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Esophagogastric junction distensibility is greater following Toupet compared to Nissen fundoplication

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Abstract
Background The goal of antireflux surgery is to create a competent antireflux valve at the esophagogastric junction (EGJ). The two most common types of fundoplications constructed are the 360° Nissen and the 270° Toupet. We sought to determine whether there was a significant difference in distensibility at the EGJ based on fundoplication geometry (full vs. partial).
Methods This is a retrospective review of prospective data. All subjects underwent laparoscopic fundoplication over a 47-month period for primary GERD or failed fundoplication. An endoluminal functional luminal-imaging probe (EndoFLIP®) was used to assess EGJ distensibility intraoperatively. Minimum esophageal diameter (D_{min}), cross-sectional area (CSA), and distensibility index (DI) were measured at 30- and 40-mL balloon distension volumes prior to abdominal insufflation, after hiatal dissection, and following fundoplication. DI is defined as the narrowest CSA divided by the corresponding pressure expressed in mm^2/mmHg. Analysis was conducted to compare distensibility metrics based on the type of fundoplication constructed (Nissen or Toupet). As a secondary outcome, we sought to determine whether there was a difference in distensibility of the EGJ prior to surgery in patients with primary GERD as opposed to those with recurrent GERD after a failed fundoplication.
Results A total of 75 patients underwent fundoplications during the study interval. There were 44 primary and 31 reoperative fundoplications. Nissen fundoplication was constructed in 45 and Toupet in 30. Based on the distensibility index, the EGJ distensibility significantly decreased from prior to surgery to following fundoplication in all patients. Patients undergoing reoperative antireflux surgery had an initial DI at the EGJ similar to that of patients with primary GERD. Following Toupet, the EGJ was significantly more distensible than that after Nissen fundoplication.
Conclusions Laparoscopic fundoplication results in decreased EGJ distensibility in patients with GERD. The EGJ following partial fundoplication is significantly more distensible than that after a full fundoplication.

Keywords Gastroesophageal reflux disease · EndoFLIP · Fundoplication · Esophagogastric junction · Distensibility

Gastroesophageal reflux disease (GERD) is an extremely common condition characterized by pathologic acid exposure of the distal esophagus due to an incompetent antireflux barrier. Current management strategies rely heavily on the use of proton pump inhibitors (PPIs), but recent studies have shown that approximately 30 % of patients fail to respond to these medications either partially or completely [1–3]. In the case of medically refractory GERD, the best treatment option remains antireflux surgery. Studies have demonstrated that fundoplication provides superior symptom control up to 7 years post-op when compared to long-term PPI use [4]. The most common type of fundoplication performed worldwide is the Nissen fundoplication, although studies have suggested that a partial fundoplication such as a Toupet

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may be associated with similar reflux control and fewer side effects [5].

The endoscopic functional luminal-imaging probe (EndoFLIP®, Crospon, Galway, Ireland) provides real-time feedback on the distensibility of the EGJ. The FLIP is a catheter-based probe that has 17 ring electrodes spaced at 5-mm intervals within a bag that can be inflated with various volumes of saline. The diameter of the balloon at a specific location is calculated based on impedance planimetry, and the pressure within the balloon itself is used to determine the distensibility of a luminal gastrointestinal structure at a specific point. *Distensibility* refers to the ability of a structure to be distended or stretched under pressure. A fundoplication that is more distensible will stretch to a greater volume or degree with lower pressures exerted to achieve the change in volume. A poorly distensible fundoplication will require higher pressures to stretch or distend. We sought to define the changes noted in EGJ distensibility during fundoplication. We assessed these characteristics during both primary and reoperative fundoplication in this study. Analysis was conducted to compare distensibility metrics based on whether the patient had undergone a previous fundoplication and based on the type of fundoplication constructed (Nissen or Toupet).

Materials and methods

After institutional review board approval, a retrospective review of prospectively collected data was undertaken to characterize the changes in EGJ distensibility for patients undergoing laparoscopic fundoplication from September 2013 to August 2015. Patients undergoing Primary Nissen or Toupet partial fundoplication as well as reoperative fundoplication (Nissen or conversion of a Nissen to a Toupet) for a failed previous attempt were included. Demographics and disease-specific information including age, sex, body mass index, and duration of symptoms were all collected preoperatively. Prior to surgery, all patients underwent upper gastrointestinal endoscopy, 24-h pH/impedance monitoring, and high-resolution esophageal manometry to confirm the diagnosis of GERD and rule out esophageal motility disorders.

Toupet fundoplication was selected as a primary GERD procedure in patients with severe esophageal dysmotility and in patients with a significant preoperative bloating. In reoperative fundoplication cases, a Toupet was constructed when dysphagia and/or impaired esophageal motility was present prior to revisional surgery. All procedures were performed laparoscopically. In primary procedures, the fundoplication was created about an esophageal bougie. In revisional cases, the original fundoplication was taken down entirely, a hiatal hernia was repaired (if present), and the new fundoplication was created as above for primary cases.

