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Review article: oesophageal complications and consequences of persistent gastro-oesophageal reflux disease

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SUMMARY

The major oesophageal complications associated with persistent gastro-oesophageal reflux disease (GERD) include erosive oesophagitis, ulceration, strictures and gastrointestinal (GI) bleeding. Although the causes of these complications are uncertain, studies indicate that erosive oesophagitis may progress to the development of ulcers, strictures and GI bleeding. Pharmacological treatment with proton pump inhibitors is favoured over that with H_2-receptor antagonists for the treatment of strictures. The treatment of strictures is accomplished with dilation and many favour the concomitant use of proton pump inhibitors. Most gastroenterologists are seeing far fewer oesophageal strictures these days since the introduction of proton pump inhibitors. In addition, research has shown that oesophageal complications have a greater impact on patients suffering from night-time GERD than on those suffering from daytime GERD. Barrett's oesophagus is a significant complication associated with persistent GERD and those at risk generally experience a longer duration of symptoms, especially those with a high degree of severity. In addition, there is a strong relationship between Barrett's oesophagus and oesophageal adenocarcinoma. This is in part due to the association of obesity and the development of hiatal hernias. Furthermore, endoscopic screening is being used to detect Barrett's oesophagus and oesophageal adenocarcinoma in persons suffering from chronic GERD, even though screening may not have an impact on outcomes (Sharma P, McQuaid K, Dent J, *et al*. A critical review of the diagnosis and management of Barrett's esophagus: The AGA Chicago Workshop. Gastroenterology 2004; 127: 310–30.).

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INTRODUCTION

The long-term consequences and complications of persistent gastro-oesophageal reflux disease (GERD) are often difficult to identify and may go undiagnosed for many years. Persistent GERD may present in several ways: (1) patients with unrecognized reflux who have not received treatment and present *de novo* with complications of GERD; (2) patients who are inadequately treated for GERD and remain symptomatic; and (3) patients who are adequately treated for GERD and are symptom-free, but still have abnormal/pathological oesophageal acid exposure and experience complications despite treatment.

GERD is a complex disorder that is associated with several pathophysiological changes leading to a breakdown in oesophageal defense mechanisms.[1] It is characterized by contact between the oesophageal epithelium and gastric refluxate.[1] Numerous complications have been associated with persistent GERD, especially when it is nocturnal (Table 1). Oesophageal complications of nocturnal GERD can include erosive oesophagitis, oesophageal haemorrhage, ulceration, strictures and Barrett's oesophagus.[2]

The ready availability and widespread use of acid suppressants has changed the presentation of GERD complications in recent years. This is especially true with the availability of over-the-counter proton pump inhibitors.

OESOPHAGEAL COMPLICATIONS OF GERD

Erosive oesophagitis, gastrointestinal bleeding, ulceration and strictures

The oesophageal complications most frequently associated with persistent GERD include erosive oesophagitis, oesophageal haemorrhage, ulceration and strictures. Although chronic acid reflux associated with GERD can occur during both day and night, nocturnal reflux is implicated in the development of more severe complications than daytime reflux.[3] This may be explained by the physiological differences between the responses to daytime and nocturnal GERD. GERD severity is determined in part by total acid contact time.[4] Patients with nocturnal reflux have more prolonged oesophageal acid exposure per reflux episode than those with daytime reflux.[2, 4]

The consequences of prolonged acid-mucosal contact have been well established. In a rabbit model of oesophagitis, the duration of oesophageal perfusion with a hydrochloric acid solution (pH 2) containing 5 mM of a bile salt (taurodeoxycholate) was directly related to the degree of back diffusion of H^+ ions into the oesophageal mucosa.[5] With exposure times ranging between 15 and 60 min, the amount of acid leaving the oesophageal lumen increased in a linear manner.[5] With exposure of the rabbit oesophagus preparation to a solution containing pepsin, similar changes in H^+ ion retrograde diffusion were seen and were further accompanied by macroscopic and microscopic changes, including linear erosions and intraluminal haemorrhage, consistent with features seen in patients with erosive reflux oesophagitis.[6]

Furthermore, patients in the supine position have a diminished ability to clear the oesophagus of refluxed acid, therefore they are predisposed to develop more damage to the

oesophageal mucosa and a higher incidence of GERD complications.[2, 4] In a study comparing daytime GERD, night-time GERD or a combination of both, the incidence of oesophagitis was higher among individuals with nocturnal GERD than in those with daytime GERD, although patients who had both experienced the highest rate of oesophagitis.[4]

