux medication was stopped immediately after the operation. The patient was then followed up at 1, 3, 6 and 12 months post procedure using a standardised questionnaire.

2.5 STATISTICAL ANALYSIS

The primary outcome measure was the resolution of the symptoms of GORD, with secondary measures being absence of adverse post-operative symptoms, requirement for re-operation, Outcome scale and Visick grading, whereas the intra-operative manometry study analysed the difference in pressures at various stages in the operation.

The values presented are the mean and, where appropriate, confidence intervals and standard deviation are provided. Data was analysed using SPSSTM for WindowsTM, version 15 (SPSS, Chicago, Illinois). The following tests were used to assist analysis: t-test, χ^2 test, Fisher's exact test and Mann-Whitney U-test. A p-value <0.050 was assumed to be statistically significant.

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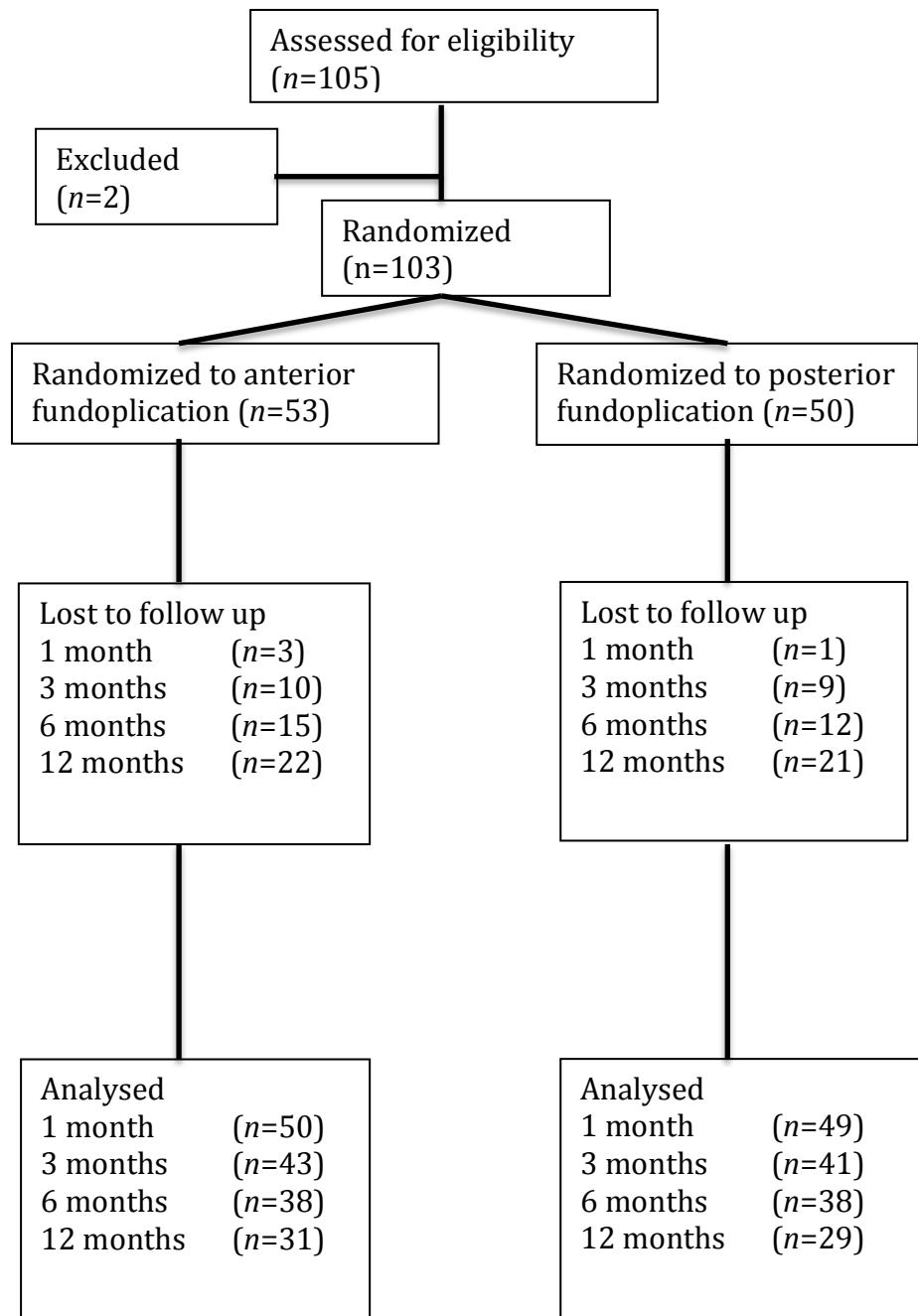
3. RESULTS

3.1 OUTCOMES FROM LAPAROSCOPIC ANTERIOR VERSUS POSTERIOR FUNDOPPLICATION RANDOMISED CONTROLLED TRIAL

During the study period, 105 patients were enrolled into the study, and 103 were randomised to either anterior or posterior fundoplication. Fifty-three individuals were randomised to anterior fundoplication and 50 to posterior fundoplication. Two patients were excluded from the analysis, as no documentation was available for analysis.

Of the 103 patients that were entered into the study, 99 (96%) attended the follow up at 1 month, 84 (82%) at 3 months, 76 (74%) at 6 months and 60 (58%) at 1 year. There were no withdrawals from the study. Numerous attempts were made to ensure individuals attended clinic appointments; however, it was not possible to contact all patients at each follow-up interval, even with attempted telephone calls (Figure 3.1.1).

Figure 3.1.1: Study flow diagram



As demonstrated in Table 3.1.2, the two groups were well matched for age, sex, height, weight, cigarette and alcohol consumption. There was an appreciable difference in the duration of symptoms in the two groups; with individuals in the posterior fundoplication group having symptoms for longer, however, this was not statistically significant ($P = 0.861$; Mann Whitney U-test). Table 3 outlines the findings at oesophagogastroduodenoscopy, and if there was presence of hiatal hernias.

Table 3.1.2: Patient Demographics

	Anterior (n=53)	Posterior (n=50)	p value
Age (years)*	43 (16-79)	43 (18-76)	0.777
Sex ratio (M:F)	36:17	38:12	0.367
Height (cm)*	169 (147-187)	170 (147-187)	0.810
Weight (kg)*	80.2 (55-129)	78.9 (46-115)	0.676
Cigarette smoker	11	17	0.131
Alcohol consumer	41	38	0.876
Previous surgery (not related)	23	20	0.730
Duration of symptoms (months)*	75.3 (12-360)	94.9 (12-480)	0.861
Preoperative medication			
Antacid	19	11	0.124
H ₂ Blocker	3	6	0.259
PPI	51	46	0.365

*Values are mean (range)

Table 3.1.3: Pre-operative OGD findings

<u>Oesophageal findings</u>	Anterior (n=52)	Posterior (n=47)
Normal	25	24
Erythema	4	4
Single ulceration	10	5
Multiple ulceration	5	5
Circumferential ulceration	1	0
Barrett's	7	3
<u>Hiatus hernia</u>		
No	27	22
Sliding	24	25
Mixed	1	0

There was no appreciable difference in the individuals' pre-operative symptoms (Table 3.1.4). Visick grading was similar for both groups pre-operatively (Table 3.1.5). Sixteen patients were found to have normal ambulatory pH studies; of these four patients demonstrated oesophagitis varying from mild erythema to Barrett's oesophagus. The remaining 12 patients were found to have hiatus hernias (n=6), wide open gastro-oesophageal junction (n=4) or reflux on barium studies (n=2).

Table 3.1.4: Number of patients with each symptom before and after surgery

	Pre-operative		1 month		3 months		6 months		12 months	
	Ant	Post	Ant	Post	Ant	Post	Ant	Post	Ant	Post
	(n=53)	(n=50)	(n=50)	(n=49)	(n=43)	(n=41)	(n=38)	(n=38)	(n=31)	(n=29)
Heartburn	50	49	9	1	12	0	13	2	7	3
Epigastric pain	31	31	2	6	6	4	2	4	3	1
Regurgitation	44	48	4	2	4	0	2	2	1	1
Lumpy solid dysphagia	10	13	16	31	5	14	4	5	2	3
Soft solid dysphagia	1	1	0	0	0	0	0	0	1	0
Liquid dysphagia	0	0	0	0	0	0	0	0	0	0
Odynophagia	7	9	2	2	2	1	1	0	0	0
Postprandial fullness	24	27	5	6	2	0	1	2	0	0
Inability to belch	0	0	3	4	0	1	0	3	0	0
Epigastric bloat	27	30	13	11	4	3	3	3	0	2
Anorexia	4	7	1	1	2	1	1	1	0	0
Nausea	12	15	1	1	0	0	0	2	1	1
Vomiting	12	22	3	0	2	0	1	0	0	1
Nocturnal cough	10	14	3	0	1	0	0	0	1	0
Nocturnal wheeze	9	13	3	0	0	0	0	0	0	0
Flatus	0	0	5	4	3	2	0	1	2	1
Diarrhoea	0	0	1	1	1	0	1	2	1	1

Table 3.1.5: Outcome scale and Visick grading

Outcome	Pre-operative				1 month				3month				6 month				12 month			
	Ant	Post	Ant	Post	Ant	Post	Ant	Post	Ant	Post	Ant	Post	Ant	Post	Ant	Post	Ant	Post		
	(n=53)	(n=50)	(n=50)	(n=49)	(n=43)	(n=41)	(n=38)	(n=38)	(n=38)	(n=38)	(n=31)	(n=31)	(n=31)	(n=29)						
Excellent	-	-	20	11	24	24	20	26	15	21										
Good	-	-	20	31	8	14	11	9	8	6										
Fair	-	-	9	7	6	3	4	3	7	2										
Poor	-	-	1	0	5	0	3	0	1	0										
Visick grade																				
1	0	0	19	7	23	22	19	25	15	21										
2	5	5	22	35	9	17	12	11	8	6										
3	15	20	8	6	7	2	3	2	6	2										
4	33	25	0	1	2	0	2	0	2	0										
5	0	0	1	0	2	0	2	0	0	0										

The mean operating time in the anterior group was 48 (21-87) minutes and for the posterior group 52.3 (21-92) minutes ($p=0.545$), and the total theatre time for the anterior group was 71.4 (40-110) minutes and in the posterior group 73.3 (40-196) minutes ($p=0.360$). There was no difference in the surgeon's perception of difficulty between the two groups; mean difficulty scores were 4.1 (1-10) for anterior, compared to 4.5 (1-10) for the posterior group ($p=0.423$). Two individuals, one from each group had to be converted to open procedure, due to bowel and liver injury respectively. The hospital stay was comparable in both groups 3.2 (1-15) *versus* 3.1 (1-9) days ($p=0.163$).

There were no fatalities in either group. In the anterior group, there were 4 post-operative complications; one respiratory tract infection, one acute renal failure and two cardiovascular complications. The posterior group demonstrated only 2 complications; one pulmonary embolus and one respiratory tract infection.

At discharge, there was no major difference in symptoms, with dysphagia to solids in 4 of 51 in the anterior group *versus* 8 of 50 in the posterior group ($p=0.205$), and inability to burp being 2 of 51 *versus* 3 of 50 ($p=0.630$) respectively. However, there was a significant difference in gas bloat, 8 of 51 *versus* 2 of 50 respectively ($p=0.049$). There was also, no major difference in the time it took individuals to get back to full activities; at one month, 35 of 48 *versus* 34 of 47 were back to full activities ($p=0.615$). The dysphagia score at all stages of assessment was comparable in both groups; 44.0 (20-45) *versus* 44.5 (40-45) at 12 months ($p=0.621$).

Eight individuals required re-operation due to symptom recurrence in the anterior group and 2 individuals in the posterior group had to be re-operated due to recurrent quantifiable reflux ($p=0.057$). Detailed analyses of the clinical assessments are displayed in Table 3.1.4 and Table 3.1.5, and demonstrate two appreciable differences between the two groups. First, the incidence of early post-operative dysphagia was slightly higher in the posterior fundoplication group as compared to the anterior group (at 1 month $p=0.002$; at 3 months $p=0.014$). Outcomes and modified Visick were similar in both groups (Table 3.1.5). Also, the number of individuals suffering from post-operative heartburn was greater in the anterior fundoplication group (at 1 month $p=0.008$, at 3 months $p=0.001$ and at 6 months $p=0.002$).

Patients were invited to attend for post-operative pH and manometry. Thirty-five of 53 patients (66%) in the anterior group and 37 of 50 patients (74%) in the posterior group underwent repeat investigations. Table 3.1.6 demonstrates the preoperative and post operative time below pH 4 ($p=0.322$ & 0.337), and pH grading was comparable between the two groups. Ten patients had persistent heartburn at 1 year; however, of these ten, only one individual had quantifiable reflux at ambulatory pH monitoring the remaining 9 having normal ambulatory pH studies. Oesophageal motility was also comparable between the two groups with 23 of 47 *versus* 15 of 49 ($p=0.066$) being abnormal pre-operatively, and 19 of 35 *versus* 13 of 36 ($p=0.124$) being abnormal post-operatively.

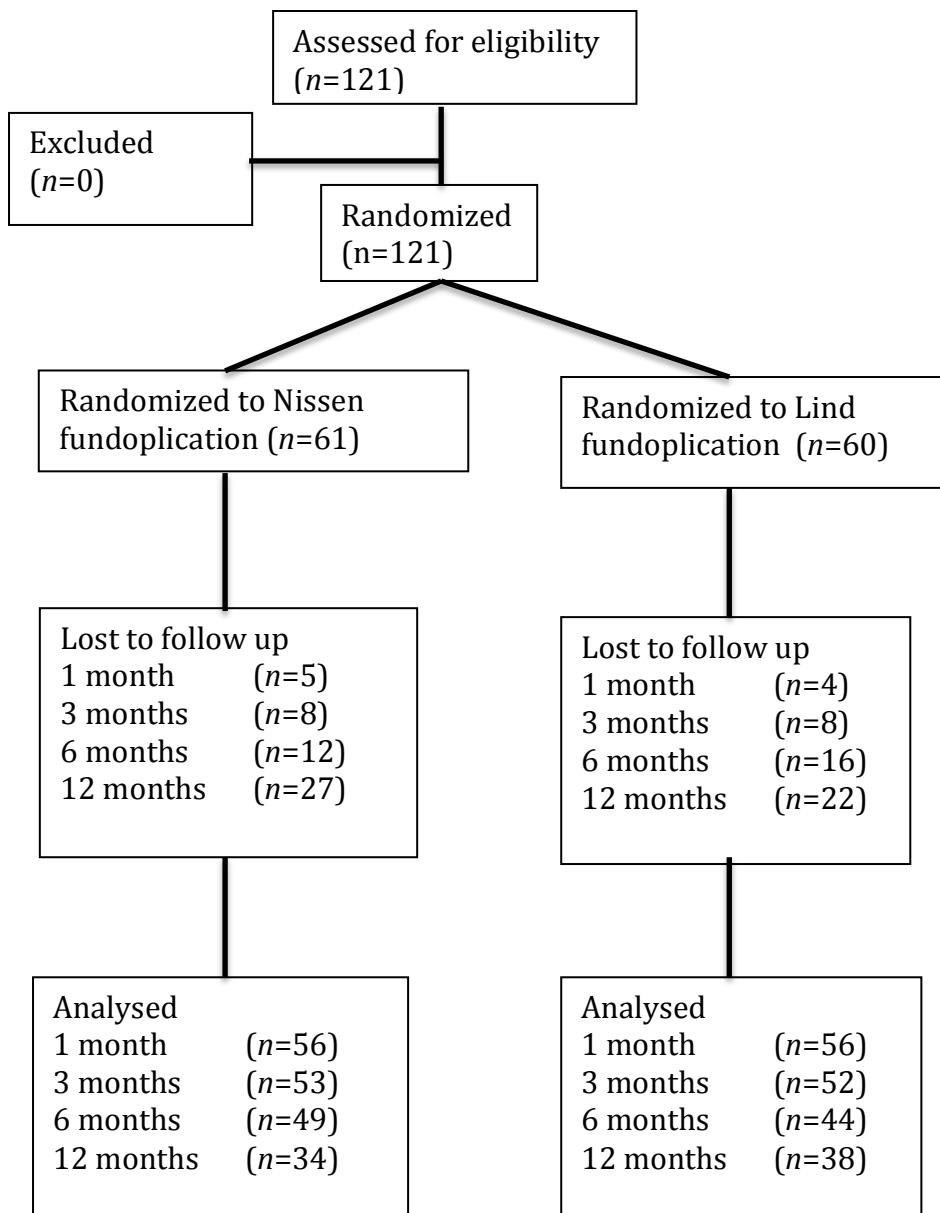
Table 3.1.6: Percentage pH below pH 4 in a 24 hour period and pH Grading

	Preoperatively Anterior (n=48)	Postoperatively Posterior (n=49)	Postoperatively Anterior (n=33)	Postoperatively (n=37)
% time below pH 4 in 24hrs	10.2(0.3-39.9)	11.7(0-58.6)	2.4(0-13.9)	1.4(0-9.5)
pH Grading				
No reflux (pH<4 less than 4%)	11	5	29	33
Mild reflux, no symptoms (pH<4 between 4-7%)	8	3	0	2
Mild reflux + symptoms (pH<4 between 4-7% with Good symptom correlation)	4	7	1	0
Severe reflux + symptoms (pH<4 more than 7%)	25	34	3	2

3.2 OUTCOMES OF LAPAROSCOPIC NISSEN *VERSUS* LIND FUNDOPPLICATION RANDOMISED CONTROLLED TRIAL

During the study period, 121 patients were enrolled into the study, and were randomised to Nissen (n=61) or Lind fundoplication (n=60). Of these, 112 (92%) attended follow up at 1 month, 105 (87%) at 3 months, 94 (78%) at 6 months and 72 (60%) at 1 year. There were no withdrawals from the study. However, despite numerous attempts to make sure that patients attended clinic appointments, there were still patients lost to follow up (Figure 3.2.1).

Figure 3.2.1: Study flow diagram



As demonstrated in Table 3.2.2, the two groups were well matched for age, sex, height, weight, cigarette and alcohol consumption. Table 3.2.3 provides the data for pre-operative endoscopy findings.

Table 3.2.2: Patient Demographics

	Nissen (n=61)	Lind (n=60)	p value
Age (years)*	45 (22-70)	49 (21-78)	0.947
Sex ratio (M:F)	38:23	39:21	0.542
Height (cm)*	170 (150-195)	171 (152-190)	0.711
Weight (kg)*	83.7 (55-172)	81.7 (45-115)	0.701
Cigarette smoker	11	14	0.402
Alcohol consumer	43	45	0.391
Previous surgery (not related)	33	34	0.583
Duration of symptoms (months)*	92.4 (12-360)	110.1 (12-860)0.476	
Preoperative medication			
Antacid	8	11	0.136
H ₂ Blocker	8	5	0.079
PPI	53	52	0.585

*Values are mean (range)

Table 3.2.3: Pre-operative OGD findings

<u>Oesophageal findings</u>	Nissen (n=58)	Lind (n=55)
Normal	24	25
Erythema	7	2
Single ulceration	10	12
Multiple ulceration	4	6
Circumferential ulceration	1	0
Stricture	2	0
Barrett's	10	10
<u>Hiatus Hernia</u>		
No	27	22
Sliding	24	25
Mixed	1	0

There was an appreciable difference in the duration of symptoms in the two groups; with individuals in the Lind fundoplication group having symptoms for longer, however, this was not statistically significant ($p=0.476$; Mann-Whitney U Test).

There was no appreciable difference in the individuals' pre-operative symptoms (Table 3.2.4). Visick grading was similar for both groups pre-operatively (Table 3.2.5).

Table 3.2.4: Number of patients with each symptom before and after surgery

Outcome	Pre-operative		1 month		3 month		6 month		12 month	
	Nissen (n=61)	Lind (n=60)	Nissen (n=56)	Lind (n=56)	Nissen (n=53)	Lind (n=52)	Nissen (n=49)	Lind (n=44)	Nissen (n=34)	Lind (n=38)
Excellent	-	-	20	30	22	36	30	34	26	28
Good	-	-	27	21	26	15	15	10	5	10
Fair	-	-	6	4	4	1	3	0	2	0
Poor	-	-	3	1	1	0	1	0	1	0
Visick grade										
1	0	0	32	40	39	41	41	39	32	31
2	9	5	18	12	10	10	4	5	1	7
3	26	27	3	3	1	1	2	0	1	0
4	26	28	0	0	2	0	1	0	0	0
5	0	0	3	1	1	0	1	0	0	0

Table 3.2.5: Outcome scale and Visick grading

Outcome	Pre-operative		1 month		3month		6 month		12 month	
	Nissen	Lind	Nissen	Lind	Nissen	Lind	Nissen	Lind	Nissen	Lind
(n=61)	(n=60)	(n=56)	(n=56)	(n=53)	(n=52)	(n=49)	(n=44)	(n=34)	(n=38)	
Excellent	-	-	20	30	22	36	30	34	26	28
Good	-	-	27	21	26	15	15	10	5	10
Fair	-	-	6	4	4	1	3	0	2	0
Poor	-	-	3	1	1	0	1	0	1	0
Visick grade										
1	0	0	32	40	39	41	41	39	32	31
2	9	5	18	12	10	10	4	5	1	7
3	26	27	3	3	1	1	2	0	1	0
4	26	28	0	0	2	0	1	0	0	0
5	0	0	3	1	1	0	1	0	0	0

The mean operating time in the Nissen group was 44.8 (12-95) minutes and for the Lind group 45 (20-132) minutes ($p=0.953$), and the total theatre time for the Nissen group was 67.7 (35-108) minutes and in the Lind group 67.7 (40-153) minutes ($p=0.997$). There was no difference in the surgeon's perception of difficulty between the two groups; mean difficulty scores were 4 (1-10) for the Nissen group, compared to 4 (1-10) for the Lind group ($p=0.968$). Only one individual (Lind group) had to be converted to an open procedure due to intra-operative bleeding. Post operative hospital stay was comparable in both groups; Nissen group 3.1 (1-6) days and Lind group 2.9 (1-10) days ($p=0.351$).

