Relationship of a Satisfactory Outcome to Normalization of Delayed Gastric Emptying After Nissen Fundoplication

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Delayed gastric emptying in patients with gastroesophageal reflux disease may be due to an incompetent distal esophageal sphincter and/or a gastric abnormality. To determine the influence of the Nissen fundoplication on gastric emptying we studied the rate of gastric emptying before and after operation in 25 patients with proved gastroesophageal reflux disease. Nine patients had no gastric pathology, 9 had gastric acid hypersecretion, 5 had gastritis, and 2 had evidence of significant duodenogastric reflux. All were treated by Nissen fundoplication. Those with gastric acid hypersecretion also had a proximal gastric vagotomy (PGV) and the two patients with pathologic duodenogastric reflux were treated by a bile diversion procedure. We found that in gastroesophageal reflux disease with associated gastric pathology there was a higher prevalence of delayed gastric emptying before operation than in patients without gastric pathology. Nissen fundoplication was associated with speeding of gastric emptying in patients with or without gastric pathology. Proximal gastric vagotomy performed in association with Nissen fundoplication augmented the speeding of gastric emptying, which was advantageous in most cases but detrimental in two. Every patient in whom gastric emptying was not normalized had postoperative symptoms. Only two of 20 patients with normal postoperative gastric emptying had postoperative symptoms. Both patients had preexisting gastric pathology. Based on these findings, the side effects associated with Nissen fundoplication are due to the failure to normalize gastric emptying rather than the operation.

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TWO THIRDS OF PATIENTS with foregut symptoms such as heartburn, regurgitation, dysphagia, cough, chest pain, or epigastric pain have increased esophageal exposure to gastric juice and one half have abnormal gastric emptying. When these are present they occur separately or together so that 41% of patients have increased esophageal acid exposure alone, 19% have abnormal gastric emptying alone, and 40% have both.[1] This suggests that an incompetent distal esophageal sphincter and/or gastric emptying abnormalities are common mechanisms that could account for these symptoms. The Nissen fundoplication procedure is reported to give relief from heartburn and regurgitation in 91% of patients followed for 10 years.[2] Despite the success in controlling reflux, some patients have persistent or new postoperative symptoms such as epigastric pain, nausea, bloating, diarrhea, and dumping.[3] These may result from persistent or induced alterations in gastric emptying. The abnormal gastric emptying associated with gastritis, gastric acid hypersecretion, and duodenogastric reflux, which may be present before operation, is not specifically addressed by fundoplication. Consequently it may persist after operation. Furthermore fundoplication, in addition to controlling reflux, speeds gastric emptying.[4] The resulting combination of these effects on gastric emptying may be beneficial or detrimental. It was the aim of this study to correlate changes in the rate of gastric emptying with the outcome after fundoplication in patients with and without evidence of gastric pathology.

Study Population and Methods

Normal Controls

Gastric emptying studies were performed on normal volunteers who did not have a history of foregut symptoms and who had normal upper gastrointestinal barium studies, esophageal manometry, and 24-hour esophageal pH monitoring. The details of this group have been described previously.[1]

Patients

The study population consisted of 25 symptomatic patients, with documented gastroesophageal reflux disease

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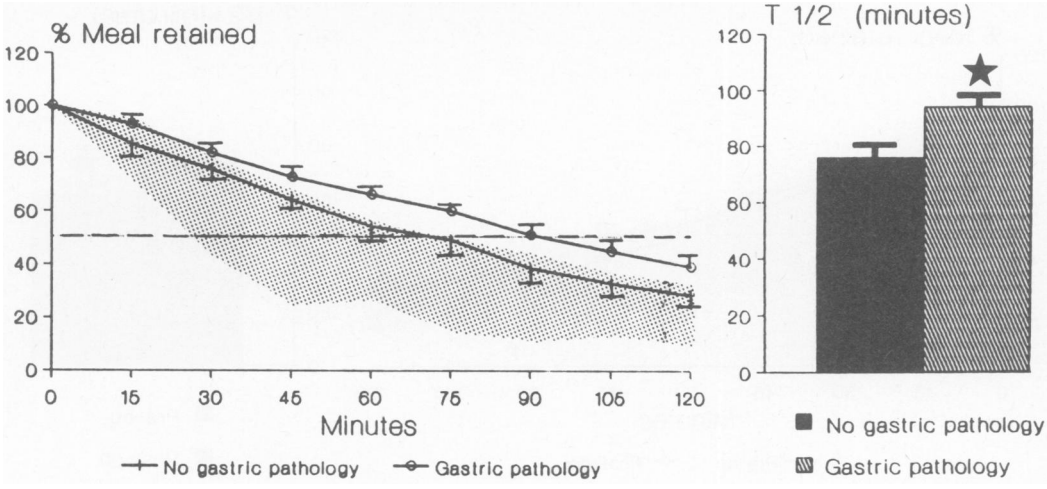


