

Endoscopic full-thickness plication versus laparoscopic fundoplication: a prospective study on quality of life and symptom control

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Abstract

Background Endoscopic antireflux techniques have emerged as alternative therapies for gastroesophageal reflux disease (GERD). Endoscopic plication receives continuing interest as an effective and safe procedure. This treatment option has not been the subject of comparison with well-established operative therapies to date. The present study aimed at comparatively evaluating the effectiveness of endoscopic plication and laparoscopic fundoplication in terms of quality of life and symptom control.

Methods Between October 2006 and April 2010, 60 patients with documented GERD were randomly assigned to undergo either endoscopic plication or laparoscopic fundoplication. Quality-of-life scores and symptom grading were recorded before treatment and at 3- and 12-month

follow-up. Outcomes were compared with the statistical significance set at a p value of 0.05.

Results Twenty-nine patients from the endoscopic group and 27 patients from the operative group were available at follow-up. Quality-of-life scores showed a substantial and similar increase for both groups after treatment. Symptoms of heartburn ($p < 0.02$), regurgitation ($p < 0.004$), and asthma ($p = 0.03$) were significantly improved in the endoscopic group, whereas laparoscopic fundoplication was more effective in controlling symptoms of heartburn ($p < 0.01$) and regurgitation ($p < 0.05$) compared to the endoscopic procedure.

Conclusions Endoscopic plication and laparoscopic fundoplication resulted in significant symptom improvement with similar quality-of-life scores in a selected patient population with GERD, whereas operative treatment was more effective in the relief of heartburn and regurgitation at the expense of higher short-term dysphagia rates.

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Laparoscopic fundoplication is considered the gold standard operative treatment for gastroesophageal reflux disease (GERD) [1, 2]. Since the early 1990s, several studies have validated this treatment option and have demonstrated its safety and efficacy with regard to long-term symptom control and healing esophagitis [3, 4]. Although a popular procedure, laparoscopic fundoplication is often accompanied by short- and mid-term adverse effects, including bloating sensation, dysphagia, and diarrhea. These symptoms usually improve or resolve within the first postoperative year; however, they may result in significant

reduction of the quality of life [5]. In case of symptom persistence, exhaustive diagnostic studies can be undertaken to exclude hernia recurrence and to elucidate the etiology of the symptoms. Conservative and interventional therapeutic measures often prove disappointing [6, 7].

Endoscopic antireflux techniques have emerged during the last decade, providing a nonoperative alternative to the armamentarium of surgeons and endoscopists for the treatment of GERD. These techniques include (1) radio-frequency thermal application at the gastroesophageal junction (Stretta System, Mederi Therapeutics, Inc., Greenwich, CT), (2) plication or sewing of the gastroesophageal junction or the cardia (NDO Plicator, NDO Surgical, Inc., Mansfield, MA; EndoCinch, CR Bard, Inc., Murray Hill, NJ), and (3) injection of biopolymers at the gastroesophageal junction (Enteryx, Boston Scientific Corporation, Natick, MA; Gatekeeper, Medtronic Foundation, Minneapolis, MN; Plexiglas).

Several devices have been abandoned due to lack of efficacy, and most endoscopic implants have been withdrawn from the market due to safety concerns [8]. Of the available devices, endoscopic full-thickness plication of the cardia continues to receive interest [8, 9] because of the documented safety of the technique and the long-term improvement in the quality of life [10]. Furthermore, this treatment option has been showed to eliminate the need for maintenance antacid therapy in a large proportion of patients [11]. Along with subjective symptom improvement, endoscopic plication seems to also improve objective evidence of reflux [12].

A direct comparison between endoscopic plication and operative modalities for the treatment of GERD has not been undertaken to date. The objective of the present study was to evaluate the effect of endoscopic full-thickness plication and laparoscopic fundoplication on quality of life and reflux symptoms in a selected group of patients with documented GERD.

Patients and methods

Between October 2007 and June 2010, a total of 60 patients with GERD were randomly assigned to undergo either endoscopic full-thickness plication or laparoscopic fundoplication. Primary outcome measures were improvement of quality-of-life and symptom scores.