Erosive oesophagitis.—Although up to 60% of patients with reflux symptoms do not have endoscopic evidence of oesophagitis, erosive oesophagitis is a potential manifestation and complication of GERD.[7, 8] Severe erosive oesophagitis is more likely to be associated with nocturnal than daytime GERD.[2] Data from 24-h pH monitoring studies have shown that nocturnal episodes of GERD lasting for more than 5 min are associated with the presence of oesophagitis.[9] Increased nocturnal acid clearance time has also been associated with oesophageal erosions, ulceration and stricture.[2] The frequency of GERD symptoms seems to be a better indicator of progression to erosive oesophagitis than duration. Lieberman *et al.* studied the correlation between GERD symptoms and complications in 662 patients who had undergone endoscopy.[10] In that study the authors found that symptom duration was not correlated with the likelihood of erosive oesophagitis, although it was correlated with the presence of Barrett's oesophagus. Forty-seven per cent of patients who reported having symptoms of GERD for 1 year or less had erosive oesophagitis, compared with 42% of patients who had experienced symptoms of GERD for more than 10 years. However, patients who experienced daily symptoms of GERD had an increased risk for erosive oesophagitis ($P < 0.001$) compared with those with less frequent episodes. These data emphasize the importance of oesophageal contact time with refluxed acidic gastric juice.

Upper gastrointestinal bleeding—Erosive oesophagitis with ulceration has been implicated as a cause of bleeding in patients with GERD. It has been proposed that oesophagitis may be responsible for a significant percentage of cases of upper gastrointestinal (GI) bleeding.[11] However, larger studies have not been performed to verify this observation. Furthermore, bleeding from erosive oesophagitis is a relatively uncommon cause for acute presentation to the hospital with haematemesis and melena. It has been suggested that chronic iron deficiency anaemia may result from inadequately managed oesophageal erosions or erosive oesophagitis.[12] Additionally it has been proposed that ongoing chemical damage, such as tight junction changes between epithelial cells due to repeated acid exposure, may result in bleeding.[1, 13]

Oesophageal strictures and ulcers.—Oesophageal strictures and ulcerations constitute more severe complications of GERD that occur in association with severe oesophagitis. Ulceration may lead to bleeding in some cases. Oesophageal strictures occur in approximately 10% of patients with untreated erosive oesophagitis.[7] Oesophageal strictures occur predominantly in older individuals and increase in prevalence with age.[14] Strictures have been associated with a hypotensive lower oesophageal sphincter, hiatal hernia, motility dysfunction and bile reflux exposure.[15] However, strictures, along with other complications of GERD, are decreasing with the increased use of proton pump inhibitor therapy in GERD.[16] There is evidence that the recurrence of strictures is reduced with the increased use of proton pump inhibitors for patients with strictures that have been effectively dilated.[17]

The pathogenesis of oesophageal strictures is unclear. Some feel that the strictures develop as a result of chronic oesophageal ulcers wherein there is damage to the substratum resulting in fibrosis. The results of endoscopies performed in over 7500 patients between 1991 and 2001 showed that 65% of oesophageal ulcers were due to GERD.[18] Most of these ulcers (80%) were found in the lower oesophagus. Morbidity associated with oesophageal ulcers included haemorrhage (34%), oesophageal stricture formation (12.5%) and oesophageal perforation (3.4%).

Causes of erosive oesophagitis, GI bleeding, strictures and ulceration.—The causes of oesophageal manifestation of nocturnal GERD, such as oesophagitis, GI bleeding, strictures and ulceration, remain unclear. Orr *et al.* found that a history of nocturnal reflux episodes lasting greater than 5 min is the most reliable factor for distinguishing patients at increased risk for erosive oesophagitis.[2] It has been postulated that the responsiveness to acid is altered with diminished alertness, leading to increased acid contact time in the oesophagus during sleep.[2, 19] However, a 24-h pH monitoring study evaluating the frequency, amount and positioning (upright or supine) of oesophageal acid exposure as a predictor for the severity of erosive reflux oesophagitis found that these factors were either not correlated or weakly correlated with the severity of erosive oesophagitis.[20] The authors suggested that the development of erosive oesophagitis was not explained solely by the duration of oesophageal acid exposure. In contrast, 24-h pH monitoring by Frazzoni *et al.* found that the total percentage of acid reflux time was greater in patients with GERD complications than in those without complications.[19] They also showed that patients with erosive GERD had a significantly higher supine nocturnal acid reflux time than those with non-erosive GERD ($P = 0.038$). These studies raise questions about the importance of prolonged or supine oesophageal acid exposure, especially the coexistence of hiatal hernia, in the development of oesophageal injury and whether other factors contribute to the process.

