Outcomes of Nissen Fundoplication in Patients With Gastroesophageal Reflux Disease and Delayed Gastric Emptying

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Objective: To investigate the effect of delayed gastric emptying (DGE) on subjective and objective outcomes of gastroesophageal reflux disease following Nissen fundoplication with or without pyloroplasty.

Design: Retrospective analysis of prospectively collected data.

Setting: Tertiary care teaching hospital.

Patients: A total of 141 consecutive patients considered for Nissen fundoplication who also had suspected DGE based on symptoms.

Interventions: Of 141 patients, 63 had a time to 50% emptying (T1/2) greater than 90 minutes; 47 of the 63 of these had severe DGE (T1/2/ > 150 minutes) and had Nissen fundoplication and pyloroplasty. Sixteen of the 141 with T1/2 greater than 90 but less than 150 minutes and 78 with normal gastric emptying findings (n=78) had Nissen fundoplication only.

Main Outcome Measures: Postoperatively, patients with symptom scores greater than 2 and/or abnormal 24-hour pH values (DeMeester score >14.7) were considered to have had unsuccessful treatment. Gastroesophageal reflux disease outcomes were compared between groups 1 and 2. Finally, the outcomes of both groups were compared with a control cohort of 418 patients with Nissen fundoplication and no DGE symptoms (group 3).

Results: At the mean follow-up of 21 months, there were no differences between the 2 groups regarding relief of reflux symptoms (DGE group, 54 of 63 [85.7%] vs NGE group, 71 of 78 [91%]; P=.47) or objective control of acid reflux (DGE group, 33 of 39 [84.6%] vs NGE group, 41 of 51 [80.3%]; P=.78). Dyspeptic symptoms were improved in the DGE group (P<.001); however, the overall incidence remained higher than the NGE group (P=.01). Postoperatively, T1/2 normalized in 88.23% (15 of 17) of patients. Postoperative objective outcomes were also no different between these groups and patients with Nissen fundoplication who did not have DGE symptoms (n=418).

Conclusions: Delayed gastric emptying does not affect outcomes of gastroesophageal reflux disease following Nissen fundoplication, but patients with DGE have more postoperative gas and bloat and/or nausea compared with patients with normal gastric emptying; this is mostly corrected by addition of a pyloroplasty.

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Nissen fundoplication is the most popular and effective antireflux procedure for patients who are referred for surgical treatment of gastroesophageal reflux disease (GERD). However, GERD is often only part of a spectrum of gastrointestinal tract dysfunction. Approximately 20% to 40% of patients with GERD have associated symptoms suggestive of delayed gastric emptying (DGE). While gastric symptoms are often secondary to reflux disease—an example being compensatory air swallowing—many of these patients have true functional disorders such as DGE due to gastroparesis or other causes. On occasion, GERD may actually be a manifestation of DGE. Whether there is any correlation between failure of antireflux procedures and DGE is controversial, although most esophageal surgeons are intuitively concerned about antireflux surgery (ARS) in patients with severe nausea, vomiting, or gas bloat owing to concerns of poor outcomes (unhappy patients) or wrap disruption. Some early studies in adults and more recent studies in the pediatric population have indicated that DGE adversely affects outcomes of antireflux procedures. On the other hand, it has been documented that gastric emptying improves, at least in patients with mild DGE, following Nissen fundoplication.

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Patients considered for ARS advocates a concomitant drainage procedure (pyloroplasty) for patients with severe DGE (solid-phase time to 50% emptying \(T_{1/2} > 150\) minutes) or for those presenting with predominant gastroparesis-related symptoms.

The objective of this study was to assess the subjective and objective outcomes of Nissen fundoplication with or without concomitant pyloroplasty in patients with DGE established preoperatively.