Study design

Adult patients referred to the Surgical Department of the General Community Hospital Zell am See, Zell am See, Austria, with the clinical diagnosis of GERD were considered for inclusion. The patients underwent a series of

diagnostic studies, including gastroscopy, barium esophagography, esophageal manometry, and esophageal multi-channel intraluminal impedance testing. Participants had to meet the following criteria: at least one typical reflux symptom (heartburn, regurgitation, or epigastric pain) and pathologic esophageal acid exposure as documented by a reflux-related DeMeester score ≥ 14.7 or symptom correlation $\geq 50\%$ or reflux episodes >73 . Patients with endoscopic or imaging evidence of hiatal hernia measuring more than 2 cm, paraesophageal hernia, or previous esophageal or gastric surgery were excluded.

Study participants were randomly assigned to undergo either endoscopic plication or laparoscopic fundoplication. A double-blind study was not planned and the patients were fully informed on the intended treatment method. Informed consent for participation in the study was obtained from all patients. All endoscopic and surgical procedures were performed by the same surgical team. Study approval was obtained from the institution's ethical committee.

Technique of endoscopic plication

Endoscopic plication was performed in the operative theatre with the patient under general endotracheal anesthesia. During standard gastroscopy, a Savary spring-tipped guidewire (Wilson-Cook Medical, Inc., Salem, NC) was introduced through the working tube and advanced to the gastric corpus. The gastroscope was then removed and the guidewire was left in place. A 45F endoscopic plicating device (NDO Surgical, Mansfield, MA) was threaded over the guidewire until its tip had reached the stomach (Fig. 1). A pediatric 5.8-mm endoscope was passed through the plicating device into the stomach and retroflexed to allow visualization of the gastric cardia. The following steps were performed under direct visualization. The plicating device was retroflexed and its arms were opened. A screwlike particle, originating from the center of the tip (Fig. 2), was advanced through all gastric layers of the cardia, 2–3 cm anterior to the gastroesophageal junction. This particle with the attached gastric wall was then retracted and the arms of the device were closed, thus grasping a part of the gastric cardia. The device was then fired and the pretied 2-0 polypropylene sutures were applied on the enclosed gastric wall and were left in place between pledgets. An additional suture was placed in the same manner, distal to the first suture. A standard control gastroscopy completed the procedure.

Technique of laparoscopic fundoplication

Patients were placed in the supine split-leg reverse Trendelenburg position. The procedure was performed using a



Fig. 1 The plicating device is threaded over the guidewire



Fig. 2 Screwlike particle at the center of the device for retraction of a full-thickness portion of the cardia

five-port technique with the surgeon standing between the patient's legs. After application of pneumoperitoneum using a Veress needle, the lesser omentum was incised up to the right crural bundle with an ultrasonic scalpel. The right crus was then exposed by blunt dissection. The phrenoesophageal ligament was incised anterior to the esophagus with direction to the left crus. The latter was then dissected free in the same manner. At this point, the short gastric vessels were divided to allow gastric mobilization and access to the left crural bundle. Dissection was continued dorsal to the esophagus and circumferentially toward the mediastinum. After 2–4 cm of esophageal length had been obtained within the abdomen without traction, the retroesophageal window was further widened by dividing gastric attachments to the retroperitoneum. The crural bundles were then approximated behind the esophagus with two or three 2-0 braided synthetic polyester sutures. If the hiatal closure was considered loose, an additional suture was placed anterior to the esophagus. A fundic 2-0 monofilament polypropylene suture served as an attachment to the left crural bundle. A 360° fundic wrap

3–5 cm long was then created using two or three 2-0 monofilament polypropylene full-thickness sutures, with one of the sutures containing the esophageal muscular layer. In the absence of adequate esophageal peristalsis, as documented by preoperative manometric and impedance data, a 270° fundoplication was constructed.

