Editorial Commentary on Current Management of Upper Gastrointestinal Malignancies

Antireflux surgery to prevent the progression from Barrett's esophagus to esophageal adenocarcinoma: yes or no?

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Gastroesophageal reflux disease (GERD) is due to the reflux of gastric contents from the stomach into the esophagus. Therefore, it is not "acid reflux" only, but a combination of acid and other substances such as bile (1,2). The pathogenesis of GERD is multifactorial, and the most important factors are the transient relaxation and/or low pressure of the lower esophageal sphincter (LES) and weak peristalsis, which causes a slower clearance of the refluxate with increased contact time with the esophageal mucosa. In addition, in obese and morbidly obese patients there is another factor that promotes reflux, the increased thoraco-abdominal gradient between the stomach and the chest, secondary to an increase in the positive intra-abdominal pressure and a more negative intra-thoracic pressure (3).

GERD causes symptoms and/or mucosal damage. Symptoms are defined as esophageal (heartburn, regurgitation, dysphagia) and extraesophageal (aspiration, cough, hoarseness). Endoscopy defines the mucosal injury. The Los Angeles (LA) classification of esophagitis is by far the most widely used system to describe the endoscopic appearance of the esophagitis and grade its severity (4). The LA classification classifies the severity of the esophagitis as follows: grade A, mucosal breaks ≤5 mm, without continuity across mucosal folds; grade B, mucosal breaks >5 mm, without continuity across mucosal folds; grade C, mucosal breaks continuous between >2 mucosal folds, involving <75% of the esophageal circumference; and grade D, mucosal breaks involving >75% of the esophageal circumference. About 10 to 15% of patients with GERD develop an intestinal metaplasia of the epithelium from squamous to columnar with goblet cells, known as Barrett's esophagus (BE) (5). The importance of this finding is due to the possibility that BE can eventually progress from metaplasia to low- and high-grade dysplasia, and cancer (6). While the risk for malignant transformation is low in patients with metaplasia, around 0.33% (7), it is higher in patients with low grade dysplasia, around 0.5% (8). In patients with high grade dysplasia the annual incidence of adenocarcinoma is remarkably high, around 7% (9).

It is very important to keep in mind the composition of the refluxate because medications available today such as proton pump inhibitors (PPI), can only decrease the production of acid by the parietal cells but they do not affect reflux through the LES. On the other hand, a fundoplication can stop any type of reflux, independent of composition and pH, by restoring the competence of the gastroesophageal junction because of an increase in LES pressure and a decrease in transient LES relaxations (10). It has been shown that a fundoplication is more effective than medications in terms of relief of symptoms, particularly regurgitation (11). But by stopping reflux and a further insult to the mucosa, can a fundoplication stop the progression from metaplasia to dysplasia and cancer? This is indeed a very controversial issue, and while some studies have shown a preventive effect, others have failed to show any impact of surgery on the natural history of the disease.

In 2003, Oelschlager and colleagues of the University of Washington in Seattle, studied the effect of laparoscopic

antireflux surgery (LARS) in 90 patients with BE (12). Heartburn improved in 96% of patients and regurgitation in 84%. At a median of 30 months, postoperative endoscopy showed complete regression of the metaplasia in 30 of 54 (55%) patients with short segment BE (< 3 cm), but in none of the 36 patients with a long segment BE (≥3 cm). The authors concluded that LARS should be recommended in patients with BE to control symptoms and prevent the progression to cancer. Unfortunately, there was no further follow-up in these patients after the initial study.

Oberg studied the development of dysplasia and adenocarcinoma in 140 patients with Barrett's metaplasia, 94 patients treated with acid suppressing therapy (H2 blocking agents or PPI) and 46 with antireflux surgery (13). At a median follow-up of 5.8 years, endoscopy showed that dysplasia development was significantly less common after antireflux surgery compared with medical therapy. Chang compared patients with BE treated medically with patients after antireflux surgery and determined that the probability of regression was much higher after surgery (1.9% versus 15.4%) (14).

Other studies, however, have shown opposite results. Parrilla *et al.* reported on the long-term results of a randomized and prospective study comparing medical and surgical treatment of BE (15). An excellent and similar control of symptoms was achieved in both groups (91%). Progression to high grade dysplasia occurred in 5% of 43 patients treated medically and in 3% of 58 patients after antireflux surgery. Corey and colleagues performed a meta-analysis to determine if an antireflux operation decreases the incidence of esophageal carcinoma in BE compared to medical therapy (16). They included 4,678 patient-years of follow-up in the surgical group and 4,906 patient-years in the medical group. There was no significant difference in the cancer rates between the two groups: 3.8 cancers/1,000 patient-years compared to 5.3 in the medical group (P=0.29). Finally, Maret-Ouda studied the incidence of adenocarcinoma after antireflux surgery in a cohort study from the 5 Nordic countries (17). They compared 48,863 patients who had surgery to 893,208 that did not, and found that the surgical treatment of GERD did not decrease the risk of developing an esophageal adenocarcinoma.

As shown, there is no consensus on the effect of LARS in terms of blocking the progression from metaplasia to dysplasia and cancer. In addition, a conclusion is made even more difficult by the existing interobserver variability in the interpretation of dysplasia, which in part explains the heterogeneity in terms of progression and treatment.

Based on the existing data, and until a properly conducted multicenter prospective and randomized trial is performed, we do not recommend LARS in patients with BE metaplasia to avoid progression to dysplasia and cancer. As stressed by the most recent guidelines of the American Gastroenterological Association, antireflux surgery should not be considered as an antineoplastic measure in patients with BE (18). The indications for surgery should be the same as for the treatment of GERD without BE, specifically for patients who have symptoms refractory to medical treatment or have complications secondary to the use of acid suppressing therapy.

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Footnote

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