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HOW-I-DO-IT ARTICLES

A modified Nissen fundoplication: subjective and objective midterm results

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Abstract

Purpose The failure rate of laparoscopic anti-reflux surgery is approximately 10–20%. The aim of our prospective study was to investigate whether a modified Nissen fundoplication (MNF) can improve reflux symptoms and prevent surgical treatment failure in the midterm.

Methods The MNF consisted of (1) suturing the esophagus to the diaphragmatic crura on each side using four non-absorbable stitches, (2) reinforcing clearly weak crura with a tailored Ultrapro mesh, and (3) fixing the upper stitch of the valve to the diaphragm. Forty-eight consecutive patients experiencing typical gastroesophageal reflux disease (GERD) symptoms at least three times per week for 6 months or longer were assessed before and after surgery using validated symptom and quality of life (GERD-HRQL) questionnaires, high-resolution manometry, 24-h impedance-pH monitoring, endoscopy, and barium swallow.

Results Mortality and perioperative complications were nil. At median follow-up of 46.7 months, the patients experienced significant improvements in symptom and GERD-HRQL scores. One patient presented with severe dyspepsia and another complained of dysphagia requiring a repeat surgery 12 months after the first operation. Esophageal acid exposure (8.8 vs 0.1; $p < 0.0001$), reflux number (62 vs 8.5; $p < 0.0001$), and symptom-reflux association (19 vs 0; $p < 0.0001$) significantly decreased postoperatively. The median esophagogastric junction contractile integral (EGJ-CI) from 31 cases (8.2 vs 21.2 mmHg cm; $p = 0.0003$) and the abdominal length of the lower esophageal sphincter (LES) (0 vs 16 mm; $p = 0.01$) increased postoperatively.

Conclusions Our data demonstrate that the MNF is a safe and effective procedure both in the short term and midterm.

Keywords Gastroesophageal reflux disease · Laparoscopic surgery · Nissen fundoplication · Anti-reflux surgery

Introduction

The main purposes of GERD management are relieving reflux symptoms, improving patients' quality of life, and preventing esophageal mucosal damage. Proton pump inhibitor (PPI) therapy is the mainstay for GERD treatment since it is effective in the majority of reflux patients without having significant side effects [1, 2]. Thus, anti-reflux surgery is indicated in a small percentage of patients in cases of refractory symptoms, poor disease control, non-compliance, or side effects with medical therapy, and young patients who refuse lifelong PPI therapy [3].

Nissen fundoplication (NF) has been shown to provide reflux control and symptomatic relief in 80–90% of GERD patients [4, 5] and is superior to medical treatment [6]. However, a failure rate of 10–20% has been reported [4, 5]. Failure can be clinically defined as persistent, recurrent, or new-onset symptoms. Failure can also be defined as (1) symptoms due to persistent or recurrent reflux and (2) symptoms mainly due to a malfunctioning fundoplication, such as dysphagia, gas bloat syndrome, inability to belch or vomit, gastric fullness, and early satiety. In many cases of failure, objective evidence of an anatomic abnormality is present; in fact, fundoplication can become herniated, disrupted, slipped,

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misplaced, or twisted, and the wrap or the crural repair can be too tight [3, 7–9].

