

Effectiveness of Laparoscopic Total and Partial Fundoplication on Extraesophageal Manifestations of Gastroesophageal Reflux Disease: A Randomized Study

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Abstract: The aim of the present study was to evaluate the clinical effect of partial and total fundoplication on extraesophageal symptoms in a selected cohort of patients with gastroesophageal reflux disease (GERD). Hundred patients with documented GERD were randomized to either undergo floppy Nissen (n = 50) or Toupet fundoplication (n = 50). Symptom scores of cough, asthma, hoarseness, and distortion of taste were prospectively evaluated using a standardized symptom questionnaire before surgery and at 3- and 12-month follow-up. Statistical significance was set at a *P*-value of 0.05. All evaluated symptoms exhibited substantial improvement after Nissen fundoplication at 3- and 12-month follow-up. Similar therapeutic results were documented for Toupet fundoplication, although statistical significance could not be reached for asthma at long-term follow-up. In conclusion, the application of laparoscopic fundoplication is justified for patients with documented GERD and atypical symptoms refractory to medical treatment. Toupet fundoplication may have a lesser effect on asthma.

Key Words: GERD, hoarseness, chronic cough, reflux-induced asthma

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Gastroesophageal reflux disease (GERD) is a common condition that results from reflux of gastric contents through the lower esophageal sphincter into the esophagus or oropharynx. GERD may cause both esophageal and extraesophageal symptoms.^{1,2} Heartburn, regurgitation, dysphagia, and chest pain are the most common, thus being considered as typical for GERD. Extraesophageal manifestations of the disease have been well investigated in the past and are now referred to as the “atypical” symptoms of GERD. In case where the larynx and/or pharynx is affected and those symptoms predominate, gastroesophageal reflux results in “laryngopharyngeal reflux disease.” Extraesophageal syndromes whose association with GERD is well established include chronic cough, laryngitis (hoarseness, throat clearing), and asthma.^{3,4}

Both acid-suppression therapy and laparoscopic anti-reflux surgery (LARS) have been proved effective in the treatment of typical symptoms of GERD.⁵ However, the therapeutic management of patients with atypical symp-

toms constitutes a significant problem, and treatment remains largely empirical. Available data regarding the effectiveness of LARS on extraesophageal symptoms of GERD are scarce and mostly controversial.³ Encouraging outcomes have been reported in patients with extraesophageal GERD symptoms documented preoperatively by pH-impedance studies.⁶ Surgical management of the extraesophageal symptoms has been the subject of several studies, which evaluated the effectiveness of laparoscopic Nissen fundoplication in highly selected groups of patients. Studies evaluating the effectiveness of LARS on symptoms specifically associated with the pharynx or larynx are lacking. Moreover, a comparative evaluation of total and partial fundoplication in the management of extraesophageal symptoms has not been undertaken yet. The purpose of the present study was to evaluate whether surgical therapy for patients with atypical symptoms is feasible and reasonable and to assess whether there is a difference in the outcome between partial and total fundoplication for extraesophageal symptoms in patients with GERD.

PATIENTS AND METHODS

Study Population/Group Assignment

The study population consisted of 100 consecutive patients with chronic GERD and no previous esophageal or gastric surgery, referred to the General Community Hospital Zell am See, Zell am See, Austria, between October 2007 and March 2010. There were 62 men and 38 women with a median age of 51.1 years (range, 25 to 78 y). The mean body mass index was 27.9 kg/m² (± 3.90).

Esophagogastroscopy, barium esophagography, esophageal manometry, and 24-hour ambulatory multichannel intraluminal impedance monitoring while off antireflux medication were routinely performed. Patients participating in the study met the following criteria: persistent or recurrent GERD symptoms despite continuous medical treatment, pathologic esophageal acid exposure as documented by a reflux-related DeMeester score ≥ 14.7, and symptom correlation ≥ 50%, and/or reflux episodes > 73.^{7–9}

Patients were randomized to laparoscopic floppy Nissen (LNF, n = 50) or Toupet fundoplication (LTF, n = 50). As it has been proven that both Nissen and Toupet can be applied independently of esophagus motility, patients were randomized irrespective of preoperative esophagus motility.¹⁰ All patients were admitted to the study only after being properly informed about the purpose of the study. An informed consent form was routinely obtained. Randomization was performed by random sampling numbers immediately before surgery by an independent member of the team.

