Laparoscopic Nissen's Fundoplication for GERD: Current Perspective

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Introduction

Fundoplication is a surgical technique used as a treatment modality for GERD with or without hiatus hernia, large symptomatic hiatus hernias and as an adjunct to Heller's cardiomyotomy in patients of achalasia cardia. Since its inception in 1991 [1], Laparoscopic Nissen's Fundoplication (LNF) has gained popularity and has largely replaced open fundoplication. Before proceeding with the description of LNF, a brief introduction of GERD, the most common indication of LNF, is in order.

GERD is a condition causing troublesome reflux of stomach contents or associated complications. The prevalence of GERD is variable, with rates of up to 20% in the west and less than 5% in Asia [2]. Studies from India show a prevalence ranging from 7.6 to 18.7% [3].

Some degree of postprandial reflux is physiological and may be asymptomatic [2]. Pathological reflux occurs consequent to disruption of the anti-reflux barrier between the stomach and esophagus and is associated with symptoms or mucosal injury. GERD may or may not co-exist with an associated hiatus hernia [4].

Hiatus hernias have been classified as: Type 1 (Sliding hernia) where the GEJ (gastroesophageal junction) migrates above the diaphragm with the stomach in its normal longitudinal axis and fundus in its normal location. Type II (Rolling) where the GEJ is in its normal position and the fundus of the stomach herniates. Type III (Mixed) where both the GEJ and fundus herniates through the hiatus (Combination of types I and II). Type IV is characterized by the presence of structures other than the stomach such as omentum, colon and small bowel [5].

A recent review published in 2017 addressed the historical practice of routine repairing of incidentally found hiatus hernia. This view has been challenged since

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studies have shown that probability of developing symptoms needing emergent repair is only around 1% per year and watchful waiting can be safely adopted in 83% of symptomatic patients. Type I hiatal hernias associated with GERD however need fundoplication with hiatal repair to prevent reflux [6, 7]. For asymptomatic paraesophageal hernia the risk of progression to symptoms is estimated to be approximately 14% per year and the need for emergency surgery is about 2% per year. Further, it has been suggested that that elective laparoscopic repair of asymptomatic paraesophageal hernia may even be detrimental in patients over 65 years of age. Recommendations are to consider the patients age and co-morbidities prior to planning intervention [7, 8]. Symptomatic para-esophageal hernia however should be repaired.

Clinical Presentation

The patients with GERD, classically present with heartburn and regurgitation. Other symptoms include chest pain, dysphagia, waterbrash, globus sensation and odynophagia. Another spectrum of symptoms includes the extraesophageal symptoms such as cough, wheeze and hoarseness. A summary of symptoms associated with GERD is included in Table 1.

For the successful outcome of fundoplication, it is important to establish GERD as the cause of patient's symptoms. It is common to find a small hiatus hernia and to operate on such patients without establishing the symptom correlation, is bound to result in a disgruntled patient.

The following investigations help in establishing the diagnosis, correlation with symptoms and planning the surgery.

1. **Barium Esophagogram:** Barium studies are losing favour in western literature with the advent of newer modalities for diagnosing GERD. It is suggested that they are now limited to evaluate the complications of GERD (e.g. peptic stricture) and in cases of post-operative dysphagia [9]. However, they are useful in setups where these advanced diagnostic modalities are not available.

Table 1 Montreal Consensus definition of symptoms of GERD

Esophageal Symptoms		Extraesophageal Syndromes	
Symptomatic Syndromes	Syndromes with Esophageal Injury	Established Associations	Proposed Association
Typical Reflux	Reflux esophagitis	Cough	Pharyngitis
Reflux Chest Pain Syndrome	Reflux stricture	Laryngitis	Sinusitis
	Barret's Esophagus (BE)	Asthma	Idiopathic Pulmonary Fibrosis
	Esophageal Adenocarcinoma (EAC)	Dental Erosion	Recurrent Otitis Media

Apart from GERD, they are helpful in locating GEJ in relation to the hiatus and help in estimating the size and reducibility of hiatus hernias. It is recommended as a key investigation in the diagnosis of Hiatus Hernia's [7].

2. **CT Scans:** A CT Scan may be useful in hiatus hernia to demonstrate cephalad migration of the GEJ and fundus especially on oral contrast films [7]. They are also useful in emergency cases of paraesophageal volvulus.
3. **Upper Gastrointestinal Endoscopy (UGIE):** It is used to evaluate symptomatic patients and especially those with alarm symptoms or suspected associated esophageal syndromes (peptic strictures, Barrett's esophagus and esophageal adenocarcinoma). Biopsies can be taken in presence of any abnormal mucosa or mass. Grading of esophagitis according to Los Angeles Classification is done. LA-C/D are considered indications for surgery in GERD [10]. UGIE also is useful to visualize hiatal hernias and remains the mainstay in its diagnosis [7].
4. **Ambulatory pH monitoring:** It provides confirmatory evidence of GERD. It is especially useful in patients with normal UGIE findings and in patients with atypical symptoms. This test provides the number of reflux episodes and acid exposure times (AET) of the esophagus. Increased yield is seen with the wireless capsule study which may be used for 48–96 h. Esophageal reflux is defined as a pH value<4 and a composite pH score or deMeester score >14.72.

   Reflux monitoring is possible in both 'off PPI (proton pump inhibitor)' and 'on PPI'. The Lyon Consensus states that testing always be performed off therapy to demonstrate baseline AET in 'unproven GERD', which includes no (or low-grade) oesophagitis at endoscopy, and no prior positive pH testing. 'On PPI' testing is recommended in patients with 'proven GERD' (prior LA grade C or D oesophagitis, long segment Barrett's oesophagus or prior abnormal pH-metry) and should be evaluated on double-dose PPI therapy to establish correlation between refractory symptoms and reflux episodes and/or to exclude inadequate acid suppression or poor compliance as the mechanism of persisting symptoms [11].
5. **High Resolution Manometry (HRM):** It is usually performed to place leads for impedance pH monitoring. Other uses include, diagnosing additional motor disorders or when symptoms don't improve with PPI.

   Recent interest has arisen on the use of HRM in GERD due to understanding of the complex anatomical and pathophysiological aberrations leading to GERD. Assessment of transient LES relaxation, GEJ location and morphology, esophageal motor function and contraction reserve have been evaluated through HRM in patients who don't respond to empiric medical therapy and have normal UGI Endoscopy [12].

Various therapeutic modules have been described in managing these patients which starts from lifestyle modification (raise head end of bed, avoid bedtime meals, weight loss) to medical therapy (proton pump inhibitors, H2 receptor antagonists, antacids and prokinetics), surgical techniques (laparoscopic fundoplication, magnetic ring implants) and endoluminal techniques (transoral incisionless fundoplication and radiofrequency ablation).

