Symptoms Are a Poor Indicator of Reflux Status After Fundoplication for Gastroesophageal Reflux Disease

Carlos Galvani, MD; Piero M. Fisichella, MD; Maria V. Gorodner, MD; Silvana Perretta, MD; Marco G. Patti, MD

Background: If a patient develops foregut symptoms after a fundoplication, it is assumed that the operation has failed, and acid-reducing medications are often prescribed. Esophageal function tests (manometry and pH monitoring) are seldom performed early in the management of these patients.

Hypothesis: In patients who are symptomatic after fundoplication for gastroesophageal reflux disease, a symptom-based diagnosis is not accurate, and esophageal function tests should be performed routinely before starting acid-reducing medications.

Design: Prospective study.

Setting: University hospital.

Patients and Methods: One hundred twenty-four patients who developed foregut symptoms after laparoscopic fundoplication (average, 17 months postoperatively) underwent esophageal manometry and pH monitoring. Sixty-two patients (50%) were taking acid-reducing medications.

Main Outcome Measures: Postoperative symptoms, use of antireflux medications, grade of esophagitis, esophageal motility, and DeMeester scores.

Results: Seventy-six (61%) of the 124 patients had normal esophageal acid exposure, while the acid exposure was abnormal in 48 patients (39%). Only 20 (32%) of the 62 patients who were taking acid-reducing medications had reflux postoperatively. Regurgitation was the only symptom that predicted abnormal reflux.

Conclusions: These results show that (1) symptoms were due to reflux in 39% of patients only; (2) with the exception of regurgitation, symptoms were an unreliable index of the presence of reflux; and (3) 68% of patients who were taking acid-reducing medications postoperatively had a normal reflux status. Esophageal function tests should be performed early in the evaluation of patients after fundoplication to avoid improper and costly medical therapy.

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FOREGUT symptoms in a patient after fundoplication may lead to the assumption that the operation failed, and acid-reducing medications may then be prescribed. This therapeutic approach is based on the assumption that a diagnosis of gastroesophageal reflux disease (GERD) can be made confidently from the clinical findings. If symptoms persist, endoscopy is often performed because it provides useful information about the reflux status. Esophageal manometry and pH monitoring (esophageal function tests) are seldom done early in the management of these patients. The goals of this study were to measure the accuracy of symptoms in the diagnosis of persistent or recurrent gastroesophageal reflux after fundoplication and to determine the role and appropriate timing of esophageal function tests in the management of these patients.

METHODS

Between October 1993 and January 2002, 124 patients with persistent or recurrent foregut symptoms after laparoscopic fundoplication for GERD were evaluated at the Swallowing Center of the University of California–San Francisco (Table 1). There were 67 men and 57 women, (mean age, 50 years [range, 20-78 years]). Forty-nine (39%) of the 124 patients had undergone a partial fundoplication (240°), and 75 patients (61%), a total fundoplication (360°). All patients had experienced symptoms for an average of 17 months (range, 1-84 months) after the operation.
SYMPTOMATIC ASSESSMENT

A GERD questionnaire derived from other GERD-specific questionnaires was used. The questions were asked by a physician before the esophageal function tests were performed. Patients were not taking medications (acid-suppressing medications were discontinued 3 days [histamine, H2 blockers] or 14 days [proton pump inhibitors] before the interview). The patients were questioned in regard to the presence, duration, and severity of heartburn, regurgitation, dysphagia, and chest pain. Symptoms were scored using a 5-point scale, ranging from 0 (no symptom) to 4 (disabling symptom). In addition, patients rated their improvement after treatment with proton pump inhibitors as follows: no response (<10%), mild response (10%-40%), good response (41%-89%), and excellent response (90%-100%).

ESOPHAGEAL MANOMETRY

Medications that interfere with esophageal motility were discontinued 3 days before the study. The patients were studied after an overnight fast, using an 8-lumen manometry catheter continuously perfused by a pneumohydraulic capillary infusion system connected to a polygraph. Position, pressure, and length of the lower esophageal sphincter were measured, using the station pull-through technique. Esophageal body function was assessed by giving 10 wet swallows of 5 mL of water at 30-second intervals. The data were analyzed by computer using a commercially available software program.

