Gastroesophageal Disease and Nausea

Does Fundoplication Help or Hurt?

Thomas T. Hui, MD; Steven M. Fass, MD; Dan I. Giurgiu, MD; Atsushi Iida, MD; Sumito Takagi, MD; Edward H. Phillips, MD

Hypothesis: Nausea associated with gastroesophageal reflux disease is cured by laparoscopic Nissen fundoplication (LNF).

Design: Prospective cohort study of unselected patients who underwent LNF from January 1, 1995, through March 31, 1999. Patients were followed up by a physician for 6 to 36 months.

Setting: A large community teaching hospital.

Patients: One hundred consecutive patients with gastroesophageal reflux disease who underwent LNF; all patients were followed up. Patients were grouped according to the presence (group A, n = 33) or absence (group B, n = 67) of preoperative nausea. Interventions were LNF, esophageal manometry, 24-hour pH monitoring, and nuclear gastric emptying studies.

Main Outcome Measures: Resolution of symptoms after LNF.

Results: Nausea was the most common atypical symptom of gastroesophageal reflux disease, occurring in 33 patients (33%). There were no differences in esophageal manometry or 24-hour pH results between groups. There was a female preponderance in group A (55% vs 33%; \( P = .003 \)). Patients in group A had a higher prevalence of preoperative dysphagia (\( P = .02 \)). Patients with persistent postoperative nausea had a higher prevalence of cough (\( P = .003 \)) and dysphagia (\( P = .009 \)). The LNF was more effective in reducing heartburn (95% reduction) and regurgitation (95% reduction) than cough and dysphagia (60% reduction). There was a 79% reduction in the number of patients with nausea (33 to 7; \( P < .001 \)).

Conclusion: Laparoscopic Nissen fundoplication is effective in eliminating nausea associated with gastroesophageal reflux disease and is not contraindicated in these patients.

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Typical symptoms of gastroesophageal reflux disease (GERD) include heartburn and regurgitation. It is estimated that 7% to 10% of the US population suffer from heartburn daily.\(^1\)\(^2\) However, patients with GERD often present with atypical symptoms such as chest pain, asthma, coughing, and nausea.\(^3\) In the study by Klauser et al,\(^4\) nausea was present in 38% of patients with symptoms of GERD and abnormal results of a 24-hour esophageal pH study.

Laparoscopic Nissen fundoplication (LNF) has been shown in nearly all published studies to be highly effective in relieving typical symptoms of GERD, specifically heartburn and regurgitation, when caused by reflux.\(^5\)\(^-\)\(^14\) It is less clear whether the same results can be achieved with atypical symptoms. While several series\(^15\)\(^-\)\(^22\) have investigated the effectiveness of LNF in improving chronic cough and asthma, to our knowledge, no study to date has addressed the effect of LNF on relief of nausea in patients with GERD. The present study was undertaken to consider this issue.

Of the 100 patients, 60 were male and 40 female, with average age 50 years (range, 11-96 years). Indications for operation included gastroesophageal reflux symptoms refractory to medical therapy in 47 patients and complications of GERD in 53 patients (esophagitis in 30, stricture in 9, esophagitis and stricture in 6, esophagitis and Barrett esophagus in 6, and Barrett esophagus in 2).

Upper gastrointestinal tract endoscopy was performed preoperatively in 81 patients and demonstrated esophagitis in 42 (52%), stricture in 12 (15%), and Barrett esophagus in 8 (10%). Barium swallow performed in 45 patients demonstrated reflux in 26 (58%) and stricture in 6 (13%). A 24-hour pH study was performed in 73 patients and showed abnormal acid reflux in all of them.

Esophageal manometry was performed in all patients. There were no differences in esophageal motility between groups. The average lower esophageal sphincter resting pressure was 12 mm Hg.
PATIENTS AND METHODS

A retrospective review was conducted on 100 consecutive unselected patients who underwent laparoscopic antireflux surgery between January 1, 1995, and March 31, 1999. A single surgical team performed all LNF procedures. All preoperative and intraoperative data were collected concurrently. Postoperative data were collected by physician interview.

Data selected for analysis included patients’ age, sex, preoperative symptoms, preoperative evaluations, indications for operation, and postoperative symptoms. All patients had at least 1 preoperative study demonstrating pathological gastroesophageal reflux, and all patients underwent esophageal manometry before operation.

