Clinical Significance of Esophageal Outflow Resistance Imposed by a Nissen Fundoplication

Shahin Ayazi, MD, Steven R DeMeester, MD, FACS, Jeffrey A Hagen, MD, FACS, Joerg Zehetner, MD, FACS, Ross M Bremner, MD, PhD, FACS, John C Lipham, MD, FACS, Peter F Crookes, MD, FACS, Tom R DeMeester, MD, FACS

BACKGROUND: Attention has been focused on the amplitude of esophageal body contraction to avoid persistent dysphagia after a Nissen fundoplication. The current recommended level is a contraction amplitude in the distal third of esophagus above the fifth percentile. We hypothesized that a more physiologic approach is to measure outflow resistance imposed by a fundoplication, which needs to be overcome by the esophageal contraction amplitude.

STUDY DESIGN: The esophageal outflow resistance, as reflected by the intra-bolus pressure (iBP) measured 5 cm above the lower esophageal sphincter (LES), was measured in 53 normal subjects and 37 reflux patients with normal esophageal contraction amplitude, before and after a standardized Nissen fundoplication. All were free of postoperative dysphagia. A test population of 100 patients who had a Nissen fundoplication was used to validate the threshold of outflow resistance to avoid persistent postoperative dysphagia.

RESULTS: The mean (SD) amplitude of the iBP in normal subjects was 6.8 (3.7) mmHg and in patients before fundoplication was 3.6 (7.0) mmHg ($p = 0.003$). After Nissen fundoplication, the mean (SD) amplitude of the iBP increased to 12.0 (3.2) mmHg ($p < 0.0001$ vs normal subjects or preoperative values). The 95th percentile value for iBP after a Nissen fundoplication was 20.0 mmHg and was exceeded by esophageal contraction in all patients in the validation population, and 97% of these patients were free of persistent postoperative dysphagia at a median 50-month follow-up.

CONCLUSIONS: Nissen fundoplication increases the outflow resistance of the esophagus and should be constructed to avoid an iBP > 20 mmHg. Patients whose distal third esophageal contraction amplitude is >20 mmHg have a minimal risk of dysphagia after a tension-free Nissen fundoplication. (J Am Coll Surg 2019;229:210–216. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

There is an attitude of uncertainty regarding the amplitude of esophageal body contraction required to avoid persistent dysphagia after a 360-degree Nissen fundoplication.[1,2] This uncertainty arises from studies that used various esophageal body contraction amplitudes to avoid persistent dysphagia after a Nissen

CME questions for this article available at http://jacscme.facs.org

Disclosure Information: Dr Bremner's institution receives preceptorship consulting fees from Ethicon Endo-Surgery. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose.

Disclosures outside the scope of this work: Dr SR DeMeester is paid consultant and receives payment for lecture from Bard-Davol, CDx Diagnostics, and Mauna Kea, and receives grant money from Bard-Davol and CDx Diagnostics; Dr TR DeMeester is a paid consultant to Torax Medical, receives payment for lecture from Ethicon and EndoStim, and is a board member for Van Andel Research Institute; Dr Lipham is a paid consultant to Ethicon and Torax Medical; and Dr Zehetner is a paid consultant to Johnson & Johnson and receives travel expenses from Johnson & Johnson and EndoStim.

Received January 23, 2019; Revised March 3, 2019; Accepted March 7, 2019.

From the Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh, PA (Ayazi); the Department of Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA (Ayazi, Hagen, Zehetner, Lipham, Crookes, T DeMeester); Foregut and Minimally Invasive Surgery, The Oregon Clinic, Portland, OR (S DeMeester); and the Norton Thoracic Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ (Bremner).

Correspondence address: Tom R DeMeester, MD, FACS, 892 Huntington Garden Dr, San Marino, CA, 91108. email: tom.demeester@med.usc.edu

https://doi.org/10.1016/j.jamcollsurg.2019.03.024
ISSN 1072-7515/19

Abbreviations and Acronyms
GERD = gastroesophageal reflux disease
iBP = intra-bolus pressure
LES = lower esophageal sphincter

fundoplication.[1-4] The varied results of these studies has led to this uncertainty regarding the use of esophageal manometry to avoid persistent postoperative dysphagia.