### METHODS

#### PATIENTS

Patients were selected from a prospective database of more than 2,500 patients who had laparoscopic antireflux surgery between October 1991, and October 2007, at our institution. Approval for entry in the database is prospectively obtained under institutional review board approval. A total of 141 patients were identified who had documented GERD and preoperative radionuclide gastric emptying assessment ordered for typical DGE symptoms (symptom score >2 for more than 1 typical symptom of gas bloat, nausea, or abdominal pain and/or fullness). For the purpose of this study, gastroparesis is defined both by a gastric symptom score higher than 2 for bloating, gastric pain, or nausea and a radionuclide gastric emptying assessment with more than 50% of tracer-labeled food remaining in the stomach after 90 minutes \(T_{1/2} > 90\).

Sixty-three patients (44.68%) had objective documentation of their DGE (group 1, solid phase \(T_{1/2} > 90\) minutes). Of 63 patients, 47 (74.60%) with solid-phase emptying and \(T_{1/2} > 150\) minutes had laparoscopic Nissen fundoplication and concomitant pyloroplasty. The remaining 16 patients (25.40%) with a solid-phase \(T_{1/2}\) value between 150 and 90 minutes as well as all patients with normal gastric emptying findings (group 2; \(n = 78\)) had laparoscopic Nissen fundoplication only. A cohort of 418 patients was selected for comparison (group 3) from the same database who had Nissen fundoplication for GERD and no symptoms of DGE. Patients with paraesophageal hernias, antireflux procedures other than a Nissen fundoplication, and those with prior antireflux surgery or pyloroplasty were excluded from the analysis.

#### OPERATIVE PROCEDURES

All surgical procedures were performed laparoscopically under the supervision of the senior investigator (L.L.S. or C.M.D.). Patients with no symptoms of DGE and those with symptomatic DGE but solid-phase \(T_{1/2}\) less than 150 on radionuclide gastric emptying studies were considered for laparoscopic Nissen fundoplication. A 360° wrap was performed using interrupted nonabsorbable sutures, as described previously. In patients with preoperative solid-phase \(T_{1/2}\) greater than 150, a concomitant laparoscopic Heineke-Mikulicz pyloroplasty was performed using a running absorbable suture for which no additional ports were required. The pyloroplasty technique remained unchanged throughout the study.

#### OUTCOME MEASURES

Baseline demographics and data on preoperative and postoperative symptoms, radionuclide gastric emptying studies, upper gastrointestinal tract studies, esophageal manometry, and 24-hour ambulatory pH were prospectively collected on standardized data collection forms that are maintained in an electronic database system (Microsoft Access 2003; Microsoft Corporation, Redmond, Washington). Symptoms were recorded with a validated symptoms assessment tool using a scale of 0 to 4, with higher ordinal values representing greater frequency of symptoms. Baseline demographics and preoperative clinical data were obtained at the time of the first office visit. All patients had preoperative esophageal manometry and 24-hour pH testing. Patients with severe esophageal motility disorders had partial fundoplication and were excluded from this analysis. Preoperative radionuclide gastric emptying studies were routinely performed only if patients had symptoms suggestive of DGE such as bloating, vomiting, epigastric fullness, and postprandial abdominal pain.

Patients were followed up 2 weeks following surgery and again at 4 to 6 weeks, if indicated. At 3 months, patients were asked to complete a symptom assessment form. After a postoperative period of 6 months, all patients were recalled and encouraged to undergo esophageal manometry and 24-hour ambulatory pH testing at no charge. Radionuclide gastric emptying studies were also advocated to all patients with moderate to severe preoperative DGE and any postoperative symptoms. Symptom assessment forms were administered at each visit. Long-term follow-up of all patients was done by telephone interview every year, and symptomatic patients were brought back for further testing. Patients with a postoperative typical GERD symptom score of 2 or higher and those with a DeMeester score greater than 14.7 were considered to have had unsuccessful treatment.