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Surgical Technique

All patients underwent laparoscopic fundoplication in a standardized way by 2 experienced laparoscopic surgeons. Irrespective of preoperative manometric findings and depending on the preoperative randomization, a laparoscopic 360-degree “floppy” Nissen fundoplication or 270-degree Toupet fundoplication was fashioned. Our technique of laparoscopic fundoplication has been described previously in detail.¹¹

Symptom Assessment

Symptom evaluation was carried out in a standardized way using written questionnaire assessing the severity and intensity of 4 typical and 4 atypical symptoms in a 4-point scale. It is similar to the symptom score evaluation used by the group around Anvari and has been used previously.^{10,12,13} In particular, typical symptoms of heartburn, regurgitation, chest pain, dysphagia and atypical symptoms asthma, hoarseness, distortion of taste, and cough were graded as none (0), once per week (1), several times per week (2), daily (3), and constantly (4). Intensity of the above symptoms was graded as none (0), mild (1), moderate (2), severe (3), and extremely severe (4). To obtain the ultimate result, the frequency of each symptom is multiplied by its degree, resulting in scores from 0 to 16 for each symptom. Higher scores indicate more severe symptoms. Symptoms were defined as clinically relevant with a score ≥ 2 points.

The questionnaire was administered to all patients by an independent observer. Typical symptoms were documented before surgery, whereas atypical symptoms were recorded, before surgery, 3 months and 1 year after surgery. At the time of symptom assessment, patients were off antireflux medication for at least 1 week.

Statistical Analysis

Statistical analysis was performed using SPSS Statistical Analysis Software (SPSS Inc., Chicago, IL). For statistical evaluation, nonparametric tests were used. All data were presented as means with ranges or SD. Statistical significance was set at a *P*-value of 0.05.

RESULTS

Demographic and reflux disease characteristics did not generally differ between the 2 surgical groups before surgery. Ninety-eight of 100 patients were available at 3-month follow-up and 89 at 12-month follow-up. Two patients from the total fundoplication group were excluded at 3-month follow-up, because they underwent repeat surgery due to severe dysphagia. At 12-month follow-up, 5 further patients were excluded due to repeat surgery owing to dysphagia (2 from the partial fundoplication group and 3

TABLE 1. Mean Typical Gastroesophageal Reflux Disease Symptom Scores at Baseline

Symptom Score	Baseline		Nissen/Toupet <i>P</i>
	Nissen	Toupet	
Heartburn	9.40 (\pm 4.88)	7.14 (\pm 4.57)	NS
Regurgitation	4.24 (\pm 4.57)	4.16 (\pm 4.38)	NS
Dysphagia	1.79 (\pm 3.55)	2.08 (\pm 3.65)	NS
Chest pain	3.20 (\pm 4.14)	3.00 (\pm 3.52)	NS

NS indicates not significant.

from the total fundoplication group), and 4 patients were not available for postoperative symptom assessment (3 from the partial fundoplication group and 1 from the total fundoplication group).

Before surgery, at least 1 typical clinically relevant symptom was present in 95.9% of patients in the LTF group and in 97.8% of the patients in the LNF group. Relevant atypical symptoms were present at baseline in 57.4% of the patients in the LNF group and 59.2% in the LTF group. Broke down to the single symptoms, 16% had distortion of taste, 12% asthma, 20% hoarseness, and 44% cough in the LTF group; in the LNF group, the apportionment at baseline was similar—10% had distortion of taste, 10% asthma, 24% hoarseness, and 46% cough.

Baseline symptom scores were similar in the 2 study groups (Tables 1 and 2).

Evaluation at 3-month follow-up demonstrated statistically significant improvement for all atypical symptoms of GERD in the total fundoplication group. However, improvement in symptom scores of asthma and hoarseness did not achieve statistical significance in the partial fundoplication group (Table 2). Although asthma symptoms persisted at 12-month follow-up in this group of patients, even approximating preoperative values, a significant improvement of hoarseness scores was recorded. Furthermore, the therapeutic effect persisted at 12-month follow-up in the total fundoplication group (Table 3; Figs. 1 and 2).

The improvement of symptoms also comes apparent when expressed in percent. At least 1 relevant atypical symptom was present 3 months postoperatively in only 18% of the patients in the LNF group and 25% in the LTF group. One year after surgery, the percentage of patients with at least 1 clinically relevant symptom persisted with 19% after LNF and with 21% of symptomatic patients after LTF; there is no statistically relevant difference between the 2 procedures 1 year after surgery. Symptom frequencies in the 2 patient groups before and after treatment are presented in Table 4.