There were no fatalities in either group; however, there were intra-operative and post-operative complications. Intra-operatively, in the Nissen group, laparoscopic dissection was extremely difficult in 2 patients due to increased intra-abdominal fat; in the Lind group, liver injury and intra-operative bleeding accounted for laparoscopic problems ($p=0.875$).

Complications were attributed to the operation if they occurred intra-operatively or in the first 30 days post procedure. Post-operatively, in the Nissen group, there were 5 complications; surgical emphysema, two patients with simple pneumothorax, a port site hernia which was repaired on day three post-operatively under local anaesthesia and one respiratory tract infection. In the Lind group, there was one case of simple pneumothorax ($p=0.106$).

Seven patients required reoperation; three in the Nissen group and 4 in the Lind Group. The Nissen re-operations were due to dysphagia; two patients were found to

have complete dysphagia and 1 patient had hiatal stenosis. Four patients from the Lind group required re-operation; two had complete dysphagia, one required removal of a crural suture and there was evidence of herniation of the wrap into the chest in one patient ($p=0.981$).

At discharge, there was no major difference in symptoms, with dysphagia to solids in 20 of 61 in the Nissen group *versus* 13 of 60 in the Lind group ($p=0.172$), and inability to burp being 5 of 61 *versus* 7 of 60 ($p=0.527$) respectively. However, there was a significant difference in the time it took individuals to return to full activities; at 1 month, 9 of 40 (22.5%) versus 2 of 45 (4.4%) had not returned to full activities ($p=0.013$). At 1 year, there was no significant difference in the dysphagia scores; Nissen 44.4 (40-45) *versus* Lind 44.8 (40-45) ($p=0.182$).

Detailed analyses of the clinical assessments are displayed in Table 4 and Table 5, and demonstrate some significant differences in the two groups. Post-operative dysphagia (qualitative) was higher in the Nissen group compared to the Lind group (At 3 months $p=0.003$; 6 months $p=0.020$), however, a significant difference in dysphagia scores (quantitative) was only demonstrable at 3 months; Nissen group 42 (15-45) *versus* Lind Group 44 (35-45) ($p=0.008$). At 1 year, there was no significant difference in dysphagia in the two groups ($p=0.066$).

Patients were invited to attend for post-operative pH and manometry. Thirty-five of 61 patients (57%) in the Nissen group and 31 of 60 (52%) in the Lind group underwent repeat investigations. Table 3.2.6 demonstrates pre and post-operative time below pH4 in a 24-hour test period ($p=0.893$ & 0.131), and pH grading was

comparable between the two groups. Oesophageal motility was also comparable between the two groups with 25 of 57 *versus* 16 of 54 ($p=0.123$) being abnormal pre-operatively, and 13 of 35 *versus* 8 of 32 ($p=0.292$) being abnormal post-operatively. Six patients complained of persistent heartburn at 1 year, however, data analysis demonstrates only one individual had quantifiable reflux.

Table 3.2.6: Percentage pH below pH 4 in a 24 hour period and pH Grading

	Preoperatively		Postoperatively		
	Nissen (n=54)	Lind (n=52)	Nissen (n=35)	Lind (n=31)	
% time below pH 4	12.7(0.2-78.7)	13.0(1.6-54.5)	3.26(0.2-20.2)	1.5(0-12.6)	
24 hour pH Grading					
No reflux (pH<4 less than 4%)	11	5	28	28	
Mild reflux, no symptoms (pH<4 between 4-7%)	5	5	2	0	
Mild reflux + symptoms (pH<4 between 4-7% and symptomatic)	5	8	1	1	
Severe reflux + symptoms (pH<4 more than 7%)	33	34	4	2	

3.3 COMPARISON AND OUTCOMES OF THE LAPAROSCOPIC ANTERIOR *VERSUS* POSTERIOR AND NISSEN *VERSUS* LIND FUNDOPPLICATION RANDOMISED CONTROLLED TRIALS

Between 2001 and 2005, 121 patients underwent Laparoscopic Total (360^0) or Subtotal ($270-300^0$) fundoplication (LTF) - 61 Nissen and 60 Lind. A further 103 underwent Laparoscopic Partial (180^0) Fundoplication (LPF) - 53 anterior and 50 posterior.

Pre-operatively, there were no statistically significant differences between the two groups regarding gender, size, smoking history, alcohol consumption or duration of symptoms. However, there was a significant difference between the ages of the groups ($p<0.05$). The mean age of patients in the LPF group was 43 years, compared with 47 years in the LTF group. More patients in the LPF group were taking a simple antacid pre-operatively (30 versus 19; $p<0.05$). Patients undergoing LTF were more likely to have had previous unrelated surgery ($p<0.05$).

For patients who had a pre-operative endoscopy and 24-hour pH studies, findings were similar in each group. The 24-hour pH studies were also similar post-operatively. Patients in the LTF group had a significantly higher rate of pre-operative dysphagia to solids (35% versus 24%; $p<0.05$). They also had greater rates of dysphagia at discharge from hospital ($p<0.001$), but this was not statistically different after one month.

There were no significant differences post-operatively in symptoms including regurgitation, post-prandial fullness, flatus and diarrhea. Heartburn control was better in the LTF group at three and six months ($p<0.05$), whereas patients in the LPF group were more likely to be taking anti-reflux medications at six months ($p<0.05$) and was more likely to require revisional surgery ($p<0.001$). There was no statistical difference in the rates of heartburn at 1 year.

Visick scores were consistently better in the LTF group in the year following surgery. Sixty-three patients in the LTF group reported a Visick score of one after one year, compared to 36 in the partial group. Overall, the Visick scores at one, three, six and 12 months were significantly better in the LTF group ($p<0.001$). Likewise patients who underwent LTF reported better overall outcomes at one year ($p<0.05$).

In our cohort, patients who underwent LPF had higher re-operation rates ($p<0.001$). A total of 12 patients required revisional surgery in the partial group. Eight patients following anterior partial fundoplication, and two patients following posterior partial needed revisional surgery for recurrent reflux. A further two patients required laparotomy for bowel or liver injury. In the total/subtotal group, three patients required re-operation for dysphagia following Nissen fundoplication. In the Lind group, two patients returned to theatre for symptoms of complete dysphagia, one required removal of a crural suture (again for dysphagia), and one patient required revisional surgery for herniation of the wrap into the chest cavity.

In total, 92 patients were lost to follow-up at one year, 49 of whom were in the LTF group and the remaining 43 in the LPF.

3.4 OUTCOMES OF INTRA-OPERATIVE MANOMETRY TO PREDICT POST OPERATIVE DYSPHAGIA PILOT STUDY

Forty patients were recruited into the study, 20 females and 20 males. The age range was 20-78 years (mean 48 years). The range of symptom duration was 1.5 years to 28 years (mean 8 years).

Of the forty patients recruited, thirty-nine underwent laparoscopic fundoplication, with one patient being cancelled due to poor lung function. Of these patients, twenty-eight underwent Lind fundoplication and 11 anterior fundoplication. Manometric data was collected for all patients pre-operatively, intra-operatively and post-operatively (Table 3.4.1-3.4.6).

Table 3.4.1: Pre-operative IOM

<u>Location of probe</u>	<u>Pressure</u>	<u>Range</u>	<u>SD</u>
Oesophageal Body Pressure (n=24)	1.75	-4 – 12	4.51
Gastric pressure (n=24)	9.13	3 – 18	4.30
Sphincter pressure (n=24)	16.32	3 – 33	7.20

Table 3.4.2: Post anaesthetic no pneumoperitoneum IOM

<u>Location of probe</u>	<u>Pressure</u>	<u>Range</u>	<u>SD</u>
Oesophageal Body Pressure (n=34)	8.88	-5 – 24	6.41
Gastric Pressure (n=30)	8.40	-7 – 26	6.87
Sphincter Pressure (n=34)	14.65	-6 – 35	8.79

Table 3.4.3: Post anaesthetic with pneumoperitoneum IOM

<u>Location of probe</u>	<u>Pressure</u>	<u>Range</u>	<u>SD</u>
Oesophageal Body Pressure (n=33)	12.97	-11 – 23	7.06
Gastric Pressure (n=23)	13.91	-17 – 29	8.67
Sphincter Pressure (n=33)	19.61	6 – 45	9.07

Table 3.4.4: Post anaesthetic with fundoplication and pneumoperitoneum IOM

<u>Location of probe</u>	<u>Pressure</u>	<u>Range</u>	<u>SD</u>
Oesophageal Body Pressure (n=29)	15.00	7 – 31	5.23
Gastric Pressure (n=17)	15.59	-21 – 30	11.22
Sphincter Pressure (n=29)	26.69	8 – 56	12.71

Table 3.4.5: Post anaesthetic and fundoplication no pneumoperitoneum IOM

<u>Location of probe</u>	<u>Pressure</u>	<u>Range</u>	<u>SD</u>
Oesophageal Body Pressure (n=29)	11.93	3 – 25	6.29
Gastric Pressure (n=14)	11.79	- 17 – 19	12.26
Sphincter Pressure (n=28)	24.18	2 – 87	16.28

Table 3.4.6: IOM 3 months post procedure

<u>Location of probe</u>	<u>Pressure</u>	<u>Range</u>	<u>SD</u>
Oesophageal Body Pressure (n=24)	2.25	-4 – 14	4.56
Gastric Pressure (n=24)	8.38	1 – 19	4.59
Sphincter Pressure (n=24)	22.58	11-37	6.36

Two patients were excluded due to the procedure being converted to open fundoplication, and four patients were excluded due to equipment malfunction.

Three patients demonstrated persistent dysphagia at the 12 month follow up point. There were no statistically significant differences in the pre-operative manometry studies in the dysphagic/non-dysphagic groups, with the dysphagic group having higher pressures, with oesophageal body pressure, sphincter pressure and gastric pressure having p-values of $p=0.299$, $p=0.997$ and $p=0.958$ respectively.

However, at operation, there were statistically significant differences in the lower oesophageal sphincter pressures: Post-anaesthetic and no pneumoperitoneum ($30.3\text{ cmH}_2\text{O}$ vs. $13.4\text{ cmH}_2\text{O}$, $p=0.002$) post-anaesthesia with pneumoperitoneum ($40.3\text{ cmH}_2\text{O}$ vs. $18.3\text{ cmH}_2\text{O}$, $p<0.001$) and post-fundoplication with pneumoperitoneum ($47.3\text{ cmH}_2\text{O}$ vs. $23.4\text{ cmH}_2\text{O}$, $p=0.001$). No statistically significant differences were demonstrated in post-operative manometry at the 3 month follow up point with oesophageal body pressure, sphincter pressure and gastric pressure having p-values of $p=0.870$, $p=0.172$ and $p=0.227$.

Three patients had persistent reflux symptoms at 12 months. There were no significant differences in the sphincter pressures in patients with reflux compared to asymptomatic patients. The only demonstrable statistical difference was in the gastric pressure post-anaesthetic with pneumoperitoneum; in patients with persistent reflux this was $16.38\text{ cmH}_2\text{O}$ compared to $5.75\text{ cmH}_2\text{O}$ ($p=0.046$).

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4. DISCUSSION

Laparoscopic fundoplication is still considered the gold standard treatment for moderate to severe gastro-oesophageal reflux disease. However, there is now an increasing tendency in many centres to utilise surgery at earlier stages of the disease [90]. Extensive debates have concluded that continuing with medical therapy does not correct the underlying motor abnormalities that exist in the upper gastrointestinal tract, but that of acid suppression [91]. In addition to this, medication may not provide adequate control of volume reflux, nocturnal symptoms and retro-sternal pain [92]. The choice is often left to patients; individuals with effective medication controlled reflux are now given the option to continue with life-long medication or undergo a potentially definitive procedure *i.e.* surgery. However, emphasis must be placed on the potential undesirable effects that can occur as a result of fundoplication when allowing patients to make an informed choice.

4.1 LAPARACOPIC ANTERIOR VERSUS POSTERIOR FUNDOPPLICATION RANDOMISED CONTROLLED TRIAL

Multiple surgical techniques exist, each with their own potential complications. It has been described in numerous studies that partial fundoplications should be reserved for individuals with mild gastro-oesophageal reflux disease [93-95]. Within the subgroup of anterior fundoplications, there exist a number of variants; commonest described in the literature as that of Watson *et al* [96] and Lundell *et al* [97]. The procedure undertaken by our centre more closely resembled that of the Lundell (Gotenburg) group, involving suturing of the fundus to one side of the oesophagus, whereas the Watson (Adelaide) group advocates suturing the fundus to both sides of the oesophagus. Both the Sheffield group and the Lundell group demonstrate higher rates of reoperation in the anterior fundoplication group, compared to the Watson group, highlighting the fact that two-side fixation may be superior to unilateral fixation.

Unfortunately, as with any trial, there were individuals who were lost to follow up periods post procedure despite the best efforts of the authors'. Of the 43 patients who failed to attend between the post-operative period and the 1-year post procedure point, 37 patients had a Visick grading 1 or 2 (Visick 1 – 26, Visick 2 – 11, Visick 3 – 4 and Visick 4 – 2) at their last clinic attendance.

In this trial, although 16 individuals demonstrated normal pH studies, they all had abnormalities detected on other investigative modalities, and were therefore offered

operative intervention. A recent study undertaken by Khajanchee *et al* [98], demonstrated that individuals with symptomatic gastro-oesophageal reflux disease but normal pH studies have significantly worse outcomes after fundoplication compared with patients with abnormal preoperative pH studies. Of the 16 individuals who had normal preoperative pH grading, only 10 attended follow-up at 1 year; and only one described the heartburn as not being controlled.

As demonstrated, there were different rates of post-operative symptoms in the two groups, with each group having a specific problem associated with it. Individuals who underwent an anterior fundoplication had a higher rate of re operation compared to individuals who underwent a posterior fundoplication (*8 versus 2*), however, this was not statistically significant as the p value was marginally outside the pre-study selected level at $p=0.057$; however, this may represent a lack of power. This has been further validated by a study by Zehetner *et al* [99], who describe that posterior funduplications have a lower rate of re-operative intervention for reflux.

The anterior fundoplication group also had a higher rate of post-operative heartburn. This was statistically significant, however, this was a qualitative measurement and postoperative pH analysis of the lower oesophagus did not support a statistically significant difference. Khajanchee *et al* [100] demonstrated that there is a poor correlation between postoperative reflux symptoms and actual reflux (abnormal DeMeester scores). Similarly, Thompson *et al* [101] demonstrated that post-operative reflux symptoms are not always due to the presence of reflux; therefore, before repeat operative intervention is undertaken, quantitative analysis of reflux

should be undertaken, or reflux could be further characterised using impedance studies [102].

The posterior fundoplication group demonstrated a higher rate of early post-operative dysphagia as compared to the anterior group. Hagedorn *et al* (2004) [74], hypothesised that increased dysphagia may be seen in the posterior wrap compared to the anterior fundoplication; this phenomenon, would be attributed to the elevation of the abdominal portion of the oesophagus from its native bed in the hiatus and increased angulation.

A meta-analysis undertaken by Broeders *et al* [103], which includes the results of this study demonstrates that oesophageal acid exposure time and the prevalence of heartburn are higher after laparoscopic anterior fundoplications compared with laparoscopic posterior fundoplication. These observations are reinforced by other studies, which demonstrate that laparoscopic posterior fundoplication provides better control of reflux symptoms, however, this is offset by an increase in the occurrence of side effects compared to the laparoscopic anterior fundoplication group [104]. Although some studies suggest that due to the recurrent incidence on reflux, laparoscopic posterior fundoplication is superior to laparoscopic anterior fundoplication, therefore, the latter should be avoided [16, 105].

More recent studies [9, 15] have demonstrated that laparoscopic anterior fundoplication offers good long-term control of reflux symptom, with modest post-fundoplication symptoms. Anterior fundoplication resulted in less dysphagia, better ability to belch and vomit than total fundoplication at 10-year follow-up compared to

Nissen fundoplication. The results suggest that laparoscopic anterior fundoplication could be an alternative to Nissen fundoplication in the surgical treatment of mild-moderate GORD.

Overall, one can conclude that each fundoplication has its benefits and disadvantages. The anterior group had a slightly higher incidence of post-operative reflux, and although marginally not statistically significant ($p=0.057$), a higher re-operation rate. The posterior group, in comparison to the anterior group, had a higher incidence of post-operative dysphagia. Therefore, potentially, according to the results obtained, a posterior fundoplication produces a better management option for controlling gastro-oesophageal reflux disease, when compared to an anterior fundoplication that utilises unilateral fixation of the gastric fundus.

4.2 LAPAROSCOPIC NISSEN VERSUS LIND FUNDOPPLICATION RANDOMISED CONTROLLED TRIAL

Unfortunately, as with any trial, there were individuals who were lost to follow up despite the best efforts of the authors. Of the 49 patients who failed to attend between the post-operative period and the 1-year post procedure point, forty-one patients had a Visick grading 1 (Visick 1 – 41, Visick 2 – 7, Visick 4 – 1) at their last clinic attendance.

The main aim of the trial was to determine whether there existed any superiority between the two procedures; and the two measurement parameters were adequate control of reflux and post-operative symptoms. One of the hypotheses being trialed was to establish whether the subtotal Lind fundoplication would decrease the rates of post-operative dysphagia encountered in a 360⁰ Nissen fundoplication. Numerous studies have stated that seniority of the surgeon and state of the fundal wrap has a direct bearing on the degree of post-operative dysphagia and symptoms in patients who undergo funduplications [106, 107]. Some studies have even evaluated hiatal suture technique as a possible predictor to post fundoplication dysphagia without success [108].

In our study, there were two major differences in the surgical groups: post-operative dysphagia and time taken to get back to full activities. Patients who underwent Nissen fundoplication had higher rates of post operative dysphagia symptoms at 3 and 6 months post-operatively compared to the Lind group; at 3 months p=0.003; 6

months p=0.020. The time taken to return to full activities at 1 month, 9 of 40 (22.5%) *versus* 2 of 45 (4.4%) had not returned to full activities (p=0.013).

Watson *et al*'s study, although comparing a total wrap with a partial (as opposed to a subtotal wrap) demonstrated that individuals who underwent a Nissen fundoplication had higher rates of post-operative dysphagia [82]. Many trials have been undertaken to determine whether post operative dysphagia in patients who undergo Nissen fundoplication can be prevented [109, 110], and there are other trials which evaluate the outcomes of subtotal wrap [111-113].

Luostarinen [110] and Hunter [109] hypothesised that full fundal mobilization may prevent dysphagia from occurring. Luostarinen *et al* randomized fifty-two patients into either having a Nissen fundoplication with or without division of the gastrophrenic/gastrosplenic ligaments and division of the short gastric vessels. No statistically significant difference was observed for post-operative dysphagia between the two groups. In our trial neither group had the short gastric vessels divided.

A recent study comparing Laparoscopic Nissen *versus* Laparoscopic Rossetti Funduplications has demonstrated that the overall incidence of severe postoperative dysphagia did not differ between the reported techniques. Only Rossetti LTF was associated with structural distortion of the fundoplication that could justify the dysphagia[114].

Unfortunately, dysphagia is a common occurrence after fundoplication and its pathophysiology is still relatively poorly understood. Studies undertaken on individuals with pre-existing motility disorders have failed to demonstrate adverse outcomes even when a Nissen fundoplication is utilized [84] and this is re-iterated in other studies which have failed to demonstrate useful criteria by which one can anticipate post fundoplication dysphagia [85].

The forerunning hypotheses in current literature are that it is due to a change in oesophageal motor function or a change in gastro-oesophageal junction characteristics. Myers *et al* conducted a study based on oesophageal manometry [101]. Patients were placed into two groups, one group to undergo laparoscopic cholecystectomy and the other to undergo laparoscopic fundoplication. The procedures were undertaken and oesophageal manometry was undertaken on the first post-operative day. This demonstrated grossly disturbed oesophageal motility following fundoplication, which was absent in the laparoscopic cholecystectomy group, indicating the occurrence of ‘oesophageal ileus’.

Multi-channel oesophageal intra-luminal impedance studies were undertaken by Yigit *et al* [115] to determine whether there was a presence of impaired oesophageal clearance in patients with post fundoplication dysphagia. The study demonstrated that there was presence of impaired oesophageal clearance in the majority of patients with post fundoplication dysphagia ($p=0.01$), compared to patients without dysphagia. It also highlighted the fact that impedance studies may demonstrate motility disorders not identified by manometric studies.

