ORIGINAL ARTICLES

Surgical Fundoplication in Laryngopharyngeal Reflux Unresponsive to Aggressive Acid Suppression: A Controlled Study

JASON SWOGER,* JEFF PONSKY,† DOUGLAS M. HICKS,§ JOEL E. RICHTER,* TOM I. ABELSON,§ CLAUDIO MILSTEIN,§ MOHAMMED A. QADEER,* and MICHAEL F. VAEZI*

*Department of Gastroenterology and Hepatology, Center for Swallowing and Esophageal Disorders; §Head and Neck Institute; and the †Department of General Surgery, Cleveland Clinic Foundation, Cleveland, Ohio

See CME exam on page 396; see editorial on page 431.

Background & Aims: In patients with persistent laryngeal symptoms despite aggressive proton pump inhibitor therapy, gastroesophageal reflux disease (GERD) continues to be implicated. The role of surgical fundoplication as the definitive therapy for these patients is uncertain. *Methods:* In this prospective concurrent controlled study, 72 patients with suspected GERD-related laryngeal symptoms received aggressive acid-suppressive therapy. Four-month symptomatic nonresponders (<50% improvement) with continued laryngeal inflammation and normalized esophageal acid exposure were offered laparoscopic Nissen fundoplication. The primary outcome was symptom improvement/resolution at 1 year after surgery. *Results:* Twenty-five of 72 (35%) patients remained unresponsive after 4 months of acid-suppressive therapy. Ten patients (40%) underwent surgical fundoplication (median age, 54 y; men, 4) and 15 patients (60%) continued medical therapy (median age, 52; men, 4). The most common laryngeal symptoms were sore throat, hoarseness, and cough. pH studies at 3 and 12 months were normal in all patients after fundoplication (median % time pH < 4, .0% and .3%; respectively). One of 10 (10%) patients in the surgery group reported improvement of laryngeal symptoms at 1 year compared with 1 of 15 in the control group (6.7%) ($P = 1.0$). Treatment of causes other than GERD improved symptoms in an additional 2 of 10 (20%) patients in the surgical group, and 10 of 15 (66%) patients in the nonsurgical cohort. *Conclusions:* Surgical fundoplication does not improve laryngeal symptoms reliably in patients unresponsive to aggressive proton pump inhibitor therapy. The argument of low volume or intermittent reflux as the cause of persistent laryngeal symptoms needs to be replaced with evaluation and therapy for other potential non-GERD causes.

Gastroesophageal reflux disease (GERD) often is implicated as the cause of chronic laryngeal inflammation, also known as laryngopharyngeal reflux (LPR). Up to 10% of visits to otolaryngologists are thought to result from complaints related to GERD.[1–4] Patients suspected of having LPR present with a variety of chronic symptoms including hoarseness, sore or burning throat, chronic cough, throat clearing, globus, nocturnal laryngospasm, otalgia, postnasal drip, and dysphagia.[2] Laryngeal abnormalities in this group may include edema and erythema, posterior pharyngeal-wall cobblestoning, vocal cord ulcers, interarytenoid changes, medial arytenoid wall edema and erythema, vocal cord granulomas, and subglottic stenosis.[2]

Although the pathophysiology is understood poorly, the symptoms and signs of LPR are believed to be caused by microaspiration of gastric contents into the hypopharynx and larynx, causing direct irritation of the affected structures.[2] Medical therapy with proton pump inhibitors (PPIs) may result in symptom and laryngeal improvement in 50%–70% of patients.[2–4] However, many patients continue to have symptoms and laryngeal irritation despite aggressive PPI therapy.[2,4] In this subset of patients, despite normalized esophageal acid exposure on acid-suppressive therapy,[2] GERD continues to be implicated as the probable cause. Laryngeal exposure to intermittent or low-volume acidic or nonacidic gastric reflux or resistance to PPIs is argued as the possible underlying cause.[5] Such contentions ultimately suggest surgical fun-

Abbreviations used in this paper: DGER, duodenogastroesophageal reflux; GERD, gastroesophageal reflux; LESP, lower esophageal sphincter pressure; LPR, laryngopharyngeal reflux; PPI, proton pump inhibitor; UESP, upper esophageal sphincter pressure.

1542-3565/06/$32.00
doi:10.1016/j.cgh.2006.01.011

doplication as the definitive treatment for suspected LPR patients refractory to medical therapy.

Surgical fundoplication is an established surgical procedure in preventing both acid and nonacid reflux and is known to be effective in patients with typical symptoms (heartburn and regurgitation) of GERD.[6] However, the role of fundoplication in treating the patient with GERD-suspected laryngeal irritation and chronic symptoms has not been well studied. Thus, the aim of this prospective concurrent control study was to assess the impact of surgical fundoplication on laryngeal symptoms and signs in individuals unresponsive to an aggressive trial of acid-suppressive therapy.