Intraoperative distensibility measurements were completed using the EndoFLIP® system. Prior to establishing pneumoperitoneum, the FLIP was advanced down the esophagus under direct endoscopic visualization until the probe was confirmed visually to be at the EGJ and an "hour-glass" visual was displayed on the FLIP monitor. Measurements were obtained at three time points: (1) prior to insufflation, (2) following hiatal takedown with the abdomen insufflated to 15 mmHg, and (3) following the construction of the fundoplication with the abdomen still insufflated. Measures were attained at bag distention volumes of 30 and 40 mL for all subjects.

The FLIP is a catheter-based probe that has 17 ring electrodes spaced at 5-mm intervals within a bag that can be inflated with various volumes of saline. These electrodes are used to calculate cross-sectional areas (CSA) at each level. When the catheter is placed across the EGJ, calculations can be made for 4 cm proximal and 4 cm distal. From the CSA, EGJ distensibility index (DI) can be calculated by dividing the minimum CSA by the intra-bag pressure. The mean minimum CSA and intra-bag pressure were calculated over a 20-s interval for each measurement and used for determining DI.

Statistical analysis was conducted using SPSS (version 22.0 Inc. Chicago, IL). All measures are reported as mean ± SD. Paired *t* test was used for intragroup bivariate analysis, and Fisher's exact tests were used for categorical variables. For intergroup comparison, a *t* test was performed. A p value of <0.05 was considered statistically significant.

Results

A total of 75 patients underwent laparoscopic primary or reoperative fundoplication with intraoperative EndoFLIP assessment during the study interval. Forty-four patients (58.7 %) underwent primary fundoplication and the remainder underwent reoperative procedures. There were 45 Nissen and 30 Toupet fundoplications constructed. Demographics of the cohort are described in Table 1.

Distensibility metrics at the pre-insufflation, post-hiatal dissection, and post-fundoplication time points for all patients are listed in Table 2. CSA increased significantly from prior to pneumoperitoneum to hiatal takedown for both the 30- and 40-mL distention volumes. A significant increase was also noted from the initial CSA to post-fundoplication at the 30-mL distention volume. A significant decrease in DI from the initial assessment to post-fundoplication occurred in both the 30- and 40-mL distention volumes for all patients.

Table 1 Patient demographics and surgery details

Subjects (*n*)	75
Mean age (years)	55.2 ± 13.9
BMI (kg/m^2)	28.9 ± 4.7
Female	49 (65.3 %)
Primary fundoplication	
Nissen	34 (77.3 %)
Toupet	10 (22.7 %)
Redo fundoplication	
Redo Nissen	14 (45.2 %)
Conversion of Nissen to Toupet	17 (54.8 %)

Table 2 Distensibility measures for all patients

Measurement	30 mL	40 mL
CSA (mm^2)		
Pre-insufflation	45.9 ± 21.7	83.7 ± 38.9
Takedown hiatus	53.0 ± 29.2*	102.6 ± 47.1*
Post-fundoplication	38.4 ± 18.7*	74.5 ± 28.1
D_{min} (mm)		
Pre-insufflation	7.5 ± 1.7	10.1 ± 2.2
Takedown hiatus	7.9 ± 2.4	11.3 ± 2.9*
Post-fundoplication	7.0 ± 1.7*	9.6 ± 2.0
Pressure (mmHg)		
Pre-insufflation	19.2 ± 9.9	26.3 ± 10.3
Takedown hiatus	25.0 ± 10.7*	31.8 ± 10.7*
Post-fundoplication	27.7 ± 9.7*	38.1 ± 9.5*
DI (mm^2/mmHg)		
Pre-insufflation	3.4 ± 3.4	3.9 ± 3.2
Takedown hiatus	2.4 ± 1.5*	3.7 ± 2.9
Post-fundoplication	1.6 ± 1.0*	2.2 ± 1.3*

CSA cross-sectional area, D_{min} minimum esophageal diameter, *pressure* intra-balloon pressure at given volume, *DI* distensibility index

* $p < 0.05$ for comparison to pre-insufflation value

Intergroup comparison between patients undergoing primary and reoperative fundoplication demonstrated that prior to surgery, the distensibility of the EGJ in patients with recurrent GERD and a fundoplication that had failed was similar to those with GERD who had never had surgery (Table 3). Patients with GERD related to a failed fundoplication had preoperative pH results similar to patients with primary GERD and no previous history of a fundoplication. A comparison between Nissen and Toupet fundoplication postoperatively demonstrated that the Toupet geometry resulted in an EGJ that was significantly more distensible than a Nissen (Table 4).