Our study demonstrated no significant differences in pre-operative oesophageal clearance and lower oesophageal sphincter resting pressures between the two groups ($p=0.265$ and $p=0.585$ respectively). However, post-operatively, there was a higher mean value of the lower oesophageal sphincter in the Nissen group ($p=0.002$) compared to the Lind group, highlighting the possibility that the total wrap may cause higher lower oesophageal sphincter pressures, giving patients better control of reflux at the expense of higher rates of post-operative dysphagia.

Open conversion was only undertaken in one patient, in the Lind group; due to intra-operative bleeding. Seven patients required re-operation due to persistent dysphagia as demonstrated by endoscopy/contrast studies, three in the Nissen group and four in the Lind group. No patients required re-operation for recurrent reflux and only one patient who had symptomatic heartburn demonstrated quantifiable reflux on 24 hour ambulatory pH monitoring.

Both operations provide good quantitative and qualitative control of gastro-oesophageal reflux. Operation time and post-operative comparators were similar in both groups. At one-year follow-up, there was no statistically significant difference in post-operative symptoms or dysphagia scores, leading to the conclusion that both operations provide good quantitative and qualitative control of gastro-oesophageal reflux.

4.3 COMPARISON AND OUTCOMES OF THE LAPAROSCOPIC ANTERIOR *VERSUS* POSTERIOR AND NISSEN *VERSUS* LIND FUNDOPPLICATION RANDOMISED CONTROLLED TRIALS

This commentary will focus on comparing the outcomes of the two randomised controlled trials [10, 11]. For the analysis of these two trials, and to aid less confusion, all the patients from the laparoscopic anterior and posterior fundoplication, the patients will be classed as having laparoscopic partial fundoplication (LPF) and for the laparoscopic Lind *versus* Nissen fundoplication, patients will be classed as undergoing a laparoscopic total fundoplication (LTF).

Pre-operatively, there were no statistically significant differences between the two groups regarding gender, size, smoking history, alcohol consumption or duration of symptoms. However, there was a significant difference between the ages of the groups ($p<0.05$). The mean age of patients in the LPF group was 43 years, compared with 47 years in the LTF group. More patients in the LPF group were taking a simple antacid pre-operatively (30 *versus* 19; $p<0.05$), whereas more patients in the LTF group were taking an H₂ antagonist or PPI pre-operatively (although not statistically significant). Patients undergoing LTF were more likely to have had previous unrelated surgery ($p<0.05$).

For patients who had a pre-operative endoscopy and 24-hour pH studies, findings were similar in each group. The 24-hour pH studies were also similar post-operatively. Patients in the LTF group had a significantly higher rate of pre-

operative dysphagia to solids (35% *versus* 24%; p<0.05). They also had greater rates of dysphagia at discharge from hospital (p<0.001), but this was not statistically different after one month. There were no significant differences post-operatively in symptoms including regurgitation, post-prandial fullness, flatus and diarrhea.

Heartburn control was better in the LTF group at three and six months (p<0.05), whereas patients in the LPF group were more likely to be taking anti-reflux medications at six months (p<0.05) and was more likely to require revisional surgery (p<0.001). There was no statistical difference in the rates of heartburn at 1 year.

Visick scores were consistently better in the LTF group in the year following surgery (Figure 4.3.1). Sixty-three patients in the LTF group reported a Visick score of one after one year, compared to 36 in the partial group. Overall, the Visick scores at one, three, six and 12 months were significantly better in the LTF group (p<0.001). Likewise patients who underwent LTF reported better overall outcomes at one year (p<0.05; Figure 4.3.2).

Figure 4.3.1: Visick scores pre and post-operatively

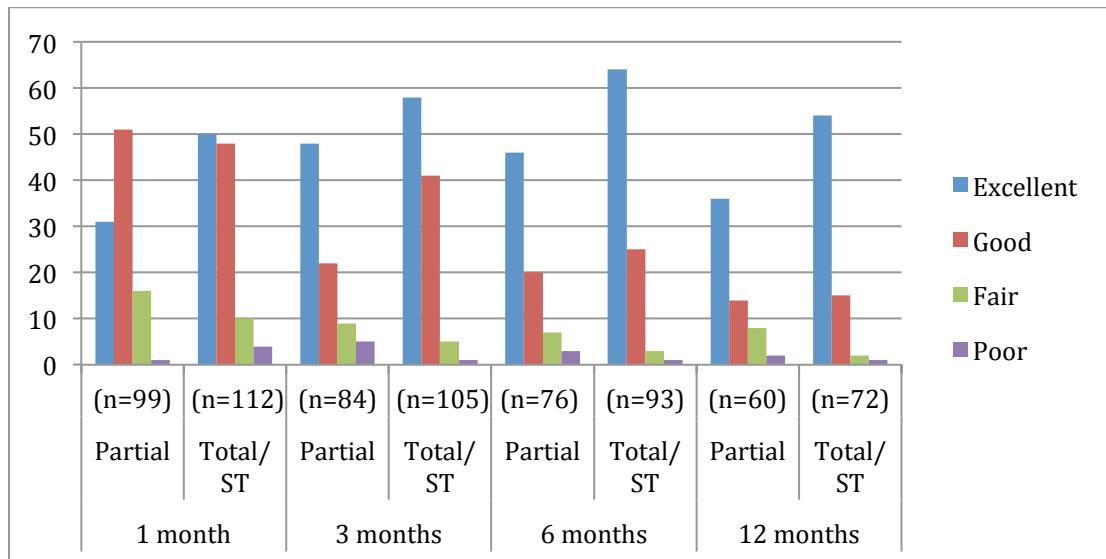
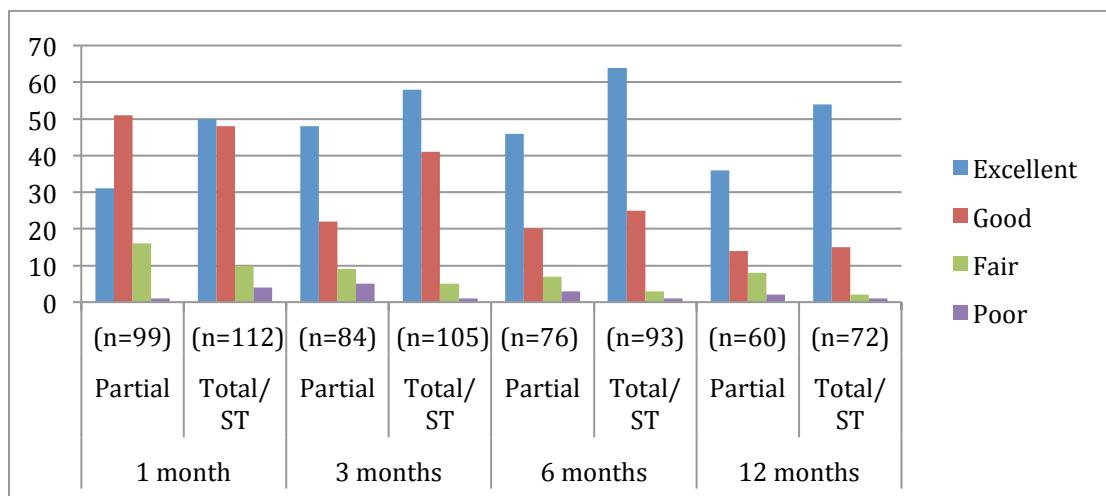


Figure 4.3.2: Patient satisfaction post-operatively



In our cohort, patients who underwent LPF had higher re-operation rates ($p<0.001$).

A total of 12 patients required revisional surgery in the partial group. Eight patients following anterior partial fundoplication, and two patients following posterior partial needed revisional surgery for recurrent reflux. A further two patients required laparotomy for bowel or liver injury. In the total/ subtotal group, three patients required re-operation for dysphagia following Nissen fundoplication. In the Lind group, two patients returned to theatre for symptoms of complete dysphagia, one

required removal of a crural suture (again for dysphagia), and one patient required revisional surgery for herniation of the wrap into the chest cavity.

In total, 92 patients were lost to follow-up at one year, 49 of whom were in the LTF group and the remaining 43 in the LPF.

Although the patients in the LTF group were older, previous research has shown that age alone does not affect post-operative patient satisfaction [116]. Few studies have documented the numbers of patients taking anti-reflux medications pre-operatively. This makes it difficult to determine whether or not the difference between patients taking PPI's or simple antacids in the LTF and LPF groups is important.

According to our randomised controlled trials, laparoscopic total fundoplication may achieve a higher lower oesophageal sphincter resting pressure so may be more successful in cases of severe reflux, but if the wrap is too tight it can result in post-operative dysphagia and abdominal bloating. Conversely, if the wrap during LPF is too loose, the patient may be left with residual symptoms of GORD. A systematic review comparing total (Nissen) with partial (Toupet) fundoplication found that the Nissen fundoplication resulted in higher rates of post-operative dysphagia, but that patient satisfaction was similar with both operations [117].

In this review, patients' health related quality of life (HRQoL) significantly improved in the short-term after LPF, compared with the LTF. However, this advantage for LPF has been shown to last for only two years, after which SF36 scores (HRQoL Inventory) become statistically insignificant [118].

On discharge, episodes of dysphagia and gas bloat were higher in the LTF group. This was similar to the findings of two previous meta-analyses [117, 119] although there was significant heterogeneity in the latter of these studies. These symptoms may reflect the tighter wrap in total/ subtotal fundoplication.

In our cohort, patients who underwent LPF had higher re-operation rates. In contrast, previous studies have found the reverse to be true, as some patients who had LTF subsequently needed dilatation for dysphagia, surgery for paraesophageal hiatus hernia [120] or revisional surgery for persistent reflux [117, 119, 120].

At three and six months post-operatively, patients in the LPF group were more likely to be taking anti-reflux medication for symptom control, suggesting that the surgery had not achieved a wrap tight enough to adequately raise the resting pressure of the LES. Interestingly, a smaller number of patients in the LPF group were on anti-reflux medication pre-operatively.

It is very difficult to determine re-operation rates for failed therapy due to mobile populations. Zhao *et al* [121] have shown that nearly one third of re-operations after failed laparoscopic fundoplication occur at a hospital different from the initial operation, which raises concern that existing literature does not reflect the true reoperation rate. The reoperation rate is highest in the first year postoperatively.

Initially, symptoms of dyspepsia were significantly reduced in the LTF group, but after one year the difference was not of statistical importance. This mirrors the

findings of a meta-analysis comprising eleven studies with nearly 1000 patients. This study demonstrated that the reduction in dyspepsia for patients following total fundoplication compared to those in the partial group was not significant ($p=0.58$) [119]. A study involving a ten-year follow up of patients after surgery also found that there was no statistical difference in heartburn symptoms between total and partial fundoplication [122].

Importantly, post-operative symptoms related to tight wraps (vomiting, postprandial fullness and regurgitation) were similar in both groups, thus demonstrating that LTF can achieve an appropriate balance between reflux control and undesirable side effects. Interestingly, vomiting was initially of greater concern in the LPF group, but this improved after one month.

Post-operative Visick scores were consistently lower in the LTF group, and patients had a significantly higher level of satisfaction. These results differ from previous studies (including a meta-analysis and ten year follow up study) into long-term patient satisfaction, which show that quality of life and patient satisfaction following surgery are similar at one and five years following partial or total/ subtotal fundoplication [118, 120, 122-124]. This may be a reflection of the experience of the surgeons involved and the techniques employed, or simply because these patients had worse pre-operative symptoms (dysphagia to solids etc.) and thus had more scope for improvement.

Total and partial fundoplication both ameliorate symptoms of GORD. However, this comparative study shows that patients undergoing total fundoplication have better

post-operative qualities of life, even if levels of GORD symptoms are statistically similar after one year. One could theorize therefore that patients with significantly severe reflux pre-operatively may benefit from a tighter wrap than those whose symptoms are milder. Although patients with pre-operative esophageal motility disorders were excluded from this study, it may be, given the smaller risk of dysphagia following a partial wrap, these patients should undergo a subtotal/ partial fundoplication, as normal to high lower esophageal sphincter pressures may be more likely to lead to dysphagia following Nissen fundoplication.

Current evidence suggests that there is little difference between the quality of life between groups in the long term. In our cohorts, differences between anterior and posterior, and partial *versus* total had resolved by 12 months following surgery. Further studies are needed to assess if this effect is still significantly higher after five to ten years.

4.4 INTRA-OPERATIVE MANOMETRY TO PREDICT POST-OERATIVE DYSPHAGIA PILOT STUDY

Dysphagia is a common occurrence after fundoplication and its pathophysiology is still relatively poorly understood. Studies undertaken on individuals with pre-existing motility disorders have failed to demonstrate adverse outcomes even when a Nissen fundoplication is utilized [84] and this is re-iterated in other studies which have failed to demonstrate useful criteria by which one can anticipate post fundoplication dysphagia [85].

The forerunning hypotheses in current literature are that it is due to a change in oesophageal motor function or a change in gastro-oesophageal junction characteristics. Myers et al conducted a study based on oesophageal manometry [101]. Patients were placed into two groups, one group to undergo laparoscopic cholecystectomy and the other to undergo laparoscopic fundoplication. The procedures were undertaken and oesophageal manometry was undertaken on the first post-operative day. This demonstrated grossly disturbed oesophageal motility following fundoplication, which was absent in the laparoscopic cholecystectomy group, indicating the occurrence of ‘oesophageal ileus’.

There is limited literature on the value of intra-operative manometry for the prediction of post-fundoplication dysphagia. Numerous studies have been published which utilise intra-operative manometry in the formation of the fundoplication wrap [125, 126], but there are no studies which have utilised it for predicting post-operative dysphagia. Hill *et al* [127], undertook intraoperative manometry in 200 patients with gastroesophageal reflux. The lower esophageal sphincter pressure was

measured at various intervals including before and during repair. Intra-operative pressures were approximately 50mmHg, and, the postoperative pressures ranged between 15 and 25 mmHg no patients with sphincter pressures higher than 15 mmHg demonstrated reflux according to postoperative pH and pressure studies. The authors concluded that measurement of intraoperative sphincter pressure is a safe, simple, and reliable technique and should be standard for all operations on the gastroesophageal junction.

Manometry measures pressure within the oesophageal lumen and sphincters, and provides an assessment of the neuromuscular activity that dictates function in health and disease. It is performed to investigate the cause of functional dysphagia, unexplained "non-cardiac" chest pain, and in the pre-operative work-up of patients referred for anti-reflux surgery [128].

The main finding in our study was the presence of abnormally high lower oesophageal sphincter pressures in the dysphagic patients. Surprisingly, the difference in these pressures only became apparent after anaesthesia. Patients who had adequate control of reflux and no symptoms of dysphagia had lower oesophageal sphincter pressure readings of about 20 cmH₂O during the intra-operative period. However, at the 3-month manometry study point, there was no significant difference between the non-dysphagic/dysphagic groups (21.9 cmH₂O *versus* 27.3 cmH₂O respectively (*p*=0.172)).

Given the above findings, intra-operative manometry may be a useful tool both in the prediction and prevention of dysphagia in patients who undergo fundoplication.

However, there is a spectrum of opinion available in current literature. Del Genio *et al* [129] undertook a retrospective analysis of 309 functional surgical procedures on the oesophagus which utilised intra-operative manometry and found it to be a useful tool in detecting the high pressure zone and calibrating lower oesophageal sphincter pressure. Prochazka *et al* [126], also concluded that intraoperative manometry may prove beneficial in predicting persistent postoperative dysphagia.

Orringer *et al* [130] undertook a study of forty-five patients who underwent a Collis-Nissen fundoplication and had several peri and intra-operative manometric studies undertaken. They concluded that oesophageal mobilisation resulted in variable intra-operative high-pressure zone values, and, were not reliable predictors of post-operative high-pressure zones.

In summary, intra-operative manometry may prove to be beneficial in predicting post-operative dysphagia, however, serial measurements at various stages of the operative procedure ranging from induction of anaesthesia to completion of the operation must be undertaken. With the advent of high resolution manometry [128] the complex functional anatomy of the oesophageal high pressure zone may be studied more closely during these stages and subsequently aid functional lower oesophageal sphincter reconstruction.

4.5 LIMITATIONS

There are a number of limitations demonstrated across the three studies discussed in this thesis. The studies were undertaken between 2001 and 2007, with subsequent data analysis. At the time of undertaking these studies, the methods used were consistent with the accepted research methodologies. However, given the progression over the last decade in the methodology of undertaking surgical trials, the limitations in these trials will be highlighted and discussed.

There is no data available on the number of patients who were available as potential recruits to the randomised controlled trials or the pilot study. This if present would be of interest as it would allow us to determine the number of patients over the recruitment period who presented with GORD and subsequently work out local prevalence and uptake rates of surgical intervention for GORD.

Recent studies have demonstrated that there is a potential for other dietary factors to predispose individuals to GORD. Suggested causative/attributing agents have included carbonated drinks, however, recent meta-analysis have demonstrated no correlation between this and GORD [131]. Caffeinated products [132] have demonstrated a positive correlation between consumption and the presence of GORD. Unfortunately, neither of these factors were recorded in the demographic and enrolling questionnaire.

Although not documented, all patients underwent OGD in the re-operative period to determine whether there was oesophagitis present. At the same endoscopy, if there was evidence that gastritis/duodenitis was present then a CLO (Campylobacter like

organism) test was undertaken to determine if *H.pylori* was present. If a positive result was obtained then eradication therapy was initiated.

The randomisation method of using a sealed paper envelope technique doesn't allow optimal randomisation. This is due to only the initial patient having a true chance of a 50:50 randomisation, with subsequent unequal chances of randomisations. Current methods include computer-generated randomisation [133], which allows for true chances of equal randomisation to either arm. On the same theme, patients and surgeons were blinded at the initial envelope selection. At follow up and subsequent investigations, attempts were made to make sure the patient and the surgeon were blinded as to the type of wrap that was undertaken.

Inhalational anaesthesia was utilised in all patients; however, there were anaesthetic variations in the type of neuromuscular blockade agent used, which could have influenced the manometric studies in the IOM study. The actual type of neuromuscular blockade agent is not of concern, but the reversal agent, especially Sugammadex has been implicated in affecting smooth muscle [134].

Another limitation, which could not be avoided due to the size of the trial and continuing clinical practice, was the number of surgeons used. Ideally, there would be one surgeon to undertake all the procedures, however, to aid in the recruitment and timely completion of the trial, two surgeons were used for this study. Inter-operator variability was reduced as CJS had trained RA in all procedures and their operative styles and the methodology to undertake the wraps were similar, thereby allowing some mitigation for having two surgeons.

The difficulty scores were on a scale measured from 1 to 10, with 1 being easy and 10 correlating to a near impossible procedure. Unfortunately, this was a perception scale and there is the potential for inter-surgeon variability as there were no strict definitions as to what defined each number on the scale.

There was an easily identifiable limitation for patient having a Nissen fundoplication; unfortunately, this was not avoidable due to safe surgical practice. The size of the oesophagus determined the size of the bougie used. It can be hypothesised that patients who had a large bougie used had lower rates of dysphagia as they had a relatively larger lumen to allow for the food bolus to propel down compared to patients who had a smaller bougie used. However, this cannot be determined from the data, as the size of the bougie was not documented in all cases.

The mean post-operative length of stay was 3 days in our patient population. This study was undertaken in the infancy of laparoscopic management of GORD, and current management strategies have the patients discharged as day case patients (within 24 hours) [135, 136]. The patients had no access to a dietitian, but were given a dietary advice sheet and advice from the surgeons. Only when the surgeons were satisfied that the patients were tolerating and following the prescribed diet were the patients allowed to be discharged.

The follow up questionnaire documented an array of symptoms, however, this only allowed a binary answer to the presence and there was no grading of severity of each symptom. This was partially mitigated by further evaluation of post-operative dysphagia if present by utilising and documenting the Dysphagia Scores, which were

a secondary outcome measure. The Visick system of scoring also was a relatively crude measure of determining patient symptoms, but at the time of the study this was a widely accepted method of determining symptoms.

As demonstrated by the study flow diagrams, there was a very high attrition rate in the patient population despite attempts at postal and telephone contacting the patients. On initial enrollment it would have been very useful to determine the postcode and socioeconomic status of each patient [137]. Even with a relatively static population, with one unit undertaking all the procedures, we could not mitigate against patients not turning up for subsequent clinic attendances. The vast majority of patients who did not attend follow up appointments were asymptomatic, or had dramatic symptomatic improvement at their last clinic attendance.

4.6 FUTURE

The past two decades have seen a dramatic advancement in the treatment of GORD. Initially, anti-reflux operations were undertaken via the open approach, later to be superseded by the laparoscopic approach, decreasing the size of the of incision and also the overall stay in hospitals.

As this thesis describes there is still widespread debate on which is the most optimal form of fundoplication to prevent reflux and alleviate the symptoms, whilst minimising adverse symptoms. It can be argued, especially after looking at IOM and recent advances in technology that the type of fundoplication no longer plays a pivotal role in determining outcome. It is possible to measure intra-operative intraluminal pressures and visualise the formation of the neo-lower oesophageal sphincter both during and after fundoplication.

This has mainly been due to the development of the EndoFLIP® device. This is an imaging catheter that is placed at the gastro-oesophageal junction and acts as a smart bougie allowing for 3-dimensional real-time monitoring of the manometric characteristics of the lower oesophageal sphincter. This subsequently allows for a tailored fundoplication to be undertaken, with emphasis on the pressure and anatomical consideration of the lower oesophageal sphincter as opposed to utilising empirical fundoplication variants [138-144].