For purposes of analysis, patients were divided into 2 groups on the basis of the presence (group A) or absence (group B) of preoperative nausea. Nausea was defined as the subjective sensation of the need to vomit. Frequency and severity of nausea were not used to further define patients in group A. Preoperative and postoperative symptoms were compared between the 2 groups. In addition, postoperative symptoms were compared for patients with and without persistent nausea at 6 weeks after operation.

Laparoscopic Nissen fundoplication was performed using a standard technique. The short gastric vessels were routinely divided in all patients. The esophagus was mobilized fully to ensure an adequate length of intra-abdominal esophagus. The crura were closed and a 360° wrap, 2 to 4 cm in length, was created.

All patients underwent follow-up examinations at 6 weeks after operation. Patients who had persistent nausea at this visit were interviewed at 6 to 36 months. Parametric and nonparametric data were analyzed with t test and χ² analysis, respectively.

Lower esophageal sphincter relaxation was normal or too low to measure in all patients. Esophageal peristalsis was normal in every patient. Twenty-six patients had mean esophageal body contraction pressures less than 50 mm Hg: 9 (27%) in group A and 17 (25%) in group B (P = .77). One patient (3%) in group A and 3 patients (4%) in group B had mean esophageal body contraction pressures of less than 30 mm Hg. There was no significant difference in 24-hour pH study results between groups A and B. The number of reflux episodes (78 vs 64; P = .23) and the percentage of reflux episodes that were symptomatic (21% [16 episodes] vs 17% [11 episodes]; P = .37) in the lower esophagus were similar. Symptoms before and after the operation are summarized in Table 1. All symptoms were reduced significantly by LNF. The 2 typical symptoms of GERD—heartburn and regurgitation—were more effectively relieved by LNF than were the atypical symptoms.

Data for patients with and without preoperative nausea are compared in Table 2. Age and manometric variables were similar, but patients with preoperative nausea were more often female.

Symptoms of the 2 groups before and after LNF are compared in Table 3. Preoperative dysphagia was more commonly found in patients with preoperative nausea and was more effectively relieved after LNF in this group of patients. Furthermore, of all atypical symptoms, preoperative dysphagia was the most likely to persist postoperatively. Cough was more effectively relieved in patients without preoperative nausea. Table 4 summarizes the postoperative symptoms of patients with and without postoperative nausea. Patients with persistent postoperative nausea had a higher prevalence of postoperative atypical symptoms, such as cough and dysphagia, than those without nausea.
Seven patients complained of nausea when seen at 6 weeks after operation. Nausea had been present preoperatively in 5 of them and had developed after operation in 2. Longer follow-up (6-36 months) of the 7 patients with nausea at 6 weeks demonstrated that all patients were free of nausea and were using no antinausea medications.

Preoperative gastric emptying studies were performed in 12 group A patients (36%) and 17 group B patients (25%). Eight (67%) of the 12 from group A and 4 (24%) of the 17 from group B had abnormal results (P = .02). Two of the 12 patients from group A had postoperative nausea, both of whom had abnormal results of gastric emptying studies. Of the 17 patients from group B who underwent preoperative gastric emptying studies, 1 patient with a normal result developed nausea postoperatively. These data show that, while patients with preoperative nausea were more likely to have delayed gastric emptying, a majority (79%) of patients with preoperative nausea and delayed gastric emptying experienced relief of their nausea after LNF.

**COMMENT**

Nausea is a nonspecific, subjective sensation of an impending urge to vomit. It can be a dominant symptom or a minor symptom in patients with GERD. Nausea can also be a symptom of other disease processes, such as peptic ulcer disease, gastroparesis, gastrointestinal tract malignant neoplasm, intestinal obstruction, and intracranial disease. In a small retrospective series by Brzana and Koch, 10 patients with chronic intractable nausea unresponsive to empiric therapies were found to have GERD on the basis of esophagastroduodenoscopy, 24-hour pH study, or a positive Bernstein test. All experienced resolution of nausea after treatment with omeprazole (7 patients), cisapride or ranitidine hydrochloride (2 patients), or open Nissen fundoplication (1 patient). That study emphasized the important relationship between GERD and nausea, as well as the effectiveness of antireflux therapies in relief of nausea caused by GERD.