AMBULATORY ESOPHAGEAL pH MONITORING

Acid-suppressing medications were discontinued 3 days (H2 blockers) or 14 days (proton pump inhibitors) before the study. During the study, patients consumed an unrestricted diet and took no medications for GERD. Ambulatory pH monitoring was performed by placing a pH probe 5 cm above the upper border of the manometrically determined lower esophageal sphincter. The probe was calibrated in standard buffer solution and took no medications (acid-suppressing medications were discontinued 3 days before the interview). The patients were questioned in regard to the presence, duration, and severity of heartburn, regurgitation, dysphagia, and chest pain. Symptoms were scored using a 5-point scale, ranging from 0 (no symptom) to 4 (disabling symptom). In addition, patients rated their improvement after treatment with proton pump inhibitors as follows: no response (<10%), mild response (10%-40%), good response (41%-89%), and excellent response (90%-100%).

ENDOSCOPY

The degree of esophagitis was graded according to the Savary-Miller classification.

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RESULTS

The pH monitoring studies showed that 76 patients (61%) had a normal reflux score (group A) and 48 patients (39%) had an abnormal score (group B). Among the 76 group A patients, 54 (71%) had a total fundoplication and 22 (29%) had a partial fundoplication. Among the 48 group B patients, 21 (44%) had a total fundoplication and 27 (56%) had a partial fundoplication. There was no difference between the 2 groups of patients with regard to age, duration of symptoms, or length of follow-up.

Table 2 presents the incidence and severity of symptoms in the 2 groups of patients. There was no difference in the incidence and severity of heartburn, dysphagia, and chest pain between the 2 groups of patients. Regurgitation was more frequent and more severe among group B patients (P<.05). Symptoms were more frequent among patients who had a poor or mild response to medication preoperatively. There was no difference between the groups in the number of patients taking medications (55% vs 42%; P=.1). Upper endoscopy was performed in 33 (27%) of the 124 patients. The degree of mucosal injury was graded as 2.0±0.1 for group A patients and 2.3±1.2 for group B patients (P=.3).

Table 3 presents the results of the postoperative manometry and pH monitoring. We did not find any correlation between the preoperative and postoperative esophageal function. While the lower esophageal sphincter pressure increased postoperatively (particularly in group A patients), the changes in esophageal peristalsis were unpredictable and not related to the reflux status. Overall, the lower esophageal sphincter pressure was lower.
and the quality of esophageal peristalsis worse (a non-specific esophageal motility disorder was more frequent) in group B patients. The esophageal acid exposure was normal in group A and abnormal (14-fold higher) in group B patients. Among group A patients, the reflux score decreased from 56±38 preoperatively to 5±4 postoperatively (P<.05). Among group B patients, the reflux score decreased from 100±76 preoperatively to 69±60 postoperatively (P<.05). Specifically, it improved in 54% of patients (141±76 to 53±47; P<.001), remained the same in 17%, and worsened in 29% (50±51 to 90±61; P=.09) (Figure). A second fundoplication was performed in 12 patients, with resolution or improvement of the symptoms in 9 of them (75%).

Sixty-two (50%) of the 124 patients had been started again on a regimen of acid-reducing medications postoperatively. Eighteen percent were taking H2 blocking agents, 74% were taking proton pump inhibitors, and 8% were taking both. Ambulatory pH monitoring results were abnormal in 20 (32%) of the 62 patients who were taking acid-reducing medications postoperatively. Among group B patients, the reflux score decreased from 100±76 preoperatively to 69±60 postoperatively (P<.05). Specifically, it improved in 54% of patients (141±76 to 53±47; P<.001), remained the same in 17%, and worsened in 29% (50±51 to 90±61; P=.09) (Figure). A second fundoplication was performed in 12 patients, with resolution or improvement of the symptoms in 9 of them (75%).

Follow-up clinical information was available in 26 (34%) of the 76 patients with normal acid exposure. After further testing, the following diseases were thought to be the cause of the symptoms: cholelithiasis (8 patients; the symptoms resolved in 5 of 6 patients who underwent a laparoscopic cholecystectomy); irritable bowel syndrome (8 patients; symptoms resolved in 2 patients with medical therapy); peptic ulcer disease (2 patients; symptoms resolved in both patients after treatment against Helicobacter pylori [proton pump inhibitors and antibiotics]); psychiatric disorder (1 patient; no resolution with medical therapy); and coronary artery disease (1 patient; symptoms resolved with medical therapy). In 6 patients, no diagnosis was established after further testing (in 3 of these 6 patients, the pH monitoring was repeated a second time and the readings were normal). Two of the 6 patients stopped taking the medications after the results of the esophageal function tests were revealed, and they remained asymptomatic.