Logic would affirm that to avoid persistent dysphagia after a Nissen fundoplication, the contraction amplitude of the peristaltic waves in the distal esophageal body must overcome the outflow resistance imposed by the fundoplication. The intra-bolus pressure (iBP) described by Cook[5] is an indicator of pharyngeal outflow resistance caused by the upper esophageal sphincter. Using simultaneous mano-fluorography, Shaw and coworkers[6] demonstrated a relationship between a high iBP and the inability of the upper esophageal sphincter to accommodate passage of a swallowed bolus.[6] This concept could also be applied to the lower esophageal sphincter (LES) to quantitate its outflow resistance. We proposed to measure the outflow resistance in normal subjects and patients with reflux disease before and after a tension-free, 360-degree Nissen fundoplication and to establish the necessary peristaltic contraction amplitude in the distal esophageal body to avoid persistent dysphagia.

METHODS

Study population

The normal subject population consisted of a group of 53 normal subjects free of foregut symptoms, no history of foregut surgery, and a normal esophageal acid exposure on 24-hour esophageal pH monitoring. There were 35 males and 18 females, with a mean age of 28 years.

The gastroesophageal reflux disease (GERD) patient population consisted of 37 symptomatic patients with documented GERD based on 24-hour esophageal pH monitoring. All had normal esophageal motility, and no patients had paraesophageal hernia. There were 25 males and 12 females, with a mean age of 48. All had a 360-degree, tension-free Nissen fundoplication performed over a 60-F bougie. All had an excellent asymptomatic outcome and were free of persistent dysphagia when assessed at a median follow-up of 6 months. This population was used to measure the outflow resistance imposed by a tension-free 360-degree Nissen fundoplication.

The threshold validation population consisted of a separate group of 100 symptomatic patients with documented GERD, based on 24-hour esophageal pH monitoring.

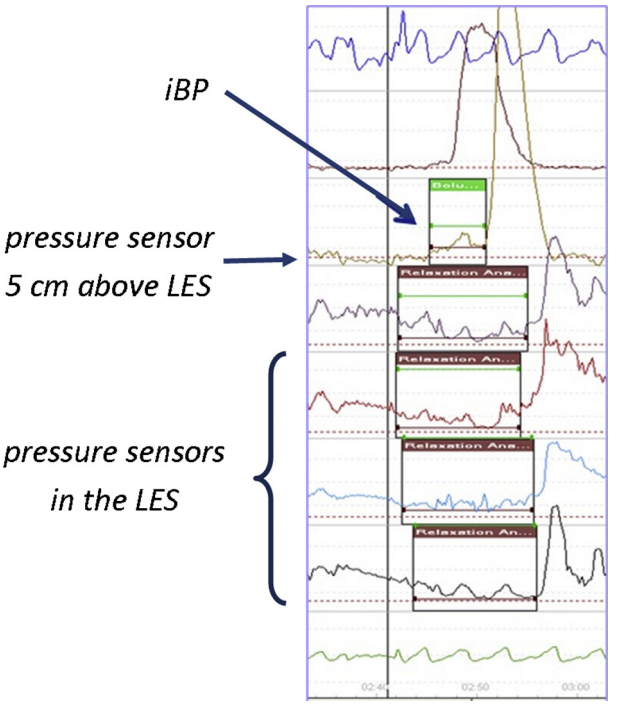

Figure 1. Intrabolus pressure (iBP) (arrow) measured by a pressure port placed 5 cm above the lower esophageal sphincter (LES). The iBP is identified by a rise in pressure to a plateau above the esophageal baseline pressure just preceding the upstroke of an esophageal contraction wave. In this illustration, 4 radial sensors located in the sphincter show relaxation of the LES.