In the series reported herein, preoperative nausea was the most common atypical symptom of GERD and was found in 33% of patients with proved GERD. Laparoscopic Nissen fundoplication was more effective in relieving typical symptoms (heartburn and regurgitation) of GERD than atypical symptoms. Patients with preoperative nausea were more commonly female and were more likely to have delayed gastric emptying but not poor esophageal contraction pressures. Heartburn and regurgitation were equally common in patients with and without preoperative nausea. Early postoperative nausea occurred in 7 patients. Persistent cough and/or dysphagia were more common in patients with postoperative nausea. All patients with early postoperative nausea experienced no nausea at longer-term follow-up.

The precise number of patients with GERD who experience nausea is unknown. Of 304 patients with a variety of esophageal and extraesophageal symptoms who underwent 24-hour pH monitoring for possible GERD, 166 had pathological results of pH monitoring indicative of reflux. Nausea was present in 38% of these patients but also occurred with similar frequency (32%) in the remaining 138 patients with normal results of 24-hour pH studies. This demonstrates the nonspecific nature of nausea. Since GERD is a relatively common condition, it may coexist with other common conditions that produce nausea, leading to problems in accurate diagnosis and treatment of these patients.

While many studies have demonstrated the effectiveness of LNF in relieving heartburn and regurgitation in patients with GERD (Table 5), few studies have examined the effect of the procedure on relief of atypical symptoms. Moreover, to our knowledge, no study has specifically examined the effectiveness of LNF in relieving nausea in patients with GERD. In Hunter and coworkers’ review of 300 patients undergoing laparoscopic antireflux surgery, 89% of patients had typical reflux symptoms (heartburn and regurgitation), while 64% also had atypical symptoms (chest pain, cough, hoarseness, and asthma) and 11% had atypical symptoms only. Treatment by LNF was found to be very effective, with improvement of 93% of typical and 81% to 91% of atypical symptoms. Preoperative nausea was seen in 18% of their patients. Postoperatively, nausea was present in 4% of patients at 6 weeks and 6% of patients at 1 year. However, it was not clear whether any patients without preoperative nausea developed nausea after LNF. In addition, the characteristics of the patients with preoperative and postoperative nausea were not studied.

In contrast, the prospective study by So et al of 150 patients undergoing LNF demonstrated that typical symptoms of GERD, such as heartburn, were reduced by 93% after surgery, compared with only 56% reduction in atypical symptoms. The authors concluded that the relief of atypical symptoms attributed to gastroesophageal reflux by LNF is less satisfactory and more difficult to predict than relief of heartburn and regurgitation. However, nausea was not included as an atypical symptom in that study. Nausea can also be a postoperative complication of LNF. In a retrospective study by Swanstrom and Wayne of 82 patients undergoing LNF, postoperative nausea immediately after surgery was present in 12 patients (15%). Of these 12 patients, 8 developed nausea only after their operation.

In our series, esophageal motility studies failed to detect differences between patients with and without nausea. Unfortunately, gastric emptying studies (although results were more often abnormal in patients with nausea) were not done on enough patients to fully elucidate a possible cause and effect. A review by Scarpignato summarized the results of 30 studies regarding gastric emptying of different meals in adult patients with GERD. In all studies reviewed, gastric emptying of liquid was normal. However, delayed gastric emptying of solid or semisolid meals

**Table 4. Persistence of Other Symptoms of Gastroesophageal Reflux Disease in Patients With and Without Early Postoperative Nausea**

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was reported in 60% of the gastric emptying studies. Since Scarpignato's review, other European studies using realtime ultrasound and electrogastrography have found increased incidence of delayed gastric emptying in patients with GERD.27,28 However, this finding could not be validated by a number of US studies, which demonstrated delayed gastric emptying in only 6% to 12% of the patients.29-31 Furthermore, in the study by Schweizer et al,32 delayed gastric emptying occurred with equal frequency in patients with or without reflux. In our series, 6 of 8 patients with preoperative nausea and delayed gastric emptying experienced complete resolution of nausea at 6 weeks after operation, and the remaining 2 patients were free of nausea when questioned 6 months later. It is known that antireflux surgery enhances gastric emptying, as shown by the work of Hinder et al33 and Viljakka et al.34 It is possible that this effect led to the resolution of nausea.