FIG. 1. Preoperative gastric emptying in 16 patients with gastric pathology (open circles) and in nine patients without gastric pathology (solid line). The shaded area represents the 10th to 90th percentiles of normal. The mean T½ is illustrated in the bar graph and shows delayed gastric emptying in patients with gastric pathology (* = $p < 0.05$).

on 24-hour esophageal pH monitoring in 23, and standard acid reflux test in two patients who were achlorhydric. All but three patients had a defective cardia on preoperative motility testing.[5] There were 13 men and 12 women, with a mean age of 53.4 years (range, 31 to 71 years). A detailed history was taken from all patients before operation and a long-term follow-up interview, either in person or by telephone, took place a median of 18 months after fundoplication (range, 5 to 48 months). In both a standard questionnaire was used by an independent observer to record the presence of foregut symptoms including heartburn, regurgitation, dysphagia, epigastric discomfort, nausea, vomiting, chest pain, and persistent cough. Patients were also asked for their own assessment of the procedure.

Before surgery all patients underwent fiberoptic endoscopy and biopsy, esophageal manometry, 24-hour esophageal pH measurement, and a gastric emptying test as described previously.[5,6,1] Acid secretory studies were performed in 19 patients with a history of ulcer disease. Hypersecretion was defined as basal acid output (BAO) > 5 mmol/h and maximum acid output (MAO) > 30 mmol/h.[7] Nine patients had preoperative documented gastroesophageal reflux without evidence of gastritis, gastric acid hypersecretion, or pathologic duodenogastric reflux on 24-hour gastric pH and hepatoiminodiacetic acid (HIDA) testing.[7,8] Sixteen patients had documented gastroesophageal reflux with gastric pathology (gastritis alone in 5 patients, gastric acid hypersecretion in 9, and duodenogastric reflux in 2). All patients had a Nissen fundoplication. The nine patients with gastric acid hypersecretion underwent fundoplication and a PGV. The two patients with duodenogastric reflux underwent Nissen fundoplication and a bile diversion procedure, the duodenal switch.[9] Gastric emptying studies were repeated a median of 12 months after surgery (range, 1 to 35 months).

Gastric Emptying Studies

A meal was given in the fasting state and consisted of 56 g of instant oatmeal, 6 g of sugar, and 175 mL of water, mixed with 500 μCi Tc-99m sulphur colloid and followed

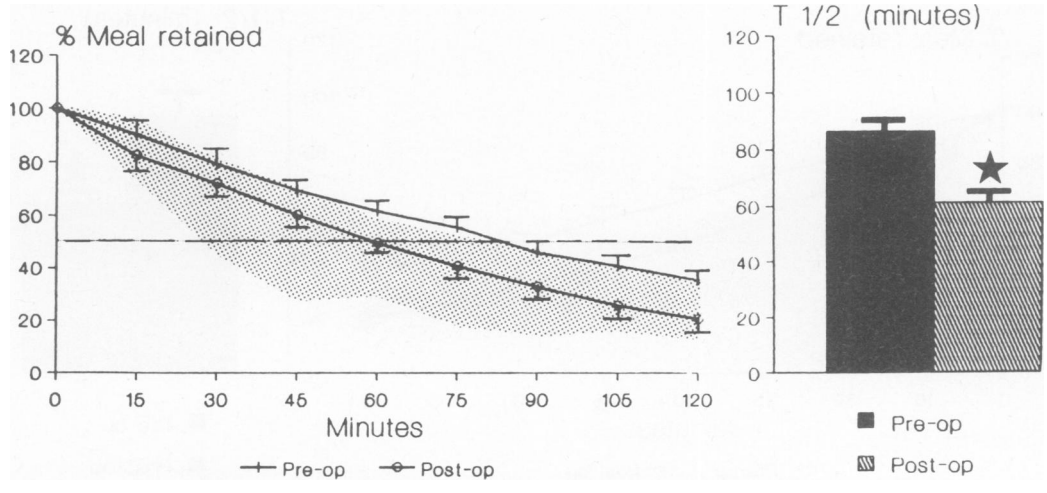


FIG. 2. Preoperative *versus* postoperative gastric emptying in all 25 patients. The shaded area represents the 10th to 90th percentiles of normal. The mean T½ is illustrated in the bar graph and shows the speeding of postoperative emptying (* = $p < 0.05$).