#### STATISTICAL ANALYSIS

Outcomes of GERD were compared between patients with objective documentation of preoperative DGE (group 1, \(n = 63\)) and those with findings of normal preoperative gastric emptying (group 2, \(n = 78\)). Finally, outcomes of both groups were compared with the cohort of 418 patients (group 3) who were considered for laparoscopic Nissen fundoplication and did not have preoperative symptoms of bloating, abdominal pain, and/or nausea severe enough to warrant preoperative gastric emptying studies (symptom score < 2). The means of all continuous variables were compared using appropriate parametric or nonparametric tests. Categorical variables and proportions were compared using the chi-square test or the Fisher exact test. P values of .05 or less were considered statistically significant when comparisons were done between 2 groups. For multiple comparisons, P values were adjusted using Bonferroni post hoc correction. All data are reported either as proportions or mean (standard deviations) or median (range).

### RESULTS

The demographics and preoperative clinical data of patients in the 3 groups are summarized in the Table. There were no significant differences in the mean age, body mass index, preoperative heartburn score, or reflux score among the 3 groups. There were no differences in the mean score of gas bloat, nausea, or abdominal pain between groups 1 and 2. However, as expected, the severity of each of these dyspeptic symptoms was significantly lower in group 3 compared with the other 2 groups \((P < .001)\). There were no conversions to open operation. No perioperative deaths were observed. Six patients had injuries to adjacent hollow viscous (1 esophageal mucosal tear, 5 gastric serosal tears). All were detected and repaired laparoscopically during the same procedure without further sequelae.
The mean (SD) blood loss was 67.02 (25) mL. Three patients had more than 300 mL of blood loss during surgery (1 phrenic artery injury, 2 liver retractor–related injuries). None required blood transfusion. One patient who had Nissen fundoplication and pyloroplasty had a non-fatal pulmonary embolism during the hospital stay. No other major complications were recorded.

**GERD OUTCOMES**

At a mean follow-up of 21 months, 54 of 63 (85.71%) patients in group 1 and 71 of 78 (91.02%) in group 2 demonstrated complete relief of reflux symptoms (P=.47). In group 3, 377 (90.19%) patients demonstrated relief of reflux symptoms. Comparison of subjective outcomes (regurgitation and heartburn) of group 1 with those of groups 2 and 3 demonstrated no significant differences (group 1 vs group 3, P=.74 and group 2 vs group 3, P=.98). Further analysis of postoperative GERD symptoms within group 1 patients demonstrated that those who had Nissen fundoplication only had a relatively poor outcome. Of 16 patients, 4 (25%) demonstrated symptomatic failure; however, the differences were not statistically significant when compared with those who had Nissen fundoplication and pyloroplasty (P=.31) or the other 2 groups (P=.16 and P=.12).

Postoperative 24-hour pH data was available for 39 patients in group 1, 51 in group 2, and 253 in group 3. Although a relatively higher proportion (84.61% [n=33]) of patients in group 1 demonstrated normalization of DeMeester score following surgery compared with groups 2 (80.39% [n=41]) and 3 (82.21% [n=208]), these differences were not found to be statistically significant (group 1 vs group 2, P=.78; group 1 vs group 3, P=.89; group 2 vs group 3, P=.90). Objective outcomes were not statistically significant when patients having Nissen fundoplication and pyloroplasty for DGE were compared with all other groups (P>.68).

**DYSPEPSIC SYMPTOMS**

The postoperative incidence of dyspeptic symptoms and/or adverse effects of surgery experienced at least once a week or more are demonstrated in the Figure. Dyspeptic symptoms demonstrated significant improvement in group 1 (P<.001). However, the overall incidence of gas bloat and nausea were significantly higher in group 1 than groups 2 and 3 (P<.02), and the incidence of abdominal pain was significantly higher in group 1 than group 3 (P=.002). Patients in group 1 also demonstrated a relatively higher incidence of postoperative diarrhea and hyperflatulence than groups 2 and 3; however, the differences were not statistically significant (P>.21). There were no significant differences in the incidence of postoperative dysphagia among the 3 groups (P>.32). Analysis of incidence of dyspeptic symptoms and the adverse effects of surgery in the subgroup of patients in group 1 who had Nissen fundoplication and pyloroplasty for DGE (n=47) and the subgroup of patients with DGE who were considered for Nissen fundoplication only (n=16) revealed that the incidence of postoperative diarrhea was highest (25.53%) among patients who had a pyloroplasty, while the patients with DGE who had only Nissen fundoplication had the high-