There were 58 males and 42 females, with a mean age of 55 years. All had an esophageal motility study performed before surgical therapy. All had a tension-free, 360-degree Nissen fundoplication performed over a 60-F bougie. All were evaluated for new onset dysphagia at a median follow-up of 50 months after surgery. Follow-up information was obtained during clinic visits in the first year after

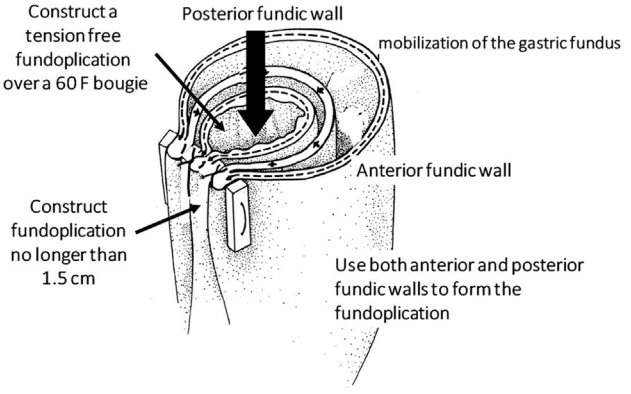

Figure 2. Technical factors that contribute to a tension-free Nissen fundoplication with low outflow resistance. (Reprinted courtesy of the author, Dr TR DeMeester.)

Table 1. Intra-Bolus Pressure Amplitude and Duration in Normal and GERD Patients

Amplitude and duration	Normal patient (n = 53), mean (SD)	Preoperative GERD patient (n = 37), mean (SD)	p Value
Amplitude, mmHg	6.8 (3.7)	3.6 (7.0)	0.003
Duration, s	16.0 (15.6)	8.6 (15.2)	0.002

GERD, gastroesophageal reflux disease.

surgery and by phone interview after that. Dysphagia was scored as none, mild (occasionally with course foods lasting for few seconds), moderate (required liquid to clear), and severe (history of meat impaction requiring medical attention).

Manometry

Esophageal manometry was performed in normal subjects and in all patients before Nissen fundoplication. All drugs with a foregut affect were discontinued for at least 48 hours before the motility study. After an overnight fast, a 12-French, 8-channel water-perfused motility catheter (Arndorfer Medical Specialties) was passed through the anesthetized nostril into the esophagus and into the stomach. The manometry study was conducted and analyzed as previously described.[7] A similar postoperative motility study was performed in 37 GERD patients after tension-free Nissen fundoplication.

The iBP was measured by a pressure port placed 5 cm above the upper border of the LES. The iBP was identified by the plateau pressure above the esophageal baseline pressure just preceding the upstroke of an esophageal contraction wave (Fig. 1). The iBP amplitude was measured for each swallow by a computer software program (Polygram Net, Medtronic Inc), and the final value for each patient was the average of 5 swallows. Distal esophageal contractility was assessed by averaging the peristaltic contraction amplitude of 10 swallows measured by sensors located in the distal third of the esophagus.

Surgical technique

A tension-free, 360-degree Nissen fundoplication was performed according to our previously published technique that included 4 modifications to reduce outflow resistance.[8] The modifications were: mobilization of the gastric fundus to remove left lateral tension on the fundoplication; construction of the fundoplication with both the anterior and posterior wall of the gastric fundus in a manner such that anterior and posterior lips of fundoplication lie on the right lateral surface of the esophagus; construction of the fundoplication without tension over a 60-F bougie; and limiting the length of fundoplication to 1.5 cm (Fig. 2).

Statistical analysis

The values are reported as mean and standard deviation (SD). The 95th percentile was used to define the upper level of iBP in normal subjects and patients. The Mann-Whitney U test was used to compare normal subjects' to patients' values. The Wilcoxon matched pairs test was used to compare preoperative to postoperative values. Correlation was assessed using Spearman's correlation analysis. A value of $p < 0.05$ was defined as significant. Approval was obtained from the Institutional Review Board of the University of Southern California before the study was started.

RESULTS

The mean (SD) for the iBP amplitude and duration in the 53 normal subjects and 37 GERD patients is shown in Table 1. The iBP amplitude and duration were significantly lower in GERD patients compared with normal subjects. After a tension-free 360-degree Nissen fundoplication, the iBP amplitude and duration were significantly higher than preoperative values as well as values obtained from normal subjects (Tables 1 and 2). There was no correlation between iBP and the amplitude of the esophageal body contraction in normal subjects or patients before and after a tension-free, 360-degree Nissen fundoplication ($p > 0.05$).