Medical vs Surgical Therapy

Use of proton pump inhibitors is the backbone of medical therapy for GERD [13] but its use is limited by long term use, patient compliance, costs, relapse of symptoms on discontinuation and side effects of long term use. Two metanalysis have been published comparing medical therapy with surgical management. The first metanalysis by Rickenbacher et al included 11 publications, 7 trials concluded that patients under the surgical arm had a better quality of life, improved symptoms and were more satisfied as compared to the medical arm. However, a considerable proportion (16–62%) of patients needed medical therapy post-surgery. They concluded that surgery is an equivalent alternative to medical therapy [14]. This study however did not include a subgroup analysis based on follow up time. Another metanalysis published a year later found similar findings to the previous study and also conducted a subgroup analysis on follow up. They observed that surgery had significantly better results in the short-term period (<3 year) but did not find statistically significant improvement on long term over medical management. De-Meester scores were lower in patients in the surgery arm. This metanalysis also favoured surgical therapy over medical therapy, especially in a follow up of three years [15].

Fundoplication

Introduction

The first fundoplication was described by Rudolf Nissen in 1955 and included a 360° wrap of the fundus of the stomach around the esophagus by plication of both the anterior and posterior walls of the gastric fundus around the lesser curvature. Several modifications to his original technique have been described and the modified Nissen's Fundoplication (NF) is the most widely performed surgical procedure for GERD [16].

Laparoscopic Nissen's Fundoplication (LNF) was first described in 1991 by Dallemagne, following which, it has gained popularity and largely replaced the open techniques [1]. LNF is commonly performed in patients of GERD and Hiatus Hernia's.

Antireflux Barrier Mechanism and Fundoplication

An intricate valve mechanism is present at the level of the GEJ that counteracts the positive gastric pressure and the negative thoracic pressures. A lack of balance in this natural antireflux mechanism is thought to be the primary cause of GERD. Components of this barrier mechanism is postulated to include [17]:

(a) Lower Esophageal Sphincter (LES) tone, length and intra-abdominal length. These may be defective in GERD and hiatus hernias.
(b) Pinchcock action of the crural diaphragm on the GEJ.

(c) Intact phreno-esophageal membrane.
(d) Acute "Angle of His" leading to a longer distance between the gastric fundus, where the food is stored, and the EGJ
(e) Intact esophageal motility contributes to adequate clearance of acid that may enter esophagus due to transient LES relaxations (TLESR). These are physiological LES relaxations occurring in the absence of swallowing, lasting more than 10 s. They are probably secondary to gastric distension, and are associated with crural inhibition.

The aim of fundoplication is to correct the defective hiatal anatomy in the hope of restoring anti reflux barrier.

Indications of Surgery

After objective confirmation for GERD and evaluation for associated problems, surgical therapy is recommended in patients with [6]:

- Failed medical management (inadequate symptom control, severe regurgitation not controlled with acid suppression, or medication side effects)
- Patient opts for surgery despite successful medical management (due to quality of life considerations, lifelong need for medication intake, expense of medications, etc.) or
- Complications of GERD (e.g., Barrett's esophagus, peptic stricture) or
- Extra-esophageal manifestations (asthma, hoarseness, cough, chest pain, aspiration) attributable to reflux

Apart from these indications individual evaluation of patients is important for improved outcomes. Results have been better in healthy, thin patients with typical symptoms. Patients who are partial responders to PPI may not have satisfactory results post fundoplication [18]. Although there has been no difference seen with age, female patients have shown worse outcomes than males [19]. Morbid obesity, psychological conditions such as depression and underlying motility disorders are some other factors which affect outcomes adversely. In presence of any of these risk factors, further evaluation and discussion with the patient is advisable prior to proceeding with surgery in order to set realistic and achievable outcomes.

The Preferred Approach: Open vs Laparoscopic?

Laparoscopic Nissen's fundoplication (LNF) was first described following the success of laparoscopic cholecystectomy. Following which several studies were performed to evaluate its advantages over open surgery. Two metanalysis including 12 RCT's (randomized controlled trials) with over 500 procedures have clearly favoured the laparoscopic approach over open technique. Advantages of the technique included

short hospital stay, early return to work, reduced risk of complications and higher patient satisfaction rates. The drawbacks seen included longer operating time and higher long-term reoperation rates. Similar outcomes were noted with both techniques in terms of safety, efficacy and dysphagia rates [20, 21]. The laparoscopic approach is hence preferred and is recommended as approach of choice [6].

Role of Fundoplication in NERD

Non-erosive reflux disease (NERD) is a spectrum of GERD defined as troublesome reflux associated symptoms without mucosal breaks on endoscopy [2]. Confirmation of reflux in these patients is done through 24 h pH monitoring or a positive response to PPI's. Poor response to PPIs have been seen in this subset of patients along with higher relapse rates [22].

Initially NERD was thought to be a milder form of GERD due to absence of endoscopic findings and physicians would be reluctant to refer patients for surgical management. However, the poor response to medical therapy supports an important role of surgery. Recent studies have shown similar benefit of laparoscopic fundoplication in NERD vs GERD patients in short and long term follow up [23, 24].

Role of Fundoplication in Obesity

Obesity has been seen to be associated with increase in GERD, erosive esophagitis and esophageal adenocarcinoma. It has been seen to increase with increasing weight (BMI >30 kg/m^2) [25, 26]. The safety and long term of effectiveness of fundoplication in this population is controversial. A recent metanalysis published on the outcomes of fundoplication in non-obese patients (n = 6246) compared to obese patients (n = 1753) included 13 studies and found no difference in rates of operative morbidity, redo surgery, need for endoscopic dilation, conversion to open surgery or return to theatre. However, recurrence of reflux was higher in the obese group (11.4%) compared to non-obese group (3.4%). This led them to conclude that laparoscopic fundoplication is safe in obese patients but risk of recurrence of GERD is higher, making it important to counsel the patients regarding the possibility of poor outcomes [27]. They were unable to perform a subgroup analysis on the best technique of fundoplication due to heterogeneity and absence of technique reporting in some studies.

LF (laparoscopic fundoplication) has been thought to improve GERD in morbidly obese patients (BMI >35 kg/m^2), however, it does not help treat the underlying disease i.e. obesity. Hence, studies have compared laparoscopic gastric bypass (LGB) with laparoscopic fundoplication (LF). It has been seen that both these techniques have similar safety and efficacy in reducing symptoms of GERD but LGB provides additional health benefits by acting as a bariatric procedure for weight loss [28–30]. SAGES (Society of American Gastrointestinal and Endoscopic Surgeons) too recommends use of LGB in morbidly obese patients while suggesting further study in the obese group [6].

Current Controversies Related to the Technique of Laparoscopic Fundoplication

There is some variation in the technique of fundoplication seen amongst different surgeons. This led to difficulty in comparison of outcomes of LNF with other methods such as oral therapy, due to heterogeneity in samples. In 2008 LOTUS trial formed a consensus document with standardized steps and found high degree of conformity amongst participating surgeons for objective assessment and comparison [31]. The same study was incorporated later to formulate guidelines by SAGES for standardization of the steps.