As the natural progression from open to laparoscopic surgery has occurred, so have the transition from laparoscopic to trans oral incision less surgery. The Medigus Ultrasonic Surgical Endostapler (MUSE™) is guided by ultrasound and video to

perform an endoscopic fundoplication. The ultrasound enables it to determine the thickness of tissues prior to deploying the staples, which complete the wrap. It is operated by one person, but currently requires a general anaesthetic, as paralysis of the diaphragm is required. Short-term outcomes are the same as for laparoscopic fundoplication; however, long-term outcomes from trials are still awaited [145, 146].

4.7 CONCLUSION

Funduplications are becoming a more popular alternative to medical therapy for the treatment of GORD. After analysis of the trials and the current literature available, there still appears to be no consensus as to which fundoplication method offers the best control of the symptoms of GORD with the least adverse symptoms.

The analysis of our studies, in the partial fundoplication trial, patients who underwent posterior fundoplication had better control of symptoms compared to those who underwent anterior fundoplication at the 12 month follow up point. There was no difference between the groups who underwent Nissen or Lind fundoplication.

When the studies were collated, the laparoscopic total/subtotal fundoplication appears to be superior in the control of reflux when compared to the laparoscopic partial fundoplication. Intraoperative manometry may be advantageous as the study does suggest that this investigation may be useful in predicting post-operative dysphagia.

Recent advances have now enabled intra-operative manometry to be utilised in helping form a neo-lower oesophageal sphincter, and technological advances may soon make laparoscopic fundoplication a historical procedure or only utilised in patients who are not eligible for incision less surgery.

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APPENDIX I

A PROSPECTIVE RANSOMISED COMPARISON OF LAPAROSCOPIC *ANTERIOR VERSUS POSTERIOR PARTIAL FUNDOPLICATION/*NISSEN VERSUS LIND FUNDOPLICATION (*DELETE AS APPROPRIATE) FOR GASTRO-OESOPHAGEAL REFLUX DISEASE

Department of Surgery
Royal Hallamshire Hospital
Sheffield

Trial number: _____

Patient's name: _____

Hospital number: _____

INVESTIGATORS:

Mr R. Ackroyd
Consultant Upper GI Surgeon
Royal Hallamshire Hospital

Mr C.J. Stoddard
Consultant Upper GI Surgeon
Royal Hallamshire Hospital

RESEARCH CONSENT FORM	
TITLE OF PROJECT: A PROSPECTIVE RANSOMISED COMPARISON OF LAPAROSCOPIC *ANTERIOR VERSUS POSTERIOR PARTIAL FUNDOPPLICATION/*NISSEN VERSUS LIND FUNDOPPLICATION (*DELETE AS APPROPRIATE) FOR GASTRO-OESOPHAGEAL REFLUX DISEASE	
THE PATIENT SHOULD COMPLETE THE WOLE OF THIS SHEET HIMSELF/HERSELF	
HAVE YOU HAD THE PATIENT INFORMATION SHEET?	YES/NO
HAVE YOU HAD OPPORTUNITIES TO ASK QUESTIONS AND DISCUSS THIS STUDY?	YES/NO
HAVE YOU RECEIVED SATIFASCTORY ANSWERS TO ALL OF YOUR QUESTIONS?	YES/NO
HAVE YOU RECEIVED ENOUGH INFORMATION ABOUT THIS STUDY?	YES/NO
WHO HAVE YOU SPOKEN TO? DR/MR/MISS..... DO YOU UNDERSTAND THAT YOU ARE FREE TO WITHDRAW FROM THE STUDY: <ul style="list-style-type: none"> • AT ANY TIME • WITHOUT HAVING TO GIVE A REASON FOR WITHDRAWING • AND WITHOUT IT AFFECTING YOUR MEDICAL CARE 	YES/NO
SIGNED:..... DATE:..... NAME (BLOCK CAPITALS):.....	
WITNESS SIGNATURE:.....	

DATE OF ENTRY INTO TRIAL: _____

PATIENT DETAILS:

NAME: _____

DATE OF BIRTH: _____ AGE AT SURGERY: _____

SEX: _____

HOSPITAL NUMBER: _____

ADDRESS: _____

TELEPHONE: HOME: _____ WORK: _____

HEIGHT: ____ FT ____ IN OR ____ CM

WEIGHT: _____ KG/LB

OCCUPATION: _____

SMOKER: Y/N

ALCOHOL: Y/N

PRE-OPERATIVE SYMPTOMS

DURATION OF SYMPTOMS: ____ YEARS ____ MONTHS

PRE-OPERATIVE MANAGEMENT (CIRCLE IF USED)

	STARTED	COMPLETED/IN USE	DURATION
ANTACID			
H ₂ BLOCKER			
PROTON PUMP INHIBITOR			
OTHER (SPECIFY)			

PRE-OPERATIVE SYMPTOMS

(CIRCLE IF PRESENT)

HEARTBURN

EPIGASTRIC PAIN

REGURGITATION

DYSPHAGIA – SPECIFY: LUMPY SOLIDS / SOFT SOLIDS / LIQUIDS

PAIN ON SWALLOWING

POST-PRANDIAL FULLNESS OR EARLY SATIETY

EPIGASTRIC BLOATING

ANOREXIA

NAUSEA

VOMITING

NOCTURNAL COUGHING

NOCTURNAL WHEEZING

MODIFIED VISICK GRADING

1. NO SYMPTOMS
2. MILD SYMPTOMS EASILY CONTROLLED BY SIMPLE CARE
SUCH AS AVOIDING CERTAIN FOODS OR SMALL MEALS, ETC.
3. MODERATE SYMPTOMS NOT CONTROLLED BY SIMPLE CARE
BUT NOT INTERFERING WITH SOCIAL OR ECONOMIC LIFE
4. MODERATE SYMPTOMS INTERFERING WITH SOCIAL OR
ECONOMIC LIFE

1. IS HEARTBURN CONTROLLED? YES/NO

GRADE ON A SCALE OF 0-10:

0 = FULLY CONTROLLED

1 0 = NOT CONTROLLED

0 ————— 5 ————— 10

2. ANY DIFFICULTY SWALLOWING? YES/NO

GRADE ON A SCALE OF 0-10:

0 = NO DIFFICULTY

10 = SEVERE DIFFICULTY

LIQUIDS:

0 ————— 5 ————— 10

SOLIDS:

0 ————— 5 ————— 10

3. ABLE TO RELIEVE ANY BLOATING EFFECTIVELY DURING EATING?

YES/NO

4. EAT A NORMAL DIET NOW? YES/NO

LIST ANY RESTRICTIONS IF APPLICABLE

DYSPHAGIA SCORE: PRE-OPERATIVELY

DYSPHAGIA SCORE (SCORE EACH LINE)

	ALWAYS	OCCASIONAL	NEVER
WATER			
MILK/THIN SOUP			
CUSTARD (YOGHURT, PUREED FRUIT)			
JELLY			
SCRAMBLED EGG (BAKED BEANS, MASHED POTATO)			
BAKED FISH (STEAMED POTATO, COOKED CARROT)			
BREAD (PASTRIES)			
APPLE (RAW CARROT)			
STEAK (PORK OR LAMB CHOP)			

TOTAL SCORE: _____

(MULTIPLE EACH NUMBER BY 0, 0.5 OR 1 AND THEN SUM
0=TOTAL DYSPHAGIA, 45 = NO DYSPHAGIA)

PAST MEDICAL HISTORY

A) SIGNIFICANT DISEASE (SPECIFY)

1. RESPIRATORY Y/N
2. CARDIOVASCULAR Y/N
3. RENAL Y/N
4. DIABETES Y/N
5. OTHER Y/N

B) PREVIOUS ABDOMINAL OR THORACIC OPERATIONS (SPECIFY NATURE AND WHEN PERFORMED)

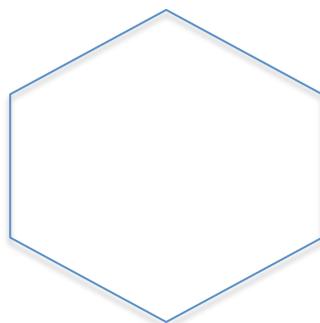
- 1.
- 2.
- 3.
- 4.
- 5.

C) CURRENT MEDICATIONS (LIST TYPE AND DOSE)

- 1.
- 2.
- 3.
- 4.
- 5.

EXAMINATION:

ABDOMINAL FINDINGS:



SCARS/MARKS:

PRE-OPERATIVE INVESTIGATIONS

ENDOSCOPY

DATE OF TEST: _____

OESOPHAGUS – GRADE OF OESOPHAGITIS: _____

0 = NORMAL

1 = ERYTHEMA ALONE

2 = ULCERATION: SINGLE OR ISOLATED LESION ONLY
 AFFECTING LONGITUDINAL FOLD

3 = ULCERATION: MULTIPLE NON-CIRCUMFERENTIAL LESIONS
 AFFECTING MORE THAN ONE LONGITUDINAL
 FOLD, WITH OR WITHOUT CONFLUENCE

4 = CIRCUMFERENTIAL ULCERATION

5 = STRICTURE

6 = BARRETT'S OESOPHAGUS

BIOPSY TAKEN: Y/N

HIATUS HERNIA: Y/N

SPECIFY LENGTH: _____ CM

SLIDING / ROLLING / MIXED

STOMACH – NORMAL/ABNORMAL

-SPECIFY: _____

DUODENUM – NORMAL/ABNORMAL

-SPECIFY: _____

24-HOUR pH STUDY

DATE OF TEST: _____

DURATION OF STUDY: _____

QUANTITATIVE REFLUX

- PERCENTAGE OF TIME OF WHICH pH<4: _____ %
- TOTAL NUMBER OF REFLUX EPISODES: _____

QUALITATIVE REFLUX

- NUMBER OF SYMPTOMATIC EPISODES WITH REFLUX EVENT: _____
- TOTAL NUMBER OF SYMPTOMATIC EPISODES: _____
- SYMPTOMATIC EPISODES CORRELATING WITH RELUX EVENTS:
_____ %

24-HOUR pH GRADING

GRADE: _____

0 = NO REFLUX: pH<4 LESS THAN 4%

1 = MILD REFLUX WITHOUT SYMPTOMS: pH<4 BETWEEN 4 TO 7 %

2 = MILD REFLUX WITH SYMPTOMS: pH<4 BETWEEN 4 TO 7 % WITH
GOOD SYMPTOM CORRELATION

3 = REFLUX WITH SYMPTOMS: pH<4 MORE THAN 7 %

OESOPHAGEAL MANOMETRY

DATE OF PROCEDURE: _____

PROXIMAL OESOPHAGUS:

RESTING PRESSURE: _____ MMHG

MEAN AMPLITUDE OF CONTRACTION: _____ MMHG

DISTAL OESOPHAGUS:

RESTING PRESSURE: _____ MMHG

MEAN AMPLITUDE OF CONTRACTION: _____ MMHG

TYPE OF CONTRACTIONS: PRIMARY: _____ %

SECONDARY: _____ %

TERTIARY: _____ %

LOWER OESOPHAGEAL SPHINCTER:

LOCATED AT: _____ CM

RESTING PRESSURE: _____ MMHG

NADIR PRESSURE: _____ MMHG

LOSP

NORMAL (>10MMHG)

ABNORMAL (<10MMHG)

PERISTALSIS (10 WET SWALLOWS)

NUMBER OF SUCCESSFUL SWALLOWS: _____

NORMAL/ABNORMAL (3 OR MORE FAILURES)

ANAESTHETICS

ASA SCORE: _____

ANAESTHETIC PROBLEMS DURING OPERATION: _____

OPERATING TIMES

24-HOUR CLOCK: _____ HRS

INDUCTION: _____ HRS

POSITIONING OF PATIENT: _____ HRS

KNIFE TO SKIN: _____ HRS

LAST STITCH: _____ HRS

TRANSFER TO RECOVERY: _____ HRS

DURATION OF PROCEDURE: _____ HRS _____ MINS

THEATRE TIME: _____ HRS _____ MINS

OPERATION DETAILS

FUNDOPLICATION RANDOMISATION:

ANTERIOR / POSTERIOR OR NISSEN / LIND

OPERATION PERFORMED:

LAPAROSCOPIC

LAPAROSCOPIC CONVERTED TO OPEN

DEGREE OF DIFFICULTY (1-10, 1- EASY)

1 2 3 4 5 6 7 8 9 10

SURGEON	ASSISTANT 1	ASSISTANT 2
CJS/RA	CONSULTANT	CONSULTANT
	SENIOR REGISTRAR	SENIOR REGISTRAR
	REGISTRAR	REGISTRAR
	INTERN	INTERN
	STUDENT	STUDENT
	NURSE	NURSE

PRE-OPERATIVE ANTIBIOTICS: Y/N ANTIBIOTIC: _____

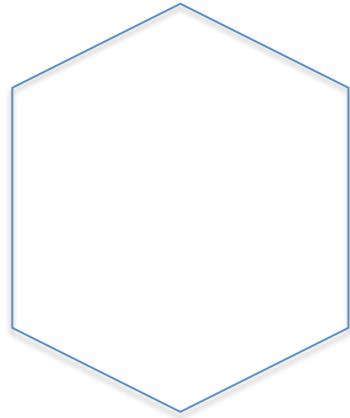
HEPARIN PROPHYLAXIS: Y/N DOSE: _____

NASOGASTRIC INTUBATION: Y/N

CONTINUED POST OPERATIVELY FOR: _____ DAYS

LAPAROSCOPIC FUNDOPPLICATION TECHNIQUE

NUMBER OF ENTRY SITES: _____ (MARK)



X = 10 MM PORT

O = 5 MM PORT

LAPAROSCOPY:

INSPECTION: NORMAL/ABNORMAL/CURSORY/NOT PERFORMED

HIATUS HERNIA: Y/N

IF YES: SLIDING/ROLLING/MIXED

SIZE: <2CM/2-5CM/>5CM

ADHESIONS: Y/N

IF YES, QUADRANT: _____

GRADE 0-5 (5=SEVERE)

LAPARASCOPIC PROBLEMS (CIRCLE):

NONE

FAILED INSUFFLATION

BLEEDING

BOWEL INJURY

BLADDER INJURY

LIVER INJURY

SPLENIC INJURY

IF ANY OF THE ABOVE, GIVE DETAILS: _____

FUNDOPLICATION REPAIR TECHNIQUES

OESOPHAGEAL SLING: Y/N

SHORT GASTRICS: NOT DIVIDED/ DIVIDED

IF DIVIDED, HOW MANY? _____

BOUGIE USED IN OESOPHAGUS: Y/N

FUNDOPLICATION TYPE: ANTERIOR/POSTERIOR/NISSEN/LIND

NUMBER OF SUTURES USED: _____

SUTURE TYPE: 2/0 PROLENE/ 2/0 NOVAFIL / ENDOSTITCH / OTHER

KNOT TYING: INTRACORPOREAL/EXTRACORPOREAL

SPECIFY ANY VARIATION FROM STANDARD TECHNIQUE: _____

HIATAL REPAIR: Y/N

ANTERIOR/POSTERIOR

SUTURES: NUMBER _____

SUTURE TYPE: 2/0 PROLENE/ 2/0 NOVAFIL / ENDOSTITCH / OTHER

KNOT TYING: INTRACORPOREAL/EXTRACORPOREAL

ANY OTHER PROCEDURES AT THE TIE OF LAPAROSCOPY? _____

CONVERSION TO OPEN PROCEDURE: Y/N

REASON: _____

ANY SPECIFIC DIFFICULTIES: _____

POST-OPERATIVE RECOVERY

DATE OF DISCHARGE: _____

LENGTH OF POST-OPERATIVE STAY: _____ DAYS

TOTAL HOSPITAL STAY: _____ DAYS

TIME FROM OPERATION TO ORAL FLUIDS: _____ DAYS

TIME FROM THE END OF THE OPERATION TO SOLID/SEMISOLID FEEDING: _____ DAYS

WOUND PROBLEMS (SPECIFY):_____

OTHER COMPLICATIONS (CIRCLE AND DETAIL):

HAEMORRHAGE

RESPIRATORY COMPLICATIONS

ILEUS GREATER THAN 2 DAYS

OTHER GI COMPLICATIONS

GU/RENAL COMPLICATIONS

CARDIOVASCULAR COMPLICATIONS

DVT

PE

SUBPHRENIC COLLECTION

DEATH

OTHER

DETAILS OF COMPLICATION: _____

RE-OPERATIONS: Y/N

REASON: _____

PROCEDURE: _____

OTHER POST-OPERATIVE PROCEDURES: _____

ADIOLOGICAL DRAINAGE: _____

SYMPTOMS AT DISCHARGE

REFLUX/HEARTBURN: Y/N

REGURGITATION: Y/N

DYSPHAGIA: Y/N

SOLIDS/LIQUIDS

ABLE TO BURP: Y/N

GAS BLOAT: Y/N

RE-ADMISSION TO HOSPITAL: Y/N

SPECIFY (WHERE, WHEN AND HOW LONG): _____

OUTPATIENT FOLLOW UP 1 MONTH

DATE: _____

FOLLOW UP AT: _____ WEEKS

_____ STILL CONVALESCENT

_____ RESUMED WORK/FULL ACTIVITY

SPECIFY WHEN AFTER SURGERY, AT FULL ACTIVITY: _____ WEEKS

AT WORK: _____ WEEKS

SYMPTOMS (CIRCLE): ASYMPTOMATIC/SYMPOMATIC

HEARTBURN

EPIGASTRIC PAIN

REGURGITATION

DYSPHAGIA – SPECIFY: LUMPY SOLIDS / SOFT SOLIDS / LIQUIDS

PAIN ON SWALLOWING

POST-PRANDIAL FULLNESS OR EARLY SATIETY

EPIGASTRIC BLOATING

ANOREXIA

NAUSEA

VOMITING

NOCTURNAL COUGHING

NOCTURNAL WHEEZING

INCREASED FLATUS

DIARRHOEA

1. IS HEARTBURN CONTROLLED? YES/NO

GRADE ON A SCALE OF 0-10:

0 = FULLY CONTROLLED
10 = NOT CONTROLLED

0 ————— 5 ————— 10

2. ANY DIFFICULTY SWALLOWING? YES/NO

GRADE ON A SCALE OF 0-10:

1 = NO DIFFICULTY
10 = SEVERE DIFFICULTY

LIQUIDS:

0 ————— 5 ————— 10

SOLIDS:

0 ————— 5 ————— 10

3. ABLE TO RELIEVE ANY BLOATING EFFECTIVELY DURING EATING?

YES/NO

4. EAT A NORMAL DIET NOW? YES/NO

LIST ANY RESTRICTIONS IF APPLICABLE

5. SATISFIED WITH THE RESULT OF SURGERY? (0-10, 10 SATISFIED)

0 1 2 3 4 5 6 7 8 9 10

6. WOULD YOU HAVE THIS OPERATION AGAIN KNOWING WHAT YOU DO NOW? Y/N

EXAMINATION

WEIGHT: _____ KG

WOUNDS: NORMAL/ABNORMA (SPECIFY)

OTHER

MEDICATIONS (LIST):

A) FOR HEARTBURN

B) OTHER

OTHER SIGNIFICANT EVENTS

OUTCOME:

EXCELLENT (COMPLETE RECOVERY)

GOOD (MAJOR IMPROVEMENT WITH MINOR PROBLEMS)

FAIR (MAJOR IMPROVEMENTS WITH STILL SIGNIFICANT PROBLEMS OR ADVERSE EFFECTS)

POOR (MINOR/NO IMPROVEMENT OR DETERIORATION)

MODIFIED VISICK GRADING AT 1 MONTH

1. NO SYMPTOMS
2. MILD SYMPTOMS EASILY CONTROLLED BY SIMPLE CARE SUCH AS AVOIDING CERTAIN FOODS OR SMALL MEALS, ETC.
3. MODERATE SYMPTOMS NOT CONTROLLED BY SIMPLE CARE BUT NOT INTERFERING WITH SOCIAL OR ECONOMIC LIFE
4. MODERATE SYMPTOMS INTERFERING WITH SOCIAL OR ECONOMIC LIFE
5. SYMPTOMS AS BAD OR WORSE THAN PRE-OPERATIVELY

DYSPHAGIA SCORE AT 1 MONTH

DYSPHAGIA SCORE (SCORE EACH LINE)

	ALWAYS	OCCASIONAL	NEVER
WATER			
MILK/THIN SOUP			
CUSTARD (YOGHURT, PUREED FRUIT)			
JELLY			
SCRAMBLED EGG (BAKED BEANS, MASHED POTATO)			
BAKED FISH (STEAMED POTATO, COOKED CARROT)			
BREAD (PASTRIES)			
APPLE (RAW CARROT)			
STEAK (PORK OR LAMB CHOP)			

TOTAL SCORE: _____

(MULTIPLE EACH NUMBER BY 0, 0.5 OR 1 AND THEN SUM
0=TOTAL DYSPHAGIA, 45 = NO DYSPHAGIA)