Table 3 Distensibility prior to insufflation for primary versus reoperative fundoplication patients

	Primary fundo	Reoperative fundo	*p* value
CSA 30 mL	43.1 ± 16.0	49.9 ± 27.7	0.63
CSA 40 mL	83.8 ± 39.6	83.6 ± 38.5	0.9
D_{min} 30 mL	7.3 ± 1.4	7.8 ± 2.1	0.42
D_{min} 40 mL	10.0 ± 2.0	10.2 ± 2.4	0.96
Pressure 30 mL	16.8 ± 8.5	22.5 ± 10.8	0.02
Pressure 40 mL	24.6 ± 9.5	28.6 ± 11.0	0.07
DI 30 mL	3.5 ± 3.2	3.2 ± 3.7	0.27
DI 40 mL	4.0 ± 3.2	3.7 ± 3.2	0.31

CSA cross-sectional area, D_{min} minimum esophageal diameter, *pressure* intra-balloon pressure at given volume, *DI* distensibility index

Table 4 Post-fundoplication distensibility for Nissen versus Toupet fundoplication

	Nissen	Toupet	*p* value
CSA 30 mL	32.8 ± 13.1	48.4 ± 23.0*	<0.01
CSA 40 mL	68.2 ± 27.5	85.9 ± 26.2	<0.01
D_{min} 30 mL	6.5 ± 1.5	7.8 ± 1.8	<0.01
D_{min} 40 mL	9.1 ± 1.8	10.6 ± 2.1	<0.01
Pressure 30 mL	26.7 ± 7.8	29.4 ± 12.4*	0.67
Pressure 40 mL	37.6 ± 8.5	38.9 ± 11.4*	0.95
DI 30 mL	1.4 ± 0.8	1.9 ± 1.2	0.02
DI 40 mL	2.0 ± 1.4	2.4 ± 1.1	0.03

CSA cross-sectional area, D_{min} minimum esophageal diameter, *pressure* intra-balloon pressure at given volume, *DI* distensibility index

There were no intraoperative complications or other complications potentially related to the placement of the EndoFLIP catheter or intraoperative distensibility assessment.

Discussion

Impedance planimetry using the EndoFLIP device during laparoscopic fundoplication for GERD demonstrates significant changes in the distensibility characteristics of the EGJ at various phases of the procedure. The addition of a fundoplication resulted in significantly decreased DI from baseline in all patients. When a fundoplication fails and GERD recurs to the point where reoperative surgery is required, the EGJ distensibility is similar to that of patients with de novo GERD and no prior esophageal surgeries. The Toupet partial fundoplication anatomy was demonstrated to result in an EGJ that was significantly more distensible than that of a full Nissen fundoplication.

Several previous studies have shown that GERD patients have significantly increased distensibility of the EGJ when compared to normal control subjects without GERD [6, 7]. This increase in distensibility allows for a greater volume of refluxate to pass through the EGJ and the EGJ to open at a lower intraluminal pressure. Pandolfino et al. [8] demonstrated that flow through the EGJ is proportional to the opening diameter raised to the fourth power, which leads to a significant increase in reflux in the setting of increased distensibility. Kwiatek et al. [6] used the EndoFLIP device to assess the distensibility of the EGJ in 20 GERD patients and 20 healthy volunteers. In this study, it was demonstrated that the EGJ DI was about twofold greater in GERD patients when compared to healthy volunteers at both the 30- and 40-mL distention volumes. GERD patients were also demonstrated to have a significantly lower distending pressure when compared to controls. In another study, Kwiatek et al. [9] examined the EGJ distensibility differences between 10 healthy controls and 10 patients who underwent laparoscopic Nissen fundoplication using the EndoFLIP device. In this study, 50 and 60 mL distention volumes were used to show that interdeglutitive EGJ compliance was comparable between fundoplication patients and healthy controls. Pandolfino et al. [10] demonstrated that fundoplication restores distensibility of the EGJ to a level similar to normal subjects without GERD using a barostat device. It was determined that trans-EGJ flow is related to EGJ length and EGJ diameter, suggesting that retrograde flow through the EGJ would be decreased by both a reduction in diameter and an increase in length of the EGJ (as takes place with the construction of a fundoplication). Based on our data as well as these previous studies, it appears that GERD patients have significantly increased EGJ distensibility when compared with healthy volunteers and that distensibility is decreased by the creation of a fundoplication. A less distensible EGJ appears to provide a better antireflux barrier and a more competent valve to prevent pathologic reflux on a physiologic basis.

