



Laparoscopic Nissen fundoplication improves disease-specific quality of life in patients with gastroesophageal reflux disease and functional gastroesophageal outflow obstruction

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Abstract

Introduction The optimal management of functional esophagogastric junction outflow obstruction (EJOO) remains controversial particularly in the setting of concomitant gastroesophageal reflux disease (GERD). There remains a paucity of data regarding the outcomes of laparoscopic Nissen fundoplication (LNF) in this patient population. We hypothesized that GERD patients with manometric findings of EJOO on preoperative manometry do not have increased rates of postoperative dysphagia compared to those with normal or hypotensive LES pressures.

Materials and methods This retrospective cohort study of patients undergoing LNF for GERD compared outcomes in patients with and without functional EJOO (fEJOO). The outcomes of interest included disease-specific quality of life improvement, dysphagia scores, and the need for endoscopic dilation following fundoplication.

Results Two hundred and eleven patients underwent LNF for GERD and 15 (7.1%) were classified as having fEJOO. Baseline GERD-HRQL [30.0 (21.5–37) vs. 31 (21–37), $p=0.57$] were similar between fEJOO and control patients, respectively. There was no difference in baseline dysphagia scores [3.5 (2–5) vs. 2.0 (1–4), $p=0.64$] between the two groups. Postoperative GERD-HRQL [5.0 (2–13) vs. 4.0 (1–8), $p=0.59$] scores did not differ between fEJOO and control patients at 6-week follow-up. One year after surgery, GERD-HRQL [8.0 (3–9) vs. 4.5 (2–13), $p=0.97$] did not differ between groups. Dysphagia rates were similar at 6-week ($p=0.78$) and 1-year follow-ups ($p=0.96$). The need for dilation at 1 year following fundoplication was similar in both cohorts (13%, $p=0.96$).

Conclusion GERD patients with functional EJOO achieved similar improvements in disease-specific quality of life without increased incidence of dysphagia postoperatively.

Keywords GERD · Nissen · Esophagogastric junction outflow obstruction · Dysphagia

Hypertensive lower esophageal sphincter (LES) is a primary esophageal motility disorder that was initially described in 1960 [1]. This finding is most often associated with dysphagia and chest pain and may represent a condition akin to achalasia and may benefit from treatments aimed at reducing LES pressure, including surgical myotomy [2]. However, it has also been shown that hypertensive LES is often

accompanied by acid reflux, and that patients presenting with symptomatic gastroesophageal reflux disease (GERD) and manometric findings of hypertensive LES may achieve better benefit from laparoscopic Nissen fundoplication (LNF) rather than from esophageal myotomy [3, 4].

The advent of high-resolution manometry has led to a reclassification of esophageal motility disorders based on these parameters, including functional esophagogastric junction outflow obstruction (EJOO) [5]. This condition has an incidence of 3–11 percent, and is characterized by the manometric finding of elevated integrated relaxation pressure (IRP) of greater than 15 mmHg in the setting of preserved esophageal peristalsis [5–7]. EJOO can represent a primary esophageal motility finding or a secondary finding related to hiatal hernia, stricture, tumor, eosinophilic

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esophagitis, or esophageal varices [8]. Functional or idiopathic EJOO (fEJOO) is associated with no structural or anatomic abnormality.

Similar to those with hypertensive LES, patients with fEJOO often present with symptoms of dysphagia and chest pain, but also may present with symptoms and objective findings of GERD [7]. Studies have shown that patients presenting with fEJOO and minimal symptoms can be managed expectantly and those with significant dysphagia or chest pain may benefit from management strategies aimed at reducing LES pressure including smooth muscle relaxants, botulinum toxin injection, pneumatic dilation, and surgical myotomy [8, 9]. There remains a paucity of data, however, regarding the management of patients with symptomatic GERD in the setting of manometric findings of fEJOO.

We hypothesized that similar to those with GERD and hypertensive LES, patients with manometric findings of fEJOO in the setting of symptomatic GERD would derive similar improvements in patient-reported outcomes following LNF as those with normal LES function. We tested this hypothesis in a retrospective cohort study with a primary outcome of improvement in disease-specific quality of life following LNF. Secondary outcomes included postoperative dysphagia scores and need for endoscopic dilation.

Materials and methods

Patients

We performed a retrospective cohort study of patients undergoing LNF for management of GERD at the Ohio State University Wexer Medical Center between 2009 and 2017. All patients underwent preoperative endoscopy, esophageal pH monitoring, and esophageal manometry. Patients with potential secondary causes of EJOO including redo operation, paraesophageal hiatal hernia, and those without the manometric data required to diagnose EJOO or hypertensive LES were excluded. Demographic variables, questionnaire results, diagnostic tests, and outcomes were extracted from a prospectively maintained database approved by the institutional review board.