OUTPATIENT FOLLOW UP 3 MONTHS

DATE: _____

FOLLOW UP AT: _____ WEEKS

_____ STILL CONVALESCENT

_____ RESUMED WORK/FULL ACTIVITY

SPECIFY WHEN AFTER SURGERY, AT FULL ACTIVITY: _____ WEEKS

AT WORK: _____ WEEKS

SYMPTOMS (CIRCLE): ASYMPTOMATIC/SYMPOMATIC

HEARTBURN

EPIGASTRIC PAIN

REGURGITATION

DYSPHAGIA – SPECIFY: LUMPY SOLIDS / SOFT SOLIDS / LIQUIDS

PAIN ON SWALLOWING

POST-PRANDIAL FULLNESS OR EARLY SATIETY

EPIGASTRIC BLOATING

ANOREXIA

NAUSEA

VOMITING

NOCTURNAL COUGHING

NOCTURNAL WHEEZING

INCREASED FLATUS

DIARRHOEA

1. IS HEARTBURN CONTROLLED? YES/NO

GRADE ON A SCALE OF 0-10:

0 = FULLY CONTROLLED
10 = NOT CONTROLLED

0 ————— 5 ————— 10

2. ANY DIFFICULTY SWALLOWING? YES/NO

GRADE ON A SCALE OF 0-10:

0 = NO DIFFICULTY
10 = SEVERE DIFFICULTY

LIQUIDS:

0 ————— 5 ————— 10

SOLIDS:

0 ————— 5 ————— 10

3. ABLE TO RELIEVE ANY BLOATING EFFECTIVELY DURING EATING?

YES/NO

4. EAT A NORMAL DIET NOW? YES/NO

LIST ANY RESTRICTIONS IF APPLICABLE

5. SATISFIED WITH THE RESULT OF SURGERY? (0-10, 10 SATISFIED)

0 1 2 3 4 5 6 7 8 9 10

6. WOULD YOU HAVE THIS OPERATION AGAIN KNOWING WHAT YOU DO NOW? Y/N

EXAMINATION

WEIGHT: _____ KG

WOUNDS: NORMAL/ABNORMA (SPECIFY)

OTHER

MEDICATIONS (LIST):

A) FOR HEARTBURN

B) OTHER

OTHER SIGNIFICANT EVENTS

OUTCOME:

EXCELLENT (COMPLETE RECOVERY)

GOOD (MAJOR IMPROVEMENT WITH MINOR PROBLEMS)

FAIR (MAJOR IMPROVEMENTS WITH STILL SIGNIFICANT PROBLEMS OR ADVERSE EFFECTS)

POOR (MINOR/NO IMPROVEMENT OR DETERIORATION)

MODIFIED VISICK GRADING AT 3 MONTHS

1. NO SYMPTOMS
2. MILD SYMPTOMS EASILY CONTROLLED BY SIMPLE CARE SUCH AS AVOIDING CERTAIN FOODS OR SMALL MEALS, ETC.
3. MODERATE SYMPTOMS NOT CONTROLLED BY SIMPLE CARE BUT NOT INTERFERING WITH SOCIAL OR ECONOMIC LIFE
4. MODERATE SYMPTOMS INTERFERING WITH SOCIAL OR ECONOMIC LIFE
5. SYMPTOMS AS BAD OR WORSE THAN PRE-OPERATIVELY

DYSPHAGIA SCORE AT 3 MONTHS

DYSPHAGIA SCORE (SCORE EACH LINE)

	ALWAYS	OCCASIONAL	NEVER
WATER			
MILK/THIN SOUP			
CUSTARD (YOGHURT, PUREED FRUIT)			
JELLY			
SCRAMBLED EGG (BAKED BEANS, MASHED POTATO)			
BAKED FISH (STEAMED POTATO, COOKED CARROT)			
BREAD (PASTRIES)			
APPLE (RAW CARROT)			
STEAK (PORK OR LAMB CHOP)			

TOTAL SCORE: _____

(MULTIPLE EACH NUMBER BY 0, 0.5 OR 1 AND THEN SUM
0=TOTAL DYSPHAGIA, 45 = NO DYSPHAGIA)

POST OPERATIVE INVESTIGATIONS

ENDOSCOPY

DATE OF TEST: _____

WHEN AFTER SURGERY: _____ WEEKS

OESOPHAGUS – GRADE OF OESOPHAGITIS: _____

0 = NORMAL

1 = ERYTHEMA ALONE

2 = ULCERATION: SINGLE OR ISOLATED LESION ONLY
 AFFECTING LONGITUDINAL FOLD

3 = ULCERATION: MULTIPLE NON-CIRCUMFERENTIAL LESIONS
 AFFECTING MORE THAN ONE LONGITUDINAL
 FOLD, WITH OR WITHOUT CONFLUENCE

4 = CIRCUMFERENTIAL ULCERATION

5 = STRICTURE

6 = BARRETT'S OESOPHAGUS

BIOPSY TAKEN: Y/N

RESULT: _____

HIATUS HERNIA: Y/N

SPECIFY LENGTH: _____ CM

SLIDING / ROLLING / MIXED

STOMACH – NORMAL/ABNORMAL

SPECIFY: _____

FUNDOPLICATION: PRESENT/ABSENT

SATISFACTORY: Y/N

GASTRIC ANATOMY: NORMAL/BILOBED/DISTORTED

DUODENUM – NORMAL/ABNORMAL

-SPECIFY: _____

24-HOUR pH STUDY

DATE OF TEST: _____

SPECIFY WHEN AFTER SURGERY: _____ WEEKS

DURATION OF STUDY: _____

QUANTITATIVE REFLUX

- PERCENTAGE OF TIME OF WHICH pH<4: _____ %
- TOTAL NUMBER OF REFLUX EPISODES: _____

QUALITATIVE REFLUX

- NUMBER OF SYMPTOMATIC EPISODES WITH REFLUX EVENT: __
- TOTAL NUMBER OF SYMPTOMATIC EPISODES: __
- SYMPTOMATIC EPISODES CORRELATING WITH RELUX EVENTS:
_____ %

24-HOUR pH GRADING

GRADE: _____

0 = NO REFLUX: pH<4 LESS THAN 4%

1 = MILD REFLUX WITHOUT SYMPTOMS: pH<4 BETWEEN 4 TO 7 %

2 = MILD REFLUX WITH SYMPTOMS: pH<4 BETWEEN 4 TO 7 % WITH
GOOD SYMPTOM CORRELATION

3 = REFLUX WITH SYMPTOMS: pH<4 MORE THAN 7 %

OESOPHAGEAL MANOMETRY

DATE OF PROCEDURE: _____

SPECIFY WHEN AFTER SURGERY: _____ WEEKS

PROXIMAL OESOPHAGUS:

RESTING PRESSURE: _____ MMHG

MEAN AMPLITUDE OF CONTRACTION: _____ MMHG

DISTAL OESOPHAGUS:

RESTING PRESSURE: _____ MMHG

MEAN AMPLITUDE OF CONTRACTION: _____ MMHG

TYPE OF CONTRACTIONS: PRIMARY: _____ %

SECONDARY: _____ %

TERTIARY: _____ %

LOWER OESOPHAGEAL SPHINCTER:

LOCATED AT: _____ CM

RESTING PRESSURE: _____ MMHG

NADIR PRESSURE: _____ MMHG

LOSP

NORMAL (>10MMHG)

ABNORMAL (<10MMHG)

PERISTALSIS (10 WET SWALLOWS)

NUMBER OF SUCCESSFUL SWALLOWS: _____

NORMAL/ABNORMAL (3 OR MORE FAILURES)

OUTPATIENT FOLLOW UP 6 MONTHS

DATE: _____

FOLLOW UP AT: _____ WEEKS

_____ STILL CONVALESCENT

_____ RESUMED WORK/FULL ACTIVITY

SPECIFY WHEN AFTER SURGERY, AT FULL ACTIVITY: _____ WEEKS

AT WORK: _____ WEEKS

SYMPTOMS (CIRCLE): ASYMPTOMATIC/SYMPOMATIC

HEARTBURN

EPIGASTRIC PAIN

REGURGITATION

DYSPHAGIA – SPECIFY: LUMPY SOLIDS / SOFT SOLIDS / LIQUIDS

PAIN ON SWALLOWING

POST-PRANDIAL FULLNESS OR EARLY SATIETY

EPIGASTRIC BLOATING

ANOREXIA

NAUSEA

VOMITING

NOCTURNAL COUGHING

NOCTURNAL WHEEZING

INCREASED FLATUS

DIARRHOEA

1. IS HEARTBURN CONTROLLED? YES/NO

GRADE ON A SCALE OF 0-10:

0 = FULLY CONTROLLED
10 = NOT CONTROLLED

0 ————— 5 ————— 10

2. ANY DIFFICULTY SWALLOWING? YES/NO

GRADE ON A SCALE OF 0-10:

0 = NO DIFFICULTY
10 = SEVERE DIFFICULTY

LIQUIDS:

0 ————— 5 ————— 10

SOLIDS:

0 ————— 5 ————— 10

3. ABLE TO RELIEVE ANY BLOATING EFFECTIVELY DURING EATING?

YES/NO

4. EAT A NORMAL DIET NOW? YES/NO

LIST ANY RESTRICTIONS IF APPLICABLE

5. SATISFIED WITH THE RESULT OF SURGERY? (0-10, 10 SATISFIED)

0 1 2 3 4 5 6 7 8 9 10

6. WOULD YOU HAVE THIS OPERATION AGAIN KNOWING WHAT YOU DO NOW? Y/N

EXAMINATION

WEIGHT: _____ KG

WOUNDS: NORMAL/ABNORMAL (SPECIFY)

OTHER

MEDICATIONS (LIST):

A) FOR HEARTBURN

B) OTHER

OTHER SIGNIFICANT EVENTS

OUTCOME:

EXCELLENT (COMPLETE RECOVERY)

GOOD (MAJOR IMPROVEMENT WITH MINOR PROBLEMS)

FAIR (MAJOR IMPROVEMENTS WITH STILL SIGNIFICANT PROBLEMS OR ADVERSE EFFECTS)

POOR (MINOR/NO IMPROVEMENT OR DETERIORATION)

MODIFIED VISICK GRADING AT 6 MONTHS

1. NO SYMPTOMS
2. MILD SYMPTOMS EASILY CONTROLLED BY SIMPLE CARE SUCH AS AVOIDING CERTAIN FOODS OR SMALL MEALS, ETC.
3. MODERATE SYMPTOMS NOT CONTROLLED BY SIMPLE CARE BUT NOT INTERFERING WITH SOCIAL OR ECONOMIC LIFE
4. MODERATE SYMPTOMS INTERFERING WITH SOCIAL OR ECONOMIC LIFE
5. SYMPTOMS AS BAD OR WORSE THAN PRE-OPERATIVELY

DYSPHAGIA SCORE AT 6 MONTHS

DYSPHAGIA SCORE (SCORE EACH LINE)

	ALWAYS	OCCASIONAL	NEVER
WATER			
MILK/THIN SOUP			
CUSTARD (YOGHURT, PUREED FRUIT)			
JELLY			
SCRAMBLED EGG (BAKED BEANS, MASHED POTATO)			
BAKED FISH (STEAMED POTATO, COOKED CARROT)			
BREAD (PASTRIES)			
APPLE (RAW CARROT)			
STEAK (PORK OR LAMB CHOP)			

TOTAL SCORE: _____

(MULTIPLE EACH NUMBER BY 0, 0.5 OR 1 AND THEN SUM
0=TOTAL DYSPHAGIA, 45 = NO DYSPHAGIA)

OUTPATIENT FOLLOW UP 12 MONTHS

DATE: _____

FOLLOW UP AT: _____ WEEKS

_____ STILL CONVALESCENT

_____ RESUMED WORK/FULL ACTIVITY

SPECIFY WHEN AFTER SURGERY, AT FULL ACTIVITY: _____ WEEKS

AT WORK: _____ WEEKS

SYMPTOMS (CIRCLE): ASYMPTOMATIC/SYMPOMATIC

HEARTBURN

EPIGASTRIC PAIN

REGURGITATION

DYSPHAGIA – SPECIFY: LUMPY SOLIDS / SOFT SOLIDS / LIQUIDS

PAIN ON SWALLOWING

POST-PRANDIAL FULLNESS OR EARLY SATIETY

EPIGASTRIC BLOATING

ANOREXIA

NAUSEA

VOMITING

NOCTURNAL COUGHING

NOCTURNAL WHEEZING

INCREASED FLATUS

DIARRHOEA

1. IS HEARTBURN CONTROLLED? YES/NO

GRADE ON A SCALE OF 0-10:

0 = FULLY CONTROLLED
10 = NOT CONTROLLED

0 ————— 5 ————— 10

2. ANY DIFFICULTY SWALLOWING? YES/NO

GRADE ON A SCALE OF 0-10:

0 = NO DIFFICULTY
10 = SEVERE DIFFICULTY

LIQUIDS:

0 ————— 5 ————— 10

SOLIDS:

0 ————— 5 ————— 10

3. ABLE TO RELIEVE ANY BLOATING EFFECTIVELY DURING EATING?

YES/NO

4. EAT A NORMAL DIET NOW? YES/NO

LIST ANY RESTRICTIONS IF APPLICABLE

5. SATISFIED WITH THE RESULT OF SURGERY? (0-10, 10 SATISFIED)

0 1 2 3 4 5 6 7 8 9 10

6. WOULD YOU HAVE THIS OPERATION AGAIN KNOWING WHAT YOU DO NOW? Y/N

EXAMINATION

WEIGHT: _____ KG

WOUNDS: NORMAL/ABNORMA (SPECIFY)

OTHER

MEDICATIONS (LIST):

A) FOR HEARTBURN

B) OTHER

OTHER SIGNIFICANT EVENTS

OUTCOME:

EXCELLENT (COMPLETE RECOVERY)

GOOD (MAJOR IMPROVEMENT WITH MINOR PROBLEMS)

FAIR (MAJOR IMPROVEMENTS WITH STILL SIGNIFICANT PROBLEMS OR ADVERSE EFFECTS)

POOR (MINOR/NO IMPROVEMENT OR DETERIORATION)

MODIFIED VISICK GRADING AT 12 MONTHS

1. NO SYMPTOMS
2. MILD SYMPTOMS EASILY CONTROLLED BY SIMPLE CARE SUCH AS AVOIDING CERTAIN FOODS OR SMALL MEALS, ETC.
3. MODERATE SYMPTOMS NOT CONTROLLED BY SIMPLE CARE BUT NOT INTERFERING WITH SOCIAL OR ECONOMIC LIFE
4. MODERATE SYMPTOMS INTERFERING WITH SOCIAL OR ECONOMIC LIFE
5. SYMPTOMS AS BAD OR WORSE THAN PRE-OPERATIVELY

DYSPHAGIA SCORE AT 12 MONTHS

DYSPHAGIA SCORE (SCORE EACH LINE)

	ALWAYS	OCCASIONAL	NEVER
WATER			
MILK/THIN SOUP			
CUSTARD (YOGHURT, PUREED FRUIT)			
JELLY			
SCRAMBLED EGG (BAKED BEANS, MASHED POTATO)			
BAKED FISH (STEAMED POTATO, COOKED CARROT)			
BREAD (PASTRIES)			
APPLE (RAW CARROT)			
STEAK (PORK OR LAMB CHOP)			

TOTAL SCORE: _____

(MULTIPLE EACH NUMBER BY 0, 0.5 OR 1 AND THEN SUM
0=TOTAL DYSPHAGIA, 45 = NO DYSPHAGIA)

OUTPATIENT FOLLOW UP 2 YEARS

DATE: _____

FOLLOW UP AT: _____ WEEKS

_____ STILL CONVALESCENT

_____ RESUMED WORK/FULL ACTIVITY

SPECIFY WHEN AFTER SURGERY, AT FULL ACTIVITY: _____ WEEKS

AT WORK: _____ WEEKS

SYMPTOMS (CIRCLE): ASYMPTOMATIC/SYMPOMATIC

HEARTBURN

EPIGASTRIC PAIN

REGURGITATION

DYSPHAGIA – SPECIFY: LUMPY SOLIDS / SOFT SOLIDS / LIQUIDS

PAIN ON SWALLOWING

POST-PRANDIAL FULLNESS OR EARLY SATIETY

EPIGASTRIC BLOATING

ANOREXIA

NAUSEA

VOMITING

NOCTURNAL COUGHING

NOCTURNAL WHEEZING

INCREASED FLATUS

DIARRHOEA

1. IS HEARTBURN CONTROLLED? YES/NO

GRADE ON A SCALE OF 0-10:

0 = FULLY CONTROLLED
10 = NOT CONTROLLED

0 ————— 5 ————— 10

2. ANY DIFFICULTY SWALLOWING? YES/NO

GRADE ON A SCALE OF 0-10:

0 = NO DIFFICULTY
10 = SEVERE DIFFICULTY

LIQUIDS:

0 ————— 5 ————— 10

SOLIDS:

0 ————— 5 ————— 10

3. ABLE TO RELIEVE ANY BLOATING EFFECTIVELY DURING EATING?

YES/NO

4. EAT A NORMAL DIET NOW? YES/NO

LIST ANY RESTRICTIONS IF APPLICABLE

5. SATISFIED WITH THE RESULT OF SURGERY? (0-10, 10 SATISFIED)

0 1 2 3 4 5 6 7 8 9 10

6. WOULD YOU HAVE THIS OPERATION AGAIN KNOWING WHAT YOU DO NOW? Y/N

EXAMINATION

WEIGHT: _____ KG

WOUNDS: NORMAL/ABNORMA (SPECIFY)

OTHER

MEDICATIONS (LIST):

A) FOR HEARTBURN

B) OTHER

OTHER SIGNIFICANT EVENTS

OUTCOME:

EXCELLENT (COMPLETE RECOVERY)

GOOD (MAJOR IMPROVEMENT WITH MINOR PROBLEMS)

FAIR (MAJOR IMPROVEMENTS WITH STILL SIGNIFICANT PROBLEMS OR ADVERSE EFFECTS)

POOR (MINOR/NO IMPROVEMENT OR DETERIORATION)

MODIFIED VISICK GRADING AT 2 YEARS

1. NO SYMPTOMS
2. MILD SYMPTOMS EASILY CONTROLLED BY SIMPLE CARE SUCH AS AVOIDING CERTAIN FOODS OR SMALL MEALS, ETC.
3. MODERATE SYMPTOMS NOT CONTROLLED BY SIMPLE CARE BUT NOT INTERFERING WITH SOCIAL OR ECONOMIC LIFE
4. MODERATE SYMPTOMS INTERFERING WITH SOCIAL OR ECONOMIC LIFE
5. SYMPTOMS AS BAD OR WORSE THAN PRE-OPERATIVELY

DYSPHAGIA SCORE AT 2 YEARS

DYSPHAGIA SCORE (SCORE EACH LINE)

	ALWAYS	OCCASIONAL	NEVER
WATER			
MILK/THIN SOUP			
CUSTARD (YOGHURT, PUREED FRUIT)			
JELLY			
SCRAMBLED EGG (BAKED BEANS, MASHED POTATO)			
BAKED FISH (STEAMED POTATO, COOKED CARROT)			
BREAD (PASTRIES)			
APPLE (RAW CARROT)			
STEAK (PORK OR LAMB CHOP)			

TOTAL SCORE: _____

(MULTIPLE EACH NUMBER BY 0, 0.5 OR 1 AND THEN SUM
0=TOTAL DYSPHAGIA, 45 = NO DYSPHAGIA)

OUTPATIENT FOLLOW UP 3 YEARS

DATE: _____

FOLLOW UP AT: _____ WEEKS

_____ STILL CONVALESCENT

_____ RESUMED WORK/FULL ACTIVITY

SPECIFY WHEN AFTER SURGERY, AT FULL ACTIVITY: _____ WEEKS

AT WORK: _____ WEEKS

SYMPTOMS (CIRCLE): ASYMPTOMATIC/SYMPOMATIC

HEARTBURN

EPIGASTRIC PAIN

REGURGITATION

DYSPHAGIA – SPECIFY: LUMPY SOLIDS / SOFT SOLIDS / LIQUIDS

PAIN ON SWALLOWING

POST-PRANDIAL FULLNESS OR EARLY SATIETY

EPIGASTRIC BLOATING

ANOREXIA

NAUSEA

VOMITING

NOCTURNAL COUGHING

NOCTURNAL WHEEZING

INCREASED FLATUS

DIARRHOEA

1. IS HEARTBURN CONTROLLED? YES/NO

GRADE ON A SCALE OF 0-10:

0 = FULLY CONTROLLED
10 = NOT CONTROLLED

0 ————— 5 ————— 10

2. ANY DIFFICULTY SWALLOWING? YES/NO

GRADE ON A SCALE OF 0-10:

1 = NO DIFFICULTY
10 = SEVERE DIFFICULTY

LIQUIDS:

0 ————— 5 ————— 10

SOLIDS:

0 ————— 5 ————— 10

3. ABLE TO RELIEVE ANY BLOATING EFFECTIVELY DURING EATING?

YES/NO

4. EAT A NORMAL DIET NOW? YES/NO

LIST ANY RESTRICTIONS IF APPLICABLE

5. SATISFIED WITH THE RESULT OF SURGERY? (0-10, 10 SATISFIED)

0 1 2 3 4 5 6 7 8 9 10

6. WOULD YOU HAVE THIS OPERATION AGAIN KNOWING WHAT YOU DO NOW? Y/N

EXAMINATION

WEIGHT: _____ KG

WOUNDS: NORMAL/ABNORMA (SPECIFY)

OTHER

MEDICATIONS (LIST):

A) FOR HEARTBURN

B) OTHER

OTHER SIGNIFICANT EVENTS

OUTCOME:

EXCELLENT (COMPLETE RECOVERY)

GOOD (MAJOR IMPROVEMENT WITH MINOR PROBLEMS)

FAIR (MAJOR IMPROVEMENTS WITH STILL SIGNIFICANT PROBLEMS OR ADVERSE EFFECTS)

POOR (MINOR/NO IMPROVEMENT OR DETERIORATION)

MODIFIED VISICK GRADING AT 3 YEARS

1. NO SYMPTOMS
2. MILD SYMPTOMS EASILY CONTROLLED BY SIMPLE CARE SUCH AS AVOIDING CERTAIN FOODS OR SMALL MEALS, ETC.
3. MODERATE SYMPTOMS NOT CONTROLLED BY SIMPLE CARE BUT NOT INTERFERING WITH SOCIAL OR ECONOMIC LIFE
4. MODERATE SYMPTOMS INTERFERING WITH SOCIAL OR ECONOMIC LIFE
5. SYMPTOMS AS BAD OR WORSE THAN PRE-OPERATIVELY

DYSPHAGIA SCORE AT 3 YEARS

DYSPHAGIA SCORE (SCORE EACH LINE)

	ALWAYS	OCCASIONAL	NEVER
WATER			
MILK/THIN SOUP			
CUSTARD (YOGHURT, PUREED FRUIT)			
JELLY			
SCRAMBLED EGG (BAKED BEANS, MASHED POTATO)			
BAKED FISH (STEAMED POTATO, COOKED CARROT)			
BREAD (PASTRIES)			
APPLE (RAW CARROT)			
STEAK (PORK OR LAMB CHOP)			

TOTAL SCORE: _____

(MULTIPLE EACH NUMBER BY 0, 0.5 OR 1 AND THEN SUM
0=TOTAL DYSPHAGIA, 45 = NO DYSPHAGIA)

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APPENDIX II

Sheffield Teaching Hospitals 
NHS Foundation Trust

General Surgery
Mr R Ackroyd MB ChB MD FRCS
Consultant Surgeon
Secretary to Mr Ackroyd: Della Oldham
0114 3052411

Mr C Kelty - Consultant Surgeon
Mr K A Patel - Consultant Surgeon
Mr A Tamhankar - Consultant Surgeon
Mr A Wyman - Consultant Surgeon

Northern General Hospital
Herries Road
Sheffield
S5 7AU

Tel: 0114 2434343

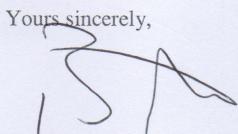
Warwick Graduate School
University of Warwick
Senate House
Coventry
CV4 7AL

Dear Colleague,

In my role as senior author in the below publications, I can confirm that Mr Mansoor Ali Khan gathered and analysed the data and also undertook writing the manuscripts for the below publications.