![Figure](reprinted/archsurg/vol144/issue9/fig8.jpg)
Many patients referred for antireflux surgery have associated symptoms suggestive of DGE such as bloating, nausea, vomiting, and abdominal pain and/or fullness, and frequently these patients will have objective evidence of DGE when evaluated with radionuclide gastric emptying studies. The reason for this association is unknown and is almost certainly multifactorial. Some patients have a generalized gastrointestinal tract motility disorder and others a true isolated gastroparesis (idiopathic or disease-related) that can be the sole etiology of their GERD. Still others have symptoms consistent with DGE but, in fact, have normal emptying and are merely dyspeptic, often owing to maladaptive habits like aerophagia related to their GERD. Controversy exists regarding whether these patients will have poor outcomes if offered antireflux surgery, although it is known that wrap herniation or disruption is frequent with chronic retching or vomiting. Cogliandolo et al have emphasized the importance of stabilizing impaired gastric emptying rates to ensure a satisfactory clinical outcome following ARS. Maddern et al compared 16 postoperative patients with recurrent reflux symptoms and objective evidence of reflux with 21 postoperative subjects with normal outcomes and demonstrated that gastric emptying was significantly delayed in patients for whom surgery failed. On the other hand, Farrell et al reported an 86.3% symptomatic success rate in patients with DGE (n = 15) compared with 91.8% without DGE. Similar results have been demonstrated by Bais and colleagues in a prospective study of 36 patients. Part of the explanation for these differing results may be the inhomogeneity of the DGE symptom population, with patients with primary neuromuscular dysfunction requiring additional treatment and dyspeptic patients doing well with their antireflux surgery.

In the present study involving 141 patients, although the symptomatic GERD outcomes were relatively worse (85.71%) among patients with objective DGE than in those without (91.02% in group 2 and 90.19% in group 3), the differences were not statistically significant. Moreover, objective control of GERD in this group was marginally better than in the other 2 groups (84.61% vs 80.39% in group 2 and 82.21% in group 3). An important observation was a 25% rate of recurrent/persistent GERD symptoms in patients with objective DGE who did not have a pyloroplasty. In our series, this subgroup of patients, despite good objective outcomes, demonstrated the worst control of reflux symptoms compared with the other groups and studies.

Good results from antireflux surgery (ie, satisfied patients) depends not only on subjective and objective control of GERD but also on the severity of other associated gastrointestinal symptoms and/or adverse effects such as dysphagia, nausea, bloating, epigastric fullness and/or pain, or diarrhea. These symptoms, if severe enough, might lead the patient to consider the ARS a failure despite good control of reflux. Bloating, nausea, and epigastric pain and/or fullness, are also typically present preoperatively in patients with GERD and DGE. Because of this, many physicians consider it important to establish preoperatively which patients with GERD experience their symptoms as a result of gastroparesis or other functional disorders. On the other hand, some investigators challenge the usefulness of preoperative screening for DGE, even in patients with preoperative symptoms of gastroparesis, arguing that DGE has been shown to improve after fundoplication. Currently, there are no clear guidelines as to how these patients should be treated once DGE is established. Some investigators strongly advocate in favor of pyloroplasty for all patients with evidence of DGE. Others suggest that pyloroplasty should be considered only for patients who have moderate to severe objective DGE. Yet others argue that nothing needs to be done, even with the most severe gastroparesis.

At our institution, all patients with GERD with severe symptoms of gastroparesis (symptom score >2 for 2 or more symptoms) are screened objectively with radionuclide scanning for DGE before ARS. Patients with T1/2 greater than 150 are offered Nissen fundoplication and pyloroplasty, while patients with mild DGE (T1/2 <90 but >50) and those with no objective DGE are considered for ARS only.