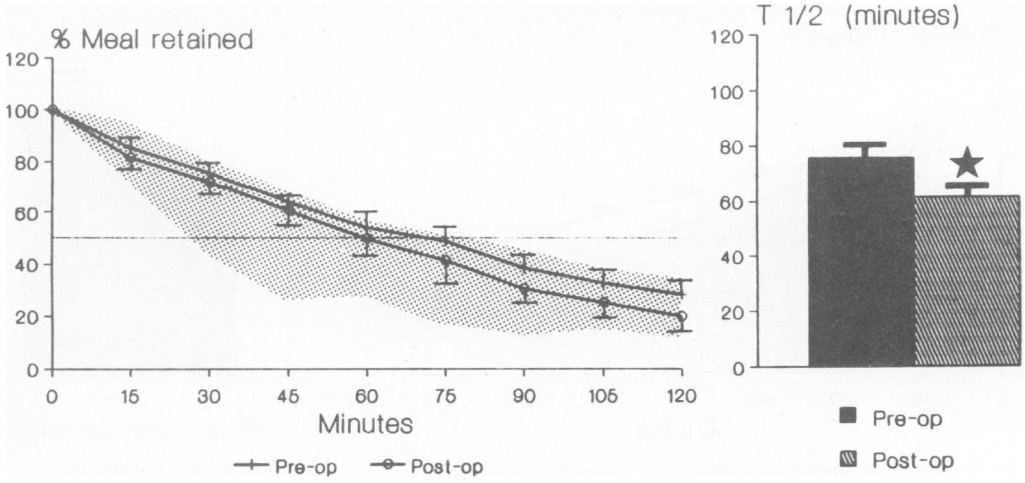


FIG. 3. Preoperative *versus* postoperative gastric emptying in nine patients without gastric pathology. The shaded area represents the 10th to 90th percentiles of normal. The mean T½ is illustrated in the bar graph and shows that fundoplication in the absence of gastric pathology increases gastric emptying (* = p = 0.05).

by 240 mL of 2% milk. (Total protein, 18 g; carbohydrate, 28 g; fat, 9 g; 380 KCal).

Gamma camera images were obtained in the upright, anterior, and posterior projections for 40 seconds at the completion of the meal and every 15 minutes for 90 to 120 minutes.[1] The geometric mean of the anterior and posterior counts per minute for the gastric region of interest were adjusted for decay of the isotope and expressed as a percentage of the initial counts over the stomach area.[10] To identify rapid or delayed emptying, either the emptying curve or T½ was used as an end point. Using the former a patient was considered to have abnormal emptying if his curve at 90 minutes was outside the 10th to 90th percentile range of normals and remained so at 105 and 120 minutes. Using the latter the patient was considered to have abnormal emptying if the T½ was outside the 5th and 95th percentile of normals.

Operative Technique

The Nissen fundoplication was performed as previously described using a 1-cm fundic wrap over a size 60 French bougie.[2] Particular care was taken to identify and preserve both vagal nerve trunks.

Statistical Methods

Nonparametric tests for paired and unpaired data were used to compare the T½ before and after operation within and between the various groups. The Fisher exact test was used to compare patients with a satisfactory or unsatisfactory outcome to the incidence of delayed, normal, or rapid emptying after operation.

Results

Gastric Emptying

Before fundoplication 17 of the 25 patients (68%) had delayed gastric emptying. Gastric emptying was more frequently delayed before operation in patients with associated gastric pathology (81%) than in patients without (45%). When grouped, patients without gastric pathology had an emptying curve within the normal range, whereas those with gastric pathology were outside the normal