The Key Components of Fundoplication as Recommended Are as Follows:

- Opening the phreno-esophageal ligament to approach the hiatus and the distal esophagus from the left to the right with preservation of the hepatic branch of the anterior vagus nerve where possible.
- Complete dissection of both crura.
- Generous transhiatal mobilization of the esophagus to allow approximately 3 cm of intra- abdominal length of the distal esophagus.
- Division of short gastric vessels to allow a tension-free wrap.
- Posterior crural repair using nonabsorbable sutures. In case of a very large hiatal defect, a few anterior crural sutures may be placed.
- Creation of short (1.5–2 cm) and floppy wrap with the most distal suture (nonabsorbable) incorporating the anterior wall musculature of the esophagus.
- At the time of the construction of the wrap, introduction of a large bougie through the esophagus is recommended but not defined as essential

The images of the aforementioned steps as performed: (Figs. 1, 2, 3, 4, 5, 6 and 7)

Complete vs Partial Wrap

Partial wraps have been described to avoid the complications associated with complete 360° Nissen's fundoplication. These include 270° Toupet fundoplication and anterior wraps such as Dor (180–200°). In the era of laparoscopic surgery, the issue of complete vs partial wrap has been revisited.

A systematic review in 2011 suggested significantly lesser dysphagia and inability to belch with partial wraps without any statistical difference in outcomes related to treatment failure when compared with complete wrap. However, the studies analyzed had heterogeneity in surgical procedure and approach, poor methodology, unclear outcome measures and publication bias [32].

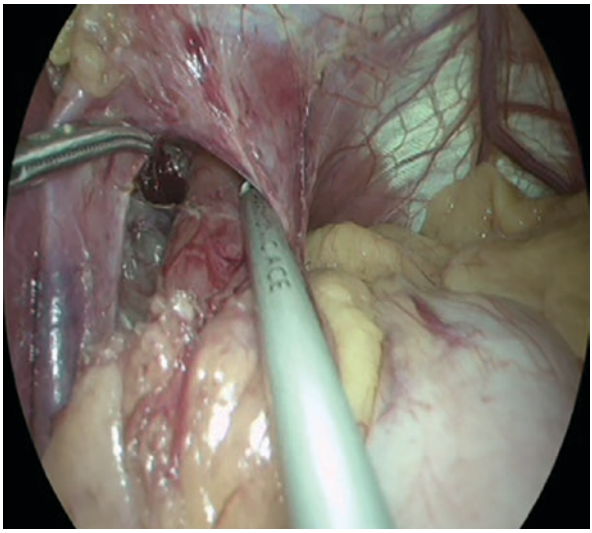

Fig. 1 Hiatal Dissection

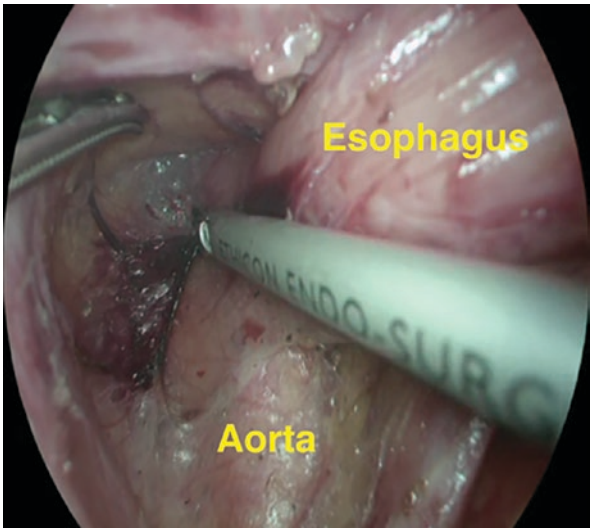

Fig. 2 Mobilization of the esophagus well into the mediastinum

A more recent metanalysis in 2016 compared the Laparoscopic Nissen fundoplication (LNF) with Laparoscopic Toupet Fundoplication (LTF). It included 8 RCTS with 625 LNF and 567 LTF. There was no difference in postoperative dysphagia, gas-bloating, inability to belch or dilatation for dysphagia between the 2 groups. Reoperation rates were seen to be higher after LNF but specific reasons could not be elucidated [33]. Another metanalysis in 2017 compared LNF (n = 266) with Laparoscopic anterior 180° fundoplication (n = 265) including 6 RCT's. The authors concluded that both methods were equally effective in reducing reflux and

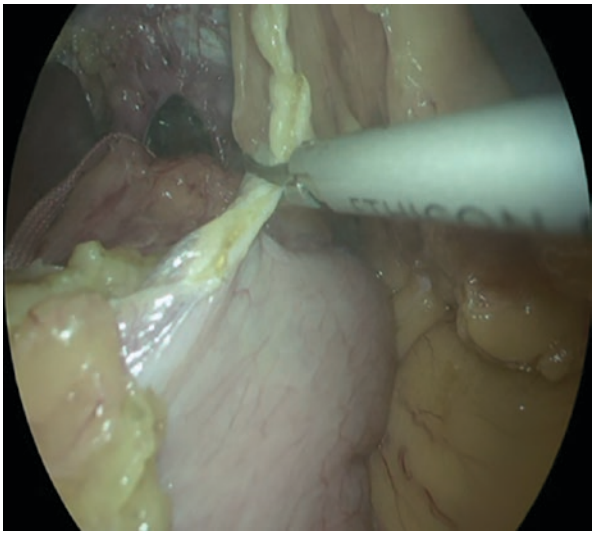

Fig. 3 Division of Short Gastric Vessels

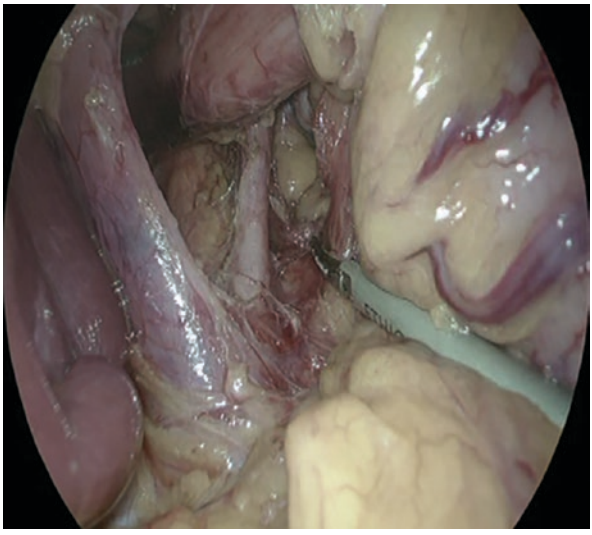

Fig. 4 Complete crural mobilization and creation of retroesophageal window

providing patient satisfaction, but there is a higher risk of reoperation for recurrent symptoms with anterior wrap [34].

Division vs Non-Division of Short Gastric Vessels

Mobilization of the fundus and cardia by division of the short gastric was added as a modification to Nissen fundoplication by Donahue [35] and De Meester [36] inorder to create a tension free floppy fundoplication and reduce some of the troublesome side effects of Nissen fundoplication.