Quality-of-life and symptom severity assessment

Participants had to complete the Gastrointestinal Quality of Life Questionnaire, a well-established quality-of-life assessment tool validated in the German language [13]. Patients enrolled in the study had to complete a second questionnaire that assessed the severity of ten reflux-associated symptoms on a 5-point scale. In particular, symptoms of heartburn, regurgitation, bloating, diarrhea, gas, epigastric pain, dysphagia, asthma, hoarseness, and cough were graded as none (0), mild (1), mild to moderate (2), moderate (3), or severe (4). Both questionnaires were filled out before treatment, after 7-day cessation of antacid medication, and at 3- and 12-month follow-up.

Statistical analysis

Comparison of demographic characteristics, baseline symptom grades, and symptom frequencies between the two groups was performed using the two-tailed Student's *t*-test for uncorrelated variables and the one-tailed Fisher's exact probability test, as appropriate. Improvement of quality-of-life and symptom scores for the two groups was evaluated using the two-tailed Student's *t*-test for correlated variables. The statistical significance was set at a *p* value of 0.05.

Results

A total of 60 patients were assigned to undergo either endoscopic full-thickness plication or laparoscopic fundoplication with a 1:1 ratio. One patient from the endoscopic group and three patients from the operative group were lost to follow-up. Thus, 29 patients in the endoscopic group and 27 patients in the operative group were included in the analysis. Demographic and disease characteristics are presented in Table 1.

Comparative data at 3-month follow-up demonstrated similar quality-of-life scores in the two study groups, whereas symptom scores of heartburn and regurgitation were significantly better in the operative group. However, symptoms of diarrhea and dysphagia were less intense in the endoscopic group (Table 2).

At 12-month follow-up, quality-of-life scores were significantly improved in the endoscopic group, from a baseline mean value of 96.3 to 119.2 after treatment

Table 1 Demographic characteristics of the two study groups

	Endoscopic group	Fundoplication group
No. of patients	29	27
Age (years)	46.5	46.3
BMI (kg/m ²)	27.12	28.20
Hiatal hernia (%)	60.0	57.9
On PPIs (%)	96.2	93.8
Quality-of-life score	96.3	88.4

BMI body mass index, PPIs proton-pump inhibitors

Data are reported as mean values, unless otherwise indicated

Table 2 Comparison of the two study groups in terms of quality-of-life and symptom scores at 3-month follow-up

	Endoscopic group	Fundoplication group	<i>p</i>
Quality-of-life score	114.2	114.7	0.99
Heartburn score	1.04	0.04	<0.0001
Regurgitation score	0.56	0.08	0.005
Bloating score	1.32	1.92	0.95
Diarrhea score	0.28	0.83	<0.04
Gas score	1.52	2.50	0.002
Epigastric pain score	0.68	0.64	0.87
Dysphagia score	0.08	0.60	0.003
Asthma score	0.28	0.12	0.33
Hoarseness score	0.80	0.60	0.57
Cough score	0.72	0.52	0.50

Data are reported as mean values, unless otherwise indicated

($p < 0.002$). Symptoms of heartburn, regurgitation, and asthma also showed significant improvement (Table 3). Furthermore, quality-of-life scores improved significantly in the operative group from a baseline mean value of 88.4 to 123.7 ($p < 0.0001$). Symptom scores of heartburn, regurgitation, bloating, epigastric pain, dysphagia, hoarseness, and cough also showed significant improvement after laparoscopic fundoplication (Tables 4, 5).

Comparative analysis demonstrated similar quality-of-life scores between the two study groups at 12-month follow-up (119.2 vs. 123.7, respectively; $p = 0.66$). Symptoms of heartburn, regurgitation, and hoarseness demonstrated greater response to operative treatment, whereas gas scores were recorded lower for the endoscopic group (Table 3). Heartburn and regurgitation resolved in the vast majority of patients who underwent laparoscopic fundoplication, whereas only about half of the patients who underwent endoscopic plication experienced complete relief of these symptoms (Fig. 3). Nevertheless, 15 of 27

Table 3 Quality-of-life and symptom scores before and after endoscopic plication at 12-month follow-up