Many surgical techniques have been described to prevent these complications. The anchorage of the esophagus in its intra-abdominal position aims to prevent a herniated, disrupted, slipped, misplaced, or twisted fundoplication. In 1948, Lortat Jacob proposed a cardiophrenopexy by fixing the gastric fundus to the sub-diaphragmatic peritoneum [10]. Nevertheless, the recurrence rate remained high. Thereafter, Allison suggested fixing the stomach to the anterior portion of the phrenoesophageal ligament, which proved to be the weakest part of this membrane, leading to a high recurrence rate (49%) [11]. In 1956, Nissen proposed a 360° fundoplication with a long valve (4–6 cm) fixed to the abdominal esophagus; typical new-onset symptoms after NF were dysphagia, gas bloat syndrome, and inability to belch [12]. A few years later, Hill suggested anchoring the gastroesophageal junction to the median arcuate ligament and preaortic fascia; however, this procedure was found to be technically difficult [13]. A partial fundoplication was proposed by Toupet in 1963 to prevent dysphagia, gas bloat syndrome, and inability to belch. The degree of fundoplication was reduced to 180° (later changed to 270°) using a posterior wrap [14], but reflux control was inadequate [15, 16]. Similarly, in 1984, Watson attempted to reduce the degree of fundoplication to 120° by fixing the intra-abdominal esophagus to the crural sling and accentuating the angle of His [17]. However, this technique also showed insufficient reflux control. (3) As NF became the procedure of choice, some modifications to the classical technique were explored between 1968 and 1986. Rossetti modified the NF by wrapping only the anterior wall of the stomach and performed manometric calibration of the new high-pressure zone [18]. Donahue introduced the concept of a "floppy" Nissen by creating a loose wrap that is still effective in preventing pathologic reflux [19, 20]. DeMeester increased the caliber of the bougie used to size the diameter of the gastric wrap; the incidence of temporary swallowing discomfort decreased from 83 to 39%. Moreover, he proposed a "short" gastric wrap (1.0 cm), which reduced the incidence of persistent dysphagia from 21 to 3%, and a division of the short gastric vessels, which increased the incidence of complete distal esophageal sphincter relaxation during swallowing from 31 to 71% [21]. Despite these different techniques, failure rates remain high.

A novel modification to the Nissen procedure was recently proposed and validated in our center [22]: it consists of anchoring the esophagus to the diaphragmatic crura with four non-absorbable sutures and fixing the upper stitch of the valve to the diaphragm. This technique has shown good preliminary results compared to traditional NF; moreover, it has demonstrated safety and feasibility.

The aim of our prospective study was to investigate clinical and pathophysiological outcomes in the midterm to assess the efficacy and failure rates of this modified surgical approach.

Patients and methods

Between March 2011 and January 2016, we prospectively screened 60 consecutive patients who were referred to the Department of Surgery, Oncology and Gastroenterology at the University Hospital of Padua, Italy, with typical GERD symptoms (i.e., heartburn and/or regurgitation) occurring at least three times weekly for 6 months or longer. We excluded 12 (20%) patients based on the following criteria: inability to provide informed consent, pregnancy, severe esophageal motility disorders (i.e., achalasia, scleroderma, and other connective tissue disorders), giant paraesophageal hiatal hernia, severe psychiatric illness, malignancies, inability to perform the required diagnostic workup, and under the age of 18. Forty-eight enrolled patients underwent anti-reflux surgery due to (a) uncontrolled acid and non-acid reflux symptoms using PPI, (b) large hiatal hernia with GERD symptoms, (c) non-compliance or side effects of medical therapy, (d) desire to avoid long-term medical therapy, and (e) Barrett's esophagus (BE) in young patients [3]. Although a uniform definition does not exist, for the purpose of this study, large hiatal hernias were defined as hiatal hernias measuring > 5 cm or hiatal hernias with at least 30% of the stomach present in the chest [23, 24].

This study was performed according to the Principles of the Declaration of Helsinki. This study was reviewed and approved by the Internal Review Board in Padova, Italy. Written consent was obtained from all patients prior to study enrollment.

Preoperative assessment

Enrolled subjects underwent careful physical and clinical examinations, and medical history was collected. GERD symptoms were scored according to their severity and frequency. Scores for heartburn, dysphagia, acid regurgitation, and pain were calculated by combining the severity (0 = none, 2 = mild, 4 = moderate, 6 = severe) and frequency (0 = never, 1 = occasionally, 2 = once a month, 3 = every week, 4 = twice a week, 5 = daily) for each symptom [25]. Each patient completed a previously validated functional dyspepsia questionnaire [26, 27]. Quality of life was measured in each patient using the GERD-HRQL questionnaire [28].