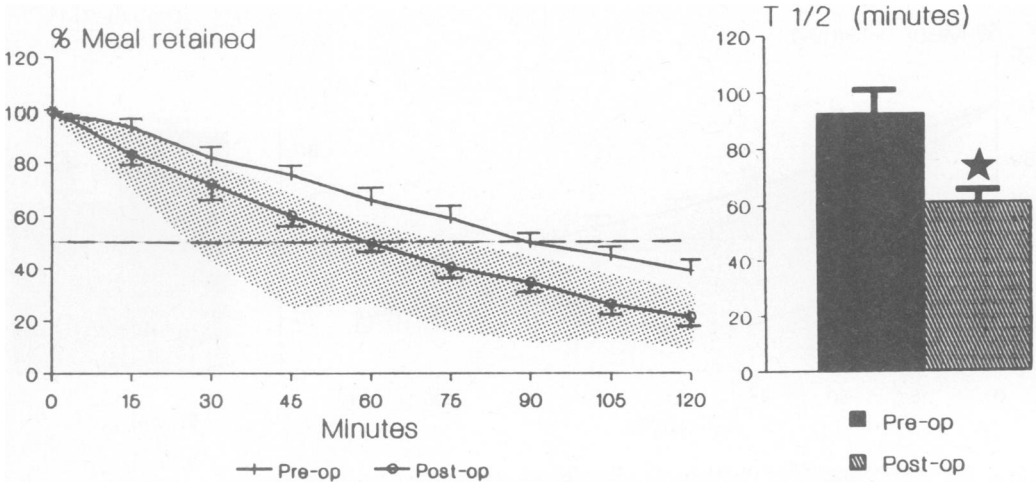


FIG. 4. Preoperative *versus* postoperative gastric emptying in the 16 patients with preoperative gastric pathology. The shaded area represents the 10th to 90th percentiles of normal. The mean T½ is illustrated in the bar graph and shows a faster rate of emptying after surgery even in the presence of gastric pathology (* = p < 0.01).

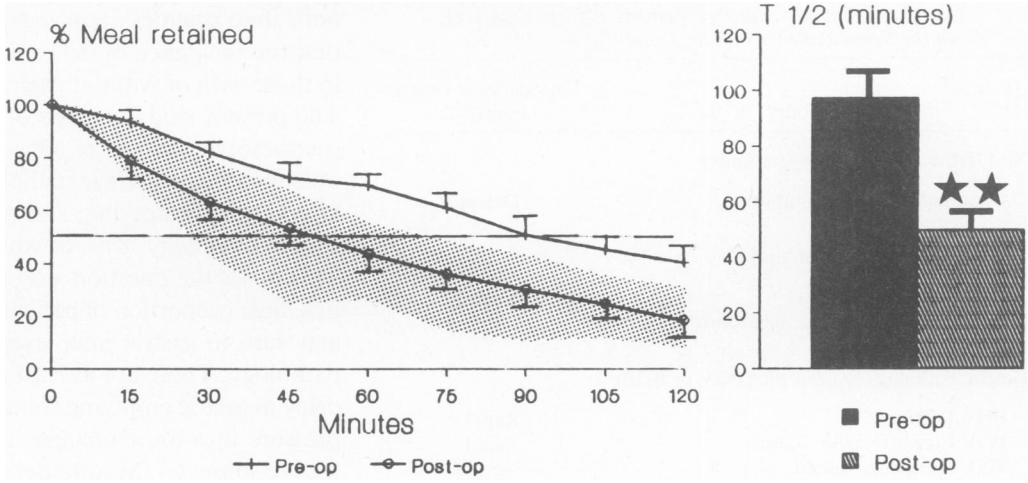


FIG. 5. Preoperative *versus* postoperative gastric emptying in nine patients with a history of ulcer disease and preoperative gastric acid hypersecretion who were treated by fundoplication and PGV. The shaded area represents the 10th to 90th percentiles of normal. The mean T½ is illustrated in the bar graph and shows the additive speeding effect of PGV and fundoplication on gastric emptying (** = $p < 0.01$).

range. The mean T½ in patients with gastric pathology was significantly higher than those without associated gastric pathology ($p < 0.05$; Fig. 1). After operation the mean gastric emptying rate of all patients was significantly faster than before operation ($p < 0.05$; Fig. 2). In patients without associated gastric pathology, fundoplication speeded gastric emptying ($p < 0.05$; Fig. 3). This normalized the emptying rate in three of the four patients who had delayed emptying before operation. Fundoplication also speeded gastric emptying in patients with associated gastric pathology ($p < 0.01$; Fig. 4). This normalized the rate of gastric emptying in 11 of 13 patients who had delayed emptying before operation. In patients in whom PGV was performed together with fundoplication, the effect of the two procedures was additive with a more marked speeding of gastric emptying than observed in patients without gastric pathology and those with untreated gastritis ($p < 0.01$; Fig. 5). This normalized the emptying rate in six of seven patients who had markedly delayed emptying before operation but resulted in abnormally rapid emptying in two patients. The five patients with gastritis who had a fundoplication alone also showed some speeding of gastric emptying ($p < 0.08$; Fig. 6).