Blom et al. [11] assessed the changes in EGJ distensibility from baseline to post-fundoplication in 15 patients using a barostat device. Prior to laparoscopic Nissen fundoplication, the barostat device was introduced into the esophagus and baseline EGJ characteristics were assessed. This was repeated following the construction of a Nissen fundoplication for each patient. Using a slightly different approach to that of the EndoFLIP device, Blom et al. showed that Nissen fundoplication significantly decreases EGJ distensibility by looking at the change in pressure for each 5 mL change in volume. Ilczyszyn et al. [12] built on this study by collecting intraoperative distensibility measurements for 17 patients undergoing laparoscopic Nissen fundoplication using the EndoFLIP device. They again showed a significant decrease in EGJ DI from prior to the establishment of pneumoperitoneum to post-fundoplication, which we observed as well.

The majority of fundoplication procedures performed worldwide for GERD are 360° Nissen fundoplications [13]. A common practice is to perform a partial fundoplication in patients with abnormal or inefficient esophageal motility [14], although the necessity of this practice has been challenged [15]. Proponents of the Toupet partial fundoplication point to studies that suggest that the Toupet is associated with similar GERD control as a Nissen with fewer side effects such as dysphagia and gas bloat [16, 17]. Advocates of the Nissen point to studies demonstrating no difference in dysphagia rates and decreased durability of the Toupet when compared to the Nissen [18, 19]. A recently published meta-analysis of 13 randomized controlled trials including 1564 patients undergoing laparoscopic Nissen and Toupet fundoplication determined that Toupet was equally effective at improving quality of life and controlling reflux compared to Nissen fundoplication, but was associated with a lower incidence of postoperative dysphagia and other gas-related symptoms [20]. In this meta-analysis, it was determined that the rate of dysphagia was 12.56 % following Nissen and 4.84 % following Toupet. When analyzed based on preoperative esophageal motility, it was the type of fundoplication (Nissen vs. Toupet) rather than esophageal function that was correlated with dysphagia. Gas bloat may be less common following Toupet because the increased distensibility of the EGJ when compared to the Nissen may allow gastric belching and the release of swallowed air more readily. A recent study demonstrated that belching pattern is altered by Nissen fundoplication by reducing gastric belching (air venting from the stomach) and increasing supra-gastric belching (no air venting from the stomach) [21]. A Toupet fundoplication may be more physiologic than a Nissen fundoplication [22].

Even today, nearly 60 years after Nissen first described the fundoplication [23], a significant variability exists in surgical technique and the procedure remains part art, part science. There is variability with regard to the extent of hiatal dissection, bougie, or no bougie, how the fundoplication is created, and other factors. The goal of most surgeons is to create a "floppy" wrap—the definition of which varies from surgeon to surgeon and is not based on an objective metric of any type. In a recent systematic review, Ip et al. [24] concluded that these subtle variations continue to hamper our ability to adequately assess the predictors of clinical and symptomatic outcomes of antireflux procedures in medically refractory GERD. A significant variability in the symptomatic outcomes and side effects associated with antireflux surgery have been observed in the community setting outside of major referral centers (which are most likely to publish their results) [25].

Intraoperative distensibility assessment may provide surgeons with real-time data to help guide the creation of the fundoplication. This may facilitate a more standardized approach to fundoplication and could potentially provide surgeons with feedback that the fundoplication they just created is more likely to be associated with significant side effects given the distensibility of the EGJ post-fundoplication. We plan to continue collecting data on the distensibility and long-term symptomatic outcomes in these patients with a goal of establishing a threshold value for distensibility attainable in the majority of properly performed fundoplications and associated with the lowest possible incidence of postoperative adverse side effects.

There are several limitations to this study. First, we did not follow patients longitudinally to determine whether there were specific distensibility characteristics or changes relative to baseline that are associated with poor symptomatic outcomes. Our initial measurements were collected prior to the establishment of pneumoperitoneum, while the latter assessments were made with the abdomen insufflated to 15 mmHg. It has been demonstrated in a previous study that insufflation of pneumoperitoneum and hiatal dissection does not impact baseline DI in a cohort of patients with achalasia [26]. In patients with GERD undergoing fundoplication however, the initiation of pneumoperitoneum leads to a significant decrease in DI and other metrics [12]. Finally, the heterogeneity of the GERD patient population creates study comparison difficulties as EGJ distensibility varies significantly between individual patients with GERD [27].

Based on our data, we have demonstrated that EGJ distensibility can be determined in real-time intraoperatively and that fundoplication results in a decreased distensibility of the EGJ in patients with GERD. We have also demonstrated that a Toupet is associated with an EGJ that is significantly more distensible than that of a Nissen fundoplication. Future studies are needed to evaluate the long-term symptomatic outcomes as they relate to intraoperative esophageal measurements to determine whether the fundoplication geometry and type can be tailored intraoperatively to improve the long-term symptomatic outcomes and to minimize the side effects.

Compliance with ethical standards

Disclosures Reece K. DeHaan, Daniel Davila, and Matthew J. Frelich declare no conflicts of interest. Jon C. Gould is a consultant for Torax Medical.

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