Most evidence thus far favors our findings that dyspeptic symptoms improve significantly in patients with DGE symptoms following ARS with or without concomitant pyloroplasty. However, patients with objective evidence of DGE (group 1) in our study, while having significant improvement in bloating, nausea, and abdominal pain and/or fullness, still had a significantly higher incidence of these symptoms postoperatively than patients without DGE (groups 2 and 3) (Figure).

Our data also highlight the importance of concomitant pyloroplasty for patients with objective DGE. Patients with objective DGE who were offered Nissen fundoplication only, though they had a good objective control of reflux, demonstrated the highest incidence of gas bloat (25%), hyperflatulence (62.5%), and abdominal pain and/or fullness (31.25%). Interestingly, these patients also had the poorest control of reflux symptoms (success rate, 75%). Our data had insufficient numbers to document definitively whether T1/2 normalizes in these patients, as postoperative radionuclide scanning was available for only 3 of 16 patients in this subgroup. All 3 demonstrated normalization of T1/2; however, objective documentation of increased gastric emptying after fundoplication in such patients has been documented previously in a larger study population. Moreover, because the criteria for inclusion of pyloroplasty were different (T1/2 >90 and <150) in our study population, we do not know whether the symptomatic outcomes would have been better had these patients been offered a pyloroplasty. Nevertheless, inclusion of pyloroplasty is associated with a significant incidence (25.53%) of postoperative diarrhea, and patients should be cautioned about this possibility.
Weaknesses of our study include that it is not a randomized prospective evaluation of treatment options for patients with DGE. Our treatment algorithm is based on 20 years of experience treating esophageal diseases and, though the present study seems to validate this treatment approach, is still a post hoc assessment of our experience. Obviously a prospective randomization between pyloroplasty/Nissen fundoplication and Nissen fundoplication alone with subjective and objective follow-up would be the definitive study. Another potential bias is the incomplete follow-up. Although all patients had symptomatic follow-up using our validated assessment tool, only 64% of patients had pH testing after surgery and even fewer had postsurgical gastric emptying studies. This potentially biases the results toward failure, as patients with problems are more likely to return for testing, in our experience. A higher percentage of postoperative objective studies may have made the differences we saw (improved outcomes after Nissen fundoplication and pyloroplasty for the DGE population) statistically significant.

The present study demonstrates that the symptoms of gastroparesis such as bloating, nausea, and/or abdominal pain and/or fullness are not uncommon in patients with GERD referred for surgery and that many of these patients (44.7%) have objective evidence of DGE. Our data further demonstrate that preoperative DGE does not affect the subjective and objective outcomes of GERD treated with an algorithm of anti-reflux surgery alone for normal or slightly delayed gastric emptying and ARS with pyloroplasty for severe DGE and that the preoperative symptoms of DGE significantly improve in these patients. However, patients with mild DGE who are considered for Nissen fundoplication only should be warned about a relatively higher incidence of reflux symptoms, gas bloat, abdominal pain and/or fullness and hyperflatulence after surgery. Finally, patients being considered for a possible pyloroplasty should be made aware of the possibility of postoperative diarrhea.

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REFERENCES


DISCUSSION

Mark A. Talamini, MD, San Diego, California: The authors have shed some important light on a murky subject: the issue of delayed gastric emptying and outcomes following fundoplication for reflux symptoms. Why do patients remain symptomatic after an antireflux operation? Their standard is to perform a complete 360° wrap in most patients and ask if altered gastric emptying is the source of symptoms after fundoplication.

The authors stratify their patients selectively into 3 groups based on gastric emptying symptoms and studies. Those with the most severe emptying scores and most impaired emptying studies were offered pyloroplasty in an effort to minimize gastroparesis symptoms. It appears from this retrospective look at their very impressive database that patients with the most severe gastric stasis might benefit from a pyloroplasty. However, not all patients in the most severely affected group had pyloroplasty. A few questions.