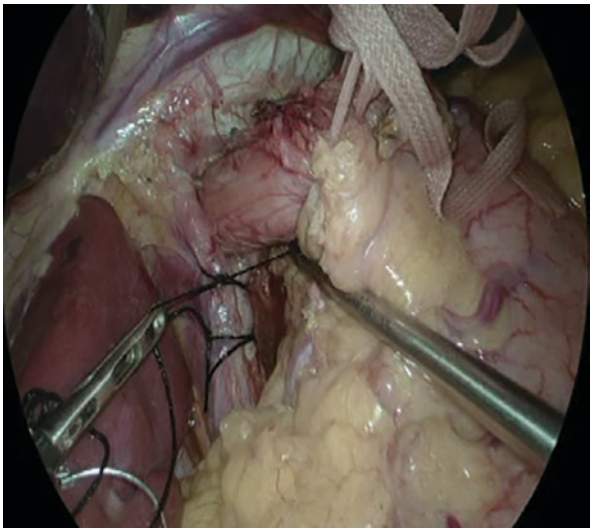

Fig. 5 Crural Approximation

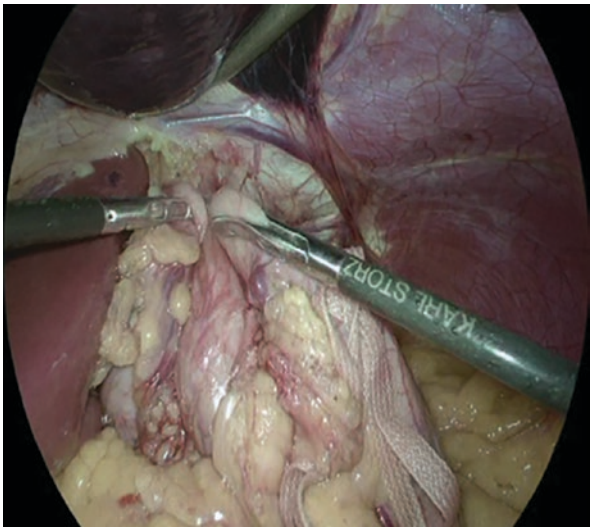

Fig. 6 Shoe shine maneuver

Six RCT's have been performed comparing division vs non-division of short gastric with a follow-up of up to 20 years. The findings suggest that routine division of short gastric do not confer any functional or clinical advantages and was associated with increased surgery time and persistent epigastric bloat syndrome [37–43]. This has been postulated to arise due to absence of the Belch reflex due to division of afferent nerves along with short gastric vessels [44]. SAGES recommends division to be undertaken when a tension free fundoplication can't be achieved with a Grade B recommendation [6].

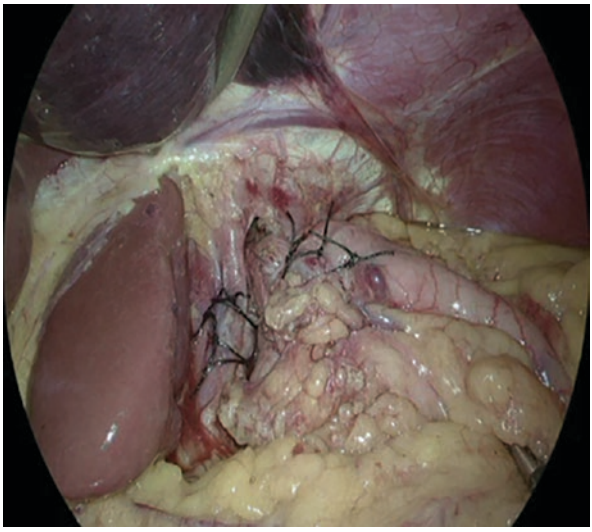

Fig. 7 Creation of Floppy Wrap

Crural Closure

Closure vs non-closure of crura is a controversial topic with some reporting benefits while others showing no benefit. No Metanalysis or RCT's are available and recommendations made are based on case series. General recommendation is to close crural when hiatal opening is large and mesh reinforcement may benefit in decreasing wrap migration [6].

One RCT comparing anterior (n = 47) vs posterior closure (n = 55) did not show any difference in dysphagia with soft solids/liquids, need for medication and overall satisfaction at 10 years follow up [45]. They concluded that anterior repair was at least as good as posterior repair.

Mesh vs Suture Closure of Hiatus Hernia

A widened hiatus or a hiatus hernia (HH) is frequently associated with GERD and has been tackled using simple suture repair. Few studies showed radiological recurrence on long term follow up which brought about an interest in the use of mesh for repair of large hiatus hernias. Recurrences were usually small and asymptomatic making the routine use of mesh controversial. A recent systematic review and metanalysis of 11 studies compared mesh (n = 719) vs suture closure (n = 755). Mesh repair was associated with lesser recurrence rates on short term follow up (<12 months), had similar patterns of complications, but increased dysphagia. QOL (quality of life) scores were similar with some improvement seen in patients with biological mesh. A major limitation was a short term follow up which does not bring out the mesh associated problems that are expected on long term [46]. So the routine use of mesh has to be considered with caution.

A systematic review of 16 studies compared use of biological mesh (n = 385) versus synthetic mesh (n = 704) with a median follow up of 53.4 months. It found that recurrence rates in synthetic mesh (6.8%) was much lower than biological mesh

(16.1%) with no significant difference in complication rates of 5.1% vs 4.6% respectively on short term. This suggested no additional advantage on the use of biological mesh [47].

Role of Bougie Dilators

Another addition to Nissen's Fundoplication was the use of bougie dilators to prevent dysphagia. Several studies have investigated use of dilator from 39-60F to prevent dysphagia [48, 49]. However, certain studies have shown no advantage in the use of bougie dilation, especially in short term follow up [50]. Use of bougie dilators has been seen to be associated with problems such as prolonged surgery, esophago-gastric mucosal damage and perforations.

Nevertheless, an RCT on the effect of bougie on dysphagia with 171 patients was conducted and revealed that use of large caliber bougie (56F) decrease long term risk of dysphagia albeit increasing risk of injury [49]. We can conclude that the use of bougie seems to have improved outcomes on dysphagia postoperatively despite a small risk of complications.

Redo Fundoplication

Although laparoscopic fundoplication has satisfactory outcomes postoperatively, some patients have persistent or recurrence of symptoms. Another problem noted with the procedure is development of dysphagia. Apart from these there is a heterogenous cause of complications associated with the procedure needing reoperation.

Several systematic reviews have been performed on the best method of treating these and outcomes associated. Recurrent reflux and dysphagia were found to be the most common reason for redo fundoplication. The most common causes of failure were seen to be wrap migration, wrap disruption and tight wrap accounting to nearly half the patients. Most of the patients were dealt with redo fundoplication and laparoscopy was the commonly used approach. Morbidity, mortality, longer operative times and conversion to open was higher in redo fundoplication when compared to index surgery. Most commonly witnessed complications were esophago-gastric perforations and bleeding. Symptomatic outcomes of redo fundoplication were good to excellent. Technically this surgery is more complex and should be performed by experienced surgeons [51–53].

Therefore laparoscopic redo fundoplication is safe, feasible and effective with higher complication rates than index surgery and due to its complexity should be performed by experienced surgeons [6].