	Before endoscopic plication	After endoscopic plication	<i>p</i>
Quality-of-life score	96.3	119.2	<0.002
Heartburn score	2.50	1.07	<0.02
Regurgitation score	1.52	0.57	<0.004
Bloating score	1.88	1.50	0.27
Diarrhea score	0.92	0.36	0.14
Gas score	1.80	1.43	0.07
Epigastric pain score	1.36	0.57	0.21
Dysphagia score	0.50	0.14	0.07
Asthma score	0.76	0.14	0.03
Hoarseness score	1.04	0.64	0.10
Cough score	1.52	0.71	0.10

Data are reported as mean values, unless otherwise indicated

Table 4 Quality-of-life and symptom scores before and after laparoscopic fundoplication at 12-month follow-up

	Before fundoplication	After fundoplication	<i>p</i>
Quality-of-life score	88.4	123.7	<0.0001
Heartburn score	2.96	0.17	<0.0001
Regurgitation score	1.96	0.11	<0.0001
Bloating score	1.96	1.33	0.09
Diarrhea score	0.88	0.50	0.39
Gas score	2.08	2.22	0.33
Epigastric pain score	1.64	0.39	<0.002
Dysphagia score	0.92	0.22	<0.03
Asthma score	0.52	0.11	0.07
Hoarseness score	0.84	0.00	<0.01
Cough score	1.08	0.29	0.02

Data are reported as mean values, unless otherwise indicated

patients (52%) in the endoscopic group received everyday or on-demand antacid medication, whereas only 3 of 29 patients (11%) in the endoscopic group continued receiving medication ($p < 0.02$).

Discussion

Laparoscopic fundoplication has been established as an effective and safe treatment for GERD. Symptom

Table 5 Comparison of the two study groups in terms of quality-of-life and symptom scores at 12-month follow-up

	Endoscopic group	Fundoplication group	<i>p</i>
Quality-of-life score	119.2	123.7	0.66
Heartburn score	1.07	0.17	0.01
Regurgitation score	0.57	0.11	<0.05
Bloating score	1.50	1.33	0.72
Diarrhea score	0.36	0.50	0.55
Gas score	1.43	2.22	<0.04
Epigastric pain score	0.57	0.39	0.48
Dysphagia score	0.14	0.22	0.47
Asthma score	0.14	0.11	0.84
Hoarseness score	0.64	0.00	0.007
Cough score	0.71	0.29	0.17

Data are reported as mean values, unless otherwise indicated

improvement may be expected in up to 95% of patients with a concomitant GERD health-related quality-of-life score approaching that of the general population [14]. However, new-onset symptoms following laparoscopic fundoplication, such as dysphagia, bloating, excessive gas, and diarrhea, may result in worsening of the quality of life in a significant proportion of patients [15]. Furthermore, there is a subgroup of individuals with mild symptoms who are not willing to undergo surgery but seek an effective, minimally invasive therapy. In view of the above, endoscopic therapies for GERD have emerged during the last decade [16].

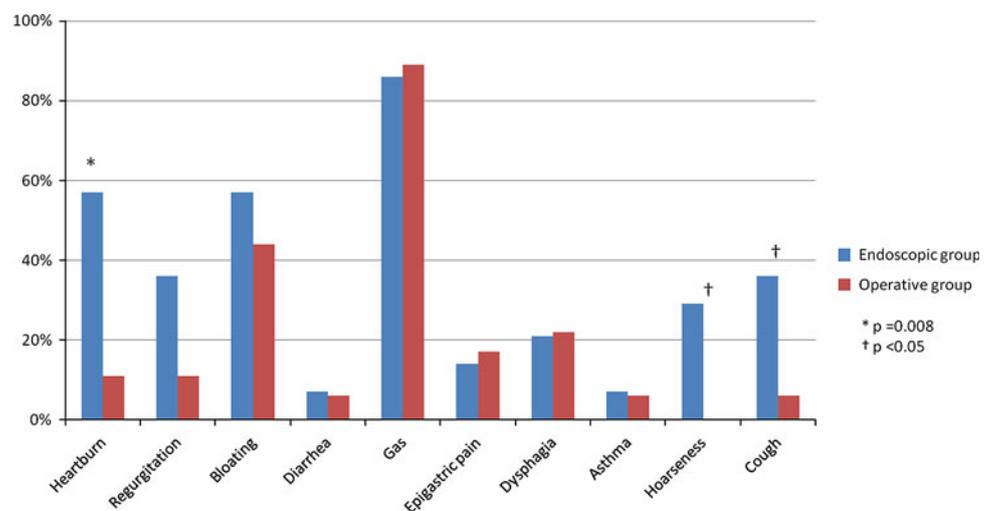
Whereas some of these techniques have fallen out of favor, others have been withdrawn from the market due to safety issues. Radiofrequency thermal application at the