Four of the 16 patients in group 1 who had failure of therapy did not undergo pyloroplasty despite your stated preference. How many did not, and what were the criteria used to omit pyloroplasty in the patients with severe gastric emptying?

Do the results hold up if patients were grouped by the type of operation received, not by the severity of delayed gastric emptying?
What were the effect of significant confounding variables such as diabetes or medications that contributed to delayed gastric emptying?

As many patients have confusing symptoms that do not correlate with objective findings, symptom-based testing is the setup for significant bias and confusion. Did any patients agree to postoperative testing without symptoms, and what can we learn from this subgroup?

If motility is a significant problem, does it make sense to offer a partial wrap to those who are also considering for a gastric emptying procedure?

Most of your patients were obese, with an average body mass index (BMI) of 30 [calculated as weight in kilograms divided by height in meters squared]. When do you offer an obesity operation instead of an antireflux operation?

All of us who deal with these complex patients find a few who were sorry they had a pyloroplasty. Is there a set of patients, if you had to do it over again, in which you would not do a pyloroplasty, and how could you find that group?

Dr Swanstrom: Patients who had documented evidence of delayed gastric emptying but did not have a pyloroplasty, which we designated as group 2, did not do as well. This group of 16 patients had more postoperative dyspepsia, abdominal pain, etc, as well as a higher failure rate: 4 of 16 were GERD treatment failures. We triaged them prospectively to not have a pyloroplasty because their objective emptying test was only mildly to moderately abnormal. Our conclusion is that this might be a mistake and perhaps all patients with documented DGE should have a concomitant pyloroplasty.

Why didn't we sort or triage based on symptoms instead of by GES [gastric emptying studies] results? For the first run we took the group of patients with gastroparesislike symptoms and those who had no gastric symptoms and sorted the same data. There was no difference in the outcomes on the whole. Patients who start with delayed gastric emptying symptoms tend to end up with at least some of the same symptoms. They are, however, better than they were preoperatively. We decided to analyze based on objective testing because it gives surgeons more of a treatment guideline.

Regarding confounding factors, it is true that these patients are complex, with many comorbidities, and this may have affected their surgical outcomes. We didn't, however, break our data down based on the etiology of their delayed gastric emptying. Causes are multifactorial and include narcotic use, peptic damage, diabetes, etc. We know that diabetics in particular are difficult to deal with but our patients have been pretty satisfied, happy with adding pyloroplasties to their fundoplication. Nissen-only groups had a postoperative study because we didn't want to subject them to the cost of a scan. But that would be a good focus for a further study.

A partial fundoplication for delayed gastric emptying in this patient population is a potentially risky combination. Partial fundoplications are less of an antireflux barrier to start with. While these patients might be able to belch and vomit more, they may have a high postoperative reflux rate due to back pressure on the valve from their delayed gastric emptying. We do, on occasion, perform a pyloroplasty plus a partial fundoplication for patients with severe esophageal motility disorders along with gastroparesis, as seen in scleroderma. These cases were specifically excluded from this study.

The average BMI was 30, so there were definitely some patients who were obese. Our standard recommendation for patients with reflux and a BMI greater than 40 is to give them the option to look into a bariatric procedure, particularly if they have gastroparesis. Undoubtedly some of the patients we initially saw went on to have a gastrectomy or bypass and were not included in this study. For obese patients who refuse to consider bypass or gastrectomy, or can't have one for other reasons, we do a fundoplication plus or minus the pyloroplasty.

Finally, while people often ask us about dumping symptoms, a notorious problem following peptic ulcer surgery, we really haven't seen much true dumping when we closely look at postoperative symptoms. Some of these patients do have fairly significant diarrhea which mostly resolves with time; some of it is a bile salts diarrhea, some of it is rapid gastric emptying, but most patients are manageable medically. Considering the complexity of these patients before surgery, we have been pretty happy with adding pyloroplasties to their fundoplication. Nausea, abdominal pain, all of these functional symptoms are difficult to deal with but our patients have been pretty satisfied, and it has been a successful treatment algorithm overall.

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