Endoscopy was performed to identify erosive esophagitis (EE) or BE and to exclude the presence of other pathologies such as eosinophilic esophagitis (in cases of dysphagia, bolus impaction history, and chest pain), gastritis associated with *Helicobacter pylori* (in case of Hp infection, the patient was treated before surgery to avoid potentially influencing clinical outcomes), peptic ulcer disease, benign strictures, and malignant disease.

A barium swallow was performed preoperatively to detect any anatomic variations (hiatal hernia, short esophagus,

diverticulum, or peptic stricture), to describe the morphological features of any previous unsuccessful fundoplication and to examine gastric and duodenal emptying.

Esophageal manometry was performed using the conventional (CM; before November 2011) or high-resolution manometry (HRM; after December 2011) systems, as described in detail elsewhere [29–32]. In addition to conventional HRM metrics according to the Chicago Classification System, a new parameter of HRM, the esophagogastric junction contractile integral (EGJ-CI), was assessed. This recently proposed feature has proven to be a valid parameter for the assessment of both lower esophageal sphincter (LES) and crural diaphragmatic contributions to the anti-reflux barrier of the esophagogastric junction and represents a more robust metric than conventional LES pressure in the assessment of adequacy of surgical interventions [33, 34]. EGJ-CI was considered abnormal when the value was below 13 mmHg cm (5th percentile among healthy volunteers in Nicodeme's study) [35].

The characteristics of gastroesophageal reflux were studied using 24-h impedance-pH monitoring with patients off medications; PPI therapy was stopped at least 14 days before testing. Impedance-pH monitoring is considered the gold standard for reflux detection because it objectively evaluates pathologic acid exposure and correlates specific symptoms with episodes of reflux (i.e., symptom association analysis). The calibration, performance, and duration of impedance-pH studies have been previously described in detail [36, 37]. For the purpose of this study, a positive impedance-pH test was defined when the esophageal acid exposure time over 24 h was higher than 4.2%, the number of reflux events was greater than 54, and/or there was positive symptom-reflux association using the symptom index (SI) or symptom association probability (SAP) [36, 38].

Surgical technique

The NF was performed according to the traditional technique described elsewhere [12]. Three modifications of NF were adopted, as previously described by our institution [22]. First, the esophagus was sutured to the diaphragmatic crura bilaterally by means of two non-absorbable sutures to guarantee the intra-abdominal stability of sufficient esophageal length. The esophagus was secured with two horizontal mattress sutures (0/0 non-absorbable braided suture thread) to the crura on either side, passing through the crus, the esophageal wall, and then back inversely, knotting the suture externally on the crura, including an abundant amount of the crus. The sutures were placed in the esophagus 1 cm apart longitudinally, catching the muscular coat and making sure to leave enough free space between the diaphragm and the anterior surface of the esophagus. Posteriorly, the hiatus was closed with a non-absorbable suture to approximate the crura. Second, in cases of clearly weak crura or repeat surgery, the crura was reinforced with Ultrapro mesh (50% absorbable poliglecaprone-25 and 50% non-absorbable polypropylene) (Ethicon-Johnson & Johnson International, Belgium; CE 0086) (Fig. 1). The mesh was tailored to envelop the crura bilaterally and extend into the mediastinum (Fig. 2a). Each piece of mesh was secured to the crura with clips laterally and medially, preventing their migration and reinforcing the suture of the esophagus to the crura. The above-described mattress suture is therefore applied to secure the mesh to the crus and the esophagus, returning to the outside (Fig. 2b). Lastly, the third modification to the classical Nissen procedure consisted of fixing the anti-reflux valve to the diaphragm above the hiatus using the upper suture of the valve to prevent the migration of the valve to the chest (Fig. 2c). A floppy Nissen was performed around the esophagus avoiding any direct constriction by the valve to prevent postoperative dysphagia. Three sutures were placed along a length of approximately three centimeters to create the anti-reflux wrap.

