UNIVERSITÀ DEGLI STUDI DI TORINO

Gastric Emptying as a Prognostic Factor for Long-term Results of Total Laparoscopic Fundoplication for Weakly Acidic or Mixed Reflux

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Abstract
Objectives: To evaluate the long-term effect of laparoscopic total fundoplication (LTF) on symptoms and reflux control in patients with combined (acidic and weakly acidic) (CR) or weakly acidic reflux (WAR), according to the gastric emptying (GE) rate.
Background: After LTF, 12% to 15% of patients experience persistent reflux symptoms and 20% and 25% develop gas-related symptoms. Both WAR and inability to belch have been suggestive of these symptoms.
Methods: Consecutive patients with CR and WAR selected for LTF were included in a prospective clinical study. Gastroesophageal function was assessed by clinical validated questionnaires, upper endoscopy, esophageal manometry, and 24-hour impedance–pH monitoring before and 12 and 60 months after LTF. Gastric scintigraphy was preoperatively performed in all patients to evaluate GE. This trial is registered with ClinicalTrials.gov (no. NCT01741441).
Results: Between June 2002 and June 2007, a total of 188 patients with CR and WAR underwent LTF; 172 (91.5%) completed the 5-year protocol. Among them, 42 (24.4%) had preoperative mild/moderate delayed GE (DGE). Quality of life at 12 and 60 months improved in patients with normal GE (Gastroesophageal Reflux Disease Health-Related Quality of Life score 18.2/2.5, $P < 0.001$; Health-Related Quality of Life score from 52.1 to 68.3, $P < 0.001$) but not in DGE patients. Manometric values of "gastroesophageal junction" significantly increased at 12 and 60 months in all patients with normal GE, whereas the values returned to the baseline at 60 months in 66.7% of DGE patients. Acidic and liquid reflux episodes significantly reduced in both groups, whereas a significant reduction of WAR and mixed (gas + liquid) reflux episodes occurred only in patients with normal GE ($P < 0.001$).
Conclusions: DGE affects long-term results of LTF in CR and WAR patients.

Gastroesophageal reflux disease (GERD) is the most common upper gastrointestinal condition in Western countries, and it accounts for about 75% of esophageal disorders.1 Laparoscopic total fundoplication (LTF) is the standard surgical treatment of GERD, with low morbidity and excellent long-term functional outcome.2 Nevertheless, 12% to 15% of patients have persistent reflux symptoms and 20% to 25% develop gas-related symptoms after LTF.3
Reflux symptoms, gas bloating, and inability to belch after the surgery have been associated with combined (acidic and weakly acidic) (CR) or weakly acidic reflux (WAR). To date, few studies 4-8 have evaluated functional outcome after LTF in patients with CR or WAR; the majority reporting only short-term results.
Delayed gastric emptying (DGE) has been described in 25% to 59% of patients with functional dyspepsia and in up to 40% of patients with GERD.9 The correlation between poor long-term outcome after LTF and DGE is controversial,10,11 and the effect of DGE in patients with CR or WAR is poorly investigated. The aim of this study was to prospectively evaluate the relationship between DGE and the long-term outcome of LTF in terms of reflux and symptom control in patients with CR or WAR.

METHODS

The study population consisted of consecutive patients with CR or WAR confirmed by 24-hour multichannel intraluminal impedance (MII)–pH monitoring and eligible for LTF. Exclusion criteria were the presence of acidic reflux alone and giant hiatal hernia. Preoperative workup included clinical examination, upper endoscopy, barium swallow, conventional esophageal manometry, 24-hour MII–pH monitoring, and gastric scintigraphy.

Patient characteristics were entered into a prospective database including preoperative assessment, intraoperative data, perioperative results, and long-term clinical and functional outcomes. Gastroesophageal function was evaluated using GERD Health-Related Quality of Life (GERD-HRQOL) score,12 reflux symptom index (RSI),13 and 36-item Short-Form Health Survey (SF-36)14 and by functional testing. The protocol was approved by the ethical committee of our institution, and patients gave informed consent.

Endoscopic Evaluation

All patients underwent upper endoscopy with a flexible endoscope. Findings of possible hiatal hernia and/or esophagitis were described in detail and, in case of macroscopic esophagitis, were graded according to the Savary-Miller classification.15 Biopsy samples were routinely taken at the gastroesophageal junction and in areas suggestive of the Barrett esophagus. All patients underwent gastric mucosal biopsy to exclude a Helicobacter pylori infection; in case of H pylori infection, eradication therapy was provided with standard amoxicillin-clarithromycin-containing triple therapy.

Radiological Evaluation

A complete radiological study of the upper gastrointestinal tract was conducted using a low-density barium sulfate suspension (45% wt/vol). Three parameters were routinely evaluated and measured: (1) esophageal body length; (2) the presence and size of a hiatal hernia; and (3) the occurrence of spontaneous gastroesophageal reflux.