### Table 3. Esophageal Manometry and pH Monitoring Among 124 Patients Referred for Evaluation of Foregut Symptoms After Fundoplication

<table>
<thead>
<tr>
<th></th>
<th>Group A*</th>
<th>Group B†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LES pressure, mean ± SD, mm Hg</td>
<td>16±6</td>
<td>11±7</td>
<td>.004</td>
</tr>
<tr>
<td>LES length, mean ± SD, cm</td>
<td>2.3±0.8</td>
<td>2.1±1.1</td>
<td>.1</td>
</tr>
<tr>
<td>Normal peristalsis, % of patients</td>
<td>64</td>
<td>19</td>
<td>.001</td>
</tr>
<tr>
<td>NSEMD, % of patients</td>
<td>36</td>
<td>81</td>
<td>.001</td>
</tr>
<tr>
<td>DeMeester score, mean ± SD‡</td>
<td>5±4</td>
<td>69±60</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: LES, lower esophageal sphincter; NSEMD, nonspecific esophageal motility disorder.
*Patients with negative pH monitoring (n=76).
†Patients with positive pH monitoring (n=48).
‡Normal, less than 14.7.

### Table 4. Demographic Data and Reflux Score of 62 Patients Taking Acid-Reducing Medications After Laparoscopic Fundoplication

<table>
<thead>
<tr>
<th></th>
<th>Normal pH (42 Patients [66%])</th>
<th>Abnormal pH (20 Patients [32%])</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>49</td>
<td>51</td>
<td>.4</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>22/20</td>
<td>10/10</td>
<td>.9</td>
</tr>
<tr>
<td>Duration of symptoms, mean ± SD, mo</td>
<td>9</td>
<td>12</td>
<td>.5</td>
</tr>
<tr>
<td>Duration of follow-up,  mean ± SD, mo</td>
<td>19±23</td>
<td>20±28</td>
<td>.7</td>
</tr>
<tr>
<td>DeMeester score, mean ± SD (normal &lt;14.7)</td>
<td>4±4</td>
<td>46±70</td>
<td>.009</td>
</tr>
</tbody>
</table>

COMMENT

These results show that (1) with the exception of regurgitation, symptoms were an unreliable index of the presence of abnormal reflux after laparoscopic fundoplication; (2) endoscopic evidence of esophagitis was diagnostically nonspecific; and (3) two thirds of patients who were taking acid-reducing medications postoperatively had a normal reflux status.

**SYMPTOMATIC ASSESSMENT IN THE DIAGNOSIS OF GERD**

It is commonly believed that a diagnosis of GERD based on clinical history is reliable, particularly when a patient complains of heartburn. However, when this strategy has been tested by comparing the symptomatic assessment with the results of esophageal function tests, symptoms have been found to be less sensitive and specific than usually thought. For instance, Johnsson and colleagues found that heartburn, a symptom considered typical of GERD, had a positive predictive value of just 59%. In other reports, reflux was shown by pH monitoring in only 65% to 70% of patients with a clinical diagnosis of GERD (based on symptoms and endoscopic findings). It is commonly believed that a diagnosis of GERD based on clinical history is reliable, particularly when a patient complains of heartburn.