Two surgeons experienced in esophageal surgery with comparable skills performed the surgical procedures.

Postoperative assessment and follow-up

All patients underwent an esophagogram on the first day after surgery and were discharged on the second day on a soft diet. Clinical outcomes were assessed by repeating the same preoperative questionnaires 6 months after surgery and every year thereafter. A barium swallow was obtained at 2 months and 2 years after surgery. Esophageal manometry and 24-h impedance-pH monitoring were performed 6 months after surgery or in cases of symptom recurrence. Endoscopy was repeated 12 months after surgery. Any esophagitis was graded according to the Los Angeles Classification [39]. Treatment failure was defined in the following cases: a postoperative symptom score greater than the 10th percentile of the preoperative score (i.e., > 8), esophagitis, recurrent hernia on barium swallow, defective LES or EGJ-CI on manometric assessment, positive postoperative 24-h impedance-pH monitoring based on acid exposure time greater than 4.2%, a number of reflux events greater than 54, and/or a positive symptom-reflux association analysis [40].

Statistical analyses

Continuous data were expressed as medians and interquartile ranges (IQR). Categorical data were compared between the preoperative and postoperative periods using Fisher's test, and continuous data were compared using the Mann-Whitney non-parametric test. Pre- versus postoperative variations in continuous data were assessed using Wilcoxon's non-parametric test for paired data. A p value of less than 0.05 was considered significant. Statistical analyses were performed using SAS 9.1 software.

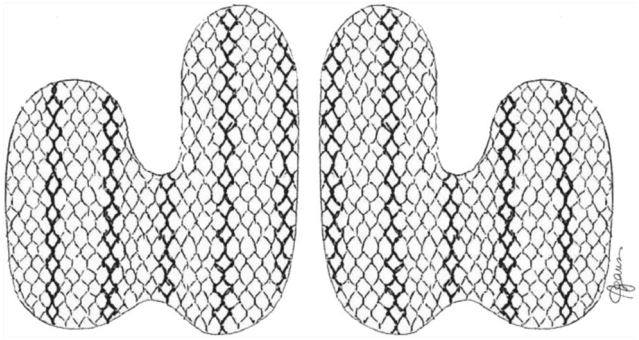

Fig. 1 Tailored Ultrapro meshes

Results

We included 48 consecutive GERD patients (25 M/23 F) with a median age of 57 years (IQR 44–63) whose demographic and clinical data are shown in Table 1.

The modified Nissen fundoplication (MNF) was performed as a repeat surgery in 10 patients with failure of a previous fundoplication due to a slipped Nissen ($N = 6$), telescoping ($N = 2$), excessively tight Nissen ($N = 1$), and disruption of the wrap ($N = 1$).

Clinical and pathophysiological characteristics

We collected subjective and objective data for all patients ($n = 48$). Symptom/GERD-HRQL scores and pathophysiological findings from the manometry and pH/impedance tests are shown in Table 2. The median preoperative symptom score was 18.5 (IQR 11–27), while the median GERD-HRQL score was 27 (20–34). At preoperative endoscopy, there was evidence of esophagitis in 42% of cases, Barrett's esophagus in 17%, and hiatal hernia in 71%. Barium swallow showed hiatal hernia in 71% of patients and normal esophageal and gastric emptying in all subjects. At HRM, we observed a median LES resting pressure of 17.1 mmHg (IQR 11.4–19.45), a median LES length of 27 mm (23–36), and a median intra-abdominal LES length of 0 mm (0–11). EGJ morphology type I was present in 42% of the patients, type II in 12%, and type III in 46%. During manometry, 76% of patients presented with normal peristalsis, 14% with ineffective esophageal motility, and 10% with weak peristalsis with small breaks. Finally, impedance-pH studies showed a median acid exposure time of 8.8% (6.4–14.7) and a median number of reflux of 62 (40.5–91.5) and 19 patients had a positive symptom-reflux association analysis.