Esophageal Manometry

Stationary manometry of the esophagus was performed before and after the operation, using 8-channel perfusion catheters, 4 disposed radially and oriented at 90 degrees to each other and 4 positioned longitudinally at intervals of 5 cm. The catheter was perfused with distilled water, using a low-compliance pneumohydraulic perfusion system (Dyno 2000 Menfis Biomedica, Bologna, Italy) at a constant infusion rate of 0.8 mL/min at 1.2 kg/cm^2. Lower esophageal sphincter (LES) pressure was calculated by withdrawing the catheter using a motorized pull-through technique at a constant speed of 1 mm/s from the stomach to the esophageal body, passing through the high-pressure zone. LES pressure was calculated as both the midexpiratory pressure at the respiratory inversion point and the average of all pressures recorded in the high-pressure zone (as analyzed by the computer). Esophageal body motility and LES relaxation were assessed by recording the changes in pressure elicited by 10 wet swallows, with the side holes of the catheter positioned inside the LES and 5, 10, 15, and 20 cm higher up. LES residual pressure was defined as the minimal pressure (nadir) recorded in the LES during swallowing. Any medications with possible effect on esophageal motility were discontinued 5 days before the examinations.

Twenty-four-Hour MII–pH Monitoring

Twenty-four hour esophageal MII–pH monitoring performed in the absence of medical therapy preoperatively and postoperatively, using an ambulatory MII–pH monitoring system (Sleuth; Sandhill Scientific INC, Highland Ranch, CO). The system included a portable data logger with impedance–pH amplifiers and a catheter with 1 antimony pH-electrode and 8 impedance electrodes at 2, 4, 6, 8, 10, 16, and 18 cm from the tip of the catheter. Each pair of adjacent electrodes represents an impedance-measuring segment (2-cm length) corresponding to 1 recording channel.

The single-use catheter was passed into the esophagus transnasally and positioned 5 cm above the proximal edge of the manometrically determined LES. The probe was calibrated in buffer solution at pH 7 and pH 1 before and after the test. Patients were encouraged to consume a normal diet during the 24-hour study, to continue normal activity, and to keep a diary of precise eating times, time spent in the upright and supine positions, and any reflux symptoms for 24 consecutive hours. The data were stored on a 128-MB Compact Flash card, downloaded to a personal computer and then analyzed using a customary reflux detection algorithm (Autoscan; Sandhill Scientific, Inc), and manually reviewed by 2 expert observers (F.R., C.G.). Reflux episodes were defined as follows: (a) liquid, as a retrograde 50% reduction in impedance starting at the level of LES and propagating to at least the next 2 more proximal impedance-measuring segments; (b) gas, as a rapid and simultaneous increase in impedance in at least 2 segments; and (c) mixed, as gas reflux episode occurring immediately before or during a liquid reflux episode. On the basis of simultaneous recording of pH values, a reflux episode was classified as acidic, with a nadir pH below 4, and weakly acidic, with a nadir pH between 4 and 7. The manual revision of combined 24-hour MII–pH monitoring identified (a) patients with acidic reflux alone if only pathological acidic reflux episodes were recorded; (b) patients with CR if both acidic and weakly acidic reflux episodes were recorded; and (c) patients with WAR if only pathological weakly acidic reflux episodes were recorded. The total number of acidic, weakly acidic, liquid, and mixed reflux episodes was calculated. Normal values for the number of total, acidic, and WAR episodes were 75, 50, and 33 for 24 hours, respectively.16 The total number of symptom episodes and the symptom index (SI), that is, the percentage of symptom episodes related to reflux, were calculated. Symptoms were defined as reflux related if the SI was more than 50%.17 The proximal extent of each single-reflux episode was measured in centimeters above the LES. The liquid component of both pure liquid and mixed reflux episodes was classified as proximal if it extended more than 15 cm above the LES, midesophageal if extended 5 to 15 cm above the LES, or distal if extended less than 5 cm above the LES.

Gastric Scintigraphy

The study was conducted in the morning after an overnight fast. Drugs that affect gastric emptying (GE), including prokinetic drugs, opiate analgesic, and anticholinergic antispasmodic agents, were stopped at least 2 days before the test. A standard test meal (282 kcal) consisting of a technetium Tc 99m sulfur colloid radiolabeled scrambled egg sandwich (2 eggs with 2 pieces of white toast) and 300 mL of water was used. All subjects were instructed to complete the intake of meal within 10 minutes. Gamma camera images were acquired using a low-energy all-purpose collimator with 20% energy window setting centered at 140 keV. Computerized digital images were required for quantification. Imaging was performed in the anterior and posterior projections at only 4 time points (0, 1, 2, and 4 hours). Between imaging sessions, the subjects were allowed to sit in a designated waiting area and to walk to and from the imaging room and the bathroom as desired. Grading for severity of DGE based on the 4-hour value in groups related to the standard deviation of the normal results was considered according to the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine Consensus Recommendations for GE scintigraphy 18: grade 1 (mild), 11% to 20% retention at 4 hours; grade 2 (moderate), 21% to 35% retention at 4 hours; grade 3 (severe), 36% to 50% retention at 4 hours; and grade 4 (very severe), more than 50% retention at 4 hours.