Clinical Outcome

Follow-up evaluation showed that significant postoperative symptoms occurred in 7 of 25 patients (Table 1). Five of these seven patients had postoperative gastric emptying rates outside of the normal range, and these were either delayed or rapid (Fig. 7). Only 2 of 20 patients with normal postoperative gastric emptying had significant postoperative symptoms ($p < 0.01$). In both patients gastric pathology was present in their preoperative evaluation. All patients who had normal postoperative gastric emptying and were free of associated gastric pathology in their preoperative evaluation were asymptomatic after fundoplication.

When questioned about their satisfaction with the operation, 89% of patients without gastric pathology and

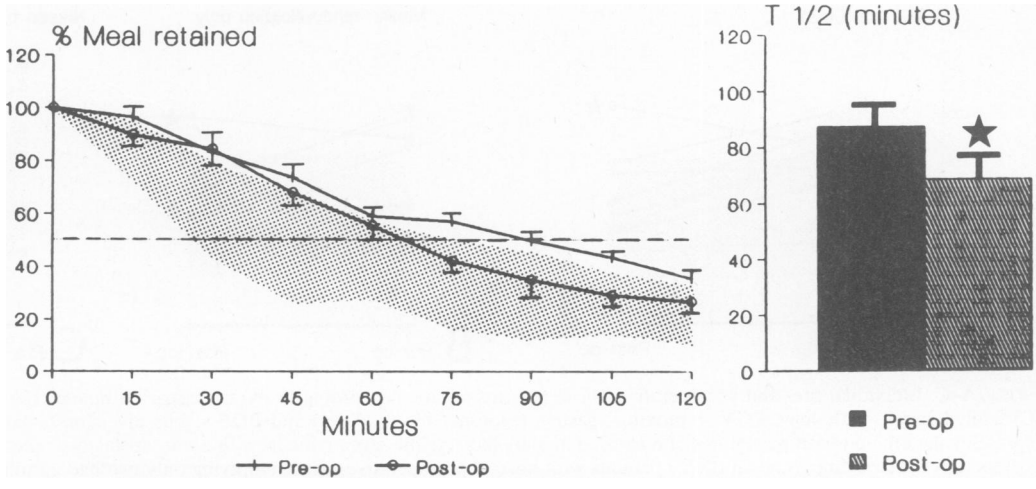


FIG. 6. Preoperative *versus* postoperative gastric emptying in five patients with gastritis alone. The shaded area represents the 10th to 90th percentiles of normal. The mean T½ is illustrated in the bar graph and shows a trend to faster emptying after fundoplication alone in patients with gastritis (* = $p < 0.08$).

TABLE 1. *Symptoms and Postoperative Gastric Emptying in the Seven Patients with an Unsatisfactory Outcome*

Symptoms	Postoperative Gastric Emptying
No Gastric Pathology (Nissen only)	
Chest pain and regurgitation	Delayed
Gastric Pathology (Nissen only)	
Epigastric pain, nausea	Normal
Epigastric pain, nausea, heartburn*	Delayed
Gastric Pathology (Nissen plus PGV or BDP)	
PGV Diarrhea	Rapid
PGV Epigastric pain, nausea	Rapid
PGV Dumping, nausea	Normal
BDP Diarrhea, constipation	Delayed

* Breakdown of fundoplication.
PGV, proximal gastric vagotomy; BDP, bile diversion procedure.