1. Khan M, Smythe A, Globe J, Stoddard CJ and Ackroyd R. (2010), Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease. ANZ Journal of Surgery, 80: 500–505. doi: 10.1111/j.1445-2197.2009.05197.x
2. Khan MA, Smythe A, Globe J, Stoddard CJ and Ackroyd R (2009), Randomized controlled trial of laparoscopic Nissen versus Lind fundoplication for gastro-oesophageal reflux disease. Scandinavian Journal of Gastroenterology, 44(3):269-275. doi:10.1080/00365520802495552
3. Khan M, Smythe A, Elghellal K and Ackroyd R (2010), Can intraoperative manometry during laparoscopic fundoplication predict postoperative dysphagia? Surgical Endoscopy, 24(9):2268-2272. doi: 10.1007/s00464-010-0949-6

Yours sincerely,


Mr Roger Ackroyd
Consultant Upper GI and Bariatric Surgeon


In hospital and in the community
proud to make a difference

Chairman: Tony Pedder OBE Chief Executive: Sir Andrew Cash OBE



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APPENDIX III

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Oct 23, 2015

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License Number	3734910588263
License date	Oct 23, 2015
Licensed Content Publisher	John Wiley and Sons
Licensed Content Publication	ANZ Journal of Surgery
Licensed Content Title	Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease
Licensed Content Author	Mansoor Khan,Anne Smythe,Jenny Globe,Christopher J. Stoddard,Roger Ackroyd
Licensed Content Date	Aug 12, 2010
Pages	6
Type of use	Dissertation/Thesis
Requestor type	Author of this Wiley article
Format	Print and electronic
Portion	Full article
Will you be translating?	No
Title of your thesis / dissertation	Outcomes of Laparoscopic Fundoplication
Expected completion date	Nov 2015
Expected size (number of pages)	160
Requestor Location	Mansoor Khan 20 Silica Crescent
Billing Type	Scunthorpe, United Kingdom DN172XA Attn: Mansoor A Khan
Billing Address	Invoice
Total	Mansoor A Khan 20 Silica Crescent
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APPENDIX IV

UPPER GUT SURGERY



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Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease

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Department of Surgery, Royal Hallamshire Hospital, Sheffield, UK

Key words

Partial fundoplication, Gastro-oesophageal reflux, Laparoscopic, Anterior fundoplication, Posterior fundoplication.

Abbreviations

GI, Gastrointestinal; OGD, Oesophagogastroduodenoscopy; PPI, Proton pump inhibitor.

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Abstract

Background: The aim of the study was to compare the effect of laparoscopic anterior and posterior fundoplication on gastro-oesophageal reflux disease by means of a prospective randomized controlled trial.

Methods: One hundred and three patients were randomised to undergo either anterior (53) or posterior (50) fundoplication. Initial enrolment and subsequent clinical appointments were undertaken 1, 3, 6 and 12 months after the procedure using a standardized questionnaire. Ambulatory pH monitoring and manometry were undertaken both preoperatively and at approximately 3 months post-procedure.

Results: The mean operating time was similar in both groups (43 versus 52 min). Two operations in each group were converted to open surgery. Post-operative dysphagia in the first month was higher in the posterior fundoplication group compared with the anterior group (at 1 month, $P = 0.002$; and at 3 months, $P = 0.014$). The number of individuals suffering from post-operative heartburn was greater in the anterior fundoplication group (at 1 month, $P = 0.008$; at 3 months, $P < 0.001$; and at 6 months, $P = 0.002$). Eight individuals required reoperation in the anterior group and two individuals in the posterior group ($P = 0.057$).

Conclusion: Anterior and posterior fundoplication each have their advantages and disadvantages. There is an increased risk of early post-operative dysphagia after posterior fundoplication. Anterior fundoplication carries a greater risk of persistent or recurrent reflux. Overall, a posterior fundoplication produces a better management option for controlling gastro-oesophageal reflux disease when compared with an anterior fundoplication technique which utilizes unilateral fixation of the gastric fundus.

Introduction

Mild reflux may be managed with proton pump inhibitors, but, surgery is accepted as the 'gold standard' treatment for moderate to severe gastro-oesophageal reflux.¹ Numerous operative procedures have been described, including Nissen, Lind, anterior and posterior fundoplication, all of which can be undertaken using either a laparoscopic or open technique.

Anterior and posterior fundoplication are partial wraps, encircling only around 180° of the oesophagus as compared with Nissen and Lind fundoplications, which encircle 360° and 270–300°, respectively. This may be advantageous, as a partial wrap may decrease postoperative symptoms such as dysphagia, inability to belch, post-prandial fullness, epigastric bloating and flatulence.^{2–5}

There is limited literature comparing anterior and posterior fundoplication in randomized controlled trials, as well as long-term symptom control and outcome of individuals who have undergone partial fundoplication.² The aim of this study was to compare the outcome of anterior versus posterior fundoplication in individuals with gastro-oesophageal reflux disease, to determine whether one is superior in the control of gastro-oesophageal reflux disease and incidence of undesired post-operative symptoms.

Methods

All individuals presenting for primary gastro-oesophageal reflux surgery were considered for entry into the trial. Similar selection criteria and methods were used, as detailed by Ackroyd *et al.*⁶ All

eligible patients underwent preoperative endoscopy and oesophageal manometry, followed by 24-h ambulatory pH investigations. If preoperative endoscopy and pH/manometric studies were found to be negative, and patients were still experiencing symptomatic reflux, they were sent for barium studies. Patients were excluded if they had an oesophageal motility disorder, required a concurrent abdominal procedure (e.g. cholecystectomy) or had undergone previous anti-reflux surgery.

Patients were randomized to undergo either anterior or posterior fundoplication. Informed consent was obtained and randomization was achieved by opening an opaque sealed envelope, after the individual was anaesthetized. The study protocol was approved by the South Sheffield Research Ethics Committee and the study was conducted in accordance with the World Medical Association declaration of Helsinki (revised 1989).

Laparoscopic anterior and posterior fundoplications were carried out as described previously.^{7,8} After introduction of the laparoscope, a brief inspection was performed to identify any hiatus hernia or the presence of adhesions; these were then subsequently graded. Intra-operative problems and the requirement to convert to open surgery were then noted. A standardized procedure was followed and any reason for variation was documented.

Both procedures were undertaken by an experienced Upper GI Consultant Surgeons (RA or CJS). The operation began with dissection of the hiatal pillars, followed by full oesophageal mobilization and posterior hiatal repair using a median of 2 nylon sutures. A tape was placed around the oesophagus to assist with oesophageal retraction and the short gastric vessels were not divided. In the anterior fundoplication, the fundus of the stomach was brought across the front of the lower oesophagus and was sutured to the right side of the oesophagus using 2 nylon sutures and then to the right crus with a further 2 nylon sutures. If necessary, the fundus was sutured to the apex of the crura. In the posterior fundoplication, the fundus of the stomach was wrapped behind the lower oesophagus and was again anchored to the right side of the oesophagus and the right crus. The operation was given a difficulty grading of 1–10 (1 = easy; 10 = difficult). The length of post-operative hospital stay and symptoms at discharge were noted.

Oral fluids were commenced on the evening of surgery, and subsequently, if tolerated, a soft diet was allowed the next day. Discharge from hospital was allowed when the patient was stable and able to manage at home. Dietary advice was given to individuals, and they were instructed not to eat bread or lumpy foods for the first 4 weeks.

On initial enrolment onto the trial, the patients were interviewed by an experienced Consultant Surgeon (RA or CJS) and questions were asked using a standard, structured questionnaire. Subsequent clinical appointments were undertaken by an experienced clinician at 1, 3, 6 and 12 months after the procedure using the same questionnaire format. At each visit, it was determined whether the individual was still convalescent or had returned to full activity. The presence or absence of a detailed list of symptoms was sought. Patients ranked the outcome of surgery on a modified Visick grading (Table 1), and were asked to score the outcome ranging from excellent to poor.

Table 1 Modified Visick grading

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

Stationary oesophageal manometry and ambulatory pH monitoring was undertaken approximately 3 months post-procedure. A standardised procedure was closely followed; patients were fasted for 6 h prior to the pH and manometry studies. A single use antimony crystal probe (Mediplus, High Wycombe, Buckinghamshire, UK) was positioned 5 cm above the lower oesophageal sphincter and connected to a Flexilog™ 2000 datalogger (Oakfield Instruments, Whitely, Oxfordshire, UK).⁹ The total number of reflux episodes and the percentage of time of the pH was less than 4 recorded.

Prior to manometry being performed, all individuals were asked to cease medication known to affect oesophageal motility. An eight lumen water-perfused catheter was used in four of the lumens placed concentrically at the region of the sphincter and amplified signals recorded using a Phoenix™ recording system (Albyn Medical, Dingwall, Ross-shire, UK). The location and resting pressure of the lower oesophageal sphincter (or high pressure zone post-fundoplication) was located by the station pull through technique. Oesophageal wave amplitude and propagation were measured by 10 mL water bolus swallowing 30 s apart.

Statistical analysis

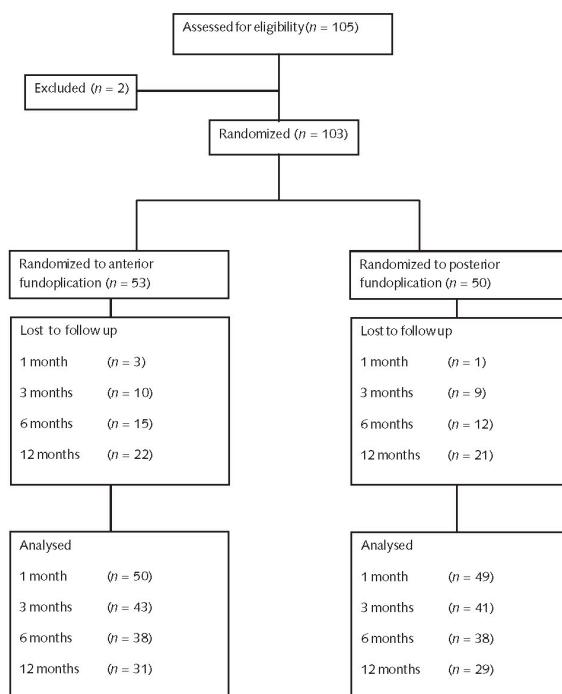
The main outcome measures used in this trial were post-operative symptoms, requirement for re-operation, outcome scale and Visick grading. It was determined that 100 patients were required to demonstrate a 20% difference in outcome measures, with a significance level of $P < 0.050$ and a power of 90%. All analyses were performed on an intention-to-treat basis.

The values presented are the mean and, where appropriate, confidence intervals and standard deviation are provided. Data was analysed using SPSS™ for Windows™, version 15 (SPSS, Chicago, IL, USA). The following tests were used to assist analysis: χ^2 test, Fisher's exact test and Mann-Whitney U-test. A P value of <0.050 was assumed to be statistically significant.

Results

During the study period, 105 patients were enrolled into the study, and 103 were randomized to either anterior or posterior fundoplication. Fifty-three individuals were randomized to anterior fundoplication and 50 to posterior fundoplication. Two patients were excluded from the analysis as no documentation was available for analysis.

Of the 103 patients that were entered into the study, 99 (96%) attended the follow up at 1 month, 84 (82%) at 3 months, 76 (74%) at 6 months and 60 (58%) at 1 year. There were no withdrawals from

**Fig. 1.** Study flow diagram.

the study. Numerous attempts were made to ensure that individuals attended clinic appointments; however, it was not possible to contact all patients at each follow-up interval (Fig. 1).

As demonstrated in Table 2, the two groups were well matched for age, sex, height, weight, cigarette and alcohol consumption. There was an appreciable difference in the duration of symptoms in the two groups, with individuals in the posterior fundoplication group having symptoms for longer; however, this was not statistically significant ($P = 0.861$; Mann–Whitney U-test). Table 3 outlines the findings at oesophagogastroduodenoscopy, and if there was presence of hiatal hernias. There was no appreciable difference in the individuals' preoperative symptoms (Table 4). Visick grading was similar for both groups preoperatively (Table 5). Sixteen patients were found to have normal ambulatory pH studies; of these four patients demonstrated oesophagitis varying from mild erythema to Barrett's oesophagus. The remaining 12 patients were found to have hiatus hernias ($n = 6$), wide open gastro-oesophageal junction ($n = 4$) or reflux on barium studies ($n = 2$).

The mean operating time in the anterior group was 48 (21–87) min and for the posterior group 52.3 (21–92) min ($P = 0.545$),

and the total theatre time for the anterior group was 71.4 (40–110) min and in the posterior group 73.3 (40–196) min ($P = 0.360$). There was no difference in the surgeon's perception of difficulty between the two groups; mean difficulty scores were 4.1 (1–10) for anterior, compared with 4.5 (1–10) for the posterior group ($P = 0.423$). Two individuals, one from each group, had to be converted to open procedure, because of bowel and liver injury, respectively. The hospital stay was comparable in both groups 3.2 (1–15) versus 3.1 (1–9) days ($P = 0.163$).

There were no fatalities in either group. In the anterior group, there were four post-operative complications; one respiratory tract infection, one acute renal failure and two cardiovascular complications. The posterior group demonstrated only two complications; one pulmonary embolus and one respiratory tract infection.

At discharge, there was no major difference in symptoms, with dysphagia to solids in 4 of 51 in the anterior group versus 8 of 50 in the posterior group ($P = 0.205$), and inability to burp being 2 of 51 versus 3 of 50 ($P = 0.630$), respectively. However, there was a significant difference in gas bloat, 8 of 51 versus 2 of 50, respectively ($P = 0.049$). There was also no major difference in the time it

Table 2 Patient demographics

	Anterior (n = 53)	Posterior (n = 50)	P value
Age (years)†	43 (16–79)	43 (18–76)	0.777
Sex ratio (M : F)	36 : 17	38 : 12	0.367
Height (cm)†	169 (147–187)	170 (147–187)	0.810
Weight (kg)†	80.2 (55–129)	78.9 (46–115)	0.676
Cigarette smoker	11	17	0.131
Alcohol consumer	41	38	0.876
Previous surgery (not related)	23	20	0.730
Duration of symptoms (months)†	75.3 (12–360)	94.9 (12–480)	0.861
Preoperative medication			
Antacid	19	11	0.124
H ₂ blocker	3	6	0.259
PPI	51	46	0.365

†Values are mean (range). PPI, Proton pump inhibitor.

Table 3 Preoperative OGD findings

	Anterior (n = 52)	Posterior (n = 47)
Oesophageal findings		
Normal	25	24
Erythema	4	4
Single ulceration	10	5
Multiple ulceration	5	5
Circumferential ulceration	1	0
Barrett's	7	3
Hiatus hernia		
No	27	22
Sliding	24	25
Mixed	1	0
OGD, oesophagogastrroduodenoscopy.		

took individuals to get back to full activities; at 1 month, 35 of 48 versus 34 of 47 were back to full activities ($P = 0.615$). The dysphagia score at all stages of assessment was comparable in both groups; 44.0 (20–45) versus 44.5 (40–45) at 12 months ($P = 0.621$).

Eight individuals required re-operation because of symptom recurrence in the anterior group and two individuals in the posterior group had to be re-operated due to recurrent quantifiable reflux ($P = 0.057$). Detailed analyses of the clinical assessments are displayed in Tables 4 and 5, and demonstrate two appreciable differences between the two groups. First, the incidence of early post-operative dysphagia was slightly higher in the posterior fundoplication group as compared with the anterior group (at 1 month, $P = 0.002$; at 3 months, $P = 0.014$). Outcomes and modified Visick were similar in both groups (Table 5). Also, the number of individuals suffering from post-operative heartburn was greater in the anterior fundoplication group (at 1 month, $P = 0.008$; at 3 months, $P < 0.001$; and at 6 months $P = 0.002$).

Patients were invited to attend for post-operative pH and manometry. Thirty-five of 53 patients (66%) in the anterior group and 37 of 50 patients (74%) in the posterior group underwent repeat investigations. Table 6 demonstrates the preoperative and post-operative time below pH 4 ($P = 0.322$ and 0.337), and pH grading was comparable between the two groups. Ten patients had persistent heartburn at 1 year; however, of these 10, only one individual had quantifiable reflux at ambulatory pH monitoring while the remaining 9 had normal ambulatory pH studies. Oesophageal motility was also

comparable between the two groups with 23 of 47 versus 15 of 49 ($P = 0.066$) being abnormal preoperatively, and 19 of 35 versus 13 of 36 ($P = 0.124$) being abnormal post-operatively.

Discussion

Laparoscopic fundoplication is still considered the gold standard treatment for moderate to severe gastro-oesophageal reflux disease. However, there is now an increasing tendency in many centres to utilize surgery at earlier stages of the disease.⁷ Extensive debates have concluded that continuing with medical therapy does not correct the underlying motor abnormalities that exist in the upper gastrointestinal tract, but that of acid suppression.¹⁰ In addition to this, medication may not provide adequate control of volume reflux, nocturnal symptoms and retro-sternal pain.¹¹ The choice is often left to patients; individuals with effective medication controlled reflux are now given the option to continue with life-long medication or undergo a potentially definitive procedure, that is, surgery. However, emphasis must be placed on the potential undesirable effects that can occur as a result of fundoplication when allowing patients to make an informed choice.

Multiple surgical techniques exist, each with their own potential complications. It has been described in numerous studies that partial funduplications should be reserved for individuals with mild gastro-oesophageal reflux disease.^{12–14} Within the subgroup of anterior funduplications, there exist a number of variants; commonest described in the literature are that of Watson *et al.*¹⁵ and Lundell *et al.*¹¹ The procedure undertaken by our centre more closely resembled that of the Lundell (Goteborg) group, involving suturing of the fundus to one side of the oesophagus, whereas the Watson (Adelaide) group advocate suturing the fundus to both sides of the oesophagus. Both the Sheffield group and the Lundell group demonstrate higher rates of reoperation in the anterior fundoplication group, compared with the Watson group, highlighting the fact that two side fixation may be superior to unilateral fixation.

Unfortunately, as with any trial, there were individuals who were lost to follow-up periods post-procedure despite the best efforts of the authors. Of the 43 patients who failed to attend between the post-operative period and the 1-year post-procedure point, 37 patients had a Visick grading of 1 or 2 (Visick 1 – 26, Visick 2 – 11, Visick 3 – 4 and Visick 4 – 2) at their last clinic attendance.