Surgical Technique

LTF was performed using a standard 5-trocar technique in all cases and carried out by 2 expert surgeons (M.M., F.R.) who had previously performed more than 50 laparoscopic fundoplications. A floppy 360-degree total fundoplication of 2 to 2.5 cm was constructed after full esophageal mobilization, clear identification of the vagus nerves, and posterior crural repair with nonabsorbable sutures.19

Outcome Assessment

Gastroesophageal function was assessed by clinically validated questionnaires, upper endoscopy, esophageal manometry, and 24-hour ambulatory MII–pH monitoring at 12 and 60 months after LTF. The primary end point was the long-term efficacy of LTF on reflux control in patients with WAR or mixed reflux at 24-hour esophageal MII–pH monitoring. The secondary end point was the occurrence of reflux symptoms at long-term follow-up after LTF.

Statistical Analysis

The outcome variables used to define changes in postoperative function were the scores derived from patient responses to the questionnaire items and functional data derived from esophageal manometry and 24-hour MII–pH monitoring. Quantitative data are given as mean and standard deviation, and categorical data are expressed as percentages. The $[chi]^2$ test was used to compare proportions. The Student t test was used to compare normally distributed variables. A stepwise logistic regression analysis was done to identify predictive factors of recurrent pathological reflux. The variables potentially related to recurrent pathological reflux, with $P <= 0.200$ in the univariate analysis entered into a multivariate analysis. The predictor variables used were patient age, sex, body mass index (BMI), the presence of DGE, the presence of hiatal hernia, and proximal reflux. Results are reported as odds ratio with 95% confidence intervals. All P values were 2-sided. A level of 5% was set as the criterion for statistical significance. The data were collected on an Excel spreadsheet. The statistical analysis was done using SPSS (version 19, Copyright 2000; SPSS Inc). This trial is registered with ClinicalTrials.gov (no. NCT01741441).

RESULTS

Between June 2002 and June 2007, a total of 296 patients underwent LTF for GERD. Of these, 108 patients were excluded from the study: 92 had acidic reflux, and 16 had a giant hiatal hernia.

The remaining 188 patients were included in the study (Fig. 1): 90 (48%) were men and 98 (52%) were women. Mean age was 49.3 ± 10.1 years.

The patients were divided into 2 groups according to the scintigraphic findings: 146 patients (77.7%) with normal gastric emptying (NGE group), and 42 patients (22.3%) with mild/moderate DGE (DGE group). No significant differences were observed in terms of age, sex distribution, BMI, and typical reflux symptoms between the NGE and DGE groups, whereas hoarseness and cough were more frequently reported in the DGE group ($P < 0.001$) (Table 1).

All patients were receiving proton pump inhibitor (PPI) therapy before surgery, taking 1 pill or double dose of PPI; in some cases, promotility drugs or bile acid binders and sucralfate were added. An adequate symptom control on PPIs was obtained in 98 NGE patients (67.1%) and in 6 DGE patients (14.3%) ($P < 0.001$), with early recurrence of symptoms when PPI therapy was discontinued. Four NGE patients (2.7%) and 3 DGE patients (7.1%) had previous laparoscopic cholecystectomy ($P = 0.387$).

Baseline esophageal function as defined by manometry is reported in Table 1. No differences were observed in terms of LES pressure and distal esophageal amplitude between the 2 groups of patients. Table 2 summarizes the baseline reflux profile in the study population. The rates of CR and WAR, such as the mean number of total, liquid, and mixed reflux episodes, were similar between the 2 groups. Proximal reflux was significantly more frequent among DGE patients than among NGE patients ($P < 0.001$). No conversion to open surgery and no perioperative complications occurred in both groups of patients. All patients were discharged on the second or third postoperative day.Table 2

All patients completed the follow-up protocol, including clinical and instrumental assessments, at 12 months. Five NGE patients (2.7%) died of other causes, and 11 NGE patients (5.9%) were lost to follow-up. Therefore, 172 patients (91.5%) were included in the 60-month analysis (Fig. 1).

Before surgery, the prevalence of esophagitis was similar between the 2 groups: 67 of 146 patients (45.8%) in the NGE group and 21 of 42 patients (50%) in the DGE group (P = 0.768); a small hiatal hernia was present in 72.6% of NGE patients and 73.8% of DGE patients (P = 0.967). After LTF, no differences were observed in terms of esophagitis between the 2 groups at 12- and 60-month endoscopic evaluation (11.6% vs 14.3%, P = 0.847, and 11.5% vs 16.7%, P = 0.549, respectively). Esophageal metaplasia was present in 8.2% of NGE patients (12/146) and 9.5% of DGE patients (4/42) (P = 0.963) preoperatively, and its prevalence at 5 years remained similar in both groups [8.5% (11/130) vs 9.5% (4/42), respectively] (P = 0.918).