The 95th percentile values for the amplitude and duration of iBP in asymptomatic normal subjects and GERD patients after a tension-free Nissen fundoplication are shown in Table 3. The 95th percentile value for the amplitude of the iBP after a tension-free Nissen fundoplication was 20 mmHg and reflects the outflow resistance that needs to be overcome by the esophageal peristaltic contractions to avoid dysphagia.

Table 2. Intra-Bolus Pressure and Duration before and after Nissen Fundoplication (n = 37)

Amplitude and duration	Preoperative, mean (SD)	Postoperative, mean (SD)	p Value
Amplitude, mmHg	3.6 (7.0)	12.0 (3.2)	$p < 0.0001$
Duration, s	8.6 (15.2)	13.6 (10.2)	$p = 0.002$

Table 3. Upper Limit of Normal (95th Percentile) for the Intra-Bolus Amplitude and Duration in Normal and GERD Patients after a Tension-Free, 360-Degree Nissen Fundoplication

Amplitude and duration	Normal patient	Patient after a Nissen
Amplitude, mmHg	10.4	20.0
Duration, s	35.5	32.4

GERD, gastroesphageal reflux disease.

In the validation population, all 100 patients had an esophageal peristaltic contraction amplitude in the distal esophagus > 20 mmHg. However, 44 patients did have abnormal esophageal motility findings consisting of a contraction amplitude in the lower third of the esophagus below the 5th percentile of normal (30 mmHg) or >20% dropped contraction waves. Only 3 of the 100 patients developed dysphagia as a new symptom after Nissen fundoplication, and in all 3, it was scored as mild. Two of these patients had normal motility and 1 had an increased number of dropped waves on the manometry before surgery.

DISCUSSION

Intrabolus pressure (iBP) is a waveform on the esophageal manometry tracing preceding a contraction upstroke. The iBP, when measured at 5 cm above the upper border of the LES, reflects the outflow resistance of the LES. The 95th percentile value for the iBP in normal subjects was 10.4 mmHg and is easily overcome by the amplitude of a normal esophageal contraction. The iBP was lower in patients with GERD, when compared with normal subjects, indicating a reduced outflow resistance, likely from a structurally defective sphincter. A tension-free, 360-degree Nissen fundoplication causes a significant increase in iBP above the level of normal subjects, indicating that the procedure increases LES outflow resistance (Fig. 3).

Fibbe and colleagues[3] categorized patients with dysmotility on the basis of a mean contraction amplitude < 40 mmHg measured 3 to 8 cm above the LES, or failed primary peristalsis > 40%. They found that the development of postoperative dysphagia was unrelated to these manometric findings and concluded that esophageal dysmotility reflects more the severity of the disease and does not predict postoperative outcome or required tailoring of the surgical procedure.[3]

This conclusion disregards the development of dysphagia secondary to outflow resistance imposed by the LES. For example, patients with a hypertensive LES have a high intrabolus pressure and require a myotomy of the sphincter to relieve the dysphagia. This indicates that there is a level of outflow resistance in the LES that induces dysphagia in patients with normal peristaltic contraction amplitudes. Consequently, to avoid persistent postoperative dysphagia, both the status of esophageal

