

# Conventional versus robot-assisted laparoscopic Nissen fundoplication: a comparison of postoperative acid reflux parameters

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## Abstract

**Background** Laparoscopic Nissen fundoplication (LNF) is a technically demanding surgical procedure designed to cure gastroesophageal reflux disease (GERD). It represents an alternative to life-long medical therapy and the only recommended treatment modality to overcome refractoriness to proton pump inhibitor (PPI) therapy. The recent development of robotic systems prompted evaluation of their use in antireflux surgery. Between 1997 and 2000, in a PPI-responsive series we found postoperative normalization of esophageal acid exposure time (EAET) in most but not all cases. Between 2007 and 2009, in a PPI-refractory series we found postoperative normalization of EAET in all cases. We decided to analyze retrospectively our prospectively collected data to evaluate whether differences other than the conventional or robot-assisted technique could justify postoperative differences in acid reflux parameters. **Methods** Baseline demographic, endoscopic, and manometric parameters were compared between the two series of patients, as well as postoperative manometric and acid reflux parameters.

**Results** There were no significant differences in the baseline demographic, endoscopic, and manometric

characteristics between the two groups of patients. The median lower esophageal sphincter tone increased significantly, and the median EAET decreased significantly after conventional as well as after robot-assisted LNF. The median postoperative EAET was significantly lower in the robot-assisted (0.2%) than in the conventional LNF group (1%;  $P = 0.001$ ). Abnormal EAET values were found in 6 of 44 (14%) and in 0 of 44 cases after conventional and robot-assisted LNF, respectively ( $P = 0.026$ ).

**Conclusions** Robot-assisted LNF provided a significant gain in postoperative acid reflux parameters compared with the conventional technique. In a challenging clinical setting, such as PPI-refractoriness, in which the efficacy of endoscopic or pharmacological treatment modalities is only moderate, even a small therapeutic gain can be clinically relevant. In centers where robot-assisted LNF is available, it should be preferred to conventional LNF in PPI-refractory GERD.

**Keywords** GERD · GORD · Laparoscopic Nissen fundoplication · Robotic surgery

Gastroesophageal reflux disease (GERD) has been defined as symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus [1]. Due to outstanding efficacy in intraesophageal acid suppression, proton pump inhibitor (PPI) therapy represents the mainstay of medical treatment for GERD, providing the most rapid symptomatic relief and healing reflux esophagitis in the highest percentage of patients [1]. However, in recent years, it has been increasingly recognized that PPIs fail to completely eliminate symptoms attributed to GERD in up to 40% of patients [2].

Laparoscopic Nissen fundoplication (LNF) is an anti-reflux surgical procedure designed to cure GERD. It has

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been shown to represent an effective alternative to life-long medical therapy in PPI-responsive GERD patients [3]. However, LNF is a technically demanding procedure with well-recognized side effects, and many authorities recommend to confine it to patients with troublesome reflux symptoms persisting despite PPI therapy, i.e., to patients with PPI-refractory GERD [4, 5].

In recent years, robotic systems have been designed to improve dissection and suturing in relatively small, confined spaces, such as the gastroesophageal junction. They have been shown to improve intracorporeal suturing performance and safety in the operating room [6] and have been recently proposed for single-trocar access LNF [7]. In a recent review, no differences have been detected between robot-assisted and conventional LNF with respect to surgery time, length of hospital stay, complications, or rate of conversion to open surgery [8], but postoperative acid reflux parameters have been compared in two relatively small series only [9, 10].

Between 1997 and 2000, we prospectively assessed before and after intervention a selected series of PPI-responsive GERD patients who requested to undergo laparoscopic fundoplication and found normalization of the esophageal acid exposure time (EAET) at postoperative pH-metry in most but not all patients [11]. Between 2007 and 2009, we prospectively evaluated before and after intervention a selected series of PPI-refractory GERD patients undergoing robot-assisted LNF and found normalization of the postoperative EAET in all cases [12]. These differences in postoperative results prompted us to analyze retrospectively prospectively collected data from GERD patients who underwent LNF at our center to evaluate whether differences other than the laparoscopic technique (conventional or robot-assisted) could justify different postoperative results in terms of acid reflux control.

## Patients and methods

We prospectively studied adult patients referred to our center because of troublesome heartburn/regurgitation, responsive to PPI therapy in the conventional LNF series and refractory to at least 4-week high-dosage PPI therapy in the robot-assisted LNF series, respectively. Patients in the conventional LNF series were studied after an adequate washout period (at least 30 days) of antisecretory drugs (PPIs and H<sub>2</sub>-receptor antagonists) during which antacids (magaldrate or aluminum/magnesium hydroxide) were allowed. In the robot-assisted LNF series, patients were studied on double-dose of their particular PPI at the time of enrolment.