Functional Results

Esophageal manometry values for NGE patients are reported in Figure 2. Compared with the preoperative values, esophagogastric junction (EGJ) pressure significantly increased at 12 and 60 months (P < 0.001). No differences were observed over time in terms of esophageal peristalsis amplitude. Figure 2

In this group of patients, the mean number of total reflux episodes significantly decreased at 12 and 60 months compared with preoperative evaluation (118.7 ± 7.5 vs 28.4 ± 3.1 vs 34.6 ± 3.8, P < 0.001). In particular, both liquid and mixed reflux episodes significantly reduced during the follow-up period at 12- and 60-month evaluation compared with baselines scores, regardless of the pH value (Fig. 3). There was a greater decrease in proximal reflux episodes than in distal reflux episodes at 12 and 60 months, compared with preoperative values (proximal reflux: 35.1 ± 3.1 vs 4 ± 1.2 vs 4.8 ± 1.0, P < 0.001; distal reflux: 64.4 ± 5.2 vs 20.3 ± 2.3 vs 23.2 ± 2.6, P < 0.001). The mean SI score significantly decreased at 12 and 60 months compared with the preoperative value (71.7 ± 9.8 vs 13.1 ± 3.6 vs 10.5 ± 2.7, P < 0.001). Overall, the proportion of patients with SI of more than 50% decreased from 94.5% (n = 138) preoperatively to 6.2% (n = 9) at 12 months and 9.2% (n = 12) at 60 months (P < 0.001), respectively. Figure 3

Among DGE patients, the mean EGJ pressure value significantly increased at 12 months (P < 0.001). At 60 months, it significantly decreased and returned to the baseline value in 28 patients (66.7%). Mean distal esophageal amplitude did not change significantly during the follow-up period (Fig. 2).

In DGE patients, on MII–pH monitoring, the mean total number of reflux episodes decreased significantly after 12 and 60 months compared with the preoperative values (120.5 ± 6.9 vs 58.4 ± 5.8 vs 97.6 ± 11.4, P < 0.001). We observed a significant improvement in the control of acidic reflux (both liquid and mixed) at 12 months. At 60 months, liquid acidic reflux was still well controlled, whereas the mean number of mixed acidic reflux episodes returned to the baseline (Fig. 4). Furthermore, LTF did not change the total number of WAR episodes (Fig. 4): there was no statistical difference in terms of the mean number of proximal episodes at 12 and 60 months compared with the preoperative values (14.1 ± 2.8 vs 13.7 ± 2.6 vs 14.2 ± 2.9, P = 0.682). The mean SI score was not significantly different at 12 and 60 months compared with the preoperative value (79.7 ± 10.1 vs 77.4 ± 17.5 vs 76.5 ± 18.8, P = 0.638). Overall, the percentage of patients with SI of more than 50% did not change during the follow-up period: 95.2% (n = 40) preoperatively, 90.5% (n = 38) at 12 months, and 92.9% (n = 39) at 60 months (P = 0.698).Figure 4

Clinical Results

In the NGE group, the mean GERD-HRQOL, RSI, and SF-36 scores were significantly lower at 12 and 60 months (P < 0.001) than the preoperative values (Fig. 5). In this group, 9 patients (6.2%) at 12 months and 12 patients (9.2%) at 60 months were receiving PPI therapy with adequate control of symptoms.Figure 5

In the DGE group, no differences were observed at 12 and 60 months compared with baseline values (Fig. 6). In this group, almost all patients [38 (90.5%) at 12 months and 39 (92.9%) at 60 months] were receiving medical therapy (double dose of PPI and prokinetic drugs) with partial and transient control of symptoms. Figure 6

Overall prevalence of gas bloating symptoms was 20.2% at 12 months and 25% at 60 months. In particular, it was significantly lower in NGE patients than in DGE patients (4.1% vs 76.2%, $P < 0.001$, at 12 months; 6.2% vs 83%, $P < 0.001$, at 60 months).

Univariate analysis showed that BMI of 27 kg/m^2 or more, DGE, WAR, mixed reflux, and proximal reflux were the factors significantly associated with recurrent pathological reflux. By multivariate analysis, the only factor to emerge as a significant predictor of recurrent pathological reflux was DGE (Table 3).

DISCUSSION

Antireflux surgery is a safe and effective procedure for the treatment of GERD, with excellent short- and long-term results. However, in some patients, reflux symptoms persist postoperatively despite a marked decrease in acidic reflux, and a subset of patients continue to use acid-suppressive therapy.20,21 Several studies have shown that some patients after surgery worsen or develop symptoms, including bloating, flatulence, abdominal pain, and epigastric fullness,3,20,21 with deterioration in GERD symptom control in up to 50% at long-term follow-up.21-23 The reason for this is multifactorial and related not only to the type of fundoplication performed (total vs partial) but also to several pathophysiological aspects involved in the genesis of GERD in each patient including esophageal and gastric dysmotility.