Newer Modalities

Robotic Fundoplication

With the advent of robotics in late 1990s and identification of its distinct advantages of improved 3D vision, precise movements, added dexterity and improved

ergonomics, it didn't take time for surgeons to implement it in performing antireflux surgeries. Several RCT's were conducted evaluating its outcomes. A metanalysis of 6 RCT's including 226 patients compared robotic fundoplication to LNF. Results from this study showed no difference in operative complications, length of hospital stay, need for reoperation or postoperative dysphagia between the two procedures. However, robotic fundoplication was found to be expensive and had longer operative times. Although results were largely comparable robotic fundoplication offered no advantage over LNF [54]. Larger scale RCT's are needed to definitively assess the role of robotics in antireflux surgery.

Magnetic Ring Implants (LINX™ Procedure)

The LINX magnetic implant system was approved for use in GERD in 2012 by the FDA. This device works through a ring of magnets implanted laparoscopically around the LES. They augment LES pressure upto 15–25 mm of Hg to prevent reflux but at same time allow passage of food through it. This device was found to be safe in patients for GERD and the changes it brought were evaluated via manometry and published in a study of 121 patients. Results have been tabulated in Table 2 [55] (Fig. 8).

Table 2 Manometry changes in magnetic ring implants

Parameter	Preoperative Value	Postoperative value	p Value
Median LES Resting pressure	18 mmHg	23 mmHg	0.0003
Residual Pressure	4 mmHg	9 mmHg	<0.0001
Distal esophageal contraction amplitude	80 mmHg	90 mmHg	0.02
Percentage of Peristalsis	94%	87%	0.71

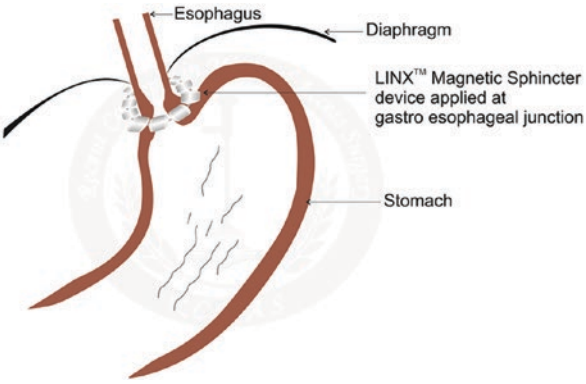

Fig. 8 Schematic diagram showing LINX™ magnetic device applied at Lower oesophageal sphinter

Apart from this, the study also showed that patients with a manometrically defective LES were restored 67% of the time to a normal sphincter and those with a structurally defective or severely defective LES improved to a normal LES in 77% and 56% of patients, respectively. Only 18% of patients with a normal preoperative manometric LES deteriorated to a lower category. The results of this study were very promising with significant improvement in LES tone without deleterious effects on the body and it managed to restore a manometrically defective LES to normal sphincter and leaving a normal sphincter stable.

The excitement following this procedure led to comparisons with the traditional surgical method of fundoplication.

Two metanalysis and systemic review comparing early outcomes of LINX vs LNF were published with the latter including 7 observational studies including 1211 patients [56, 57]. In both the metanalysis LINX and LNF were both seen to be safe and effective at 1 year follow-up. PPI suspension, need for endoscopic dilatation and QOL rates were similar for both groups with LINX procedure associated with less gas/bloat symptoms and increased ability to vomit and belch. LNF was found to take longer operative times and was technically challenging needing skilled surgeons. The findings need to be assessed with caution as these included only observational studies and no RCT's were available. Long term safety, efficacy and durability are yet to be ascertained for the LINX procedure.

Conclusion

Although newer modalities such as robotics, magnetic sphincter implants and also the advent of endoscopic fundoplication bring excitement to the field of antireflux surgery, the definite role, safety and reliability are yet to be ascertained on long term follow up studies. Laparoscopic Nissen's Fundoplication remains a tested modality for over four decades and can be considered to be the gold standard surgical approach. LNF remains the alternate therapy of choice for long term/refractory medical management.

Key Clinical Points

1. Laparoscopic Nissen's Fundoplication (LNF) has gained popularity since 1990s and has largely replaced open fundoplication.
2. Postprandial physiological reflux is quite common and may be asymptomatic. Pathological reflux occurs consequent to disruption of the anti-reflux barrier between the stomach and esophagus and is associated with symptoms or mucosal injury.
3. Elective laparoscopic repair of asymptomatic paraesophageal hernia may even be detrimental in patients over 65 years of age.
4. The role of barium esophagogram is currently limited to evaluation of the complications of GERD and is helpful in locating the GEJ in relation to the hiatus, thereby helping in estimating the size and reducibility of hiatus hernias.

5. CT Scan is useful to demonstrate cephalad migration of the GEJ and fundus especially on oral contrast films. It is also useful in emergency cases of paraesophageal volvulus.
6. Ambulatory pH monitoring is especially useful in patients with normal UGI Endoscopy findings and in patients with atypical symptoms.
7. Proton pump inhibitors are the backbone of medical therapy for GERD, but its use is limited by long term use, patient compliance, costs and relapse of symptoms on discontinuation and side effects of long term use.
8. Laparoscopic fundoplication bestows a shorter hospital stay, early return to work, reduced risk of complications and higher patient satisfaction rates. The drawbacks are longer operating time and higher long-term reoperation rates.
9. Complete and partial fundoplication have no difference in postoperative dysphagia, gas-bloating, inability to belch or dilatation for dysphagia.
10. Routine division of short gastric do not confer any functional or clinical advantages and is associated with increased surgery time and persistent epigastric bloat syndrome.
11. Mesh repair of the hiatus is associated with lesser recurrence rates on short term but had similar patterns of complications with increased dysphagia.
12. Presence and size of a bougie may define the incidence of dysphagia. It should be weighed against the risk of possible oesophageal injury and prior consent for it needs to be taken.
13. Laparoscopic redo fundoplication is safe, feasible and effective with higher complication rates than index surgery and due to its complexity should be performed only by experienced surgeons.
14. Robotic fundoplication is expensive and has a longer operative time. No difference has been noted in operative complications, length of hospital stay, need for reoperation or postoperative dysphagia in robotic vs laparoscopic fundoplication.

Editor's Note[1]

Insertion of the Bougie Across the Esophageal Junction

Insertion of a bougie is often recommended in numerous guidelines including SAGES (Grade B). Few randomized trials have shown significant lower dysphagia rates 12 months later after using bougies, however the size of bougie used made the most important impact in dysphagia rates [1]. Reports are so varied and complex to interpret with many variables, that the results are frequently suggested to have a relation between post-operative dysphagia to undiagnosed pre-operative dysmotility, timing of dysphagia assessment (months after surgery) and scoring system used in assessing post-operative dysphagia [2].

There is definite evidence, which suggest that the presence and size of a bougie may define the incidence of dysphagia. It is always weighed against the risk of possible oesophageal injury and prior consent for it needs to be taken [2].

Incidence of perforation during LF is around 0.8% which is attributed to lack of direction at the tip of bougie and thought to be aggravated due to anterior angulation of the GE junction after posterior crural repair.