In both series, patients requested to undergo LNF after receiving comprehensible and detailed explanations. Both

study protocols were conducted according to the Declaration of Helsinki and were approved by our institutional review board. A written, informed consent was obtained by all patients.

The severity of symptoms was rated by means of a validated reflux/dyspepsia questionnaire, based on a standard four-grade, Likert-type scale scoring system [11, 13]. Patients were asked to refer to the last month. Symptoms were graded as follows: 0 = none; 1 = mild/occasional, symptom could be ignored; 2 = moderate/frequent, symptom could not be ignored, but neither daily activities nor sleep were influenced; 3 = severe/constant, symptom influenced daily activities and/or sleep. Symptoms of the typical reflux syndrome (heartburn and regurgitation) were assessed, as well as dysphagia, chest pain, and dyspeptic symptoms (belching, early satiety, postprandial fullness, epigastric pain/burn, vomiting, and epigastric bloating). Symptoms were considered clinically relevant when the score was >1. A heartburn/regurgitation score of at least 2 was required for enrollment.

Standardized criteria were adopted to evaluate and report endoscopic esophageal abnormalities. Reflux esophagitis was defined by the presence of at least one mucosal break in the distal esophagus. Hiatal hernia was considered to be present when the distance between the gastroesophageal junction and the diaphragmatic impression was >2 cm on withdrawing the endoscope.

Traditional pH-metry is still regarded as the standard diagnostic tool for diagnosing GERD in patients off PPI therapy [2] and was utilized in the PPI-responsive series evaluated between 1997 and 2000. Impedance-pH monitoring is considered the most sensitive diagnostic tool for establishing a cause-and-effect relationship between PPI-refractory symptoms and reflux in patients on PPI therapy [2] and was utilized in the PPI-refractory series evaluated between 2007 and 2009. For the purposes of this study, we compared acid reflux parameters between the two series only after intervention, as both traditional pH-monitoring and impedance-pH monitoring were performed off PPI therapy postoperatively and both allow assessment of EAET. Reflux monitoring studies before intervention were not compared, because they were performed off PPI therapy in the conventional and on PPI therapy in the robot-assisted LNF series, respectively.

## Esophageal manometry

Standard esophageal manometry was performed before and 3 months after interventions (MF). The station pull-through method was used to locate the lower esophageal sphincter (LES). Briefly, an 8-channel, water-perfused manometry catheter was placed nasally into the stomach

and slowly withdrawn. The LES was identified and then, at each 0.5-cm station, the resting pressure was measured at the end of expiration and the relaxation was assessed with wet swallows. Esophageal body peristalsis was assessed and pressures measured with at least 10 wet swallows. The upper esophageal sphincter was finally identified and the catheter was removed. All manometric data were processed by using the Polygram module (Medtronic Functional Diagnostics A/S, Tonsbakken, Denmark) to obtain the mean LES tone and the mean distal esophageal amplitude (DEA). LES hypotension was defined by a basal LES tone <10 mmHg, and defective peristalsis was defined as a mean DEA <30 mmHg, according to standard criteria [14].

### Reflux monitoring

In the conventional LNF series, patients underwent a traditional ambulatory pH-metry before intervention, in the absence of any acid suppressive therapy from at least 1 month, and 3 months after intervention, in the absence of any acid suppressive therapy from at least 1 month (MF). In the robot-assisted LNF series, impedance-pH monitoring was performed on high-dose PPI therapy before surgical intervention, and 3 months after intervention in the absence of any acid suppressive therapy from at least 1 month (MF). A pH-metry or impedance-pH monitoring catheter, respectively, was passed nasally such that an antimony pH electrode was placed 5 cm above the manometrically defined LES upper border. Patients were discharged and encouraged to maintain normal activities, sleep schedule, and eat their usual three meals at their normal times. They were asked to remain upright during the day and lie down only during their usual nocturnal bedtime. Patients returned to the lab the following day for catheter removal and data review. Tracings were analyzed by automated plus visual analysis. Acid reflux was considered to take place when pH dropped below 4.0. The esophageal acid exposure time (EAET) was calculated for the total study period with commercial analysis software (Polygram module, Medtronic Functional Diagnostics A/S, Tonsbakken, Denmark; Bioview Analysis, Sandhill Scientific, Inc.; Highland Ranch, CO), the upper normal limit was considered 5.8% according to standard criteria [15]. The symptom association probability (SAP) and the symptom index (SI) also were calculated. A positive SAP was defined by 95% or more of symptoms associated with reflux. A positive SI was defined by 50% or more of symptoms associated with reflux. A negative SAP was defined by less than 95% of symptoms associated with reflux. A negative SI was defined by less than 50% of symptoms associated with reflux.