gastroesophageal junction (Stretta system), cinching of the gastroesophageal junction mucosa (EndoCinch), and endoscopic full-thickness plication of the gastric cardia (NDO Plicator) are under continuing evaluation [9]. Those endoscopic techniques offer a minimally invasive approach to patients with GERD and allow further potential treatment by means of repeated treatment sessions or a subsequent laparoscopic antireflux procedure.

Although the therapeutic effect of endoscopic plication has been adequately reported in the past, a clinical comparison with conventional, well-established operative methods has not been undertaken to date. A clinical comparison would elucidate the hypothesis that plication provides symptom control comparable to that of current operative modalities in select patients, with minimal concomitant morbidity. The present study prospectively evaluated the symptomatic short- and mid-term outcome in individuals with documented GERD who have undergone endoscopic plication or laparoscopic fundoplication. Statistical analysis demonstrated a significant improvement of quality-of-life scores in both groups and similar postoperative quality-of-life scores following treatment.

Endoscopic plication resulted in a significant improvement of typical reflux symptoms. Extraesophageal manifestations of hoarseness and cough showed a lesser degree of improvement. Interestingly, symptoms of dysphagia and bloating were also downgraded or resolved in 80% and 64%, respectively. Eventually, significant improvement was achieved for four of the ten examined symptoms; however, a significant proportion of patients who underwent endoscopic plication continued receiving antacid medication.

Different patterns of treatment effect were recorded for laparoscopic fundoplication. Six of the ten examined symptoms showed significant improvement, namely, heartburn, regurgitation, epigastric pain, dysphagia,

Fig. 3 Symptom frequencies at 12-month follow-up

hoarseness, and cough. Comparative analysis showed a greater degree of effectiveness for the laparoscopic procedure with respect to heartburn and regurgitation at the expense of increased short-term dysphagia frequency and severity. Furthermore, endoscopic plication both eliminated dysphagia in 89% of patients and had a low potential of 6.6% for new-onset dysphagia at 3-month follow-up. Considering the corresponding values for laparoscopic fundoplication (35.7% and 14.3%, respectively), this observation may suggest that endoscopic plication could be preferable for patients experiencing preoperative dysphagia.

Since endoscopic plication has significant therapeutic potential but symptom-specific results seem to be inferior to those of laparoscopic fundoplication, identification of factors for success may be the most interesting issue for further investigation. A prospective multicenter trial by Khajanchee et al. [17] demonstrated optimal treatment outcome for patients with a lower body mass index and mild reflux as documented by 24-h pH studies. Furthermore, positive therapeutic results have also been exhibited for a cohort of obese patients, with a reduction of antacid medication from 91 to 51% [18]. Further subgroup identification of patients who will benefit from the procedure is essential for a rational and evidence-based application of what seems to be a valuable therapeutic tool.

Conclusion

The prospective evaluation of endoscopic plication and laparoscopic fundoplication demonstrated comparable quality-of-life scores following treatment in a select patient population. Laparoscopic fundoplication was, however, superior in terms of reflux symptom improvement at the expense of higher short-term dysphagia rates. Further studies are necessary to identify patient subgroups that will most benefit from this endoscopic tool and to validate its objective effectiveness in reflux control.

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