WAR is suggested to play a major role in persistent reflux complaints. To date, only few studies with limited sample sizes and short follow-up have evaluated the effect of fundoplication on WAR. The results of these studies, however, are contradictory, because some reported that fundoplication mainly controls acidic reflux with the persistence of WAR causing postoperative symptoms,6,7 whereas others demonstrated a similar reduction in both acidic and WAR episodes.4,5,8

Although severe DGE is considered a contraindication to LTF, only few retrospective studies have assessed the effect of preoperative mild/moderate DGE on long-term outcome of fundoplication for acidic reflux.23 No data are available regarding symptom and reflux control in patients with WAR and CR.

This prospective study shows that LTF reduces acidic reflux and WAR with good functional and clinical results in the long-term follow-up of NGE patients. On the contrary, functional and clinical results in DGE patients are unsatisfactory. Although the acidic component of liquid reflux episodes was well controlled at 12 and 60 months, we observed no significant changes in WAR in this group of patients. In addition, a progressive deterioration in the number of mixed acidic reflux episodes was observed, with no differences at 60 months compared with preoperative data.

Recent studies have demonstrated that proximal extent of WAR is the most important determinant of symptomatic reflux events.24,25 Others have reported that in addition to proximal extent, WAR episodes that are associated with symptoms have both gas and liquid components.26

This is the first study that demonstrates a persistent high incidence of proximal mixed WAR episodes in patients with GERD and DGE who underwent LTF. The persistence of WAR, mixed, and proximal reflux episodes in DGE patients was strongly correlated with poor control of typical and atypical symptoms at 12- and 60-month follow-up. In the NGE group, mean GERD-HRQOL, RSI, and SF-36 scores were significantly lower at 12 and 60 months ($P < 0.001$) than those at baseline, whereas no differences were observed in the DGE group. Quality of life was impaired in DGE patients because of a higher incidence of atypical symptoms as reported by worse RSI scores and abdominal symptoms. In particular, our results regarding the occurrence of gas bloating

symptoms after LTF in the whole study population compare favorably with the literature data 3; however, when analyzed separately, DGE patients showed a significantly higher rate of gas bloating symptoms than NGE patients at both short- and long-term follow-ups. Some authors 23 have proposed a pyloroplasty concomitant to LTF in patients with severe DGE to improve the GE; however, this procedure is associated with a high incidence of diarrhea, and very few data concerning GERD-related symptom control over a long follow-up period in patients with mild to moderate DGE are available.

The crucial role of DGE in long-term clinical results is confirmed by the multivariate analysis that shows that DGE is the only independent factor associated with recurrent pathological reflux. Several mechanisms may explain the differences observed after LTF between the 2 groups of patients included in this study in terms of functional and clinical results. For instance, the compliance of the proximal stomach after total fundoplication in GERD patients with NGE has been demonstrated to be similar to healthy volunteers.27,28 On the contrary, DGE is associated with proximal gastric distension and low compliance of the stomach.9 The fundal wrap that is not able to accommodate to intragastric pressure increments in DGE patients 9 in our series controls only the acidic component of refluxate in the short-term period whereas it is ineffective in controlling WAR.

In the absence of specific studies on this topic, we hypothesize that different chemical and physical properties of weakly acidic refluxate in the presence of DGE may be responsible for the poor outcome related to the persistent WAR observed after LTF.

In addition, the chronic distention of the gastric cavity secondary to DGE may be a critical factor for the progressive reduction of EGJ pressure over time after LTF. We found significantly increased EGJ pressure in NGE patients during the follow-up period compared with preoperative values, whereas it returned to the baseline value in 66.7% of DGE patients at 60-month manometric evaluation.

CONCLUSIONS

Our study clearly shows that mild/moderate DGE is a frequently occurring condition associated with WAR and CR and that it is an independent risk factor for poor outcome after LTF in terms of both reflux and symptom control.

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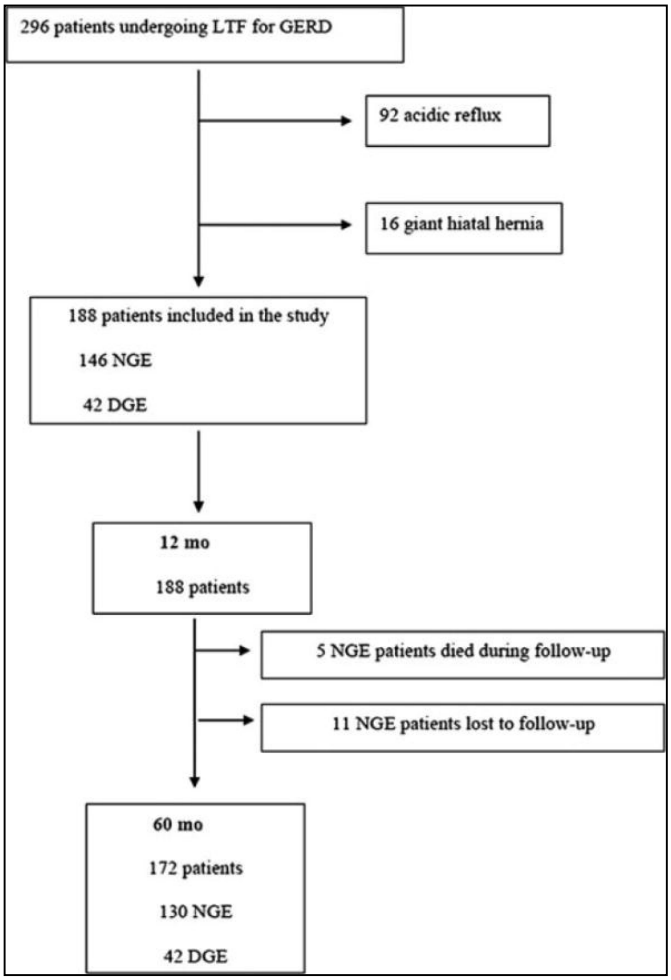