### Indications for surgery

The conventional LNF series consisted of patients with PPI-responsive heartburn who requested to undergo anti-reflux surgery because of concerns about chronic medication use. GERD had been diagnosed on the basis of reflux esophagitis detected at endoscopic examination and/or abnormal pH-metric findings [11]. Data from patients who underwent a partial posterior Toupet fundoplication on account of defective peristalsis (11 cases) were excluded from the present analysis. Scleroderma esophagus represented exclusion criteria.

The robot-assisted LNF group consisted of an extension of a recently published series of patients with heartburn/regurgitation persisting despite high-dose PPI therapy [12]. GERD had been diagnosed on the basis of reflux esophagitis detected at endoscopic examination and/or abnormal impedance-pH monitoring findings. Scleroderma esophagus but not defective peristalsis was an exclusion criterion.

### Surgical intervention

All procedures were performed laparoscopically by a senior surgeon (GM) beyond the learning curve for both the techniques. For the conventional LNF group, a floppy 360° Nissen fundoplication of 2.5–3 cm was constructed after full esophageal mobilization and posterior crural repair with nonabsorbable sutures. The wrap was not anchored to the crura. The robot-assisted LNF was performed identically to the conventional technique with the support of the Da Vinci surgical system (Intuitive Surgical, Goleta, CA). The robotic instruments were controlled by the senior surgeon from behind the console and a tableside assistant (GC) was responsible for changing instruments, retraction, suction, and passing sutures into the abdomen.

To ensure that the completed fundoplication was tension-free, a 52-Fr bougie was routinely inserted into the esophagus during construction of the wrap in the conventional as well as in the robot-assisted procedures.

### Outcome assessment

Endoscopy was scheduled only for postoperative severe symptoms (score = 3) reported at monthly-settled telephonic contact. Postoperative evaluation was scheduled 3 months after intervention, in the absence of any acid-suppressive therapy during the last month. It consisted of questionnaire administration, esophageal manometry, and pH monitoring or impedance-pH monitoring (MF). Six-month follow-up visits with questionnaire administration were scheduled for patients complaining of residual

relevant symptoms (score = 2). Patients rated their symptoms with reference to the last month as described previously and returned the questionnaire only after the visual analysis of the pH or impedance-pH tracing (MF) had been completed. Total symptom remission was defined by a score = 0 for heartburn and regurgitation. Subtotal symptom remission was defined by a score = 1 if the score for that particular symptom before intervention was = 3. Partial symptom remission was defined by a score = 1 if the presurgical score was = 2 or by a score = 2 if the score before intervention was = 3.

### Statistics

For the continuous variables, the Mann–Whitney and the Wilcoxon test for unpaired and paired data, respectively, were adopted. For the categorical variables, the Fisher's exact test was used.  $P < 0.05$  was considered significant.

### Results

The conventional LNF group consisted of 44 patients who underwent intervention between June 1997 and November 2000. The robot-assisted LNF group consisted of 44 patients who underwent intervention between June 2007 and December 2009. The main baseline characteristics before intervention, including endoscopic and manometric findings did not differ between the two groups (Table 1). One patient in the robot-assisted LNF group had defective esophageal peristalsis.

In both series, median hospital stay was 4 days, with ranges 3–6 days for the conventional LNF group and 2–5 days for the robot-assisted LNF group ( $P =$  not significant [NS]). Postoperative manometric and pH-metric findings are reported in Table 2.

**Table 1** Patient characteristics before intervention

	Conventional LNF (44 patients)	Robot-assisted LNF (44 patients)	<i>P</i>
Age (median) (IQR)	49 (39–51)	42 (32–56)	NS
Males/females (%)	26/18 (59)	28/16 (63)	NS
Reflux esophagitis (%)	29/44 (66)	19/44 (43)	NS
Hiatal hernia (%)	34/44 (77)	30/44 (68)	NS
LES tone (mmHg) (median) (IQR)	18 (8–22)	15 (9–21)	NS
DEA (mmHg) (median) (IQR)	79 (51–99)	87 (53–106)	NS

LNF laparoscopic Nissen fundoplication, LES lower esophageal sphincter, DEA distal esophageal amplitude, IQR interquartile range

After intervention, the median LES tone increased significantly in the conventional LNF group as well as in the robot-assisted LNF group ( $P = 0.023$  and  $P = 0.001$ , respectively), whereas no significant variation in the median DEA was detected.

