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

Role of Esophageal Functions Tests

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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.1 This therapeutic approach is based on the assumption that a diagnosis of gastroesophageal reflux disease (GERD) can be made confidently from the clinical findings.2,3 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 (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.
The degree of esophagitis was graded according to the Savary-Miller classification. 4

### 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. 5 The data were analyzed by computer using a commercially available software program.

### AMBULATORY ESOPHAGEAL pH MONITORING

Acid-suppressing medications were discontinued 3 days (H2 blocking agents) to 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 at pH 7 and a pH of 1 before and after monitoring; whenever a drift of more than 0.2 was present during the postprocedure calibration, the study was considered invalid, and it was repeated with a new catheter. The data were incorporated into a composite score (ie, DeMeester score) that took into account 6 elements: (1) number of reflux episodes; (2) number of episodes longer than 5 minutes; (3) longest reflux episode; (4) percentage of time the pH was less than 4 total; (5) percentage of time the pH was less than 4 in the upright position; and (6) percentage of time the pH was less than 4 in the supine position. A score greater than 14.7 was set as abnormal based on data obtained from 50 volunteers. 6 A symptom score was calculated for heartburn and regurgitation. Symptoms were considered to be due to reflux if they occurred during or within 3 minutes of an episode of reflux documented by pH monitoring.

### STATISTICAL ANALYSIS

An analysis of variance, $x^2$ test, t test, and Wilcoxon signed rank test were used for the statistical evaluation of the data. Data are expressed as mean ± SD. Differences were considered significant at $P<.05$.

### 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

### Table 1. Demographic Data on 124 Patients Referred for Evaluation of Foregut Symptoms After Laparoscopic Fundoplication

<table>
<thead>
<tr>
<th>Value</th>
<th>Group A</th>
<th>Group B</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>54 ± 14</td>
<td>51 ± 14</td>
<td>.1</td>
</tr>
<tr>
<td>Gender, F/M</td>
<td>37/39</td>
<td>21/27</td>
<td>.7</td>
</tr>
<tr>
<td>Duration of symptoms, mean ± SD, mo</td>
<td>16 ± 20</td>
<td>17 ± 20</td>
<td>.7</td>
</tr>
<tr>
<td>Patients taking medications, %</td>
<td>55</td>
<td>42</td>
<td>.1</td>
</tr>
<tr>
<td>Follow-up, mean ± SD, mo</td>
<td>24 ± 24</td>
<td>25 ± 25</td>
<td>.7</td>
</tr>
</tbody>
</table>

*Patients with negative pH monitoring (n = 76).
†Patients with positive pH monitoring (n = 48).

### Table 2. Incidence and Severity of Symptoms Among 124 Patients Referred for Evaluation of Foregut Symptoms After Fundoplication

<table>
<thead>
<tr>
<th>Value</th>
<th>Group A</th>
<th>Group B</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn, % of patients</td>
<td>76</td>
<td>69</td>
<td>.4</td>
</tr>
<tr>
<td>Regurgitation, % of patients</td>
<td>17</td>
<td>40</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Dysphagia, % of patients</td>
<td>7</td>
<td>8</td>
<td>.9</td>
</tr>
<tr>
<td>Chest pain, % of patients</td>
<td>12</td>
<td>12</td>
<td>.8</td>
</tr>
<tr>
<td>Heartburn, mean ± SD score ‡</td>
<td>1.5 ± 1.2</td>
<td>1.9 ± 1.4</td>
<td>.1</td>
</tr>
<tr>
<td>Regurgitation, mean ± SD score ‡</td>
<td>0.4 ± 1.0</td>
<td>1.8 ± 1.2</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Dysphagia, mean ± SD score ‡</td>
<td>0.6 ± 1.2</td>
<td>0.4 ± 1.0</td>
<td>.7</td>
</tr>
<tr>
<td>Chest pain, mean ± SD score ‡</td>
<td>0.6 ± 1.0</td>
<td>0.3 ± 0.8</td>
<td>.8</td>
</tr>
</tbody>
</table>

*Patients with negative pH monitoring (n = 76).
†Patients with positive pH monitoring (n = 48).
‡Range, 0 to 4.
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 5±4; 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 while 42 patients (32%) had a normal reflux score (Table 4).

There was no difference in the response to medications between patients with normal and patients with abnormal pH. Specifically, 57% of patients with normal pH and 33% of patients with abnormal pH had no response or poor response to medications (P=.1). Similarly, 43% of patients with normal pH and 65% of patients with abnormal pH had a good or excellent response to medications (P=.1).

Follow-up clinical information was available in 26 (516) of the 62 patients with abnormal pH monitoring postoperatively.

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).

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...
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 H\(_2\) 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 injury\(^{6}\) and major inter-observer 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.\(^{1,11}\) 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 colleagues\(^{11}\) 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**

Endoscopic 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 (54%), 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**

plain 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 you are looking at 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 cardia. 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, amitryptiline, and other agents?

Stephen G. Jolley, MD, Anchorage, Alaska: There are 3 questions I have. The first is, how many patients had paraesoph-
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), 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.

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.