LES Electrical Stimulation

It is a novel technique that has been designed to be a successful, minimally invasive and minimal disturbing approach to GERD than laparoscopic fundoplication [3]. Temporary LES stimulation leads to durable increase in LES pressure, without impairing LES relaxation and esophageal peristalsis [3]. It has 3 different components: a bipolar electrical stimulation lead, implantable pulse generator and external programmer. It delivers stimulation waves in sessions which can be adjusted in non-invasive fashion.

Procedure: Anterior right side of esophageal wall is exposed laparoscopically and electrodes are superficially implanted and fixed into LES 1 cm apart along the longitudinal axis of the esophagus. Correct position of electrode is checked under endoscopy at the LES level and to rule out esophageal perforation. Subcutaneous pocket is created for the generator and is attached to the pulse generator.

High success rate is claimed by the proponents, suggesting normalization or a decrease of 50% of more of acid exposure of the distal esophagus in 71% of patients and complete cessation of PPI use in 76% of patients. LES electrical stimulation might have promising results in GERD patients. Robust data will confirm the preliminary outcomes.

Laparoscopic Sleeve Fundoplication

Laparoscopic sleeve gastrectomy has been noted to increase gastroesophageal reflux. It may be beneficial in GERD with concomitant obesity. Therefore, authors have

[1] References: Main chapter references are included after the "References Editor's Note" section.

investigated the concept of adding a fundoplication to laparoscopic sleeve gastrectomy termed as laparoscopic sleeve fundoplication (Fig. EN1). Though weight loss and GERD resolution has been promising in the short term, long term results are awaited. A higher incidence in perforation and complications has also been observed [4].

Endoscopic Fundoplication/Transoral Incisionless Fundoplication

TIF (Transoral incisionless fundoplication) is being investigated as a minimally invasive technique for treatment of GERD refractory to PPI and small hiatal hernia (<2 cm). The recommended technique consists of esophagogastric plications in the region of intraabdominal esophagus with fundus being wrapped around the distal

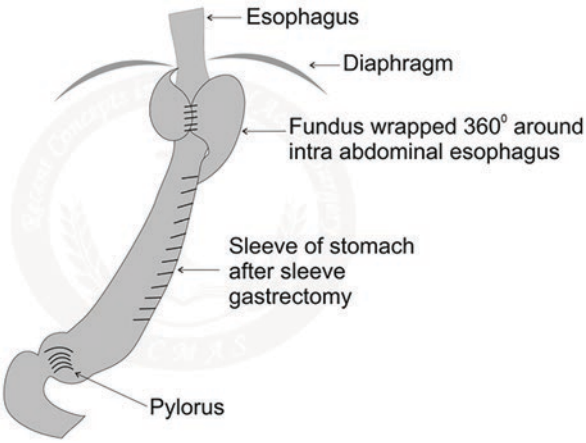

Fig. EN1 Schematic diagram of Laparoscopic sleeve fundoplication

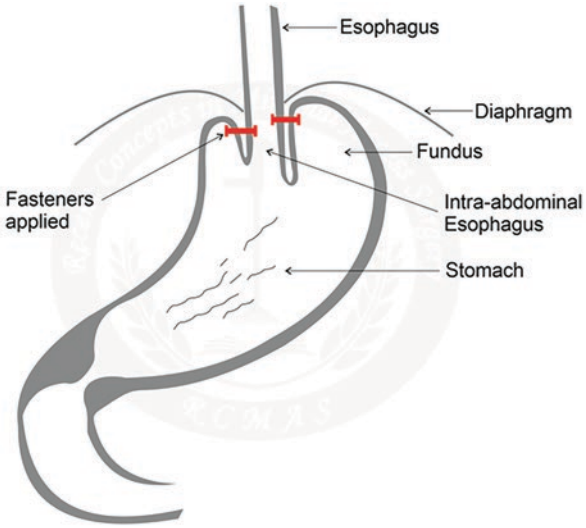

Fig. EN2 Schematic diagram showing the end result of Endoscopic Fundoplication/Transoral incisionless fundoplication

esophagus and secured with fasteners above the Z line (Figure EN2). Though it appears to be promising in PPI refractory GERD in the short term, its long-term efficacy is yet to be evaluated and when compared with LNF currently TIF appears to have an inferior outcome [5–8].

Stretta Procedure

Stretta is a procedure by which radiofrequency treatment is delivered to the lower esophageal sphincter by endoscopic balloon mounted needles. It remodels LES and gastric musculature at cardia and thus improves symptoms of GERD. A recent meta-analysis on the procedure concluded that Stretta improved subjective and objective parameters of GERD. It decreased (improved) health related quality of life score and pooled heartburn score. Only 49% patients receiving PPI required to continue the medicine after the procedure. It reduced erosive esophagitis by 24%, decreased lower esophageal acid exposure, and increased lower esophageal sphincter basal pressure [9]. An earlier metaanlysis however did not find any difference in outcome after Stretta procedure for GERD [10].

Quality of Life

GERD-Health Related Quality of Life Questionnaires convey that heartburn and regurgitation due to GERD is relieved in 84% to 97% after laparoscopic fundoplication [11, 12] and 86% to 96% are well pleased with the end result [13]. No change or worsening related to bloating and swallowing is reported after Laparoscopic fundoplication [11].

Comparison of various meta-analyses has been done and data is included in the following tables:

Table EN1: Meta-analysis on efficacy and safety of endoscopic, transoral incisionless fundoplication

Table EN2: Meta-analysis comparing magnetic sphincter augmentation versus fundoplication in GERD

Table EN3: Meta-analysis comparing robotic with laparoscopic fundoplication

Table EN4: Meta-analyses comparing total and partial laparoscopic fundoplication

Table EN5: Meta-analyses comparing short gastric division versus non division in laparoscopic fundoplication

Table EN1 Metanalysis on efficacy and safety of endoscopic, transoral incisionless fundoplication

Study, first author, year	Result/conclusion
Transoral Incisionless Fundoplication (TIF 2.0): A Meta-Analysis of Three Randomized, Controlled Clinical Trials Lauren Gerson, 2018 [5]	TIF subjects at 3 years had improved esophageal pH, a decrease in PPI utilization & improved quality of life.
Efficacy of Laparoscopic Nissen Fundoplication vs Transoral Incisionless Fundoplication or Proton Pump Inhibitors in Patients With Gastroesophageal Reflux Disease: A Systematic Review and Network Meta-analysis. Richter JE, 2018 [6]	• LNF had greatest ability to improve physiologic parameters of GERD, including increased LES pressure and decreased percent time pH <4. • TIF produced the largest increase in health-related quality of life, this could be due to the shorter follow-up time of patients treated with TIF vs LNF or PPIs.
Efficacy of transoral incisionless fundoplication for refractory gastroesophageal reflux disease: a systematic review and meta-analysis. Thomas R Mc Carty, 2018 [7]	TIF success rate 99% (95% confidence interval (CI) 97 to 100; P < 0.001), adverse event rate of 2% (95%CI 1 to 3; P < 0.001). Following parameters improved significantly post-TIF • GERD HRQL, GERSS and RSI • Hernia reduction occurred in 91% of patients (95%CI 83 to 98; P < 0.001). • DeMeester scores improved significantly (mean difference 10.22, 95%CI 8.38 to 12.12; P < 0.001). • PPI therapy was discontinued post-procedure in 89% of patients (95%CI 82 to 95; P < 0.001).
Efficacy of transoral incisionless fundoplication (TIF) for the treatment of GERD: a systematic review with meta-analysis Xiaoquan Huang, 2017 [8]	TIF vs PPI sham The pooled relative risk of response rate to TIF versus PPIs/sham was 2.44 (95% CI 1.25–4.79, p = 0.0009. The total number of refluxes was reduced after TIF compared with the PPI sham group. Following parameters did not improve after TIF: • Esophageal acid exposure time and acid reflux episodes • Proton-pump inhibitors (ppis) usage in long-term follow-up. T Total satisfaction rate after TIF was about 69.15% in 6 months. The incidence of severe adverse events consisting of gastrointestinal perforation and bleeding was 2.4%. TIF is an alternative intervention with comparable short-term patient satisfaction. Long-term results showed decreased efficacy with time.