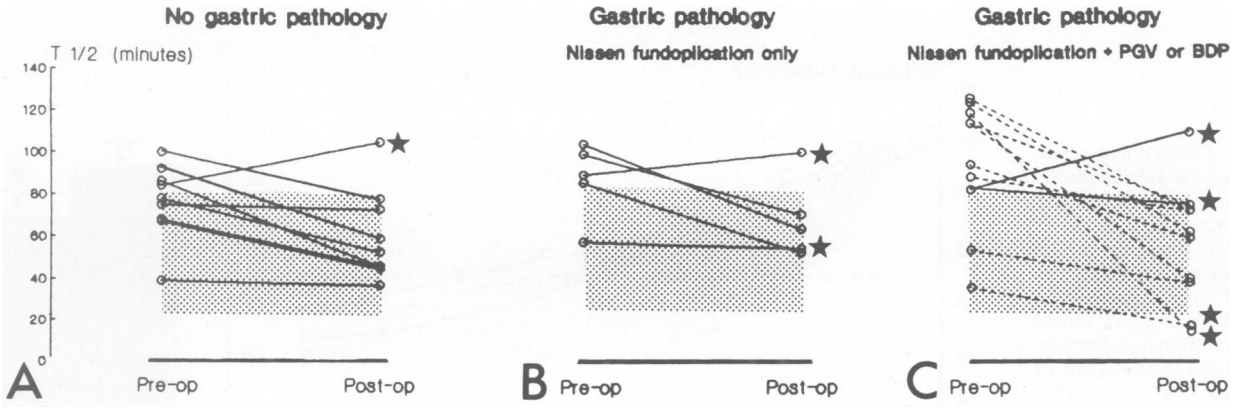
81% with associated gastric pathology were satisfied with the result of the operation (Table 2). Seventy-seven per cent of patients without and 63% with associated pathology believed that the operation has cured their disease. The remaining patients all believed that the operation had improved their condition. No patient stated that the operation worsened his condition. All the patients without and 93% with associated gastric pathology were satisfied with the result of surgery and if they had to make the decision to have the operation again they would do so again in light of their current experience.

Discussion

Increased esophageal exposure to gastric juice and abnormal gastric emptying are common findings in patients with foregut symptoms.[1] We have shown previously that both abnormalities occur independently of each other and that the incidence of delayed gastric emptying is similar in those with or without gastroesophageal reflux[1] (Fig. 8). The present study consists of patients with documented gastroesophageal reflux. One third of these patients had no concomitant gastric pathology, 45% of whom had delayed gastric emptying, and two thirds had concomitant gastric pathology, 81% of whom had delayed emptying. This raises the question why gastric emptying is delayed in a large proportion of patients with increased esophageal exposure to gastric juice even in the absence of gastric pathology. There are at least three possibilities. First the delay in gastric emptying could be due to venting of fundic pressure into the esophagus through a mechanically defective sphincter. Second delayed gastric emptying could be due to neutralization of fundic pressure by the effect of the negative thoracic pressure on the intrathoracic portion of the stomach in patients with a hiatal hernia. Third patients with a mechanically defective lower esophageal sphincter may also have a muscle abnormality involving the gastric fundus, resulting in decreased fundic tone.

Reduction of the radius of the proximal stomach by fundoplication increased the rate of gastric emptying in our study. This resulted in normalization of emptying in 13 of 17 patients with delayed preoperative gastric emptying. The mechanism by which this happened could be explained by Laplace's Law, which states that a decrease in radius results in disproportionately less wall tension required to generate a greater intraluminal pressure. This would promote the fundic contribution to the forward passage of chyme. Wilbur and Kelly[11] have shown previously that reducing the radius of the proximal stomach by fundectomy in dogs resulted in a speeding of the rate of gastric emptying of liquids.

Of the 25 patients, 17 had delayed gastric emptying before operation and none had rapid emptying. An un-



FIGS. 7A–C. Individual pre- and postoperative T½ in patients grouped according to (A) no gastric pathology, (B) untreated gastric pathology, and (C) treated gastric pathology. PGV = proximal gastric vagotomy (dotted lines) and BDP = bile diversion (solid lines C only). The shaded area represents the 5th and 95th percentiles of normal. The stars indicate the seven patients with an unsatisfactory outcome, five of whom had abnormal postoperative gastric emptying. Of the 20 patients with normal postoperative gastric emptying only two had an unsatisfactory outcome.

satisfactory outcome occurred in every patient in whom gastric emptying was not normalized after operation. Based on this finding, the side effects of fundoplication, other than dysphagia and the inability to vomit or belch, are more a consequence of the failure to normalize gastric emptying than of the procedure. Our findings show that the persistence of delayed gastric emptying after operation was most likely due to the presence of concomitant gastric pathology. Only two of the 20 patients with normal postoperative gastric emptying had an unsatisfactory outcome. In one the symptoms were most likely due to induced dumping and the other from persistent gastric mucosal damage secondary to duodenogastric reflux. These results suggest that to disregard or fail to recognize mild gastric pathology is the most common cause of an unsatisfactory outcome. This may explain the high incidence of burning epigastric pain induced by eating, postprandial fullness, and postprandial distention reported by Negre[3] after Nissen fundoplication. It is important that from the patient's point of view the benefit derived from fundoplication in controlling reflux outweighs the side effect. This point was underscored by the report that 100% of the patients without and 93% with gastric pathology would have the operation again.