Surgical data

The median operating time was 138 min (IQR 120–180). Mortality and perioperative morbidity were nil. In 39 cases (81%), surgery was completed laparoscopically, while an open conversion was necessary in 3 patients (6%) because of strong adhesions resulting from previous surgery. In another 6 cases (13%), an open approach was chosen due to history of previous open surgery. In 28 patients (58%), mesh was used to reinforce weak crura. No complications related to the mesh (e.g., erosion, migration, or infection) were observed during the entire follow-up period in this cohort of patients (median 42 months).

Clinical and objective outcome data after surgery

Clinical and pathophysiological features are reported in Table 2. The median follow-up was 46.7 months (IQR 36.3–58.9). Overall, patients experienced a significant improvement in symptoms and GERD-HRQL scores, and manometry and pH-metry findings after surgery. At postoperative endoscopy, no evidence of esophagitis was detected. Barium swallow excluded the presence of significant hiatal hernia in all subjects.

One patient (2%) presented with severe dyspepsia and another complained of dysphagia, requiring a repeat surgery 12 months after the first operation. At surgical exploration, a floppy wrap and correct position of the mesh were observed; however, the wrap was disassembled and re-fashioned. The

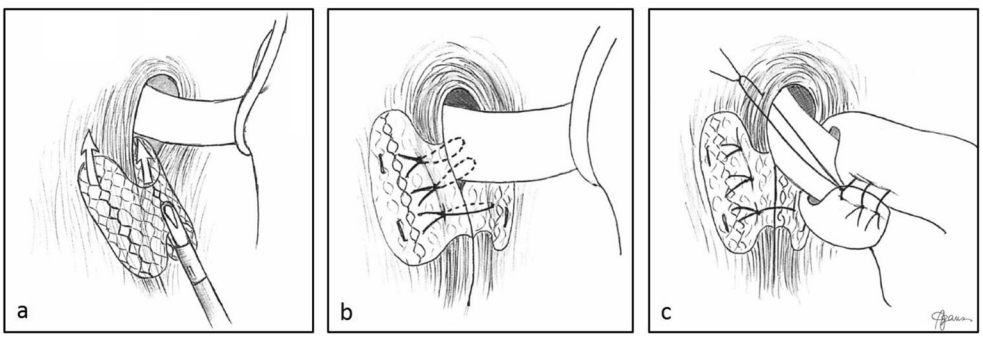

Fig. 2 **a** The mesh is placed to wrap the crura bilaterally and extend into the mediastinum. **b** The meshes are placed to flap onto and around the crura and fixed by metallic clips. Then, two sutures are placed to fix the esophagus to the crura and meshes bilaterally. **c** The anti-reflux valve is fixed to the diaphragm above the hiatus using the upper suture of the valve

Table 1 Demographic and clinical data

Number of patients	48
Sex (M/F)	25/23
Median age, years (IQR)	57 (44–63)
Mean body mass index (range), kg/m^2 (IQR)	25.7 (16.0–33.6)
Smoking, *n* (%)	7 (15%)
The American Society of Anesthesiology classification of physical status (ASA)	
ASA 1 e 2, *n* (%)	42 (87.5%)
ASA 3, *n* (%)	6 (12.5%)
Median duration of symptoms, months (IQR)	60 (21.5–162)
Patients with hiatal hernia, *n* (%)	34 (71%)
Patients undergoing repeat surgery for GERD, *n* (%)	10 (21%)
Patients with previous laparotomy for digestive surgery, *n* (%)	9 (19%)
Helicobacter pylori status	
Previous infection, *n* (%)	2 (4%)
Negative, *n* (%)	46 (96%)
Patients with clinically relevant dyspeptic symptoms*, *n* (%)	4 (8%)

*Grades 4 and 5 for frequency of dyspeptic symptoms according to the Rome III criteria [41]

patient continued to complain of dysphagia and manometry was performed, which showed 100% failed peristaltic waves during swallows. He underwent pneumatic dilation of the LES twice, after which he reported improvement of symptoms. He is now undergoing regular follow-up in the outpatient clinic.