Patients were divided into two groups: fEJOO versus control. Functional EJOO was defined as an IRP above 15 mmHg or elevated mean LES residual pressure with preserved peristalsis, not meeting criteria for achalasia. The control group included all patients who underwent LNF for GERD and did not meet criteria for functional EJOO.

Primary and secondary outcomes

The primary outcomes for this study were improvement in GERD symptoms as assessed using the gastroesophageal

reflux symptom scale (GERSS) and disease-specific quality of life as measured by the gastroesophageal reflux disease health-related quality of life (GERD HRQL) questionnaire [10]. Patients completed the questionnaire preoperatively in the clinic, again at their early postoperative follow-up appointment (4–8 weeks) and were then contacted by telephone for long-term follow-up results. Secondary outcome variables included dysphagia scores and need for endoscopic dilation to manage postoperative dysphagia.

Statistical analysis

Statistical analyses were performed using Stata 15 statistical software (Statacorp LLC, College Station, Tx). Data are presented as mean \pm standard deviation (SD), median (IQR), or number (%) as appropriate. Differences between continuous and categorical variables were evaluated using Mann–Whitney U-test and Chi-square test, respectively. A *p* value of <0.05 was considered statistically significant.

Results

Two hundred and eleven patients meeting the inclusion and exclusion criteria underwent LNF for GERD during the study period and were included in this study. Fifteen (7.1%) patients met criteria for fEJOO and 196 (92.9%) represented the control arm for the study.

There were no differences in patient age ($p=0.82$), BMI ($p=0.12$), race ($p=0.52$), or insurance status ($p=0.36$) between the two groups (Table 1). There were no significant differences in presenting predominant complaints. All patients in the fEJOO group had typical symptoms of GERD, expressing either heartburn or regurgitation, compared with 95% ($n=187$) in the control arm. Patients in both groups had similar incomplete bolus clearance of approximately 40% ($p=0.85$) and symptom association probability in reference to heartburn ($p=0.64$). Baseline GERD-HRQL [30.0 (21.5–37) vs. 31 (21–37), $p=0.57$] and GERSS [36.5 (31–54) vs. 40.0 (26–50), $p=0.78$] scores were similar between fEJOO and control patients, respectively. There was no difference in baseline dysphagia scores [3.5 (2–5) vs. 2.0 (1–4), $p=0.64$] between the two groups (Table 1).

Following LNF, GERD-HRQL and GERSS scores improved significantly in both groups. Postoperative GERD-HRQL [5.0 (2–13) vs. 4.0 (1–8), $p=0.59$] and GERSS [11.0 (0–15) vs. 6.0 (1–13.5), $p=0.71$] scores did not differ significantly between those with and without fEJOO, respectively (Table 2). At 1-year follow-up, GERD-HRQL [8.0 (3–9) vs. 4.5 (2–13), $p=0.97$] and GERSS [20.0 (4–23) vs. 8.0 (1–22), $p=0.82$] scores did not differ between groups.

Early postoperative dysphagia rates were similar for those with [1.0 (0–3)] and without fEJOO [1.0 (0–2),

Table 1 Demographics, baseline symptom scores, and results of reflux testing for patients with and without functional EJOO

| Variable | FEJOO (<i>N</i> =15) | Control (<i>N</i> =196) | <i>P</i> -value |
|---|-----------------------|--------------------------|-----------------|
| Age, SD (years) | 51.8 ± 12.9 | 51.0 ± 12.9 | 0.82 |
| BMI, SD (kg/m ²) | 33.1 ± 5.4 | 30.8 ± 5.1 | 0.12 |
| Race, <i>N</i> (%) | | | 0.52 |
| Caucasian | 14 (93.3) | 165 (84.6) | |
| African American | 0 (0) | 15 (7.7) | |
| Other | 1 (6.7) | 15 (7.7) | |
| Insurance status, <i>N</i> (%) | | | 0.36 |
| Medicare | 2 (13.3) | 50 (25.6) | |
| Medicaid | 0 (0) | 4 (2.1) | |
| Private | 13 (86.7) | 127 (65.1) | |
| Self-pay | 0 (0) | 14 (7.2) | |
| ASA category, SD | 2.6 ± 0.6 | 2.4 ± 0.5 | 0.26 |
| Predominant symptoms | | | |
| Typical GERD, <i>n</i> (%) | | | |
| Heartburn | 14 (93) | 160 (81) | |
| Regurgitation | 12 (80) | 132 (67) | |
| Either | 15 (100) | 187 (95) | |
| Atypical GERD, <i>n</i> (%) | | | 0.22 |
| Dysphagia | 2 (13) | 62 (31) | |
| Cough | 5 (33) | 54 (28) | |
| Chest pain | 5 (33) | 57 (29) | |
| DeMeester score, mean ± SD | 49.9 ± 32.6 | 44.9 ± 28.8 | 0.55 |
| % peristalsis, mean ± SD | 81.6 ± 18.2 | 86.5 ± 16.8 | 0.28 |
| % incomplete bolus clearance ± SD | 39.4 ± 27.4 | 37.5 ± 30.6 | 0.85 |
| Symptom association probability, % ± SD | 93.0 ± 6.1 | 89.0 ± 23.8 | 0.63 |
| Heartburn | | | |
| Baseline dysphagia, median (IQR) | 3.5 (2–5) | 2.0 (1–4) | 0.64 |
| Baseline GERD-HRQL score, median (IQR) | 30.0 (21.5–37) | 31.0 (21–37) | 0.56 |
| Baseline GERSS score, median (IQR) | 36.5 (31–54) | 40.0 (26–40) | 0.78 |