In some patients damage to the vagus nerves while performing the fundoplication, particularly when associated with a PGV, may induce postoperative symptoms or make existing gastric-based symptoms worse. This was suggested by the observation that one patient without and one with gastric pathology developed further delay of their emptying after fundoplication and two patients with gastric pathology developed rapid emptying after fundoplication and PGV. The former could be explained by postvagotomy gastric stasis and the latter by the dumping syndrome. Vansant and Baker[12] reported that the incidence of specific symptoms of delayed emptying, such as bloating, nausea, and vomiting, were almost identical after an antireflux procedure, regardless of the addition of truncal vagotomy, but the incidence of diarrhea and dumping was significantly increased in vagotomized patients. This suggests that vagotomy is unlikely to cause delayed gastric emptying in patients with reflux disease and supports our observation that proximal gastric vagotomy and fundoplication can actually speed gastric emptying. Performing a PGV can cause dumping and diarrhea and, because it does not contribute to the control of reflux, should be reserved for those patients with a history of ulcer disease and documented hypersecretion.

TABLE 2. *Patient Satisfaction After Operation*

Degree of Satisfaction	No Gastric Pathology (%)	Gastric Pathology (%)
Cured	77	63
Improved	23	37
Worsened	0	0
Satisfied	89	81
Would have operation again	100	93

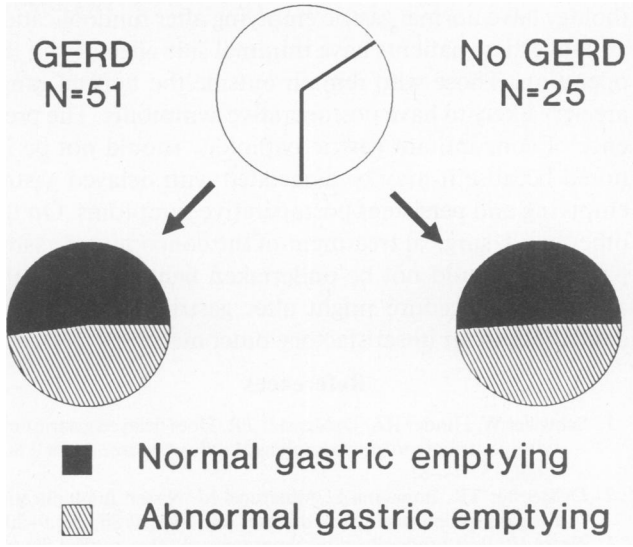


FIG. 8. Similar incidence of abnormal gastric emptying in patients with foregut symptoms with or without gastroesophageal reflux.

It was not possible to predict the pattern of postoperative gastric emptying from the pattern of preoperative emptying. Five of the patients with an unsatisfactory outcome had delayed preoperative emptying and the remaining two had normal emptying. This was similar to the ratio found in patients with a satisfactory outcome. This emphasizes that postoperative side effects of fundoplication, other than dysphagia and the inability to vomit or belch, can come from persistent delayed gastric emptying, persistent gastric mucosa damage, or rapid emptying from an inadvertent truncal vagotomy.

We used radiolabeled oatmeal as the test meal because it is convenient to use, well tolerated by the patients, and adequately reflects the characteristics of a liquid and a solid meal.[1] We used two methods to assess the rate of gastric emptying, both based on the rate of emptying in a normal population: If the T½ fell outside the 95th and 5th percentile of normal or if the emptying curve remained outside of the 90th and 10th percentile of normal after 90 minutes it was regarded as abnormal. There was total agreement between the two methods in the preoperative evaluation of gastric emptying. After operation some patients showed rapid initial gastric emptying that was more accurately identified by the T½ method. Similarly regression lines or expression of the rate of emptying as percentage emptied per minute would have been less accurate when emptying was no longer linear in nature.