A symptom-based diagnosis is even less sensitive in assessing the presence of persistent or recurrent reflux after fundoplication. Our study showed that 61% of...
patients thought to have abnormal reflux after laparoscopic fundoplication had a normal reflux status when measured by pH monitoring. We found that there was no difference between patients with normal and abnormal reflux in the incidence and severity of heartburn, dysphagia, and chest pain. Only the presence of regurgitation was of value in predicting that abnormal reflux was due to failure of the operation. Our findings are in accord with other reports that have shown that abnormal reflux is present in only 23% to 41% of patients who are symptomatic after fundoplication.10,12 The response to medications was also of limited value in distinguishing group A from group B patients. A similar percentage of patients in the 2 groups had a poor or good response to H2 blockers or proton pump inhibitors. In addition, among the 62 patients (50%) who were taking acid reducing medications, an abnormal reflux score on pH monitoring was found in only 20 (32%). Similar findings have also been reported by Lord and colleagues,11 who found that only 24% of patients taking acid suppressing medications postoperatively had abnormal esophageal acid exposure on 24-hour pH monitoring. It is of concern that the correct diagnosis had been missed in so many patients. Although follow-up information was available in only one third of group A patients, it is clear that diseases other than recurrent reflux had caused the symptoms. As a consequence, expensive medications had been prescribed and the real disease had gone for a long time without proper treatment. Directed treatment determined resolution of the symptoms and cure of the underlying disease in most of these patients.

ENDOSCOPY IN THE DIAGNOSIS OF GERD

Endoscopy is most often the first test performed to confirm a symptom-based diagnosis of GERD. However, this approach has several pitfalls since many patients with GERD do not have any mucosal injury9 and major interobserver variation exists for endoscopy, particularly for the low grades of esophagitis.13 In our study, a similar degree of mucosal injury was found between group A and group B patients, which indicated that the test failed to provide any useful information. These findings have been confirmed by other reports.1,12 It has been proposed that the appearance of the fundoplication on the retroflex view during endoscopy might help predict the reflux status. For instance, Lord and colleagues11 found that the pH monitoring was positive in 75% of patients whose fundoplication appeared disrupted or abnormally positioned on endoscopy. This type of evaluation, however, requires a very skilled physician who is familiar with the gastroesophageal junction changes observed endoscopically at the site of the fundoplication. No comments had been made by the endoscopist about the appearance of the fundoplication in our patients.

ESOPHAGEAL FUNCTION TESTS IN THE DIAGNOSIS OF GERD

Esophageal function tests are of key importance in the evaluation of patients who are symptomatic after fundoplication for GERD. While endoscopy detects esophagitis, a complication of GERD, pH monitoring directly measures the reflux of acid. In addition, this test stages the disease according to severity. Among our group B patients, pH monitoring clearly identified 2 different patterns of failure. In 22 patients (46%), the reflux score either remained the same (8 patients [17%]) or got worse (14 patients [29%]), suggesting complete failure of the operation. In contrast, in 26 patients (34%), the reflux score improved significantly (from 141±76 preoperatively to 53±47 postoperatively, P<.001), becoming almost normal in 8 patients. These findings might have important therapeutic implications. In the case of complete failure, a second operation should be considered, but might not be necessary if a major improvement in the esophageal acid exposure is documented. For instance, a second operation would not be indicated for a patient whose reflux score has decreased from 200 preoperatively to 20 to 30 postoperatively (normal reflux score <14.7). In this case, acid reducing medications should be prescribed for symptomatic control of the residual reflux since a second operation would not improve the results or eliminate the symptoms. In summary, esophageal function tests should be performed early in the evaluation of patients who are symptomatic after fundoplication. More liberal use of these tests would avoid improper and costly medical therapy and would single out cases where the operation has failed.

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REFERENCES

Carlos A. Pellegrini, MD, Seattle, Wash: This is a very important paper, for at least 2 reasons. First, from the point of view of the individual patient with symptoms after an antireflux operation, it clearly suggests that the presence of symptoms alone is not a good enough reason to start treatment with proton pump inhibitors (PPIs)—appropriate testing should, instead, be done. Second, we hear more and more at gastrointestinal society meetings that some 60% of patients who undergo antireflux surgery are back on proton pump inhibitors 10 years after the operation. This statement is based on the number of patients who reported PPI use when interviewed several years after an antireflux operation and reported by Spechler in JAMA. Dr Galvani's paper shows that the practice of prescribing PPIs almost universally to patients who have undergone an antireflux operation on the assumption that whatever symptoms they have are suggestive of an incompetent sphincter is incorrect. Indeed, the authors have shown that most of the patients who were taking this medication did not have abnormal reflux. Previous studies by Ron Hinder and by Jeff Peters and DeMeester have shown a similar pattern: about half of the patients who are taking this medication after an antireflux procedure do not have reflux.

