The Effect of Antireflux Surgery on Esophageal Carcinogenesis in Patients With Barrett Esophagus

A Systematic Review

Eugene Y. Chang, MD, Cynthia D. Morris, PhD, MPH,† Ann K. Seltman, MD,* Robert W. O'Rourke, MD,* Benjamin K. Chan, MS,† John G. Hunter, MD,* and Blair A. Jobe, MD*‡*

Objective: To determine whether patients with Barrett esophagus who undergo antireflux surgery differ from medically treated patients in incidence of esophageal adenocarcinoma and probability of disease regression/progression.

Summary Background Data: Barrett esophagus is a risk factor for the development of esophageal adenocarcinoma. A question exists as to whether antireflux surgery reduces this risk.

Methods: Query of PubMed (1966 through October 2005) using predetermined search terms revealed 2011 abstracts, of which 100 full-text articles were reviewed. Twenty-five articles met selection criteria. A review of article references and consultation with experts revealed additional articles for inclusion. Studies that enrolled adults with biopsy-proven Barrett esophagus, specified treatment-type rendered, followed up patients with endoscopic biopsies no less than12 months of instituting therapy, and provided adequate extractable data. The incidence of adenocarcinoma and the proportion of patients developing progression or regression of Barrett esophagus and/or dysplasia were extracted.

Results: In surgical and medical groups, 700 and 996 patients were followed for a total of 2939 and 3711 patient-years, respectively. The incidence rate of esophageal adenocarcinoma was 2.8 (95% confidence interval, 1.2–5.3) per 1000 patient-years among surgically treated patients and 6.3 (3.6–10.1) among medically treated patients ($P = 0.034$). Heterogeneity in incidence rates in surgically treated patients was observed between controlled studies and case series ($P = 0.014$). Among controlled studies, incidence rates were 4.8 (1.7–11.1) and 6.5 (2.6–13.8) per 1000 patient-years in surgical and medical patients, respectively ($P = 0.320$). Probability of progression was 2.9% (1.2–5.5) in surgical patients and 6.8% (2.6–12.1) in medical patients ($P = 0.054$). Probability of regression was 15.4% (6.1–31.4) in surgical patients and 1.9% (0.4–7.3) in medical patients ($P = 0.004$).

Conclusions: Antireflux surgery is associated with regression of Barrett esophagus and/or dysplasia. However, evidence suggesting that surgery reduces the incidence of adenocarcinoma is largely driven by uncontrolled studies.

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Esophageal adenocarcinoma occurs in an estimated 7000 patients each year in the United States, and its incidence has risen 350% since 1970.[1] Although still a relatively rare disease, esophageal adenocarcinoma is associated with a dismal prognosis, with a 5-year overall survival rate of less than 10%.[2–4] Furthermore, conventional curative treatment involves esophagectomy, which is associated with an in-hospital mortality rate of 7.5% to 14.5%[5] and a correspondingly high morbidity rate.[6]

Because of the relative rarity of esophageal adenocarcinoma and the associated morbidity of esophagectomy, a preventative strategy should focus on individuals at greatest risk for developing disease. Barrett esophagus, a complication of gastroesophageal reflux disease (GERD) characterized by esophageal mucosa metaplasia, is associated with a 30- to 125-fold increase in risk for the development of esophageal adenocarcinoma[7] and therefore represents a marker for patients at risk for disease progression. Barrett's metaplasia may progress from low-grade dysplasia (LGD), to high-grade dysplasia (HGD), and eventually to invasive adenocarcinoma, which may be present in up to 30% of cases of HGD and go unrecognized because of sampling error associated with endoscopic screening and surveillance.[8] The presence of HGD is therefore considered an indication for esophagectomy.[9]

In patients with GERD and Barrett esophagus without dysplasia, however, the appropriate choice of therapy (medical or surgical) is debated. A theoretical advantage of antireflux surgery is the creation of a mechanical valve which prevents all forms of gastroesophageal reflux. In contrast, proton pump inhibitors and histamine receptor antagonists reduce the acidity of gastric secretions but do not prevent nonacidic reflux,[10] which has been implicated in carcinogenesis.[11] These observations have fueled speculation that surgical antireflux procedures may prevent the development of

From the Departments of *Surgery and †Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, Portland, OH; and ‡Surgical Services, Portland VA Medical Center, Portland, OR.

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Reprints: Blair A. Jobe, MD, Portland VA Medical Center, Surgical Service–P3Surg, PO Box 1034, Portland, OR 97207. E-mail: jobeb@ohsu.edu.

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