Table 4 Number of patients with each symptom before and after surgery

	Preoperative		1 month		3 months		6 months		12 months	
	Anterior (n = 53)	Posterior (n = 50)	Anterior (n = 50)	Posterior (n = 49)	Anterior (n = 43)	Posterior (n = 41)	Anterior (n = 38)	Posterior (n = 38)	Anterior (n = 31)	Posterior (n = 29)
Heartburn	50	49	9	1	12	0	13	2	7	3
Epigastric pain	31	31	2	6	6	4	2	4	3	1
Regurgitation	44	48	4	2	4	0	2	2	1	1
Lumpy solid dysphagia	10	13	16	31	5	14	4	5	2	3
Soft solid dysphagia	1	1	0	0	0	0	0	0	1	0
Liquid dysphagia	0	0	0	0	0	0	0	0	0	0
Odynophagia	7	9	2	2	2	1	1	0	0	0
Postprandial fullness	24	27	5	6	2	0	1	2	0	0
Inability to belch	0	0	3	4	0	1	0	3	0	0
Epigastric bloat	27	30	13	11	4	3	3	3	0	2
Anorexia	4	7	1	1	2	1	1	1	0	0
Nausea	12	15	1	1	0	0	0	2	1	1
Vomiting	12	22	3	0	2	0	1	0	0	1
Nocturnal cough	10	14	3	0	1	0	0	0	1	0
Nocturnal wheeze	9	13	3	0	0	0	0	0	0	0
Flatus	0	0	5	4	3	2	0	1	2	1
Diarrhoea	0	0	1	1	1	0	1	2	1	1

Table 5 Outcome scale and Visick grading

	Preoperative		1 month		3 months		6 months		12 months	
	Anterior (n = 53)	Posterior (n = 50)	Anterior (n = 50)	Posterior (n = 49)	Anterior (n = 43)	Posterior (n = 41)	Anterior (n = 38)	Posterior (n = 38)	Anterior (n = 31)	Posterior (n = 29)
Outcome										
Excellent	—	—	20	11	24	24	20	26	15	21
Good	—	—	20	31	8	14	11	9	8	6
Fair	—	—	9	7	6	3	4	3	7	2
Poor	—	—	1	0	5	0	3	0	1	0
Visick grade										
1	0	0	19	7	23	22	19	25	15	21
2	5	5	22	35	9	17	12	11	8	6
3	15	20	8	6	7	2	3	2	6	2
4	33	25	0	1	2	0	2	0	2	0
5	0	0	1	0	2	0	2	0	0	0

Table 6 Percent pH below pH 4 in a 24-h period and pH grading

% time below pH 4 in 24 h	Preoperatively		Postoperatively	
	Anterior (n = 48)	Posterior (n = 49)	Anterior (n = 35)	Posterior (n = 37)
10.2 (0.3–39.9)	10.2 (0.3–39.9)	11.7 (0.5–6.6)	2.4 (0–13.9)	1.4 (0–9.5)
pH Grading				
No reflux (pH < 4 less than 4%)	11	5	29	33
Mild reflux, no symptoms (pH < 4 between 4 and 7%)	8	3	0	2
Mild reflux + symptoms (pH < 4 between 4 and 7% with Good symptom correlation)	4	7	1	0
Severe reflux + symptoms (pH < 4 more than 7%)	25	34	3	2

In this trial, although 16 individuals demonstrated normal pH studies, they all had abnormalities detected on other investigative modalities, and were therefore offered operative intervention. A recent study undertaken by Khajanchee *et al.*,¹⁷ demonstrated that individuals with symptomatic gastro-oesophageal reflux disease but normal pH studies have significantly worse outcomes after fundoplication compared with patients with abnormal preoperative pH studies. Of the 16 individuals who had normal preoperative pH

grading, only 10 attended follow-up at 1 year, and only one described the heartburn as not being controlled.

As demonstrated, there were different rates of post-operative symptoms in the two groups, with each group having a specific problem associated with it. Individuals who underwent an anterior fundoplication had a higher rate of re-operation compared with individuals who underwent a posterior fundoplication (8 versus 2); however, this was not statistically significant as the *P* value was

marginally outside the pre-study selected level at $P = 0.057$; however, this may represent a lack of power. This has been further validated by a study by Zehetner *et al.*¹⁸ who describe that posterior funduplications have a lower rate of re-operative intervention for reflux.

The anterior fundoplication group also had a higher rate of post-operative heartburn. This was statistically significant; however, this was a qualitative measurement and postoperative pH analysis of the lower oesophagus did not support a statistically significant difference. Khajanchee *et al.*¹⁹ demonstrated that there is a poor correlation between postoperative reflux symptoms and actual reflux (abnormal Demeester scores). Similarly, Thompson *et al.*²⁰ demonstrated that post-operative reflux symptoms are not always because of the presence of reflux; therefore, before repeat operative intervention is undertaken, quantitative analysis of reflux should be undertaken, or reflux could be further characterized using impedance studies.²¹

The posterior fundoplication group demonstrated a higher rate of early post-operative dysphagia as compared with the anterior group. Hagedorn *et al.*² hypothesized that increased dysphagia may be seen in the posterior wrap compared with the anterior fundoplication; this phenomenon would be attributed to the elevation of the abdominal portion of the oesophagus from its native bed in the hiatus and increased angulation.

Conclusion

Overall, one can conclude that each fundoplication has its benefits and disadvantages. The anterior group had a slightly higher incidence of post-operative reflux, and although marginally not statistically significant ($P = 0.057$), a higher re-operation rate. The posterior group, in comparison with the anterior group, had a higher incidence of post-operative dysphagia. Therefore, potentially, according to the results obtained, a posterior fundoplication produces a better management option for controlling gastro-oesophageal reflux disease, when compared with an anterior fundoplication that utilizes unilateral fixation of the gastric fundus.

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ORIGINAL ARTICLE

Randomized controlled trial of laparoscopic Nissen versus Lind fundoplication for gastro-oesophageal reflux disease

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Abstract

Objective. To compare the effect of laparoscopic Nissen and Lind fundoplication on gastro-oesophageal reflux disease by means of a prospective randomized controlled trial. **Material and methods.** One hundred and twenty-one patients were randomized to undergo either Nissen (61) or Lind (60) fundoplication. Initial enrolment and subsequent clinical appointments were undertaken 1, 3, 6 and 12 months after the procedure using a standardized questionnaire. Ambulatory pH monitoring and manometry were undertaken both preoperatively and at approximately 3 months post-procedure. **Results.** The mean operating time was similar in both groups (44.8 versus 45 min). One operation in the Lind group was converted to open surgery. Postoperative dysphagia symptoms at 3 and 6 months were higher in the Nissen fundoplication group than in the Lind group (3 months $p=0.003$; 6 months $p=0.020$). The time taken to return to work was statistically longer in the Nissen group: at 1 month, 9 of 40 versus 2 of 45 patients had not returned to full activities ($p=0.013$). Three individuals required re-operation in the Nissen group and 4 individuals in the Lind group because of dysphagia caused by mechanical obstruction. Both procedures demonstrated good Visick scores at 12 months; the Nissen group having 33 (97%) patients with a Visick score of 1 or 2, and the Lind group having 38 (100%) patients with a Visick score of 1 or 2. **Conclusions.** Both operations provide good quantitative and qualitative control of gastro-oesophageal reflux. Operation time and postoperative comparators were similar in both groups. There were no statistically significant differences between the groups at 1 year.

Key Words: General, health-economy, laparoscopy, motility, oesophageal disorders

Introduction

Mild reflux can be managed with proton-pump inhibitors (PPIs), but surgery is accepted as the “gold standard” treatment for moderate to severe gastro-oesophageal reflux [1]. There has been an increase in the incidence of anti-reflux surgery in recent decades with the introduction of laparoscopic surgery, and as more centres are utilizing the procedure in the earlier stages of the disease [2], this trend has continued. It has been debated that continuing medical treatment for gastro-oesophageal reflux disease does not correct the underlying abnormalities, but instead suppresses acid formation, and hence only provides relief of symptoms [3].

Various operations are described in the literature, including Nissen and Lind fundoplication. Nissen

fundoplication is a total wrap encircling the oesophagus by 360°, whereas Lind fundoplication is a subtotal wrap encircling the oesophagus by 270–300°. A total wrap may have disadvantages in that it can increase postoperative symptoms of dysphagia [4,5], bloating, inability to belch and increased flatus as compared to a subtotal wrap. Conversely, it can have the advantage of decreasing the rates of recurrent reflux when compared to subtotal wrap.

There are many trials in the literature comparing a variety of fundoplications [6–8], but there is a dearth of data comparing the outcomes of laparoscopic Nissen and laparoscopic Lind fundoplication. The aim of this study was to identify whether the one procedure is superior to the other for postoperative control of reflux and occurrence of unwanted symptoms.

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Material and methods

All individuals presenting for primary gastro-oesophageal reflux surgery were considered for entry in the trial. Similar selection criteria and methods were used, as detailed by Ackroyd et al. [6]. All eligible patients underwent preoperative endoscopy and oesophageal manometry, followed by 24-h ambulatory pH investigations. Patients were excluded if they had an oesophageal motility disorder, required a concurrent abdominal procedure (e.g. cholecystectomy) or had undergone previous anti-reflux surgery.

Monitoring of stationary oesophageal manometry and ambulatory pH was undertaken approximately preoperatively and at 3 months post-procedure. A standardized procedure was closely followed; patients were fasted for 6 h prior to the pH and manometry studies. A single-use antimony crystal probe (Mediplus, High Wycombe, UK) was positioned 5 cm above the lower oesophageal sphincter and connected to a Flexilog 2000 datalogger (Oakfield Instruments, Whitney, UK) [6]. The total number of reflux episodes was recorded and the percentage of time the pH was less than 4.

Prior to manometry, all individuals were asked to stop taking medication known to affect oesophageal motility. An 8-lumen water-perfused catheter was used in four of the lumens placed concentrically at the region of the sphincter and amplified signals were recorded using a Phoenix recording system (Albyn Medical, Dingwall, UK). The location and resting pressure of the lower oesophageal sphincter (or high pressure zone post-fundoplication) was located by the station pull-through technique. Oesophageal wave amplitude and propagation were measured by ten 10-ml water boluses swallowed at intervals of 30 s.

Patients were randomized to undergo either Nissen or Lind fundoplication. Informed consent was obtained and randomization was achieved by opening an opaque sealed envelope, after the individual was anaesthetised, i.e. both patient and surgeon were blinded to the procedure until after the patient was anaesthetized. The study protocol was approved by the South Sheffield Research Ethics Committee and the study was conducted in accordance with the World Medical Association Declaration of Helsinki (revised 1989).

Laparoscopic Nissen and Lind fundoplications were performed as described previously [9] by one of two experienced consultant upper gastro-intestinal surgeons (R.A. and C.J.S.). After introduction of the laparoscope, a brief inspection was carried out to identify any hiatus hernia or the presence of adhesions; these were then subsequently graded. Intra-operative problems and the requirement to

convert to open surgery were then noted. A standardized procedure was followed and any reason for variation was documented.

Both procedures began with dissection of the hiatal pillars, followed by full oesophageal mobilization and posterior hiatal repair. A tape was placed around the oesophagus to assist with oesophageal retraction and the short gastric vessels were not divided. In the Nissen fundoplication, a bougie was always used. The posterior fundus of the stomach was then wrapped behind the lower oesophagus and the anterior fundus of the stomach was brought across the front of the lower oesophagus and three sutures were placed fundus to fundus (one suture incorporating the oesophagus). In the Lind fundoplication, a bougie was not used. A procedure similar to the Nissen one was undertaken; however, a "bare" area was left between the anterior and posterior fundal wraps resulting in a 270° 300° wrap being formed using six sutures (3 on each side). The operation was given a difficulty grading of 1–10 (1 = easy; 10 = difficult). The length of post-operative hospitalization and symptoms at discharge were registered.

Oral fluids were commenced on the evening of surgery, and subsequently, if tolerated, a soft diet was allowed the next day. Discharge from hospital was allowed when the patient was stable and able to manage at home. Dietary advice was given to individuals, and they were instructed not to eat bread or lumpy foods for the first 4 weeks.

On initial enrolment in the trial, the patients were interviewed by an experienced consultant surgeon (R.A. or C.J.S.) and questions were asked using a standard, structured questionnaire. Subsequent clinical appointments were undertaken by an experienced clinician at 1, 3, 6 and 12 months after the procedure using the same questionnaire format. At each visit, it was determined whether the individual was still convalescent or had returned to full activity. The presence or absence of a detailed list of symptoms was sought. Patients ranked the outcome of surgery on a modified Visick grading scale (Table I) and were asked to score the outcome, ranging from excellent to poor.

Table I. Modified Visick grading.

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



The patients were also assessed for the occurrence of postoperative dysphagia; an attempt was made quantitatively as well as qualitatively to measure the outcome. The patients were asked to quantify their dysphagia by identifying whether certain food types varying from ice cream to steak were causing dysphagia, and the frequency of this occurrence. The score used the following parameters: 0 = absolute dysphagia, 45 = no dysphagia.

Statistical analysis

The main outcome measures used in this trial were postoperative symptoms, requirement for re-operation, outcome scale and Visick grading. It was determined that 100 patients were required to demonstrate a 20% difference in outcome measures, with a significance level of $p < 0.050$ and a power of 90%. All analyses were performed on an intention-to-treat basis.

Data are expressed as mean values and, where appropriate, reference ranges are provided. Data were analysed using SPSS for Windows, version 15 (SPSS, Chicago, Ill., USA). The following tests were used to assist analysis: the χ^2 test, the Fisher exact test and the Mann-Whitney U-test. A p -value < 0.050 was assumed to be statistically significant.

Results

During the study period, 121 patients were enrolled into the study, and were randomized to Nissen ($n = 61$) or Lind fundoplication ($n = 60$). Of these, 112 (92%) attended follow-up at 1 month, 105 (87%) at 3 months, 94 (78%) at 6 months and 72 (60%) at 1 year. There were no withdrawals from the study. However, despite numerous attempts to make sure that patients attended clinic appointments, there were still patients lost to follow-up (Figure 1). As demonstrated in Table II, the two groups were well matched for age, gender, height, weight, and cigarette and alcohol consumption. Table III presents the data for preoperative endoscopy findings. There was an appreciable difference in the duration of symptoms between the two groups; with individuals in the Lind fundoplication group having symptoms for longer, but this was not statistically significant ($p = 0.476$; Mann-Whitney U-test). There was no appreciable difference in the individuals' preoperative symptoms (Table IV). Visick grading was similar for both groups preoperatively (Table V).

The mean operating time in the Nissen group was 44.8 (12–95) min and for the Lind group 45 (20–132) min ($p = 0.953$), and the total time in the theatre for the Nissen group was 67.7 (35–108) min and in the Lind group 67.7 (40–153) min

Table II. Patient demographics.

	Nissen ($n = 61$)	Lind ($n = 60$)	p -value
Age (years)*	45 (22–70)	49 (21–78)	0.947
Gender ratio (M:F)	38:23	39:21	0.542
Height (cm)*	170 (150–195)	171 (152–190)	0.711
Weight (kg)*	83.7 (55–172)	81.7 (45–115)	0.701
Cigarette smoker	11	14	0.402
Alcohol consumer	43	45	0.391
Previous surgery (not related)	33	34	0.583
Duration of symptoms (months)	92.4 (12–360)	110.1 (12–860)	0.476
Preoperative medication			
Antacid	8	11	0.136
H ₂ -blocker	8	5	0.079
PPI	53	52	0.585

Abbreviation: PPI = proton-pump inhibitor.

*Values are expressed as means (range).

($p = 0.997$). There was no difference in the surgeon's perception of difficulty between the two groups; mean difficulty scores were 4 (1–10) for the Nissen group, compared with 4 (1–10) for the Lind group ($p = 0.968$). Only one individual (Lind group) had to be converted to an open procedure owing to intra-operative bleeding. Postoperative hospital stay was comparable in both groups; Nissen group 3.1 (1–6) days and the Lind group 2.9 (1–10) days ($p = 0.351$).

There were no fatalities in either group, but there were intra-operative and postoperative complications. Intra-operatively, in the Nissen group, laparoscopic dissection was difficult in two patients because of increased intra-abdominal fat; in the Lind group, liver injury and intra-operative bleeding accounted for laparoscopic problems ($p = 0.875$).

Complications were deemed to be related to the operation if they occurred intra-operatively or in the first 30 days post-procedure. Postoperatively, in the Nissen group, there were five complications: 1 patient with surgical emphysema, 2 patients with simple pneumothorax, 1 patient with port-site hernia which was repaired on day 3 postoperatively under local anaesthesia and 1 patient with respiratory tract infection. In the Lind group, there was one case of simple pneumothorax ($p = 0.106$).

Seven patients required re-operation; 3 in the Nissen group and 4 in the Lind group. The Nissen re-operations were due to dysphagia; 2 patients were found to have complete dysphagia and 1 patient had hiatal stenosis. Four patients from the Lind group required re-operation: 2 patients had complete dysphagia, 1 patient required removal of a crural



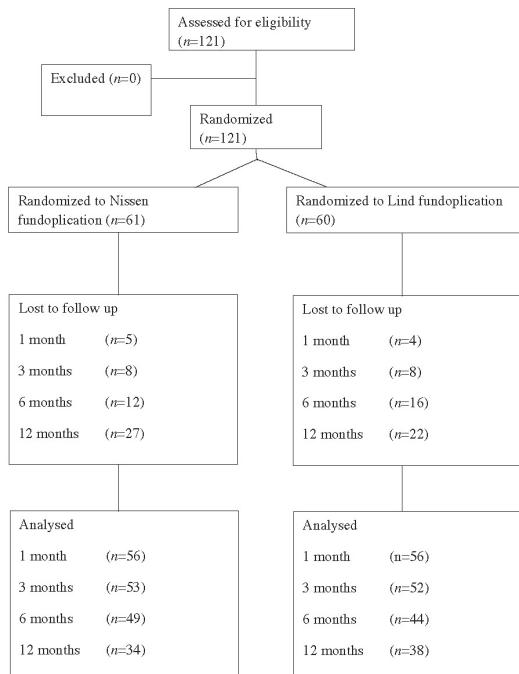


Figure 1. Study flow diagram.

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suture and there was evidence of herniation of the wrap into the chest in 1 patient ($p=0.981$).

At discharge, there was no major difference in symptoms, with dysphagia to solids in 20 of 61 patients in the Nissen group versus 13 of 60 in the Lind group ($p=0.172$), and inability to burp being 5 of 61 versus 7 of 60 ($p=0.527$) respectively. However, there was a significant difference in the time it took individuals to return to full activities: at 1 month, 9 of 40 (22.5%) versus 2 of 45 (4.4%) individuals had not returned to full activities ($p=0.013$). At 1 year, there was no significant difference in the dysphagia scores: Nissen 44.4 (40–45) versus Lind 44.8 (40–45) ($p=0.182$).

Detailed analyses of the clinical assessments are displayed in Table IV and Table V, and demonstrate some significant differences between the two groups. Postoperative dysphagia (qualitative) was higher in

the Nissen group compared with the Lind group (At 3 months $p=0.003$; 6 months $p=0.020$), but a significant difference in dysphagia scores (quantitative) was only demonstrable at 3 months: Nissen group 42 (15–45) versus Lind group 44 (35–45) ($p=0.008$). At 1 year, there was no significant difference in dysphagia between the two groups ($p=0.066$).

Patients were invited to attend postoperative pH and manometry. Thirty-five of 61 patients (57%) in the Nissen group and 31 of 60 (52%) in the Lind group underwent repeat investigations. Table VI demonstrates pre- and postoperative time below pH4 in a 24-h test period ($p=0.893$ and 0.131), and pH grading was comparable between the two groups. Oesophageal motility was also comparable between the two groups with 25 of 57 versus 16 of 54 patients ($p=0.123$) being abnormal preoperatively,

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Table III. Preoperative OGD findings.

Oesophageal findings	Nissen (n=8)	Lind (n=5)
Normal	24	25
Erythema	7	2
Single ulceration	10	12
Multiple ulceration	4	6
Circumferential ulceration	1	0
Stricture	2	0
Barrett's oesophagus	10	10
Hiatus hernia		
No	27	22
Sliding	24	25
Mixed	1	0

and 13 of 35 versus 8 of 32 ($p=0.292$) being abnormal postoperatively. Six patients complained of persistent heartburn at 1 year, but a data analysis shows that only one individual had quantifiable reflux.

Discussion

Although PPIs are the treatment of choice for patients with mild gastro-oesophageal reflux disease, the gold standard management of this disease is considered to be laparoscopic fundoplication. There is an increasing trend towards offering patients

surgical correction for reflux disease at earlier stages of the disease. There is a range of surgical techniques that can be employed in this treatment, each with its own potential benefits and complications.

Unfortunately, as with any trial, there were individuals who were lost to follow-up despite the best efforts of the investigators. Of the 49 patients who failed to attend between the postoperative period and the 1-year post-procedure point, 41 patients had a Visick grading 1 (Visick 1–41, Visick 2–7, Visick 4–1) at their last clinic attendance.

The main aim of the trial was to determine whether the one procedure was superior to the other, the two measurement parameters being adequate control of reflux and postoperative symptoms. One of the hypotheses being trialled was to establish whether the subtotal Lind fundoplication would decrease the rates of postoperative dysphagia encountered in a 360° Nissen fundoplication. Numerous studies have stated that the seniority of the surgeon and the state of the fundal wrap has a direct bearing on the degree of postoperative dysphagia and symptoms in patients who undergo fundoplications [10,11]. Some studies have even evaluated the hiatal suture technique as a possible predictor of post-fundoplication dysphagia, but without success [12].

Table IV. Number of patients with each symptom before and after surgery.