None of the patients reported early inability to vomit, while bloating after surgery or during the entire follow-up period was reported in 17 cases (35%). Two patients were still taking PPIs at follow-up, in one case, for prophylaxis during low-dose aspirin therapy and, in the other case, for habitual use without any clinical or pathophysiological evidence of recurrent gastroesophageal reflux or hernia.

Nissen fundoplication versus repeat fundoplication

We compared the results of patients undergoing first versus repeat fundoplication. No significant difference was observed in age, sex, demographic characteristics, postoperative symptom scores, quality of life scores, and manometry and pH-metry features (Table 3).

Discussion

Laparoscopic NF has become the procedure of choice for anti-reflux surgery [42]. However, 10-year follow-up studies have shown that reflux control and symptom relief after surgery are achieved in approximately 80–90% of patients [43–45], while 10 to 20% of patients experience persistent or recurrent reflux symptoms or other complications.

In this study, we added new technical details to reduce the potential failure rate of the modified Nissen procedure that we previously proposed. We designed a procedure with the aim to re-establish the anatomy of the lower esophagus and the

Table 2 Comparison of clinical and pathophysiological findings before and after surgery. Data are expressed as *n* (%) or median (IQR)

	Before surgery	After surgery	*p* value
Symptom score	18.5 (11–27)	0 (0–0)	$p < 0.0001$
GERD-HRQL score	27 (20–34)	0.5 (0–5)	$p = 0.001$
Acid exposure time (%)	8.8 (6.4–14.7)	0.1 (0–0.4)	$p < 0.0001$
Number of reflux	62 (40.5–91.5)	8.5 (3–25)	$p < 0.0001$
Symptom-reflux association (SI/SAP)	19 pos	0 pos	$p < 0.0001$
LES* resting pressure (mmHg)	17.1 (11.4–19.45)	16 (12.3–25.3)	$p = 0.49$
LES residual pressure (mmHg)	5.2 (3.15–9.1)	8 (5.2–11-9)	$p = 0.05$
LES total length (mm)	27 (23–36)	31 (26–36)	$p = 0.44$
LES abdominal length (mm)	0 (0–11)	16 (1–19)	$p = 0.01$
EGJ-CI** (mmHg cm)	8.2 (3.7–14.1)	21.2 (16.1–25.2)	$p = 0.0003$

**LES* lower esophageal sphincter

***EGJ-CI* esophagogastric junction contractile integral, calculated during HRM in 31 cases

Table 3 Comparison of outcomes in patients undergoing first versus repeat fundoplication

	First surgery	Repeat surgery	*p* value
Symptom score	0.5 (0–5)	2 (0–5)	*p* = ns
GERD-HRQL score	0 (0–0)	0 (0–0)	*p* = ns
LES resting pressure (mmHg)	16.5 (13.1–27)	14.2 (9.1–18.9)	*p* = ns
LES residual pressure (mmHg)	8.7 (4.8–12.4)	7.9 (6.4–11.5)	*p* = ns
LES length (mm)	33 (27–38)	26 (24.7–31.5)	*p* = ns
LES abdominal length (mm)	12 (8–19)	17 (14–19)	*p* = ns
EGJ-CI (mmHg cm)	19.7 (14.7–24.1)	18.8 (16.3–28.4)	*p* = ns
Acid exposure time (%)	0.1 (0–0.4)	0 (0–0.3)	*p* = ns
Number of reflux	8.5 (3–26.5)	13.5 (1.5–25.5)	*p* = ns
Symptom-reflux association (SI/SAP)	0 pos	0 pos	*p* = ns

ns not significant

esophagogastric junction in its intra-abdominal position as close to normal as possible. This was achieved by placing sutures in the esophagus to the crura bilaterally to prevent possible thoracic migration of the wrap and the occurrence of a paraesophageal hernia by closing the space between the esophagus and crura, both laterally and posteriorly. A free space is left anteriorly between the diaphragm and the anterior esophageal surface to allow the esophagus to enlarge in diameter during swallowing, thereby preventing postoperative dysphagia.