In conclusion, nausea is a common symptom of patients with GERD, occurring in one third of patients. Laparoscopic Nissen fundoplication is effective in relieving nausea in this group of patients, with 79% symptom reduction after 6 months. Although the efficacy of LNF is not as dramatic in curing atypical symptoms of GERD, it is still highly effective and more effective in relieving nausea than cough or dysphagia. The patient with nausea and reflux should anticipate a good outcome after antireflux surgery.

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REFERENCES


23. Peters et al31

24. Jamieson et al9

25. Peters et al13

26. Wetscher et al21

27. Deveney et al19

28. Hunter et al11

29. Peters et al13

30. Wetscher et al21

31. Allen and Mehran22

32. Hinder et al14

33. Jamieson et al9

34. Peters et al13

35. Wetscher et al21

36. Allen and Mehran22

37. Present study

38. Table 5. Studies Examining the Efficacy of Antireflux Surgery in Relieving Symptoms Secondary to GERD*"
Second question: Did you stratify these symptoms with respect to the presence or absence of hiatus hernia, for example, sizable type 2 or type 3 hiatus hernias? Lastly, do you ever perform gastric emptying studies in conjunction with your fundoplication?

J. Bradley Aust, MD, San Antonio, Tex: How do you define nausea? How do you grade or measure it? This is critical.

Dr Phillips: We did not identify gastric or duodenal pathology with greater or lesser frequency in the patients with nausea than in those without nausea. Gastric emptying was by nuclear emptying study with solids; we did not test for abnormal emptying of liquids. Is it possible to quantitate the delay in emptying? Yes, but we chose to analyze the data using abnormal or normal. When is gastric emptying impaired sufficiently to consider pyloroplasty? That is a difficult question to which we have given considerable thought without reaching any definite conclusions. To date, our protocol is not to perform drainage procedures at the primary operation, waiting instead to see whether the fundoplication itself improves emptying and symptoms. So far, this approach has been successful, and no reoperations have been needed. This issue is certainly of concern, particularly in patients with diabetes or connective-tissue disorders resulting in gastroparesis. As to the question of gastric emptying studies being performed postoperatively, they were done on selected patients with persistent symptoms, usually for continued heartburn or regurgitation. Two patients with nausea and delayed gastric emptying had persistence of nausea, but because it eventually improved, they were not re-studied. Clearly, a prospective analysis utilizing gastric emptying studies in all patients would be ideal, as the present data are insufficient for definitive conclusions.

Before commenting on our preoperative testing, may I emphasize that we did only 360° wraps and have abandoned partial fundoplications. We do manometry in all patients and, perhaps inappropriately, will modify the length of the wrap based on manometric data. The wrap is always floppy, and we always divide the short gastric vessels. When the esophageal body contraction pressures are less than 30 mm Hg or peristalsis is less than 50% propagated, the wrap is limited to 1 cm in length. Regarding 24-hour pH studies: we will omit them in selected patients with proven GERD such as patients with Barrett’s, GI strictures with regurgitation, or reflux confirmed on esophagram.

Dr Aust asked our definition of nausea. Like pornography, I can’t define it but I know it when I see it. The correct definition, in fact, is “the sensation of an impending urge to vomit.”

Dr Donahue asked about our interview techniques. This is a critical issue and one with which we’ve become familiar in our outcome studies of other laparoscopic procedures. To avoid bias and patients’ trying to please their doctors, the operating surgeon must not conduct the interview regarding the presence of postoperative symptoms and patient satisfaction. In this study, a physician, who was not a member of the operative team nor participated in the present or future care of the patient, conducted all of the postoperative interviews. The initial history was performed by the operating surgeon and the endoscopic fellow. We developed an intake survey tool to document preoperative symptoms prospectively. It is impossible to get an accurate retrospective assessment of a patient’s preoperative symptoms as the patient’s memory is selective at best.

Dr Dayton, thank you for your questions that give me the opportunity to clarify our patient population. All patients with partial fundoplications and patients with hiatus hernias greater than 4 cm and paraesophageal hernias were excluded from this analysis. I cannot explain the preponderance of female patients in the nausea group. Of note, frequency of abnormalities in gastric emptying was not related to sex of the patient. This question deserves further study.