TABLE 2. Mean Atypical Gastroesophageal Reflux Disease Symptom Scores at 3-month Follow-up

Symptom Score	Baseline	3 mo po		Baseline	3 mo po	
	Nissen	Nissen	Before/After <i>P</i>	Toupet	Toupet	Before/After <i>P</i>
Cough	3.12 (\pm 4.01)	0.66 (1.86)	0.000	3.08 (\pm 4.34)	1.31 (3.15)	0.001
Hoarseness	2.11 (\pm 3.99)	0.71 (\pm 2.00)	0.004	1.35 (\pm 2.62)	0.80 (\pm 2.24)	NS
Distortion of taste	0.65 (\pm 1.89)	0.02 (\pm 0.14)	0.003	1.04 (\pm 2.89)	0.10 (\pm 0.58)	0.006
Asthma	0.81 (\pm 2.26)	0.18 (\pm 0.89)	0.004	0.56 (\pm 1.55)	0.22 (\pm 0.84)	NS

NS indicates not significant; po, postoperative.

TABLE 3. Mean Atypical Gastroesophageal Reflux Disease Symptom Scores at 12-month Follow-up

Symptom Score	Baseline	1 y po		Baseline	1 y po	
	Nissen	Nissen	Before/After <i>P</i>	Toupet	Toupet	Before/After <i>P</i>
Cough	3.12 (± 4.01)	1.38 (± 2.51)	0.007	3.08 (± 4.34)	0.94 (± 2.08)	0.004
Hoarseness	2.11 (± 3.99)	0.76 (± 2.03)	0.034	1.35 (± 2.62)	0.24 (± 0.78)	0.003
Distortion of taste	0.65 (± 1.89)	0.03 (± 0.17)	0.031	1.04 (± 2.89)	0.32 (± 1.55)	0.017
Asthma	0.81 (± 2.26)	0.19 (± 0.64)	0.048	0.56 (± 1.55)	0.52 (± 1.42)	NS

NS indicates not significant; po, postoperative.

In addition, before surgery and on follow-up, correlation analysis was performed between body mass index and atypical symptom scores. No correlations were found in both the groups.

DISCUSSION

For the surgical treatment of GERD, laparoscopic Nissen fundoplication has been the procedure of choice for the last decades. Laparoscopic Nissen fundoplication is highly successful in controlling typical reflux symptoms, with a reported success rate of 90% at 10 years after surgery.¹⁴ A recent systematic review and meta-analysis of

laparoscopic Nissen versus Toupet fundoplication favoured Toupet fundoplication in terms of postoperative dysphagia, reoperation rate, prevalence of inability to belch, and gas bloating.¹⁵ Concerning atypical GERD symptoms, a recent review was not able to identify any hard data on the therapeutic effect of antireflux surgery in atypical GERD symptoms, although some degree of symptom improvement has been demonstrated by the majority of studies.¹⁶

The present study aimed to investigate whether surgical therapy for patients with atypical symptoms is feasible and reasonable and to assess whether there is a difference in the outcome between partial and total fundoplication for extraesophageal symptoms in patients with GERD.

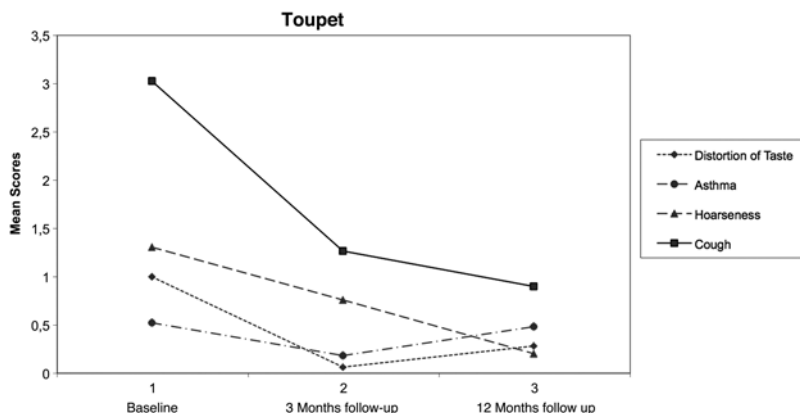


FIGURE 1. Preoperative and postoperative symptom scores in the laparoscopic Toupet fundoplication group.