To avoid disruption of the hiatoplasty, weak crura are reinforced using a mesh that ensures direct support and support when the growth of connective tissue occurs soon after implantation, as described by other authors [46].

The use of a mesh is typically suggested for skilled surgeons. Laparoscopic anti-reflux surgery, in fact, requires a high degree of two-handed laparoscopic skill and has a longer learning curve than simpler laparoscopic procedures such as cholecystectomy or appendectomy [47]. Watson showed that complication and reoperation rates were greater during the first 50 procedures and particularly high during the first 20 procedures performed. He suggested 20 laparoscopic anti-reflux procedures as the individual's learning curve [48]. Many experts believe that any laparoscopic anti-reflux surgeon not only should be trained and familiar with all aspects of management of such patients, but also needs to do a minimum of 12 procedures a year to maintain the necessary level of skill [49]. Increasing evidence suggests that surgeon's skill and experience have a direct impact on the morbidity and success of the procedure [50, 51]. Herbella et al. also underlined the importance of a particular expertise in hiatal mesh repair, as the use of a mesh shows a learning curve even to surgeons who earlier had experience with anti-reflux surgery [52].

Longer follow-up studies are needed before establishing the long-term safety of this procedure; however, a recent meta-analysis, including 915 patients with paraesophageal hernia, showed a significantly lower recurrence rate for laparoscopic mesh-augmented hiatoplasty compared to mesh-free hiatoplasty (12.1 vs 20.5%; $p = 0.04$), with comparable complication rates in both groups (15.3 vs 14.2%; $p = 0.94$). The authors concluded that mesh use should be considered for laparoscopic paraesophageal hernia repair, as it reduces recurrences in the midterm without increasing overall complications and mortality, despite of potential mesh-associated complications [53].

Prusa et al. also described their experience with the implantation of dual-sided composite PTFE/ePTFE meshes: during a median follow-up of 43.3 months, no repeat surgeries were required, while two patients complained of dysphagia (20%), which resolved after endoscopic interventions [54]. Among the rare complications of mesh fixation to the diaphragm, a few cases of pericardial injuries have been reported. Frantzides reviewed a total of 10 cases of cardiac tamponade in hiatal hernia repair, which was caused by the helical tacker (up to 7 mm in depth) in the majority of cases and by sutures less frequently [55]. Pericardial injury by laparoscopic staples has not been reported in the literature, as their shorter length (up to 4.8 mm) avoids deeper damage [56]. Moreover, a concrete risk of cardiac injury is present if the suture is applied on the central tendon of the diaphragm (thickness 2.9–3.0 mm) and not on the crura. The staples should therefore only be used on the crura and should be avoided on the diaphragm itself. In all cases, we used staples for mesh fixation and performed this procedure carefully, under direct view.

We maintained the original concept of a 360° wrap, as it has shown excellent results over the years in terms of symptomatic relief [57]. In the MNF, wrap disruption is prevented by the three non-absorbable sutures that keep the posterior and anterior parts of the valve together in a tension-free manner and by suturing the valve to the diaphragm just above the hiatus to avoid any traction to the left.

Our cohort of patients experienced significant improvement in symptom and GERD-HRQL scores after surgery; subjective symptoms were objectively confirmed by impedance-pH measurements, which showed significant

decreases in acid exposure time and reflux number, in accordance with the literature [3].