Materials and Methods

This study was approved by Institutional Review Board of the Cleveland Clinic Foundation and each participant provided written informed consent before inclusion in the study.

Patient Population and Study Design

Since 1997 an ongoing cohort study at the Cleveland Clinic Foundation's Department of Gastroenterology and Hepatology and Head and Neck Institute has investigated the response of patients with chronic laryngeal symptoms and signs to a 4-month trial of aggressive acid-suppressive therapy.[7] In this study, patients with chronic laryngeal signs and symptoms presumed to be GERD related were tested initially with esophagogastroduodenoscopy, manometry, and 24-hour ambulatory pH monitoring, and, irrespective of findings, were treated aggressively with high-dose PPI therapy (40 mg of omeprazole twice a day or 60 mg of lansoprazole twice a day) for 4 months. Between August 1, 2001, and August 31, 2003, patients unresponsive to the earlier-described therapy (<50% symptomatic improvement) were screened for potential enrollment in the current study and were offered laparoscopic Nissen fundoplication. Inclusion criteria were age older than 18 years, chronic symptoms (cough, throat clearing, sore/burning throat, hoarseness, and globus), and laryngoscopic findings suggestive of LPR despite aggressive acid suppression. In addition, patients were required to have abnormal pH monitoring or evidence of reflux by barium esophagram off therapy. Patients were excluded from the study if they had Barrett's esophagus, prior surgical therapy for GERD, or if they were unwilling to participate in the study.

All patients meeting the inclusion criteria completed a 4-page nurse-administered questionnaire at the start of the study. The questionnaire consisted of demographic information, medical history, tobacco and alcohol use, current medication regimen, history of allergies, presence of other potential laryngeal irritants (asthma, sinusitis, sinus congestion, allergies, postnasal drip, viral illness, and vocal abuse), and a description of specific laryngeal symptoms. Patients were asked to report the presence or absence of symptoms (cough, hoarseness, throat clearing, sore throat, globus sensation, heartburn, regurgitation, problem swallowing, chest pain, and discomfort to talk) by answering yes or no on the questionnaire and score the severity using a scale of 1 to 4 (1 = rare: once a month or less; 2 = occasional: once a week or less; 3 = frequent: several times a week; and 4 = all the time: several times daily).

Patients electing to undergo surgery underwent baseline evaluation, including esophageal manometry, dual-probe 24-hour ambulatory pH and bilirubin (Bilitec 2000; Synectics, Stockholm, Sweden) monitoring on PPI therapy, and preoperative laryngoscopy. An ambulatory pH study on twice-daily PPI therapy had to show evidence of a normalized esophageal acid pattern (% time pH < 4 of less than 5.52 total time) for inclusion in the study. Participants also had a complete preoperative evaluation including chest radiograph, 12-lead electrocardiogram, blood testing (complete blood count, basic metabolic panel, and coagulation panel), and had a consultation with the surgeon (J.P.) and an anesthesiologist.

Postfundoplication patients were monitored for 1 year. All patients kept daily symptom diaries during the study period using the earlier-described severity scoring system. All patients also had blinded symptom assessment using a standard questionnaire at 1, 3, 6, and 12 months after surgery. Patients were asked to score their symptoms (as compared with the previous visit) on a scale of 0%–100% improvement. They underwent objective evaluation including esophageal manometry and 24-hour pH monitoring at 3 months after fundoplication and pH monitoring (Bravo pH capsule; Medtronic Corp, Shoreview, MN) at 12 months after fundoplication. The response of laryngeal signs to surgical fundoplication was evaluated at 6 and 12 months after fundoplication by a single endoscopist blinded to patients' symptomatic response status. Clinical (symptomatic and laryngoscopic) response to fundoplication at 12 months was compared with PPI-unresponsive patients who declined surgery and continued on twice-daily PPI therapy for the same length of time. The control group also underwent objective baseline testing including 24-hour ambulatory pH monitoring, esophageal manometry, esophagogastroduodenoscopy, and laryngoscopy. Follow-up symptom assessments were performed in the controls by using the same questionnaire used in fundoplication patients assessing laryngeal symptoms and medication usage.

Laryngoscopy

Patients underwent a videotaped fiberoptic laryngoscopy at the Cleveland Clinic Head and Neck Institute before surgery and at 6 and 12 months after surgery. The laryngoscopy was performed by 1 specialist (D.M.H.) who was blinded to patient symptoms and group allocation. To ensure technical consistency, all examinations followed a standard protocol of patient instructions and tasks, and used the same equipment. The patients were seated comfortably and asked to sniff 3 sprays of a mixture of topical anesthetic and decongestant (1% neosynephrine; 4% Xylocaine [AstraZeneca, Wilmington, DE]) through 1 nostril. The flexible nasopharyngoscope (Pentax model FNL 13S; Pentax Precision Instrument Corp, To-