This brings me to the first question, which has to do with the indication for the first operation, ie, the one that preceded the presentation to the authors' practice. You showed that in 54% of patients, esophageal acid exposure had improved from that of the preoperative state, and that in 17%, it had remained the same. Did all patients undergo pH testing before the first operation? We have observed that a number of patients with symptoms after an antireflux procedure have not been adequately worked up before the first operation.

Second, in our study, you talk about "symptoms." But while heartburn and regurgitation would certainly raise the concern of recurrent reflux postoperatively, other symptoms, such as dysphagia, may well be the result of the operation but certainly would not suggest recurrent reflux. We have always preferred to group patients who come with symptoms after an antireflux procedure into those whose symptoms are suggestive of a defective sphincter, those whose symptoms are suggestive of an incompetent sphincter, and those who have "other" symptoms. In our published series of reoperations, we found that about one third of the patients who come to us with "symptoms" after an operation were complaining of dysphagia and not of reflux-related symptoms. Another third come with symptoms of gas bloat, dyspepsia, and bloating. Other authors have had similar observations. Could you comment on (a) what were not just the symptoms but the most important or the real presentation for which these patients came to you and (b) why such a low incidence of patients with dysphagia, gas bloat, and other problems? Wouldn't it be better, if you were just looking at the question of reflux, to study a group of patients whose symptoms are indeed just suggestive of an incompetent sphincter? Similarly, it appeared to me on reading the manuscript that when someone did not have reflux, then the patient had to have some other nonsurgical diagnosis. Again, about one third of the reoperations we do are to relieve dysphagia in patients who do not complain of reflux at all. How many of your patients had to undergo reoperation in the absence of reflux, ie, your group A patients, for other problems although they did not have reflux?

Third, you did not mention the use of an upper gastrointestinal (UGI) series in the management of the patient who has symptoms following an antireflux operation. We believe the anatomic integrity of the previous procedure plays an important role in deciding whether or not an operation is indicated. How many of these patients had an UGI (upper gastrointestinal) and how did the UGI relate to the results of 24-hr pH monitoring? Specifically, was a normal UGI more commonly seen among group A patients?

Lastly, I was surprised by the findings of positive endoscopy among patients in group A. As you know, esophagitis is almost always the consequence of abnormal reflux. When it is not, other causes are easily identified. To what do you attribute such a large number of esophagitis patients in group A?

The above notwithstanding, the message of this paper is clear and serves the surgical community well. The message is twofold: not all patients with symptoms after antireflux procedures have reflux, and for purposes of outcome reporting, the fact that someone is on a PPI after an operation for reflux should not necessarily be taken as recurrent reflux.

Philip E. Donahue, MD, Chicago, Ill: This is another interesting paper with great data trying to help us figure out a correlation between symptoms and esophageal function tests. This study has lots of evidence about postoperative reflux status, endoscopic esophagitis, and medication use in patients with foregut symptoms after operation; the data are very convincing but they might become grist for the "evidence-based medicine mill," though, regarding the fact that operations really don't change much about the underlying pathology in the esophagus. As PPIs and other good medications have virtually abolished the peptic strictures in the GI tract, those physicians who employ only medications can look at a large series like this and say that, "Gee, whatever you are doing symptomatically really doesn't change so much, especially if you have to use one of these symptom-score analyses to show that the operated patients are slightly better than the others. Not that I believe that, but it is definitely something to think about.

My question will get to one basic point about the basic cause of the symptoms. Is it possible that what you are looking at are patients with afferent nerve hypersensitivity, ie, a group of patients with lots of foregut symptoms with minimal reflux? If you did an autopsy series of patients, in this room, for example, 75% would have severe inflammatory changes at the cardioesophagus. It is fascinating. We don't know what is going on there.

The last question is about radiofrequency energy treatments (Stretta therapy) that you fellows are using in San Francisco. Are any of these patients candidates for radiofrequency energy in subsequent treatment?

Raymond J. Joehl, MD, Chicago, Ill: As Dr Pellegrini alluded to, esophageal emptying is very important in patients who have symptoms after an antireflux procedure. Can you tell us more about peristaltic function in your patients?

Additional information can be obtained from an upper GI series or barium swallow. Did you specifically look at how well the esophagus empties using a timed barium swallow where a known amount of liquid barium is given and then measure how well the esophagus empties at 1 minute, 3 minutes, 5 minutes, or other specific time intervals?