Furnée and Coll. published a systematic review of the complications and failure rates associated with anti-reflux surgery [58]. They analyzed 4509 cases reported in a total of 81 different publications of repeat fundoplication after unsuccessful primary anti-reflux surgery. The mean time between primary and repeat surgery was 38.3 ± 4.1 months. Dallemagne et al. also analyzed long-term clinical results (5 and 10 years after surgery) and found that all complications requiring reoperation occurred within the first 5 years, while surgical outcomes tended to stabilize between the 5th and 10th year of follow-up [43]. Since anti-reflux surgery usually fails within 5 years, we relied on a follow-up period of 4 years for the current study, during which time we did not observe any cases of failure (e.g., recurrence or wrap migration).

To prevent dysphagia, we performed a wide wrap leaving a free space between the anterior wall of the esophagus and the hiatus. Although one case of postoperative dysphagia occurred in our cohort, the lack of this subjective symptom in 47 patients was objectively validated by the radiological finding of a proper esophagogastric contrast progression; in fact, upper GI series were performed immediately and 24 months after surgery in all patients and excluded the presence of any kind of stenosis or peristaltic abnormalities due to the fixation of the esophagus to the diaphragmatic crura. Nevertheless, 35% of our patients complained of postoperative bloating; this value is in accordance with the 40% rate of bloating reported in the LOTUS study [59]. The reasons for the development of severe bloating are unclear, although a higher incidence has been reported after complete fundoplication compared to partial fundoplication [60]. Watson reduced the degree of fundoplication to 120°; despite better results in comparison to NF in terms of prevention of dysphagia, gas bloat syndrome, and inability to belch, this technique showed insufficient outcomes in terms of reflux control compared to posterior partial fundoplication (Toupet) [61]. A Chinese randomized prospective trial of Nissen and Toupet fundoplications showed similar results among the two techniques in terms of reflux control but showed a higher frequency of dysphagia in the NF group [62]. These results were confirmed by a recent meta-analysis that compared long-term outcomes of laparoscopic Nissen versus Toupet (270°) fundoplications: no significant difference in terms of postoperative heartburn and regurgitation was detected, but occurrence of dysphagia, gas bloating, and inability to belch was lower for patients who underwent the Toupet procedure [63].

In our study, the MNF was performed as a repeat surgery in some cases. Symons reported a higher morbidity rate and worse outcomes of repeat laparoscopic surgery compared to primary laparoscopic fundoplication [64]. In 10 of our patients (21%), one or more previous surgical procedures for reflux had been performed elsewhere but their subjective and objective results after repeat surgery were as satisfactory as those of the patients who underwent primary surgery, suggesting the effectiveness and safety of this approach in high-risk patients.

This study has intrinsic limitations such as the lack of a control group, lack of randomization, and a small and heterogeneous sample. A strength of our study is the structured clinical and instrumental measures obtained over an adequate duration of follow-up.

Conclusion

MNF has proven to be a safe and feasible anti-reflux procedure, as confirmed by clinical and instrumental evaluations over a median follow-up duration of 4 years. In fact, there were no cases of reflux recurrence and a low rate of complications (2%). Although a longer follow-up is needed to draw definitive conclusions, our data suggest safety and efficacy of MNF without many of the known complications of NF, not only as primary treatment but even as repeat surgery in cases of previously failed anti-reflux procedures. This technique needs to be evaluated in multicenter randomized trials for comparison with other surgical techniques before definitive conclusions can be drawn, according to internationally accepted levels of evidence.

Authors' contributions Sabrina Rampado: study conception and design, acquisition of data, analysis and interpretation of data, drafting the manuscript, and critical revision of the manuscript. Angelica Ganss: drafting the manuscript and critical revision of the manuscript. Giulia Pozza: acquisition, analysis, and interpretation of data. Edoardo Savarino: critical revision of the manuscript. Romeo Bardini: study conception and design and critical revision of the manuscript.

Compliance with ethical standards

Institutional review board statement The study was reviewed and approved by the Internal Review Board in Padova, Italy.

Informed consent statement All study participants provided written consent prior to study enrollment.

Conflict of interest The authors declare that they have no conflicts of interest.

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