TIF Transoral incisionless Fundoplication, *GERD* Gastroesophageal Reflux Disease, *HRQOL* Health Related quality of life, *GRESS* Gastroesophageal reflux Symptom score, *RSI* Reflux Symptom Index, *PPI* Proton pump inhibitor, *LNF* Laparoscopic Nissen Fundoplication, *LES* Lower Esophageal Sphincter

Table EN2 Meta-analysis comparing magnetic sphincter augmentation versus fundoplication in GERD

Study, first author, year	Result/Conclusion
Laparoscopic magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: systematic review and pooled analysis. Guidozzi N 2019 [14]	MSA had: • Less gas bloating (POR = 0.34; 95%CI 0.16–0.71) • Greater ability to belch (POR = 12.34; 95%CI 6.43–23.7). No significant difference in: • Postoperative PPI therapy • GERD-HRQOL score • Dysphagia • Reoperation
Early results of magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: Systematic review and meta-analysis. Aiolfi A 2018 [15]	MSA group had less:Gas/bloat symptoms, 0.39 (95% CI 0.25–0.61; $p < 0.001$), MSA group had better: • Ability to vomit 10.10 (95% CI 5.33–19.15; $p < 0.001$) • Ability to belch 5.53 (95% CI 3.73–8.19; $p < 0.001$). No significant difference: • Dysphagia requiring endoscopic dilatation, $p = 0.119$. • Postoperative GERD-HRQL ($p = 0.101$). • PPI suspension ($p = 0.548$), • Endoscopic dilation ($p = 0.119$) • Reoperation $p = 0.183$.
LINX(®) magnetic esophageal sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease: a systematic review and meta-analysis. Skubleny D 2017 [16]	No statistically significant difference between MSA and LNF in • Gas/bloating (26.7 vs 53.4%, $p = 0.06$), • Postoperative dysphagia (33.9 vs 47.1%, $p = 0.43$) • Proton pump inhibitor (PPI) elimination (81.4 vs 81.5%, $p = 0.68$).
Efficacy of Magnetic Sphincter Augmentation versus Nissen Fundoplication for Gastroesophageal Reflux Disease in Short Term: A Meta-Analysis. Chen MY 2017 [17]	MSA had less: • Operative time (MSA and NF: RR = −18.80, 95% CI: −24.57 to −13.04, and P = 0.001) • Length of stay (RR = −14.21, 95% CI: −24.18 to −4.23, and P = 0.005). • Postoperative gas or bloating (RR = 0.71, 95% CI: 0.54–0.94, and P = 0.02) Similar results in • Proton-pump inhibitor use, • Complication • Severe dysphagia for dilation • Number of adverse events, • Ability to belch and ability to vomit.

MSA magnetic sphincter augmentation, *LF* Laparoscopic Fundoplication, *LNF* Laparoscopic Nissen Fundoplication, *GERD HRQL* gastroesophageal reflux Disease Health related quality of life, *RR* risk ratio, *POR* pooled odds ratio

Table EN3 Meta-analysis comparing robotic with laparoscopic fundoplication

Study, first author, year	Result / Conclusion
Meta-analysis of robot-assisted versus conventional laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease. Wang Z 2012 [18]	RALF had longer Operative time of fundoplication (WMD 3.17 (95% confidence interval. 2.33–4.00) min; P < 0.00001). No difference in • Operative complication, • Antisecretory medication use, • Patient satisfaction with intervention, • Time needed for hiatal dissection, • Time from incision to completion of sutures, • Total operation time • Total cost
Robotic vs. laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease: systematic review and meta-analysis. Markar SR 2010 [19]	No significant difference in rates of: • Re-operation • Postoperative dysphagia • Hospital stay • Operative complications Significantly reduced total operative time in the laparoscopic group (weighted mean difference = 4.154; 95% CI = 1.932–6.375; p = 0.0002). Higher costs in roboti
Whether robot-assisted laparoscopic fundoplication is better for gastroesophageal reflux disease in adults: a systematic review and meta-analysis. Mi J 2010 [20]	RALF had lower postoperative complication rate (OR = 0.35, 95% CI = [0.13, 0.93], p = 0.04) RALF had higher total operating time (WMD = 24.05, 95% CI = [5.19, 42.92], p = 0.01) No significant difference in • Perioperative complication rate (OR = 0.67, 95% CI = [0.30, 1.48], p = 1.00) • Length of hospital stay (WMD = 0.00, 95% CI = [−0.25, 0.26], p = 0.04).
Robot-assisted laparoscope fundoplication for gastroesophageal reflux disease: a systematic review of randomized controlled trials. Zhang P 2010 [21]	RAF and conventional laparoscopic fundoplication (CLF) were similar in • Postoperative antisecretory medication (p = 1.0), • Intraoperative conversion to open surgery (p = 0.94), • Postoperative dysphagia (p = 1.0), • Pneumothorax (p = 1.0), • Total intraoperative complications (p = 0.24), • Time of hiatal dissection (p = 0.98), • Time of incision to completion of sutures (p = 0.95), • Total operation time (p = 0.16), • Hospital stay (p = 0.97), • Total cost (p = 0.25).