Table 2 Postoperative outcomes of laparoscopic Nissen fundoplication in patients with and without functional EJOO

| Variable | FEJOO (<i>N</i> =15) | Control (<i>N</i> =196) | Probability |
|--------------------------------------|-----------------------|--------------------------|-------------|
| 6-week GERD-HRQL score, median (IQR) | 5.0 (2–13) | 4.0 (1–8) | 0.59 |
| 6-week GERSS score, median (IQR) | 11.0 (0–15) | 6.0 (1–13.5) | 0.71 |
| 6-week dysphagia score, median (IQR) | 1.0 (0–3) | 1.0 (0–2) | 0.78 |
| 1-year GERD-HRQL score, median (IQR) | 8 (3–9) | 4.5 (2–13) | 0.97 |
| 1-year GERSS score, median (IQR) | 20 (4–23) | 8 (1–22) | 0.82 |
| 1-year dysphagia score, median (IQR) | 0.5 (0–2.5) | 0.0 (0–2) | 0.74 |
| Endoscopic dilation, <i>n</i> (%) | 2 (13.3) | 27 (13.8) | 0.96 |

$p = 0.78$]. At 1-year follow-up, dysphagia scores did not differ between the groups [0.5 (0–2.5) vs. 0.0 (0–2), $p = 0.96$]. During the 1st year following LNF, 2 (13.3%) patients in the fEJOO group underwent endoscopic dilation for management of dysphagia compared to 27 (13.8%) patients in the control groups ($p = 0.96$, Table 2). No patient in either group required revision to a partial fundoplication, botulinum toxin injection, or surgical myotomy during the study period.

Discussion

Functional EJOO represents a heterogeneous condition that may present as a condition analogous to achalasia with symptoms of dysphagia and chest pain, but may also present in conjunction with severe symptomatic GERD. The aim of the current study was to assess the role of LNF in patients with symptomatic GERD and manometric findings

consistent with fEJOO. This represents a distinct subgroup population of reflux patients with incidentally discovered elevated LES pressures on manometry. We found that GERD can be successfully managed in this patient cohort with laparoscopic fundoplication without specific management aimed at reducing LES pressure. This approach led to substantial improvements in disease-specific quality of life without increased rates of postoperative dysphagia or need for further endoscopic or surgical intervention during the first year after surgery.

Currently, there is no consensus as to the best management of functional EJOO due in part to the infancy of the diagnosis, the relatively few numbers of patients afflicted, and the heterogeneity of this patient population [11]. The presenting symptoms in patients with findings of fEJOO may represent the most important consideration when considering treatment strategies for this condition. Asymptomatic or minimally symptomatic functional EJOO can be managed effectively with observation alone, with or without a therapeutic trial of botox, and nearly half of these patients will have spontaneous resolution of symptoms within 6 months [5, 8, 11, 12].

The most common clinical presentation for patients with fEJOO is significant dysphagia or chest pain. These patients were excluded from the current study as this condition likely represents a primary esophageal motility disorder similar to achalasia. In this clinical scenario, studies have reported success of interventions aimed at reducing LES pressure including botulinum toxin injection, pneumatic dilation, or surgical myotomy [6, 13]. In our study cohort of fEJOO patients presenting with predominant reflux symptoms and objective testing demonstrating pathologic acid reflux, the incidence of dysphagia was 13% compared to the overall rate of greater than 50% for all patients with fEJOO reported in the literature suggesting that this represents a fundamentally different patient population from those with primary esophageal dysmotility. This is also supported by both groups displaying similar esophageal bolus clearance rates.

