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Acid suppression and surgical therapy for Barrett's oesophagus

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A B S T R A C T

Gastro-oesophageal reflux disease is a common medical problem in developed countries, and is a risk factor for the development of Barrett's oesophagus and oesophageal adenocarcinoma. Both proton pump inhibitor therapy and antireflux surgery are effective at controlling endoscopic signs and symptoms of gastro-oesophageal reflux in patients with Barrett's oesophagus, but often fail to eliminate pathological oesophageal acid exposure. The current available studies strongly suggest that acid suppressive therapy, both pharmacological as well as surgical acid suppression, can reduce the risk the development and progression in patients with Barrett's oesophagus, but are not capable of complete prevention. No significant differences have been found between pharmacological and surgical therapy. For clinical practice, patients should be prescribed a proton pump inhibitor once daily as maintenance therapy, with the dose guided by symptoms. Antireflux surgery can be a good alternative to proton pump inhibitor therapy, but should be primarily offered to patients with symptomatic reflux, and not to asymptomatic patients with the rationale to protect against cancer.

Abbreviations: BE, Barrett's oesophagus; OAC, oesophageal adenocarcinoma; HGD, high grade dysplasia; GORD, gastro-oesophageal reflux disease; LGD, low grade dysplasia; LSBE, long segment Barrett's oesophagus; PPI, proton pump inhibitor; SSBE, short segment Barrett's oesophagus.

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Introduction

Gastro-oesophageal reflux disease (GORD) is defined as symptoms or mucosal damage as a result of reflux of gastric contents into the oesophagus [1]. GORD symptoms are ubiquitous in the general population, with prevalence estimates ranging from 18.1% to 27.8% in North America, and 8.8%–25.9% in Europe [2]. Its prevalence has been increasing in Western countries over the past 30 years, most likely to be explained by the epidemic increase of obesity, changes in lifestyle and perhaps by a decreasing prevalence of *Helicobacter pylori*.

GORD entails a spectrum of disease manifestations, which can present as non-erosive disease, or erosive oesophagitis, and in a small minority lead to more severe presentations such as bleeding and peptic strictures. It is also associated with premalignant and malignant complications; Barrett's oesophagus (BO) end oesophageal adenocarcinoma (OAC) [3].

Barrett's oesophagus is an important complication of longstanding GORD, with population prevalences of BO ranging between 2 and 6%, and white males over 60 years predominantly affected [4]. It is defined by the replacement of oesophageal squamous epithelium by columnar epithelium with intestinal metaplasia, which can progress via a cascade from low grade dysplasia (LGD) to high grade dysplasia (HGD) to eventually adenocarcinoma. Published estimates on the annual risk of OAC in patients with BO range from 0.4% to 2.9%, which predominantly have come from small cohort studies with relatively short follow-up, and mostly from referral centers, which likely are affected by ascertainment bias showing a higher cancer incidence than may be observed in larger population-based studies. In a recent meta-analysis, the annual OAC incidence rates in BO cohorts with less than 2000 patient years widely ranged between 0 and 3.55%, and fell to 0.07–0.82% in cohorts with more than 2000 patient years of follow-up [5]. Recently, three large population-based BO follow-up studies were published in which national cancer registries provided complete ascertainment of OAC incidence [6–8]. These nationwide registries minimize selection bias. All three studies consistently demonstrated a risk of less than 0.2% per year, far lower than previously reported. The first and largest of these studies consisted of 42,207 patients with BO entered in a Dutch nationwide histopathology registry between 1991 and 2006, reporting an annual OAC risk of 0.14% [6], undermining the effectiveness of generalized surveillance of BO patients.

The majority of patients with BO have symptoms of GORD, especially heartburn and regurgitation. Multiple studies observed that BO patients suffer from more frequent and larger acid exposure than non-Barrett GORD patients. However, BO may occur in patients with no history of reflux symptoms. In population-based studies of the prevalence of BO, over 45% of identified BO patients did not report symptoms of GORD [9,10]. This can be explained by a decreased sensitivity to acid exposure of the Barrett's segment [11]. Acid suppression is the cornerstone for treatment of all manifestations of GORD. PPIs are the most efficient pharmacotherapy to alleviate reflux symptoms, heal oesophagitis, and prevent symptomatic relapses. Antireflux surgery is as effective as medical therapy for carefully selected patients with chronic GORD when performed by an experienced surgeon [12]. The general approach to GORD also pertains to BO patients, although maintenance therapy with a PPI is advised for all BO patients irrespective of their symptoms. This recommendation is based on indirect evidence that control of acid reflux may interfere with the development and progression of dysplasia and subsequent OAC. However, whether acid suppression by pharmacy or surgery really prevents neoplastic progression in BO remains a matter of debate.

In this review, we provide an overview of current knowledge on the effects of pharmacological and surgical therapy on GORD symptoms in patients with BO, and discuss the existing evidence on the potential preventive effect on neoplastic progression in BO of acid suppressive therapy.

Pharmacological acid suppression in Barrett's oesophagus

Proton pump inhibitor therapy

Since its introduction in 1989, PPIs have become the mainstay of therapy for reflux symptoms and prophylaxis of gastrointestinal injury due to NSAID use. For these purposes, PPIs combine high efficacy