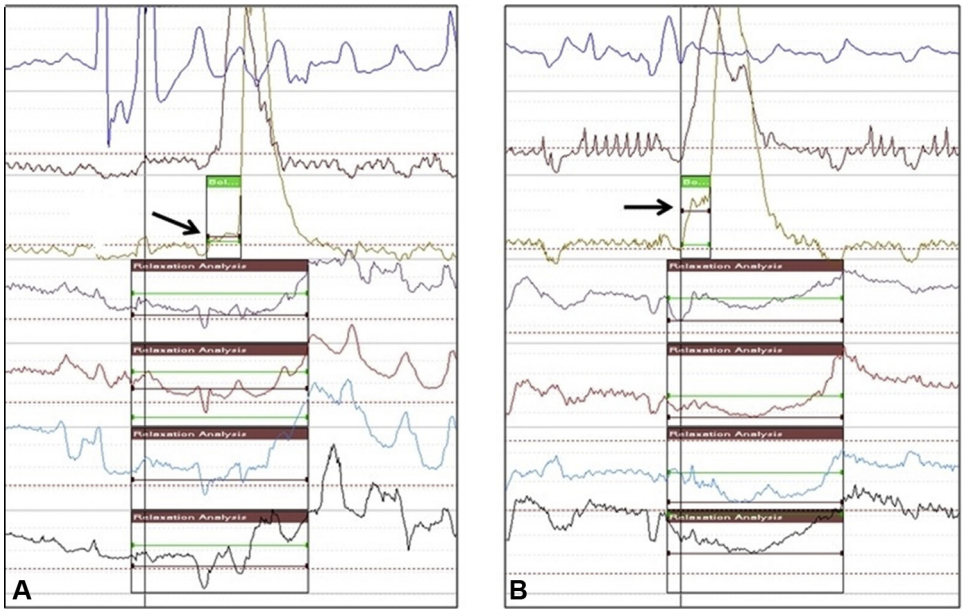

Figure 3. Intrabolus pressure (iBP) recorded in (A) a normal patient, and (B) a gastroesophageal reflux disease patient after Nissen fundoplication, illustrating elevated iBP after Nissen fundoplication.

motility and the outflow resistance imposed by the fundoplication must be considered.

In an attempt to avoid postoperative dysphagia, we used the iBP at 5 cm above the upper border of the LES rather than the esophageal body criteria used in the Fibbe and associates' study.[3] The 95th percentile value for the iBP after a tension-free Nissen fundoplication was 20 mmHg. This is the outflow resistance that needs to be overcome by the esophageal body contraction.

Verification of a contraction amplitude >20 mmHg as a threshold to avoid postoperative dysphagia was validated in a population of 100 patients, 44 of whom had contraction amplitude in the lower third of the esophagus >20 mmHg but <30 mmHg, and none of the patients had a named motility disorder, but dropped waves were occasionally seen. Only 3 of the 100 patients developed new onset dysphagia. This finding has important implications in the preoperative selection of patients for a fundoplication provided the fundoplication does not overly increase the outflow resistance of the LES.

An interesting observation in the patients with GERD is that the iBP amplitude was less and its duration was shorter than in normal subjects, indicating less resistance to the bolus transport. A tension-free Nissen fundoplication increased both these parameters significantly, indicating greater resistance to bolus transport and the potential for dysphagia. This emphasizes the importance of technique in performing a Nissen fundoplication, which can vary between surgeons.[9,10] Consequently, the outflow resistance caused by a Nissen fundoplication can vary. Surgeons need to keep the outflow resistance caused by the fundoplication low, ie below an iBP of 20 mmHg. This can be accomplished by mobilizing the gastric fundus to minimize lateral tension, using both the anterior and posterior gastric walls to construct and avoid twisting of the fundoplication, calibrating the size of the fundoplication using a 60-F bougie, and limiting the length of fundoplication to 1.5 cm (Fig. 2). In our experience, this resulted in only 3% of our patients developing postoperative dysphagia, all of which were mild in degree.

Experience has shown that if outflow resistance, ie the iBP, exceeds 20 mmHg, the probability of postoperative dysphagia is high.[11-13] The observation of pseudo-achalasia after a Nissen fundoplication supports the concept that there is a level of resistance that prevents emptying of the esophagus, despite the amplitude of the peristaltic contractions, and leads to esophageal dilatation and peristaltic failure.[14,15] The following patient example illustrates the above phenomenon. A 44-year-old white woman with a 3-year history of heartburn, regurgitation, and chest pain, underwent a Nissen fundoplication. She was referred to our center for management of her persistent postoperative dysphagia 2 years after the operation. Our measurement of iBP was 22.5 mmHg, which is slightly above the 95th percentile, after a tension-free, 360-degree Nissen fundoplication. Her esophageal contraction amplitude in the distal third of the esophagus was in excess of 80 mmHg (Fig. 4). Reconstruction of the Nissen fundoplication reduced her iBP to 10.9 mmHg and alleviated her dysphagia. This clinical example shows that to avoid postoperative dysphagia, not only must the distal esophageal contraction amplitude be greater than 20 mmHg, but the fundoplication must not be constructed in a manner that increases the outflow resistance to greater than 20 mmHg.

We acknowledge that a limitation of our study is the lack of testing the presence and degree of postoperative dysphagia in a separate group of patients with contraction amplitude < 20 mmHg in the distal third of the esophagus.

