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Antireflux Surgery for Esophageal Adenocarcinoma Prevention: Is it Worth it?

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Abstract

In contempo years, there has been growing affair apropos the assurance of this closing chic of drugs, prompting the American Gastroenterological Association to absolution an all-embracing technical review of GERD management, free that bereft affirmation exists to warrant increased anticipation or testing for patient's demography PPIs. Despite the broader AGA findings, research continues to advance two capital assurances apropos associated with PPI use: malabsorption and an added accident of infection.

Keywords:

Introduction

Barrett's esophagus (BE) is a precursor to esophageal adenocarcinoma (EAC) in which the squamous lining of the esophagus is replaced with intestinal columnar epithelium. Gastroesophageal reflux disease (GERD) is associated with BE, and is a significant risk factor for EAC [1]. The presence of GERD symptoms increases the odds of developing EAC by 7.7-fold as compared to those lacking any such symptoms [1]. The more frequent the symptoms and the longer their duration, the greater the risk of EAC. Indeed, approximately 61% of EAC patients and 70% of BE patients report having GERD symptoms (heartburn or regurgitation) [2]. Many have suggested that the prevention or amelioration of GERD symptoms is a key factor in BE management [3].

The mainstay of GERD management is medical treatment with acid suppression drugs including antacids, histamine-receptor-2 antagonists and proton pump inhibitors (PPIs). In recent years, there has been growing concern regarding the safety of this latter class of drugs, prompting the American Gastroenterological Association (AGA) to release an in-depth technical review of GERD management, determining that insufficient evidence exists to warrant increased precaution or testing for patients taking PPIs [4]. Despite the broader AGA findings, research continues to suggest two main safety concerns associated with PPI use: malabsorption and an increased risk of infection. Calcium malabsorption is of particular concern, as it can lead to decreased bone density and an increased risk of bone fracture. The Nurses' Health Study examined the relationship between PPI use and hip fracture, and found that women who had been taking PPIs for at least 2 years had a 35% increased risk of hip fracture as compared to non-PPI users [5]. Additionally, a 2011 meta-analysis of 11 studies investigating the association between fractures (hip, spine, and any-site) and PPI use and found an increased relative risk for all three types of fractures in both men and women [6]. Concerning PPI-related infection risk, a meta-analysis of 42 studies including 313,000 patients found a relative risk (RR) of 1.74 of Clostridium difficile infection for PPI users when compared to non-users. This risk was further increased (RR 1.96) in patients who were also taking antibiotics [7]. These data are not from randomized controlled trials which raises legitimate concerns regarding biases and the verity of the findings. Nonetheless, given these PPI concerns, there has been an increased interest in antireflux surgery as an alternative to medical therapy.

In patients with BE, who have an increased risk of progression to dysplasia and EAC, it has been suggested that antireflux surgery could lower the risk of cancer. While antireflux surgery has been well-established for the treatment of severe GERD, a consensus has not been reached regarding its benefits for patients with BE. Here, we briefly review some of the recent evidence and attempt to answer the question: Should antireflux surgery be recommended for patients with BE, solely for EAC prevention?

Antireflux Surgery for BE Management

The AGA recommends antireflux surgery in a number of instances. If a patient's GERD symptoms are not well controlled with medical treatment, or if a patient doesn't respond to medical treatment, surgery is advised. Additionally, surgery is recommended if a patient has extraesophageal symptoms such as asthma or cough [4]. Due to a lack of clinical evidence, the AGA does not yet recognize BE as an indication for antireflux surgery. However, a number of clinical studies have examined the efficacy of a variety of antireflux procedures for BE, in the form of controlled randomized trials, cohort studies and case series. A 2007 systematic review by Chang et al [8] attempted to pool the available data into a succinct set. Twenty-five studies were included, and 1696 patients were divided into a medically treated group and a surgically treated group: 700 medically treated patients with 3711 patient-years of follow-up and 996 surgically treated patients with 2939 patient-years of follow-up. When investigators excluded case series from the pooled data, the EAC incidence rates between the two groups did not differ significantly (p=0.32). They also determined that the progression rate from BE to low grade dysplasia (LGD) or high grade dysplasia (HGD) was 2.9% in the surgically treated group and 6.8% in the medically treated group (p=0.054). Additionally, the progression rate from BE (no dysplasia, LGD or HGD) to EAC was 1.2% in the surgically treated group and 2.3% in the