In the conventional LNF group, the median EAET after intervention (1%, off PPI therapy) was significantly lower than before intervention (17%, off PPI therapy) ( $P = 0.001$ ) but higher than normal postoperative EAET values were found in 6 of 44 (14%) patients and lower than before intervention in 3 of 6 cases. In the robot-assisted LNF group, the median EAET after intervention (0.1%, off PPI therapy) was significantly lower than before intervention (1%, on PPI therapy;  $P = 0.001$ ) and normal postoperative values were found in all patients.

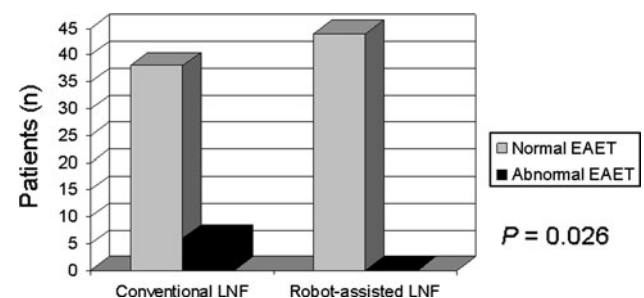
Comparing the results observed after intervention between the two series (Table 2), no significant differences in manometric parameters were detected, whereas the median EAET was significantly lower after robot-assisted than after conventional LNF. Moreover, a normal EAET was significantly less frequently observed after conventional LNF than after robot-assisted LNF (86% vs. 100%;  $P = 0.026$ ; Fig. 1).

**Table 2** Manometric and pH-metric findings after intervention

	Conventional LNF (44 patients)	Robot-assisted LNF (44 patients)	<i>P</i>
LES tone (mmHg) (median) (IQR)	23 (15–30)	21 (15–26)	NS
DEA (mmHg) (median) (IQR)	71 (49–103)	87 (46–114)	NS
%EAET (median) (IQR)	1.0 (0.3–4.0)	0.2 (0–0.4)	0.001

Values expressed as median (interquartile range)

LNF laparoscopic Nissen fundoplication, LES lower esophageal sphincter, DEA distal esophageal amplitude, IQR interquartile range



**Fig. 1** Normal values of EAET after conventional and robot-assisted LNF. EAET esophageal acid exposure time; LNF laparoscopic fundoplication

In the conventional LNF group, total/subtotal remission of heartburn and regurgitation was reported by all patients. At the 3-month follow-up visit, persistent moderate epigastric bloating (score = 2) was reported by nine patients, in three of whom associated with belching (score = 2) and in two of whom with early satiety (score = 2); dyspeptic symptoms persisted (score = 2) at the 6-month follow-up visit in all nine patients.

In the robot-assisted LNF group, severe intractable dysphagia with inability to eat solid food was reported by two patients in the early postoperative period (one of the two was the patient with defective peristalsis) ( $P = \text{NS}$  vs. the conventional LNF group). They were successfully treated with a single-session endoscopic dilation (RC). Postoperative total/subtotal symptom remission of heartburn and regurgitation was reported by 43 of 44 patients. One patient still complained of heartburn (score = 2) at 3-month follow-up but impedance-pH monitoring findings were normal, including a negative SI and a negative SAP: reflux-unrelated (functional) heartburn (2) was diagnosed, persisting at the 6-month follow-up visit. Moderate dysphagia (score = 2) was reported by one patient at 3-month follow-up: as normal postoperative manometric findings were found and food intake was not impaired, the patient was reassured and at the 6-month follow-up visit dysphagia improved (score = 1). Two patients complained of belching (score = 2) and three patients of epigastric bloating (score = 2;  $P = \text{NS}$  vs. the conventional LNF group), in two of whom associated with early satiety (score = 2) and in one of whom associated with belching (score = 2); dyspeptic symptoms persisted (score = 2) at the 6-month follow-up visit in 3 patients ( $P = \text{NS}$  vs. the conventional LNF group).

## Discussion

In this retrospective analysis of prospectively collected data, better postoperative results in terms of acid reflux control were found after robot-assisted than after conventional LNF. The median EAET was significantly lower and a normal EAET was significantly more frequently found after the robot-assisted than after the conventional technique.