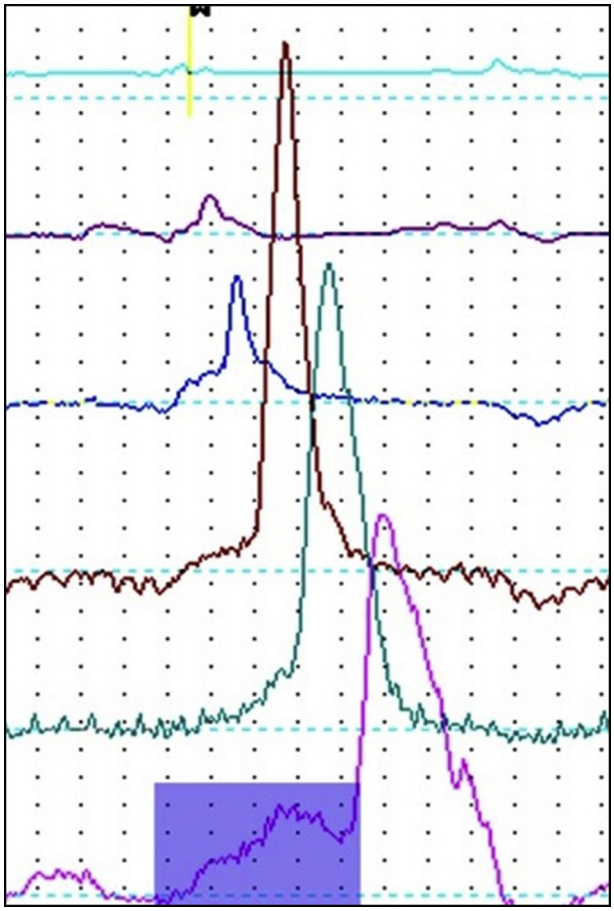

Figure 4. Manometric tracing in patient demonstrating an intrabolus pressure (iBP) amplitude of 22.5 mmHg (highlighted) and a contraction amplitude in the distal third of the esophagus in excess of 80 mmHg.

Ethically, it would be inappropriate to perform a full Nissen fundoplication in such patients just to measure the prevalence of persistent postoperative dysphagia. For this reason, we chose to affirm that peristaltic contraction amplitudes above 20 mmHg in the distal third of esophagus would overcome the outflow resistance imposed by a tension-free Nissen fundoplication and not result in persistent dysphagia. Indeed, in the validation population, 97% of the patients were free of new onset dysphagia.

Our study was performed using conventional manometry. This was done in order to obtain absolute measurements of the LES. This is difficult to do with the current high-resolution manometry catheters.[16] Our findings showed that the critical measurement was the LES outflow resistance, as measured by the iBP 5 cm above the LES. However, other investigators have studied the utility of iBP using high resolution manometry after fundoplication. Scheffer and colleagues[17] and Rerych and associates,[18] using high-resolution manometry, found an increase in intrabolus pressure after fundoplication. Wilshire and coworkers[19] showed that gastroesophageal junction integrated relaxation pressure (IRP) was significantly higher in patients with dysphagia after fundoplication compared with those without dysphagia. They suggested that impaired relaxation of the neo-high−pressure zone, recognizable as an elevated IRP on high resolution manometry, can discriminate patients with dysphagia from those without this complaint after fundoplication.[19] There is concern, however, that pressure measured at a given point will differ between conventional manometry and high resolution manometry.

In summary, LES outflow resistance can be measured by the iBP in the esophagus 5 cm above the upper border of the LES. Patients with reflux have a mean iBP of 3.6 mmHg, which is less than the 6.8 mmHg measured in normal subjects. After a Nissen fundoplication, the mean iBP rises to 12 mmHg, with a 95th percentile value of 20 mmHg. Only 3% of the patients are likely to develop dysphagia if the global contraction amplitude in the distal third of the esophagus exceeds 20 mmHg and the Nissen fundoplication is constructed in a manner that maintains the outflow resistance of the LES below an iBP of 20 mmHg.

CONCLUSIONS

Nissen fundoplication increases the outflow resistance of the esophagus and should be constructed to avoid an iBP >20 mmHg. Patients whose distal third esophageal contraction amplitude is >20 mmHg have a minimal risk of dysphagia after a tension-free Nissen fundoplication.