medically treated group [8]. Although the surgical group appears to be trending towards a more favorable progression rate, these differences are statistically not significant. A similar meta-analysis of 34 publications found no significant difference in the number of cancers per patient year for the surgically treated group versus the medically treated group [9]. Furthermore, no differences arose after controlling for country of origin, length of the BE segment, or the definition of BE used by investigators.

A handful of studies have also suggested that antireflux surgery is associated with regression, or can revert LGD to BE without dysplasia and BE to normal squamous epithelium. In a case series of 125 patients with short segment BE undergoing antireflux surgery, no patients progressed to EAC, and regression was observed in 61-65% of patients in a mean follow-up length of 56-106 months [10]. A retrospective study comparing medical therapy and surgical therapy for patients with LGD found that after 18 months, 100% of patients who received surgical therapy regressed to BE without dysplasia, as compared to 63.2% in the medical group [11]. In a comparison of patients with long-segment BE versus short segment BE (defined as greater than or less than 3 cm), surgery successfully reverted BE to normal epithelium in patients with short segments, but was not effective for long segments [12]. While these studies suggest a promising potential for BE management, they are not statistically significant, possibly because they are underpowered [10-12] and have a short follow-up period [9,11].

Antireflux Surgery Concerns: Complications and Side Effects

As with any operative procedure, complications can arise during antireflux surgery, whether it is with an open or laparoscopic approach. The LOTUS randomized trial comparing antireflux surgery to medical PPI treatment observed a 13.3% treatment failure in the surgical group (defined as needing additional treatment for symptoms, needing dilation or having serious adverse events postfundoplication) as compared to 7.1% treatment failure in the medical group (defined as failure to control symptoms) [13]. The number of patients reporting serious adverse events was similar in both groups (28.6% in the surgical group and 24.1% in the medical group). The most common adverse event after fundoplication is dysphagia, with 20% of patients experiencing dysphagia immediately after surgery; these symptoms persist long-term in 4% of patients [14]. Other postoperative dysphagia rates between 0% and 17.6% have been reported [15]. Due to the nature of the fundoplication procedure and the anatomical alterations that are made, patients are left with the inability to vomit or affectively vent air from the stomach [14]. Finally, an observational study measuring quality-of-life (QoL) scores before and after antireflux surgery found that patients with BE reported less quality-of-life improvement when compared to patients without BE, though QoL scores did improve slightly after surgery [16].

Conclusion

The current evidence supporting antireflux surgery in BE patients to reduce the risk of cancer progression is suggestive, but is not yet conclusive. Most notably, larger studies with longer follow-up duration are needed to assess whether or not surgery can prevent progression to EAC, as annual progression rates to cancer as low as 0.12% have been reported [17]. Therefore, given the lack of convincing decisive evidence that antireflux surgery prevents EAC progression, and in light of the potential for long-term discomfort post-fundoplication, we cannot currently recommend it for cancer prevention in patients with BE. Specifically, patients with nondysplastic short-segment BE, patients with BE without GERD symptoms, or patients whose GERD symptoms are well-controlled with moderate medical treatment should consider antireflux surgery with particular caution. For these groups of patients, the risk of progression, and therefore any potential benefit, may be lower than the high-risk and high-symptom patient, while assuming similar risks in complications and side effects. Antireflux surgery may be a consideration when more convincing data regarding effectiveness becomes available.

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