Similar to a previous study assessing the outcomes of LNF in patients with hypertensive LES, we found that patients with fEJOO and typical GERD symptoms achieve good control of reflux symptoms with a Nissen fundoplication [2]. Similar to the current study, Timratana et al. found that a subgroup of their functional obstructive patients with GERD and positive pH studies benefited from a fundoplication [14]. These studies suggest that clinicians should not avoid performing antireflux surgery for patients with significant GERD and manometric findings of fEJOO for patients without significant complaints of dysphagia prior to surgery, as LNF has been shown to significantly improve disease-specific quality of life without significantly increased postoperative dysphagia in this population.

Our study is limited by observational design and the small number of patients meeting the manometric diagnosis of fEJOO. Also, this cohort represents a carefully selected cohort of patients with findings of fEJOO without significant baseline dysphagia complaints, and the finding that fundoplication does not carry an increased risk of significant postoperative dysphagia should be generalized to the broader fEJOO population. Also, the study endpoint of 1 year does not allow us to assess the long-term impact of fundoplication in these patients, and the natural history of functional EJOO in these patients remains poorly understood and, therefore, requires further evaluation in longitudinal studies.

Conclusion

GERD patients with functional EJOO or hypertensive LES achieved postoperative outcomes following LNF similar to those for patients without elevated LES pressures. There was no increased risk for dysphagia or the need for endoscopic dilation in the first year following surgery. These results suggest that LNF can be safely performed with excellent results in carefully selected patients with objectively confirmed GERD and manometric findings of functional EJOO.

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Compliance with ethical standards

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References

1. Code CF, Schlegel JF, Kelley ML Jr, Olsen AM, Ellis FH Jr (1960) Hypertensive gastroesophageal sphincter. Proc Staff Meet Mayo Clin 35:391–399
2. Tamhankar AP, Almogy G, Arain MA, Portale G, Hagen JA, Peters JH, Crookes PF, Sillin LF, DeMeester SR, Bremner CG, DeMeester TR (2003) Surgical management of hypertensive lower esophageal sphincter with dysphagia or chest pain. J Gastrointest Surg 7:990–996 **discussion 996**
3. Gockel I, Lord RV, Bremner CG, Crookes PF, Hamrah P, DeMeester TR (2003) The hypertensive lower esophageal sphincter: a motility disorder with manometric features of outflow obstruction. J Gastrointest Surg 7:692–700
4. Katzka DA, Sidhu M, Castell DO (1995) Hypertensive lower esophageal sphincter pressures and gastroesophageal reflux: an apparent paradox that is not unusual. Am J Gastroenterol 90:280–284
5. Samo S, Qayed E (2019) Esophagogastric junction outflow obstruction: where are we now in diagnosis and management? World J Gastroenterol 25:411–417

6. Richter JE, Clayton SB (2019) Diagnosis and management of esophagogastric junction outflow obstruction. *Am J Gastroenterol* 114(4):544–547
7. Lynch KL, Yang YX, Metz DC, Falk GW (2017) Clinical presentation and disease course of patients with esophagogastric junction outflow obstruction. *Dis Esophagus* 30:1–6
8. Garbarino S, von Isenburg M, Fisher DA, Leiman DA (2018) Management of functional esophagogastric junction outflow obstruction: a systematic review. *J Clin Gastroenterol*. <https://doi.org/10.1097/MCG.0000000000001156>
9. Scherer JR, Kwiatek MA, Soper NJ, Pandolfino JE, Kahrilas PJ (2009) Functional esophagogastric junction obstruction with intact peristalsis: a heterogeneous syndrome sometimes akin to achalasia. *J Gastrointest Surg* 13:2219–2225
10. Velanovich V, Karmy-Jones R (2001) Psychiatric disorders affect outcomes of antireflux operations for gastroesophageal reflux disease. *Surg Endosc* 15:171–175
11. Perez-Fernandez MT, Santander C, Marinero A, Burgos-Santamaria D, Chavarria-Herbozo C (2016) Characterization and follow-up of esophagogastric junction outflow obstruction detected by high resolution manometry. *Neurogastroenterol Motil* 28:116–126
12. Song BG, Min YW, Lee H, Min BH, Lee JH, Rhee PL, Kim JJ (2019) Combined multichannel intraluminal impedance and high-resolution manometry improves detection of clinically relevant esophagogastric junction outflow obstruction. *J Neurogastroenterol Motil* 25:75–81
13. Pereira PF, Rosa AR, Mesquita LA, Anzolch MJ, Branchi RN, Giongo AL, Paixao FC, Chedid MF, Krueel CD (2019) Esophagogastric junction outflow obstruction successfully treated with laparoscopic Heller myotomy and Dor fundoplication: first case report in the literature. *World J Gastrointest Surg* 11:112–116
14. El-Hayek K, Timratana P, Brethauer SA, Chand B (2013) Complete endoscopic/transgastric retrieval of eroded gastric band: description of a novel technique and review of the literature. *Surg Endosc* 27:2974–2979

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