FIGURE 1 . Study design.

	NGE (n = 146)	DGE (n = 42)	*P*
Age, yr	48.2 ± 10.1	49.6 ± 11.6	0.445
Sex (males), n (%)	70 (47.9)	20 (47.6)	0.890
BMI, kg/m^2	27.5 ± 1.5	27.9 ± 1.7	0.141
Hiatal hernia, n (%)	106 (72.6)	31 (73.8)	0.967
Typical symptoms, n (%)			
Heartburn	112 (76.7)	37 (88)	0.165
Regurgitation	135 (92.4)	38 (90)	0.923
Dysphagia	12 (8.2)	4 (9.5)	0.963
Atypical symptoms, n (%)			
Hoarseness	38 (26)	27 (64.2)	<0.001
Cough	17 (11.6)	15 (35.7)	<0.001
Chest pain	39 (26.7)	12 (28.5)	0.967
LES pressure, mm Hg	8.4 ± 3.3	7.8 ± 3.3	0.300
Distal esophageal amplitude, mm Hg	76.1 ± 28.1	76.5 ± 30.4	0.936

Values are given as mean ± SD unless indicated otherwise.

TABLE 1 . Preoperative Data

	NGE (n = 146)	DGE (n = 42)	*P*
Patients with combined reflux, n (%)	133 (91)	34 (81)	0.118
Patients with WAR, n (%)	13 (9)	8 (19)	
Total reflux episodes	118.7 ±7.5	120.5 ± 6.9	0.165
Acidic	82.2 ± 5.4	81.2 ± 4.5	0.275
Weakly acidic	36.5 ± 4.1	39.3 ± 4.2	0.214
Liquid reflux	76.8 ± 4.1	77.9 ± 3.9	0.123
Acidic	63.7 ± 3.5	63.2 ± 3.7	0.872
Weakly acidic	13.1 ± 2.1	14.7 ± 2.3	0.112
Mixed reflux	41.9 ± 2.9	42.6 ± 3.7	0.270
Acidic	20.5 ± 2.1	20.1 ± 3.3	0.346
Weakly acidic	21.4 ± 2.4	22.5 ± 2.2	0.809
Patients with proximal reflux, n (%)	38 (26.1)	32 (76.1)	<0.001
Patients with distal reflux, n (%)	108 (73.9)	10 (23.9)	

Values are given as mean ± SD unless indicated otherwise.

TABLE 2 . Reflux Profile in NGE and DGE Patients

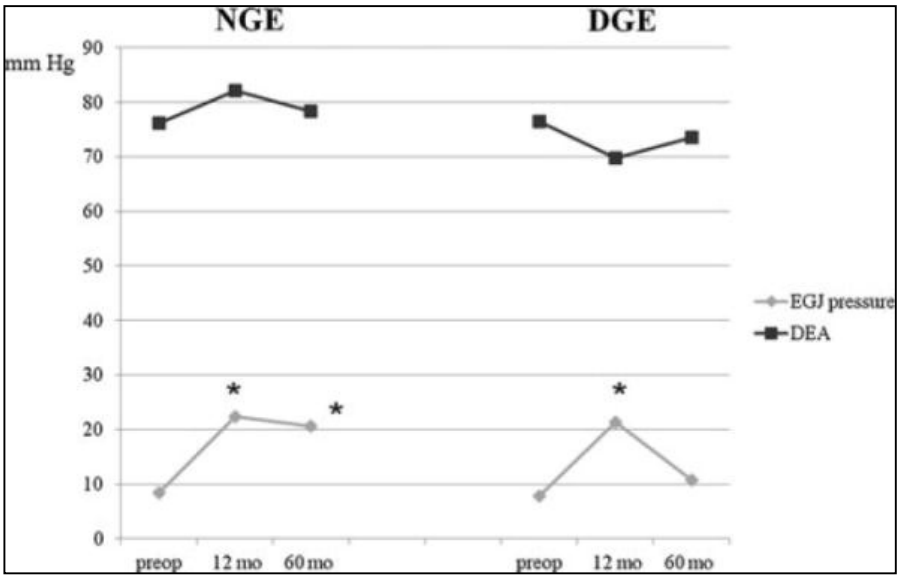

FIGURE 2 . Manometric findings before and after LTF in NGE patients versus DGE patients. preop indicates preoperatively. *P < 0.001 compared with preoperative values.