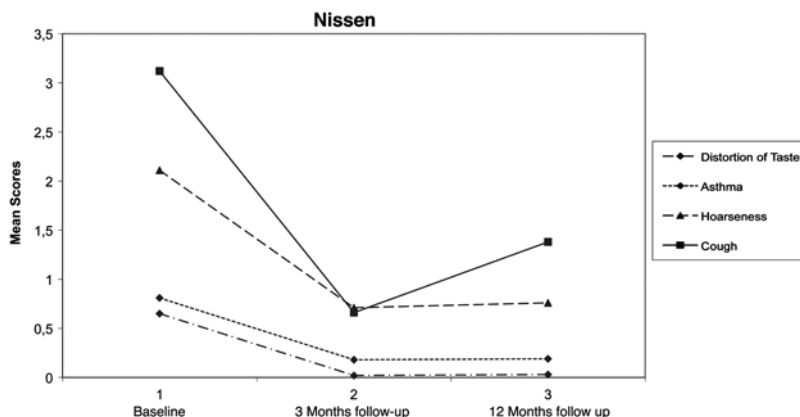


FIGURE 2. Preoperative and postoperative symptom scores laparoscopic floppy Nissen fundoplication group.

TABLE 4. Presence of Extraesophageal Symptoms in Patients With Gastroesophageal Reflux Disease Before and After Surgery

Symptom Score	Baseline		3 mo po		1 y po	
	Nissen N = 50 (%)	Toupet N = 50 (%)	Nissen N = 48 (%)	Toupet N = 50 (%)	Nissen N = 43 (%)	Toupet N = 45 (%)
Cough	46	44	6	12	10	10
Hoarseness	24	20	10	8	8	4
Distortion of taste	10	16	0	2	0	2
Asthma	10	12	2	4	2	6

NS indicates not significant; po, postoperative.

The results demonstrate that selected on the basis of pH-impedance monitoring, the application of laparoscopic fundoplication is justified for patients having persistent or recurrent symptoms despite continuous medical treatment. It seems that partial fundoplication has a lesser effect in the treatment of asthma and hoarseness as compared with total fundoplication, although the latter symptom tended to improve over time.

In a prospective study, Rakita and colleagues demonstrated good or excellent outcome with regard to asthma improvement in 83% of patients. Consistent with our results, if symptoms of asthma had not improved in the early postoperative period, they were unlikely to improve in the long term.¹⁷

Furthermore, this study confirms findings of previous reports where in half of the patients with GERD extraesophageal symptoms were present.^{18–20} The even higher preoperative percentage of patients with atypical symptoms in our patient population, almost 60% in the LTF group, could be because of the scoring system we used, multiplying the frequency of each symptom by its degree to get the ultimate result.

The clinical effectiveness of laparoscopic fundoplication in patients with persisting symptoms despite medical therapy remains a matter of debate. Similarly, the operative outcome with regard to extraesophageal symptoms of GERD has been also disputed.³ The results of this study show that LARS results in a significant improvement of extraesophageal manifestations of GERD but cannot relieve all of the patients of their symptoms. Discrepancies in clinical results suggest that specific patient groups may benefit from antireflux surgery. Assessment of objective patient characteristics, with pulmonary function tests and impedance testing, may identify patient groups, which will more likely respond to surgical treatment. In view of the results of the present study, it may be suggested that total fundoplication has a greater therapeutic effect in patients with symptoms of asthma.

A recent review reported that cough and reflux may precipitate each other.⁶ Of the entire atypical symptoms evaluated, cough showed the highest preoperative scores and was present in about 45% of the patients. The preoperative score of cough was higher than the score of dysphagia and as high as the score for chest pain. Dysphagia and chest pain are considered as typical for GERD, because they are very common. As the results of this study show that cough is also most common, the description as atypical GERD symptom does no longer seem to be appropriate.

In conclusion, laparoscopic fundoplication is feasible and reasonable for patients with extraesophageal manifesta-

tions of GERD despite medical treatment. Partial fundoplication seems to have a lesser effect on asthma and hoarseness as compared with total fundoplication. Further studies are required, to identify those patients with extraesophageal symptoms who will benefit from antireflux surgery.

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