Finally, as Dr Donohue alluded to, many of these patients have a hypersensitive distal esophagus. Did any of these patients respond to agents that are known to reduce esophageal hypersensitivity, specifically trazadone, amitriptyline, and other agents?

Stephen G. Jolley, MD, Anchorage, Alaska: There are 3 questions I have. The first is, how many patients had paraesophageal hernia?
ageal hiatal hernias on their upper GI series postoperatively? The second is, were gastric emptying studies done on these patients with persistent symptoms, and how many of them have gastric emptying abnormalities as the cause of their symptoms? Thirdly, in the patients who had positive endoscopy with a negative pH study, were those patients tested for food allergies?

John R. Edwards, MD, Auburn, Ind: Why do you think these people have the symptoms in the first place if they don’t have reflux, and do the PPIs or Pepcid, etc, help their symptoms?

Dr Patti: Dr Pellegrini asked about the indications for the operation and the preoperative reflux status of these patients; in addition, he stressed the value of a barium swallow in the preoperative evaluation and questioned the findings of endoscopy.

This is a group of patients who was operated on for gastroesophageal reflux disease. Every patient had preoperative esophageal function tests performed in the Swallowing Center at the University of California–San Francisco, and all of them had an abnormal reflux score. Subsequently, about two thirds of them were operated on at UCSF, while one third was operated on elsewhere. These patients were referred back for esophageal function tests because they experienced again, postoperatively, typical symptoms of gastroesophageal reflux disease, such as heartburn and regurgitation, suggesting failure of the fundoplication in controlling reflux. We excluded patients who presented with dysphagia as the primary complaint, as this symptom does not suggest recurrent reflux but rather a complication of the operation. In addition, the treatment of patients with severe dysphagia differs from that of patients who have only recurrent reflux symptoms.

A barium swallow is very important in delineating the anatomy of the gastroesophageal junction and the appearance of the wrap. A barium swallow, however, should not be performed as the initial screening test in patients who complain of heartburn postoperatively (low sensitivity and specificity for gastroesophageal reflux disease), but rather, in patients who are found to have an abnormal reflux score by pH monitoring; in these patients, it will help understanding the cause of failure and help planning further treatment.

Contrary to Dr Pellegrini, we were not surprised in finding an average low degree of esophagitis among patients with no reflux postoperatively (average, 2.0; range, 0–4). Some of these patients, in fact, had Barrett’s esophagus preoperatively (grade IV) and it remained the same postoperatively. Some patients were found to have no esophagitis (grade 0) or grade I or II injury. Therefore, this test failed to identify which patients had recurrent reflux postoperatively. Overall, it has been shown that endoscopy has a very limited value in the evaluation of patients with recurrent heartburn postoperatively, as it has low sensitivity and specificity and because major interobserver variation is present among endoscopists, particularly for the low levels of esophagitis.

As suggested by Dr Donahue, hypersensitivity of the lower esophagus might explain the symptoms experienced by some patients in the absence of reflux. However, there is no way to document this hypothesis. We were able to follow-up about one third of the symptomatic patients who had a normal reflux status postoperatively and found that cholelithiasis and irritable bowel syndrome were the 2 most common alternative diagnoses. In some patients, however, an alternative diagnosis was not found. Radiofrequency ablation of the lower esophagus could be beneficial, as it seems to decrease the sensitivity of the lower esophagus.

Dr Joehl asked about eventual changes in esophageal peristalsis postoperatively. Overall, peristalsis remained the same postoperatively. Abnormal peristalsis was more frequent before and after the operation among patients who had recurrent reflux postoperatively. We do not have experience with the timed barium swallow or with the use of antidepressant medications.

When a second antireflux operation was performed, we found that a herniated or an unfolded wrap were the 2 most common findings. Often, these findings had been shown by the barium swallow, which we perform routinely before any antireflux operation.

We do not perform routinely gastric emptying studies. We have not tested patients for food allergies.

Finally, I am not sure of why some of these patients had symptoms postoperatively even though the abnormal reflux had been corrected by the fundoplication. It might be because of hypersensitivity or because another disease process was missed preoperatively. Interestingly, these patients are often treated by proton pump inhibitors, but once they know that the pH monitoring is normal, they are often able to stop these medications without noticing any difference.