This study has shown that most patients with gastroesophageal reflux disease without concomitant gastric pa-

thology have normal gastric emptying after fundoplication and that these patients have minimal side effects from the operation. Those who remain outside the normal range are very likely to have postoperative symptoms. The presence of concomitant gastric pathology should not be ignored because it may be associated with delayed gastric emptying and persistent postoperative symptoms. On the other hand, surgical treatment of the concomitant gastric pathology should not be undertaken lightly because the additional procedure might alter gastric emptying and contribute to an unsatisfactory outcome.

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Discussion

DR. C. THOMAS BOMBECK III (Chicago, Illinois): The authors have very bravely attacked what was initially a very simple problem and what is now a very complicated one. In the late 1970s, there were several reports that patients with gastroesophageal reflux had delayed gastric emptying. Indeed I believe that when Dr. DeMeester was at the University of Chicago he reported one of the first of these. In 1985 it was first reported that the Nissen fundoplication corrected the delayed gastric emptying, normalizing it or at least accelerating it from the preoperative levels.

More recently, in our own laboratories, Drs. Carrallho and Richter have demonstrated in the experimental animal that a Wendell cardioplasty, a mechanical procedure that destroys the lower esophageal sphincter without at all endangering the vagi or impinging on the stomach, markedly increases or delays gastric emptying. We have questioned exactly why this occurs. Now we are trying to sort out whether it is due to acid contact with the esophageal mucosa producing, if you will excuse the pun, a reflux-reflex inhibition of gastric emptying, or if it is due to a simple mechanical effect, venting of gastric fundic pressure thereby destroying the efficiency of gastric peristalsis.

I would first like to ask the authors why they think some patients do have delayed gastric emptying. Second the authors demonstrated a group of patients who had no evidence of gastric pathology, some of whom had delayed gastric emptying and others who did not. There must be a difference between those two groups of patients. It is interesting to speculate that it might be in the degree of LES failure.

Two years ago before this association we presented a method of quantitating LES sphincter strength, which was considerably more detailed than the standard pull-back procedure, and I wonder if the authors have used that or any other in an attempt to distinguish these two groups of patients. Do patients with delayed emptying have a worse degree of LES failure than patients without?

At the same time that all of this has been going on, we have known very well that various types of gastric pathology have caused delayed gastric emptying, such as gastric outlet obstruction for one reason or another or gastric mucosal disease. This causes us to wonder, in terms of reflux and delayed emptying, which was coming first, the chicken or the egg? The results that you have heard here today seem to suggest that they arrive simultaneously. In fact it seems that these authors have defined two groups of patients. Those who have delayed gastric emptying because they have gastric pathology and those who have delayed gastric emptying because they have a failed lower esophageal sphincter. It would seem to be of great importance to be able to define those two groups of people before operation.

Would the authors recommend, therefore, that all patients should have studies of gastric emptying, perhaps gastric secretory studies, before they have a Nissen fundoplication? If not, why not?

DR. JAMES A. O'NEILL, JR. (Philadelphia, Pennsylvania): Dr. Hinder and his colleagues clearly describe that some patients with gastroesophageal reflux have delayed gastric emptying, and that the incidence of this problem in his patients may be as high as two thirds of those with gastroesophageal reflux. This is important because, at least in the past, some have suggested that some sort of gastric emptying procedure should be performed in such cases.

This very suggestion led us to look at this issue 5 years ago when we reported 18 patients with reflux strictures of the esophagus to this Association. At that time, we noted that 4 of our 18 patients had delayed emptying, and all of these patients were carefully studied. In all of these patients, the emptying normalized after operation following a Nissen fundoplication.

Recently one of our fellows reviewed more than 200 patients in whom a Nissen fundoplication was done. The incidence of delayed gastric emptying was 25%. It was 20%, as you saw in the reflux stricture group. Now what was noted, however, was that the majority of these patients had severe esophagitis. This leads me then to ask three questions. Why do you think that your incidence is 2.5 to 3 times what we have seen in our patients, although I must say the fact that our patients were children would place them in your no gastric pathology group? We have followed our patients with both milk technetium scans and scrambled egg scans as opposed to oatmeal.

Do you think that esophagitis is an issue in etiology that would perhaps suggest that the lower esophageal sphincter is to be indicted? And finally, as you did, I think all of us have rare patients who are not relieved after operation, and I wonder, does your data help you to identify these patients so that perhaps gastric emptying procedures could be applied selectively and appropriately?

DR. CARLOS PELLEGRINI (San Francisco, California): Indeed this paper illustrates some interesting physiologic and pathologic aspects that have direct clinical application.