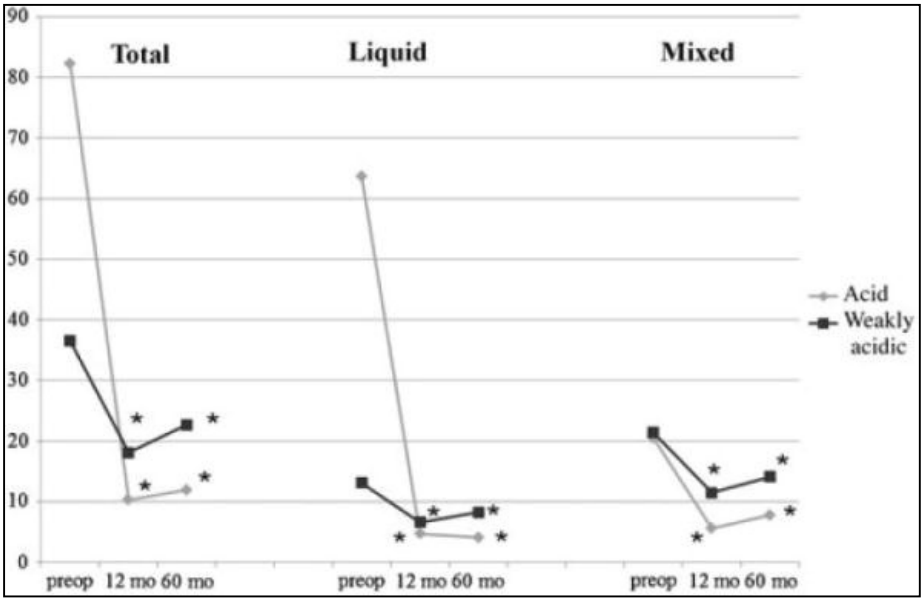

FIGURE 3 . Mean number of reflux episodes at 24-hour MII-pH monitoring before and after LTF in NGE patients. preop indicates preoperatively. *P < 0.001 compared with preoperative values.

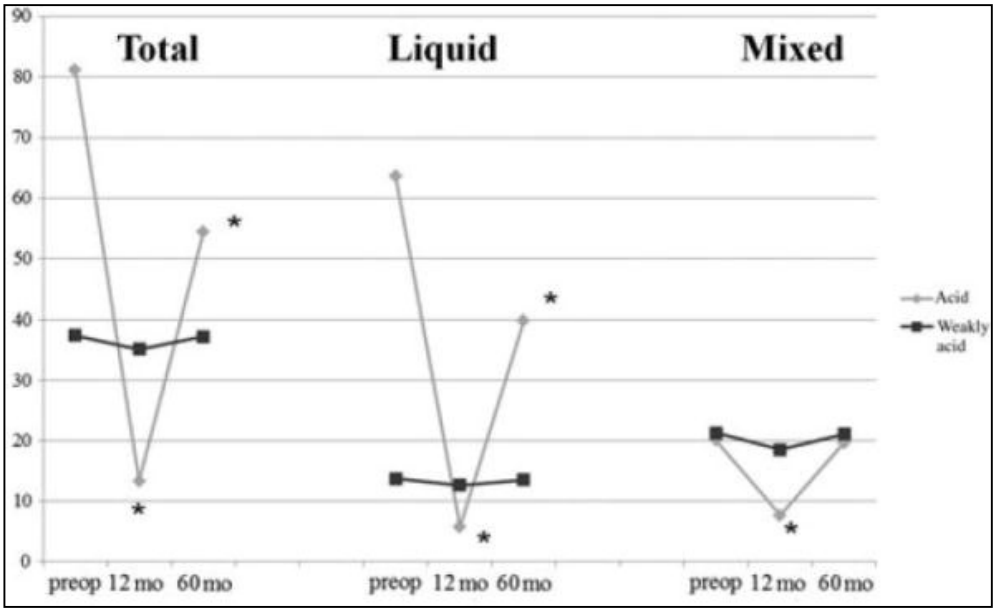

FIGURE 4 . Mean number of reflux episodes at 24-hour MII-pH monitoring before and after LTF in DGE patients. preop indicates preoperatively. *P < 0.001 compared with preoperative values.