Author Contributions

Study conception and design: Ayazi, S DeMeester, Crookes, T Demeester

Acquisition of data: Ayazi, Zehetner, Bremner, Lipham, Crookes

Analysis and interpretation of data: Ayazi, Hagen, Zehetner, Bremner

Drafting of manuscript: Ayazi, S Demeester, Hagen, Lipham, T DeMeester

Critical revision: S DeMeester, Hagen, Bremner, Crookes, T DeMeester

REFERENCES

1. Rydberg L, Ruth M, Abrahamsson H, et al. Tailoring antireflux surgery: A randomized clinical trial. World J Surg 1999; 23:612−618.
2. Mughal MM, Bancewic ZJ, Marples M. Oesophageal manometry and pH recording does not predict the bad results of Nissen fundoplication. Br J Surg 1990;77:43−45.
3. Fibbe C, Layer P, Keller J, et al. Esophageal motility in reflux disease before and after fundoplication: a prospective, randomized, clinical, and manometric study. Gastroenterology 2001; 121:5−14.
4. Bremner RM, DeMeester TR, Crookes PF, et al. The effect of symptoms and nonspecific motility abnormalities on outcomes of surgical therapy for gastroesophageal reflux disease. J Thorac Cardiovasc Surg 1994;107:1244−1249.
5. Cook IJ. Cricopharyngeal function and dysfunction. Dysphagia 1993;8:244−251.
6. Shaw DW, Cook IJ, Gabb M, et al. Influence of normal aging and oral-pharyngeal and upper esophageal sphincter function during swallow. Am J Physiol 1995;268:G389−G396.
7. Zaninotto G, DeMeester TR, Schwizer W, et al. The lower esophageal sphincter in health and disease. Am J Surg 1988; 155:104−111.
8. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. Ann Surg 1986; 204:9−20.
9. Huntington TR, Danielson L. Variation in fundic dimensions with respect to short gastric vessel division in laparoscopic fundoplication. Surg Endosc 2001;15:76−79.
10. Frazzoni M, Piccoli M, Conigliaro R, et al. Laparoscopic fundoplication for gastroesophageal reflux disease. World J Gastroenterol 2014;20:14272−14279.
11. Bais JE, Wijnhoven BP, Masclee AA, et al. Analysis and surgical treatment of persistent dysphagia after Nissen fundoplication. Br J Surg 2001;88:569−576.
12. Blom D, Peters JH, DeMeester TR, et al. Physiologic mechanism and preoperative prediction of new-onset dysphagia after laparoscopic Nissen fundoplication. J Gastrointest Surg 2002; 6:22−28.
13. Peters JH, DeMeester TR, Crookes P, et al. The treatment of gastroesophageal reflux disease with laparoscopic Nissen fundoplication: prospective evaluation of 100 patients with "typical" symptoms. Ann Surg 1998;228: 40−50.

14. Bonavina L, Bona D, Saino G, et al. Pseudoachalasia occurring after laparoscopic Nissen fundoplication and crural mesh repair. Langenbecks Arch Surg 2007;392:653–656.
15. Liu W, Fackler W, Rice TW, et al. The pathogenesis of pseudoachalasia: a clinicopathologic study of 13 cases of a rare entity. Am J Surg Pathol 2002;26:784–788.
16. Ayazi S, Hagen JA, Zehetner J, et al. The value of high-resolution manometry in the assessment of the resting characteristics of the lower esophageal sphincter. J Gastrointest Surg 2009;13:2113–2120.
17. Scheffer RC, Samsom M, Haverkamp A, et al. Impaired bolus transit across the esophagogastric junction in postfundoplication dysphagia. Am J Gastroenterol 2005;100:1677–1684.
18. Rerych K, Kurek J, Klimacka-Nawrot E, et al. High-resolution manometry in patients with gastroesophageal reflux disease before and after fundoplication. J Neurogastroenterol Motil 2017;23:55–63.
19. Wilshire CL, Niebisch S, Watson TJ, et al. Dysphagia postfundoplication: more commonly hiatal outflow resistance than poor esophageal body motility. Surgery 2012;152:584–592.