Biases related to the retrospective nature of a case-control study are difficult to eliminate. However, the main baseline demographic, endoscopic, and manometric characteristics of the two series were comparable. The conventional LNF group consisted of 44 cases, because patients with defective esophageal peristalsis were excluded from the original series of 55 cases [11], because they underwent a partial posterior Toupet fundoplication, according to the old concept of a “tailored” antireflux

surgical technique [16]. After the study by Fibbe et al. [17], which did not support the concept that the type of antireflux procedure should be tailored based on preoperative motility findings, we adopted from 2002 the floppy 360° Nissen fundoplication as the routine antireflux procedure at our center, even in patients with defective esophageal peristalsis. Only one patient in the robot-assisted LNF group had preoperative defective peristalsis. The overall incidence of postoperative dysphagia in our series was lower than that reported in a recent systematic review [18] and did not significantly differ between the two groups of patients. We compared postoperative results between the two series by means of objective criteria, i.e., the EAET, which is the most useful parameter for the analysis and interpretation of esophageal pH-metry [19] and provides a clear-cut differentiation of GERD patients from controls [20, 21]. The diagnostic tool adopted to evaluate postoperatively the conventional and robot-assisted LNF series was represented by traditional pH-monitoring and impedance-pH monitoring, respectively, but acid reflux parameters were assessed in the same manner (EAET) and therefore data can be compared.

The baseline characteristics of the two groups of patients were quite similar with the only notable exception of indications for laparoscopic fundoplication. GERD is a chronic disease and indications for surgery are an area of controversy, mainly because data concerning long-term efficacy are scanty [3]. Recently, 10-year follow-up studies showed high efficacy of laparoscopic antireflux surgery in terms of symptoms [22] and also acid reflux control [23] in patients with typical reflux symptoms responsive to PPI therapy. Currently, however, PPI-resistant heartburn/regurgitation represent the most demanding clinical problem in GERD: it is the most common presentation of reflux syndromes in third referral gastrointestinal practices [2], and according to the American Gastroenterological Association, it should be considered the main indication for antireflux surgery [4]. Refractory GERD is therefore a challenging clinical setting [5], whereas PPI-responsive patients are well-recognized optimal surgical candidates [24, 25]. Therefore, the better results that we observed in the robot-assisted LNF series cannot be attributed to a selection bias.

Our retrospective analysis of postoperative pH-metric results after robot-assisted and conventional LNF are at variance with those reported in a previous study in which 25 patients treated with conventional LNF were compared with 25 patients treated with robot-assisted LNF [9]; similar postoperative pH-metric results were found in the two groups of patients in that study but it was powered to detect a 35% difference and the two surgical procedures were performed by seven surgeons. In another study, 50 patients underwent conventional or robot-assisted LNF performed

by three expert surgeons; again, nonsignificant differences were found in the postoperative pH-metric parameters between the two groups of patients [10]. In our study, all 88 surgical procedures were performed by the same surgeon who adopted the same surgical technique with the only exception of the support of the Da Vinci instrument in the robot-assisted series. We found normal postoperative values of EAET significantly more frequently in the robot-assisted (100%) than in the conventional (86%) LNF group, a result confirmed by a slightly but significantly lower median EAET in the former. Such a modest therapeutic gain in pH-metric parameters after robotic LNF could have been undetected in previous studies in which fewer patients were evaluated. Our results after conventional LNF met a high standard as the median postoperative EAET that we found (1%) was the same detected in a larger series at a tertiary center [26].

The potential advantages of the Da Vinci surgical system over conventional laparoscopic surgery include greater precision due to anti-tremble filter, better vision due to three-dimensional imaging of the surgical field, and reduced bleeding [8]. Taken together, these advantages can explain our slightly but significantly better results after robot-assisted LNF in terms of postoperative acid reflux control. Currently, antireflux surgery is mainly advised for PPI-refractory GERD patients [4, 5]. The efficacy of endoscopic [27] or pharmacological [28] treatment modalities is only moderate in the clinical setting of PPI resistance. GERD is due to abnormal reflux of gastric contents into the esophagus [1] and even a 14% gain in normalization of postoperative acid reflux parameters provided by the robot-assisted over the conventional LNF technique can be clinically relevant for PPI-unresponsive patients. We conclude that in centers where robot-assisted LNF is available, it should be preferred to the conventional technique in PPI-refractory GERD.

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