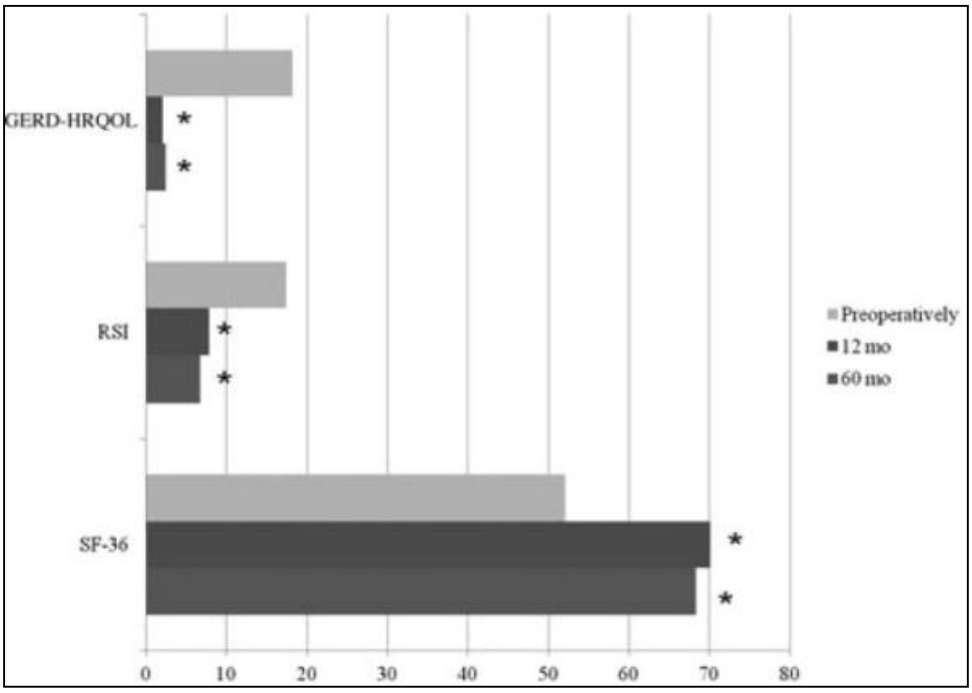

FIGURE 5 . Reflux symptoms and quality of life before and after LTF in the NGE group. *P < 0.001 compared with preoperative values.

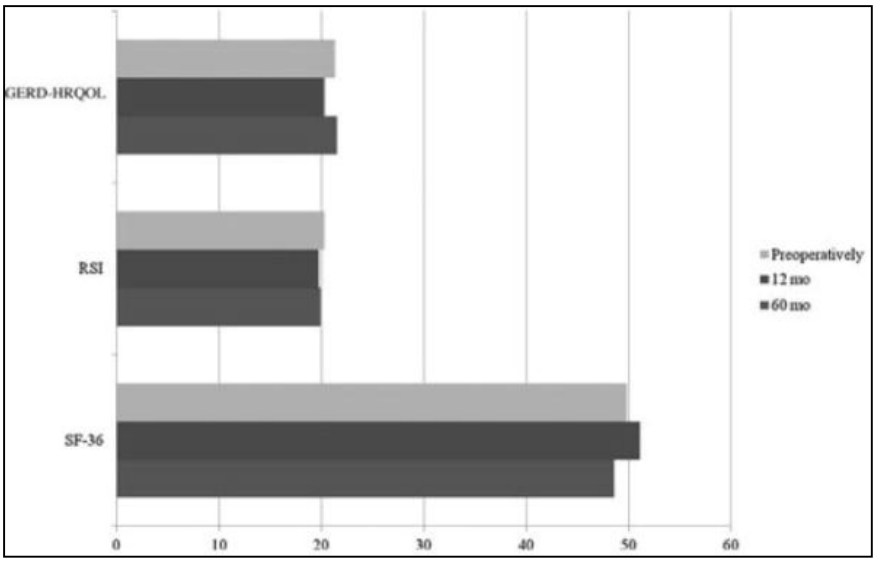

FIGURE 6 . Reflux symptoms and quality of life before and after LTF in the DGE group.

	Univariate Analysis		Multivariate Analysis	
Variable	**Odds Ratio**	***P***	**Odds Ratio**	***P***
Age, yr				
≤50	1	0.643		
>50	2.04 (0.54–3.27)			
Sex				
Male	1	0.788		
Female	1.30 (0.61–1.85)			
BMI, kg/m^2				
<27	1	0.020	1	0.332
≥27	3.15 (1.87–5.05)		1.88 (0.87–4.67)	
DGE				
No	1	0.010	1	0.030
Yes	6.25 (3.48–10.12)		4.13 (2.09–11.01)	
Hiatal hernia				
No	1	0.887		
Yes	1.51 (0.45–1.67)			
WAR				
No	1	0.041	1	0.145
Yes	2.88 (1.77–5.88)		1.79 (0.81–3.14)	
Mixed reflux				
No	1	0.038	1	0.176
Yes	2.77 (1.69–4.58)		1.83 (0.76–3.84)	
Proximal reflux				
No	1	0.035	1	0.241
Yes	2.25 (1.69–3.15)		1.66 (0.77–3.71)	

Values in parentheses are 95% confidence intervals.

TABLE 3 . Risk Factors for Recurrent Pathological Reflux