	Preoperatively		1 month		3 months		6 months		12 months	
	Nissen (n=61)	Lind (n=60)	Nissen (n=56)	Lind (n=56)	Nissen (n=53)	Lind (n=52)	Nissen (n=49)	Lind (n=44)	Nissen (n=34)	Lind (n=38)
Heartburn	57	57	2	3	1	4	4	1	1	5
Epigastric pain	35	37	5	2	4	1	2	2	3	0
Regurgitation	56	52	1	2	1	2	3	0	1	0
Lumpy solid dysphagia	25	17	30	22	26	11	14	4	5	1
Soft solid dysphagia	0	1	0	0	0	0	0	0	0	0
Liquid dysphagia	0	0	0	0	0	0	0	0	0	0
Odynophagia	0	10	12	2	1	1	0	0	1	0
Postprandial fullness	20	27	4	2	1	1	1	0	2	0
Inability to belch	0	0	0	3	3	1	1	0	0	0
Epigastric bloat	33	35	14	10	9	3	3	3	2	0
Anorexia	1	5	1	1	0	0	0	0	0	0
Nausea	14	27	3	3	3	1	3	1	2	0
Vomiting	16	21	3	4	4	2	3	1	1	0
Nocturnal cough	14	17	5	0	0	0	0	0	0	0
Nocturnal wheeze	9	12	0	0	0	0	0	0	0	0
Flatus	1	2	5	4	2	6	2	4	1	2
Diarrhoea	1	1	1	1	0	1	0	1	0	1

Table V. Outcome scale and Visick grading.

	Preoperatively		1 month		3 months		6 months		12 months	
	Nissen (n=61)	Lind (n=60)	Nissen (n=56)	Lind (n=56)	Nissen (n=53)	Lind (n=52)	Nissen (n=49)	Lind (n=44)	Nissen (n=34)	Lind (n=38)
Outcome										
Excellent	—	—	20	30	22	36	30	34	26	28
Good	—	—	27	21	26	15	15	10	5	10
Fair	—	—	6	4	4	1	3	0	2	0
Poor	—	—	3	1	1	0	1	0	1	0
Visick grade										
1	0	0	32	40	39	41	41	39	32	31
2	9	5	18	12	10	10	4	5	1	7
3	26	27	3	3	1	1	2	0	1	0
4	26	28	0	0	2	0	1	0	0	0
5	0	0	3	1	1	0	1	0	0	0

In our study, there were two major differences between the surgical groups: postoperative dysphagia and time taken to resume full activities. Patients who underwent Nissen fundoplication had higher rates of postoperative dysphagia symptoms at 3 and 6 months postoperatively compared with the Lind group: at 3 months $p=0.003$; 6 months $p=0.020$. The time taken to return to full activities at 1 month, 9 of 40 (22.5%) versus 2 of 45 (4.4%) had not returned to full activities ($p=0.013$).

Although their study compared a total wrap with a partial wrap (as opposed to a subtotal wrap), Watson et al. demonstrated that individuals who underwent a Nissen fundoplication had higher rates of postoperative dysphagia [7]. Many trials have been undertaken to determine whether postoperative dysphagia in patients who undergo Nissen fundoplication can be prevented [13,14], and there are other trials which evaluate the outcomes of a subtotal wrap [15].

Luostarinen & Isolauri [14] and Hunter et al. [13] hypothesized that full fundal mobilization may

prevent dysphagia from occurring. Luostarinen & Isolauri randomized 52 patients to having a Nissen fundoplication either with or without division of the gastrophrenic/gastroesophageal ligaments and division of the short gastric vessels. No statistically significant difference was observed for postoperative dysphagia between the two groups. In our trial, neither group had the short gastric vessels divided.

Unfortunately, dysphagia is a common occurrence after fundoplication and its pathophysiology is still relatively poorly understood. Studies undertaken on individuals with pre-existing motility disorders have failed to demonstrate adverse outcomes even when a Nissen fundoplication is utilized [16] and this is reiterated in other studies that have failed to demonstrate useful criteria by which post-fundoplication dysphagia can be anticipated [17].

The fore-running hypotheses in current literature are that dysphagia is due to a change in oesophageal motor function or a change in gastro-oesophageal junction characteristics. Myers et al. conducted a study based on oesophageal manometry [18].

Table VI. Percentage pH below pH4 in a 24-h period and pH grading.

	Preoperatively		Postoperatively	
	Nissen (n=54)	Lind (n=52)	Nissen (n=35)	Lind (n=31)
% time below pH4	12.7(0.2–78.7)	13.0(1.6–54.5)	3.26(0.2–20.2)	1.5(0–12.6)
24-h pH grading				
No reflux (pH <4 less than 4%)	11	5	28	28
Mild reflux, no symptoms (pH <4 between 4% and 7%)	5	5	2	0
Mild reflux+symptoms (pH <4 between 4% and 7% and symptomatic)	5	8	1	1
Severe reflux+symptoms (pH <4 more than 7%)	33	34	4	2

Patients were placed into two groups: one group to undergo laparoscopic cholecystectomy and the other to undergo laparoscopic fundoplication. The procedures were undertaken and oesophageal manometry was done on the first postoperative day. This demonstrated grossly disturbed oesophageal motility following fundoplication, which was absent in the laparoscopic cholecystectomy group, indicating the occurrence of "oesophageal ileus".

Multichannel oesophageal intraluminal impedance studies were undertaken by Yigit et al. [19] to determine whether impaired oesophageal clearance was present in patients with post-fundoplication dysphagia. The study demonstrated that there was impaired oesophageal clearance in the majority of patients with post-fundoplication dysphagia ($p = 0.01$) compared with patients without dysphagia. The study also highlighted the fact that impedance studies can demonstrate motility disorders not identified by manometric studies.

Our study did not demonstrate any significant differences in preoperative oesophageal clearance and lower oesophageal sphincter resting pressures between the two groups ($p = 0.265$ and $p = 0.585$ respectively). However, postoperatively, there was a higher mean value of the lower oesophageal sphincter in the Nissen group ($p = 0.002$) compared with that in the Lind group, highlighting the possibility that the total wrap may cause higher pressure of the lower oesophageal sphincter, thereby predisposing patients to higher rates of postoperative dysphagia.

Open conversion was only undertaken in one patient (in the Lind group) because of intra-operative bleeding. Seven patients required re-operation owing to persistent dysphagia as demonstrated by endoscopy/contrast studies, 3 in the Nissen group and 4 in the Lind group. None of the patients required re-operation for recurrent reflux and only one patient who had symptomatic heartburn demonstrated quantifiable reflux on 24-h ambulatory pH monitoring.

Both operations provide good quantitative and qualitative control of gastro-oesophageal reflux. Operation time and postoperative comparators were similar in both groups. At 1-year follow up, there was no statistically significant difference in postoperative symptoms or dysphagia scores, leading to the conclusion that both operations provide good quantitative and qualitative control of gastro-oesophageal reflux.

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Can intraoperative manometry during laparoscopic fundoplication predict postoperative dysphagia?

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Abstract

Background Many trials have used intraesophageal manometry (IEM) to measure the adequacy of fundoplication. This pilot study aimed to assess the value of IEM in predicting postoperative dysphagia.

Methods A series of 40 patients underwent IEM studies before operative correction of gastroesophageal reflux disease and repeat studies 3 months after the procedure. During the operation, IEM studies were undertaken before pneumoperitoneum was established, after pneumoperitoneum, after pneumoperitoneum with fundoplication, and after fundoplication without pneumoperitoneum. All the patients were followed up 1, 6, and 12 months after the procedure for assessment to detect persistent reflux and postfundoplication dysphagia.

Results Three patients demonstrated persistent dysphagia at the 12-month follow-up point. No statistically significant differences in preoperative manometry findings were observed in the dysphagic and nondysphagic groups, with the dysphagic group showing higher pressures. However, at the operation, statistically significant differences in the lower esophageal sphincter pressures were observed after anesthesia and no pneumoperitoneum (30.3 vs. 13.4 cm H₂O; $p = 0.002$), after anesthesia with pneumoperitoneum (40.3

vs. 18.3 cm H₂O; $p < 0.001$), and after fundoplication with pneumoperitoneum (47.3 vs. 23.4 cm H₂O; $p = 0.001$). No statistically significant differences were demonstrated in postoperative manometry at the 3-month follow-up point.

Conclusion Intraoperative manometry may be a useful tool compared with postoperative manometry in identifying patients who may experience postfundoplication dysphagia.

Keywords Gastroesophageal reflux disease · GERD · GORD · Pneumoperitoneum

Mild reflux may be managed with proton pump inhibitors, but surgery is accepted as the “gold standard” treatment for moderate to severe gastroesophageal reflux [1]. Numerous operative procedures have been described including Nissen, Lind, and anterior and posterior fundoplication, all of which can be undertaken using either a laparoscopic or an open technique.

A major problem associated with antireflux surgery is the potential for postoperative dysphagia. Many trials have aimed to establish a pattern or potential methods for identifying patients at risk for the development of these symptoms.

Unfortunately, dysphagia is a common occurrence after fundoplication, and its pathophysiology still is relatively poorly understood. Studies of individuals with preexisting motility disorders have failed to demonstrate adverse outcomes even when a Nissen fundoplication is used [2]. This is reiterated in other studies that have failed to demonstrate useful criteria by which postfundoplication dysphagia can be anticipated [3].

This pilot study aimed to determine whether postoperative dysphagia can be predicted by using intraoperative manometry at various stages of the operation.

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Patients and methods

The study protocol was approved by the South Sheffield Research Ethics Committee, and the study was conducted in accordance with the World Medical Association declaration of Helsinki (revised 1989).

After establishment of anesthesia, an eight-lumen water-perfused catheter (Oakfield Instruments Ltd., Oxford, England) was placed into the esophagus of the patient via the nose. The catheter was attached to a Flexilog 3000 data-logger (Oakfield Instruments Ltd.), which in turn was connected to a portable pneumohydraulic pump (Oakfield Instruments Ltd.). Gastric pressure, the location and resting pressure of the lower esophageal sphincter (or high-pressure zone after fundoplication), and esophageal body pressure were obtained using the station pull-through technique.

Manometry readings then were undertaken at predetermined intervals: after anesthesia with no pneumoperitoneum, after anesthesia with pneumoperitoneum, after fundoplication with pneumoperitoneum, and after fundoplication with no pneumoperitoneum. Laparoscopic fundoplications were performed as described previously [4, 5].

After introduction of the laparoscope, a brief inspection was performed to identify any hiatal hernia or adhesions. These then were subsequently graded. Intraoperative problems and the requirement for conversion to open surgery then were noted. A standardized procedure was followed, and any reason for variation was documented.

Anterior fundoplication began with dissection of the hiatal pillars, followed by full esophageal mobilization and posterior hiatal repair using a mean of two sutures. A tape was placed around the esophagus to assist with esophageal retraction, and the short gastric arteries were not divided. In anterior fundoplication, the fundus of the stomach was brought across the front of the lower esophagus and sutured first to the right side of the esophagus and then to the right crus.

Lind fundoplication began with dissection of the hiatal pillars, followed by full esophageal mobilization and posterior hiatal repair. A tape was placed around the esophagus to assist with esophageal retraction, and the short gastric vessels were not divided. No bougie was used. A “bare” area was left between the anterior and posterior fundal wraps, resulting in a 270° to 300° wrap being formed using six sutures (3 on each side).

Oral fluids were started the evening after surgery. Then, if tolerated, a soft diet was allowed the next day. Discharge from the hospital was allowed when the patient was stable and able to manage at home. Dietary advice given to the individuals instructed them not to eat bread or lumpy foods for the first 4 weeks.

At their initial enrollment in the trial, the patients were interviewed by an experienced consultant surgeon (R.A.). Questions were asked using a standard, structured questionnaire. Subsequent clinical appointments were undertaken by an experienced clinician 1, 6, and 12 months after the procedure using the same questionnaire format. The patients ranked the outcome of surgery on whether they still had reflux symptoms or dysphagia.

Stationary esophageal manometry, including the response to several swallows of water and ambulatory pH monitoring, was undertaken before operative intervention, during the procedure, and approximately 3 months after the procedure. A standardized procedure was closely followed. The patients were fasted for 6 h before the pH and manometry studies. A single-use antimony crystal probe (Mediplus, High Wycombe, UK) was positioned 5 cm above the lower esophageal sphincter and connected to a Flexilog 2000 data-logger (Oakfield Instruments, Whitney, UK) [6]. The total number of reflux episodes and the percentage of time the pH was lower than 4 were recorded.

Before manometry was performed, all the individuals were asked to cease medication known to affect esophageal motility. Esophageal wave amplitude and propagation were measured by ten 10-ml water bolus swallowings 30 s apart. All readings obtained were in cm H₂O.

Statistical analysis

The main outcome measures used in this trial were postoperative symptoms. The values presented are means, and where appropriate, confidence intervals and standard deviations are provided. Data were analyzed using SPSS for Windows, version 15 (SPSS, Chicago, IL, USA). The following tests were used to assist analysis: Chi-square test, Fisher's exact test, and Mann-Whitney *U* test. A *p* value less than 0.050 was assumed to indicate statistical significance.

Results

The study recruited and enrolled 40 patients (20 women and 20 men) ranging in age from 20 to 78 years (mean, 48 years). The duration of symptoms ranged from 1.5 to 28 years (mean, 8 years).

Of the 40 patients recruited, 39 underwent laparoscopic fundoplication. For the remaining patient, the procedure was cancelled due to poor lung function. Of these patients, 28 underwent Lind fundoplication and 11 had anterior fundoplication. Manometric data were collected for all the patients preoperatively, intraoperatively, and postoperatively (Tables 1, 2, 3, 4, 5, 6).

Table 1 Preoperative intraesophageal manometry (IEM)

Location of probe	Pressure	Range	SD
Esophageal body pressure (<i>n</i> = 24)	1.75	-4–12	4.51
Gastric pressure (<i>n</i> = 24)	9.13	3–18	4.30
Sphincter pressure (<i>n</i> = 24)	16.32	3–33	7.20

SD standard deviation

Table 2 Intraesophageal manometry (IEM) after anesthesia and no pneumoperitoneum

Location of probe	Pressure	Range	SD
Esophageal body pressure (<i>n</i> = 34)	8.88	-5–24	6.41
Gastric pressure (<i>n</i> = 30)	8.40	-7–26	6.87
Sphincter pressure (<i>n</i> = 34)	14.65	-6–35	8.79

SD standard deviation

Table 3 Intraesophageal manometry (IEM) after anesthesia with pneumoperitoneum

Location of probe	Pressure	Range	SD
Esophageal body pressure (<i>n</i> = 33)	12.97	-11–23	7.06
Gastric pressure (<i>n</i> = 23)	13.91	-17–29	8.67
Sphincter pressure (<i>n</i> = 33)	19.61	6–45	9.07

SD standard deviation

Table 4 Intraesophageal manometry (IEM) after anesthesia with fundoplication and pneumoperitoneum

Location of probe	Pressure	Range	SD
Esophageal body pressure (<i>n</i> = 29)	15.00	7–31	5.23
Gastric pressure (<i>n</i> = 17)	15.59	-21–30	11.22
Sphincter pressure (<i>n</i> = 29)	26.69	8–56	12.71

SD standard deviation

Table 5 Intraesophageal manometry (IEM) after anesthesia with fundoplication and no pneumoperitoneum

Location of probe	Pressure	Range	SD
Esophageal body pressure (<i>n</i> = 29)	11.93	3–25	6.29
Gastric pressure (<i>n</i> = 14)	11.79	-17–19	12.26
Sphincter pressure (<i>n</i> = 28)	24.18	2–87	16.28

SD standard deviation

Two patients were excluded from the study because their procedure was converted to open fundoplication, and four patients were excluded due to equipment malfunction. Three patients demonstrated persistent dysphagia at the 12-month follow-up point. The preoperative manometry

Table 6 Intraesophageal manometry (IEM 3 months after the procedure)

Location of probe	Pressure	Range	SD
Esophageal body pressure (<i>n</i> = 24)	2.25	-4–14	4.56
Gastric pressure (<i>n</i> = 24)	8.38	1–19	4.59
Sphincter pressure (<i>n</i> = 24)	22.58	11–37	6.36

SD standard deviation

studies showed no statistically significant differences between the dysphagic and nondysphagic groups, although the dysphagic group had higher esophageal body pressure ($p = 0.299$), sphincter pressure ($p = 0.997$), and gastric pressure ($p = 0.958$).

However, at the operation, the lower esophageal sphincter pressures showed the following statistically significant differences: after anesthesia and no pneumoperitoneum (30.3 vs. 13.4 cm H₂O; $p = 0.002$), after anesthesia with pneumoperitoneum (40.3 vs. 18.3 cm H₂O; $p < 0.001$), and after fundoplication with pneumoperitoneum (47.3 vs. 23.4 cm H₂O; $p = 0.001$). At the 3-month follow-up point, no statistically significant differences in postoperative manometry were demonstrated for esophageal body pressure ($p = 0.870$), sphincter pressure ($p = 0.172$), or gastric pressure ($p = 0.227$).

Three patients had persistent reflux symptoms at 12 months. There were no significant differences in the sphincter pressures of the patients with reflux compared with the asymptomatic patients. The only demonstrable statistical difference was in the gastric pressure after anesthesia with pneumoperitoneum. For patients with persistent reflux, this pressure was 16.38 cm H₂O compared with 5.75 cm H₂O ($p = 0.046$).

Discussion

Although proton pump inhibitors are the treatment of choice for patients with mild gastroesophageal reflux disease, the gold standard management for gastroesophageal reflux disease is considered to be laparoscopic fundoplication. There is an increasing trend to offer patients surgical correction for reflux disease at earlier stages of the disease.

Dysphagia is a common occurrence after fundoplication, and its pathophysiology still is relatively poorly understood. Studies undertaken to investigate individuals with preexisting motility disorders have failed to demonstrate adverse outcomes even when a Nissen fundoplication is used [2], and this is reiterated in other studies that have failed to demonstrate useful criteria by which postfundoplication dysphagia can be anticipated [3].

The forerunning hypotheses in current literature are that postfundoplication dysphagia is due to a change in esophageal motor function or gastroesophageal junction characteristics. Myers et al. [7] conducted a study based on esophageal manometry. Patients were placed into two groups: one group to undergo laparoscopic cholecystectomy and another group to undergo laparoscopic fundoplication. The procedures were undertaken, and esophageal manometry was performed on postoperative day 1. This demonstrated grossly disturbed esophageal motility after fundoplication, which was absent in the laparoscopic cholecystectomy group, indicating the occurrence of "esophageal ileus."

The literature on the value of intraoperative manometry for the prediction of postfundoplication dysphagia is limited. Numerous published studies have used intraoperative manometry in the formation of the fundoplication wrap [8, 9], but no studies have used it for predicting postoperative dysphagia. Hill [10] performed intraoperative manometry for 200 patients with gastroesophageal reflux. The lower esophageal sphincter pressure was measured at various intervals including before and during repair. The intraoperative pressures were approximately 50 mmHg, and the postoperative pressures ranged from 15 to 25 mmHg. No patients with sphincter pressures higher than 15 mmHg demonstrated reflux according to postoperative pH and pressure studies. The authors concluded that measurement of intraoperative sphincter pressure is a safe, simple, and reliable technique that should be standard procedure for all operations on the gastroesophageal junction.

Manometry measures pressure within the esophageal lumen and sphincters to provide an assessment of the neuromuscular activity that dictates function in health and disease. It is performed to investigate the cause of functional dysphagia and unexplained noncardiac chest pain. It also is used in the preoperative workup of patients referred for antireflux surgery [11].

The main finding in our study was the presence of abnormally high lower esophageal sphincter pressures in the dysphagic patients. Surprisingly, the difference in these pressures became apparent only after anesthesia. The patients who had adequate control of reflux and no symptoms of dysphagia had lower esophageal sphincter pressure readings of about 20 cm H₂O during the intraoperative period. However, at the 3-month manometry study point, no significant difference was observed between the non-dysphagic (21.9 cm H₂O) and dysphagic (27.3 cm H₂O) ($p = 0.172$) groups.

Given the aforementioned findings, intraoperative manometry may be a useful tool in both the prediction and prevention of dysphagia for patients who undergo fundoplication. However, a spectrum of opinion can be found in the current literature. Del Genio et al. [12] undertook a

retrospective analysis of 309 functional surgical procedures on the esophagus that used intraoperative manometry and found it to be a useful tool for detecting the high-pressure zone and for calibrating lower esophageal sphincter pressure. Prochazka et al. [9] also concluded that intraoperative manometry may prove beneficial in predicting persistent postoperative dysphagia.

Orringer et al. [13] undertook a study of 45 patients who underwent a Collis-Nissen fundoplication and had several peri- and intraoperative manometric studies. They concluded that esophageal mobilization resulted in variable intraoperative high-pressure zone values and was not a reliable predictor of postoperative high-pressure zones.

In summary, intraoperative manometry may prove to be beneficial in predicting postoperative dysphagia. However, serial measurements at various stages of the operative procedure ranging from induction of anesthesia to completion of the operation must be undertaken. With the advent of high-resolution manometry [11], the complex functional anatomy of the esophageal high-pressure zone may be studied more closely during these stages.

Disclosures M. Khan, A. Smythe, K. Elghellal, and R. Ackroyd have no conflicts of interest or financial ties to disclose.

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