RALF/RAF Robotic assisted fundoplication, *CLF* conventional laparoscopic fundoplication, *OR* odds ratio, *WMD* weighted mean difference

Table EN4 Meta-Analyses comparing total and partial laparoscopic fundoplication

Study, first author, year	Result/ conclusion
Assessing the efficacy and safety of laparoscopic antireflux procedures for the management of gastroesophageal reflux disease: a systematic review with network meta-analysis. Andreou A 2020 [22]	Laparoscopic 270°, anterior 180°, and anterior 90° were equally effective as 360° for control of heartburn. The odds were lower after 270° and anterior 90° compared to 360° as follows: • Dysphagia 270° (OR 0.38, 95%, CI 0.24–0.60), • Gas-bloat were 270° (OR 0.51, 95% CI 0.27, 0.95) • Regurgitation, morbidity, and reoperation were similar across treatments.
Laparoscopic Nissen (total) versus anterior 180° fundoplication for gastro-esophageal reflux disease: A meta-analysis and systematic review. Du X 2017 [23]	LNF & 180° LAF: • Equally effective in controlling reflux symptoms • Comparable prevalence of patient satisfaction. 180° LAF: • Reduced incidence of postoperative dysphagia • Higher risk of reoperation for recurrent symptoms.
A meta-analysis of long follow-up outcomes of laparoscopic Nissen (total) versus Toupet (270°) fundoplication for gastro-esophageal reflux disease based on randomized controlled trials in adults. Du X, 2016 [24]	Higher prevalence in LNF of: • Postoperative dysphagia, • Gas-bloating, • Inability to belch, • Dilatation for dysphagia • Reoperation • Higher les sphincter pressure *(differences with respect to dysphagia disappeared over time)* No significant differences between LNF and LTF in: • Hospitalization duration, • Perioperative complications, • Patient satisfaction, • Postoperative heartburn, • Regurgitation, • Postoperative demeester scores, • Esophagitis. 3. A shorter operative time with LNF. 4. Subgroup analyses did not support “tailored therapy” according to preoperative esophageal motility.
Laparoscopic anterior versus posterior fundoplication for gastro-esophageal reflux disease: a meta-analysis and systematic review Memon MA 2015 [25]	LAF vs LPF: • Significant reduction in the odds ratio for dysphagia in the LAF • Significant reduction in the odds ratio for heartburn in LPF Comparable effects for both groups for other variables: • Redo surgery, • Operating time, • Overall complications, • Conversion rate, • Visick’s grading, patients’ satisfaction, • Length of hospital stay, and • Postoperative 24-h ph scores.

Table EN4 (continued)

Study, first author, year	Result/ conclusion
A Meta-Analysis of Randomized Controlled Trials to Compare Long-Term Outcomes of Nissen and Toupet Fundoplication for Gastroesophageal Reflux Disease. Tian ZC 2015 [26]	No difference between the procedures in the following: • Operative time, • Perioperative complications, • Postoperative satisfaction, • Recurrence, • Rates of medication adoption • Re-operation due to recurrence Significantly higher following parameters after LNF: • Dysphagia, • Gas-bloat syndrome, • Inability to belch • Re-operation due to severe dysphagia
Laparoscopic anterior 180-degree versus Nissen fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. Broeders JA 2013 [27]	180° LAF vs LNF 1 and 5 years: Dysphagia and gas-related symptoms are lower after LAF No difference in: • Esophageal acid exposure • Esophagitis • Heartburn scores, • Patient satisfaction, • Dilatations • Reoperation rate
A meta-analysis comparing laparoscopic partial versus Nissen fundoplication. Ma S 2012 [28]	LPF: • Less post-operative dysphagia (OR = 0.44, P < 0.0001) and • Less inability to belch (OR = 0.41, P < 0.005) LNF: • Significant reduction of post-operative heartburn (OR = 1.94, P < 0.01). • Patient satisfaction comparable between the two groups.
Laparoscopic anterior versus posterior fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. Broeders JA 2011 [29]	LAF vs LPF short term (6–12 months) Higher after LAF • Esophageal acid exposure time (3.3% vs. 0.8%: wmd 2.04; 95% confidence interval [ci] [0.84–3.24]; p < 0.001), • Heartburn (21% vs. 8%; rr 2.71; 95%ci [1.72–4.26]; p < 0.001) • Reoperation rate (8% vs. 4%; RR 1.94; 95%CI [0.97–3.87]; P = 0.06) Lower after LAF: • Dakkak dysphagia score (2.5 vs. 5.7; WMD −2.87; 95%CI [−3.88 to −1.87]; P < 0.001). No short-term differences in prevalence of • Esophagitis, • Regurgitation • Perioperative outcomes. LAF vs LPF long term (2–10 years) Higher after LAF • Heartburn (31% vs. 14%; RR 2.15; 95% CI [1.49–3.09]; p < 0.001) • More PPI use (25% vs. 10%; RR 2.53; 95% CI [1.40–4.45]; p = 0.002). • Reoperation rate (10% vs. 5%; RR 2.12; 95% CI [1.07–4.21]; p = 0.03). No long term difference Long-term Dakkak dysphagia scores, inability to belch, gas bloating and satisfaction were not different.

(continued)

Table EN4 (continued)

Study, first author, year	Result/ conclusion
Meta-analysis of laparoscopic total (Nissen) versus posterior (Toupet) fundoplication for gastro-oesophageal reflux disease based on randomized clinical trials.Tan G 2011 [30]	LNF versus LTF: • Control of reflux was good • Occurrence of heartburn similar • Lower early and late post-operative dysphagia ltf group. • Patient's satisfaction similar
Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. Broeders JA 2010 [31]	LNF vs LTF higher prevalence in LNF of: • Postoperative dysphagia (RR 1.61 (95 per cent confidence interval 1.06 to 2.44); P = 0.02) • Dilatation for dysphagia (RR 2.45 (1.06 to 5.68); P = 0.04). • Surgical reinterventions (RR 2.19 (1.09 to 4.40); P = 0.03), • Inability to belch (RR 2.04 (1.19 to 3.49); P = 0.009) • Gas bloating (RR 1.58 (1.21 to 2.05); P < 0.001 No differences regarding: • Recurrent pathological acid exposure (RR 1.26 (0.82 to 1.95); P = 0.29), • Oesophagitis (RR 1.20 (0.78 to 1.85); P = 0.40), • Subjective reflux recurrence, • Patient satisfaction, • Operating time • In-hospital complications

LNF Laparoscopic Nissen Fundoplication, *LAF* Laparoscopic anterior fundoplication, *LPF* Laparoscopic posterior fundoplication, *LTF* Laparoscopic Toupet fundoplication, *OR* Odds ratio, *RR* Relative risk, *LES* Lower esophageal Sphincter, *WMD* Weighted Mean difference, *PPI* Proton Pump Inhibitors

Table EN5 Meta-analysis comparing short gastric division versus non division in laparoscopic fundoplication

Study, first author, year	Result/ conclusion
Laparoscopic Nissen fundoplication with or without short gastric vessel division: a meta-analysis. Khatri K 2012 [32]	SGVD had longer: • Operative time • Hospital stay. No difference in terms of functional outcomes for 1- and 10-year follow-up
Systematic review and meta-analysis of laparoscopic Nissen fundoplication with or without division of the short gastric vessels. Markar SR 2011 [33]	No statistically significant effect on rates of: • Reoperation, • Postoperative dysphagia • Reflux. • Length of hospital stay, • Postoperative complications, • Postoperative gas bloat syndrome • Demeester score. SGV division was associated with: • Longer duration of operation • Reduced postoperative lower oesophageal sphincter pressure.

Table EN5 (continued)

Study, first author, year	Result/ conclusion
Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of the short gastric vessels during Nissen fundoplication. Engström C 2011 [34]	No significant differences in: • Heartburn • Dysphagia, • Ability to belch or vomit, • Use of antisecretory medications. Division of the short gastric vessels was associated with a higher rate of bloating symptoms (72 versus 48 per cent; P = 0.002) at 10-12 years follow up

SGV/SGVD short gastric vessel division

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