Several mechanisms are responsible for the progression from erosive oesophagitis to the formation of oesophageal ulcers, strictures and upper GI bleeding.[21] Repeated exposure of oesophageal epithelial cells to refluxed gastric acid and pepsin causes caustic effects on the epithelial cells, leading to a progression from oesophageal erosions to ulcerations and bleeding.[21] In some cases, oesophageal ulcers can be complicated by haemorrhage and, rarely, perforations. Strictures may result when chronic oesophageal inflammation is replaced by fibrous tissue and the deposition of collagen and scar tissue.[15, 21] When omeprazole, 20 mg daily, was administered to 34 individuals with dysphagia who had erosive oesophagitis and peptic stricture, it produced significantly higher rates of oesophageal healing following dilation ($P < 0.01$) than an H_2-receptor antagonist.[17]

The current definition of Barrett's oesophagus, published by the American College of Gastroenterology in 1998, states that the disorder involves endoscopically recognized changes in oesophageal epithelium of any length, with intestinal metaplasia confirmed by biopsy.[22] In the general population, the prevalence of long-segment Barrett's oesophagus is between 0.4% and 0.9%, but many cases may go undiagnosed.[23-25] A population-based study examining clinically-detected Barrett's oesophagus vs. autopsy findings showed a rate of 22.6 cases per 100 000 individuals in the clinically-diagnosed group and a rate of 376

cases per 100 000 individuals in the autopsy group.[23] This suggests that many more patients have Barrett's oesophagus than are diagnosed. However, diagnosis of Barrett's oesophagus has increased over the past 30 years with the increased use of diagnostic endoscopy.[23] In the population of patients with chronic GERD, the prevalence of Barrett's oesophagus is between 7% and 12%.[10, 26] Barrett's oesophagus prevalence increases with age. In a study of 228 patients with GERD, a significantly higher percentage of patients over the age of 60 years had erosive oesophagitis and Barrett's oesophagus compared with those aged less than 60 years ($P < 0.001$).[27] It has been suggested that when oesophageal ulcers heal, the oesophageal mucosa undergoes a metaplastic process in which the damaged squamous cells are replaced by the columnar cells, forming Barrett's oesophagus.[21]

Risk factors for Barrett's oesophagus.—It is still unclear why some patients with GERD develop Barrett's oesophagus and others do not. Patients with GERD who are at increased risk for Barrett's oesophagus typically have a longer duration of symptoms, more severe nocturnal symptoms, symptoms occurring at an earlier age, and a greater incidence of complications of GERD.[28, 29] Unlike erosive oesophagitis, which does not show a correlation between increased prevalence and duration of GERD symptoms, the frequency of Barrett's oesophagus seems to vary with symptom duration. Patients who have had GERD symptoms for < 1 year have a 3% prevalence of Barrett's oesophagus, yet the prevalence increases to > 20% among patients who have had GERD symptoms for > 10 years.[10] Data from 24-h pH monitoring have shown that patients with Barrett's oesophagus have a higher degree of oesophageal acid exposure than patients with erosive and non-erosive GERD.[30] Furthermore, the duration of acid exposure has been correlated with the length of Barrett's mucosa.[31] This was true in both the supine and upright positions. These findings indicate that the duration of oesophageal acid exposure may influence the length of Barrett's mucosa. However, patients with Barrett's oesophagus seem to have a reduced sensitivity to acid exposure, which may be influenced by age.[32] A study evaluating responses to acid infusion demonstrated that, compared with younger patients, older patients with Barrett's oesophagus had a reduced response.[32] In a study of 12 and 10 male subjects with Barrett's oesophagus aged > 65 years (mean age, 76 ± 1.6 years; age range, 66–83 years) and ≤ 50 years (mean age 44 ± 1.8 years; age range, 34–50 years), respectively, sensitivity to acid infusion was explored. The purpose of the study was to compare perception thresholds to acid infusion between the older and younger patient populations by measuring chemosensitivity using an acid perfusion test. This assessment was done through patient feedback indication when acid reflux was reproduced. Patients reported their symptom perspective at lag time (time in seconds to initial typical symptom perception), sensory intensity rating (perception of symptom intensity at the end of acid perfusion), and acid perfusion sensory score (APSS) (score calculated from lag time and sensory intensity rating figures).[32]

Nocturnal acid exposure is also a factor in Barrett's oesophagus. During sleep, patients with Barrett's oesophagus experience a notable increase in episodes of spontaneous gastro-oesophageal reflux.[28]

Relationship between oesophageal adenocarcinoma and Barrett's oesophagus

The incidence of oesophageal adenocarcinoma has been increasing in recent years. Over the 20-year period between 1975 and 1995, the incidence of oesophageal adenocarcinoma rose dramatically from 0.7 to 3.2 per 100 000 person-years, an increase of nearly 5-fold.[33] This increase has been found predominantly in white men over the age of 65 years (Table 2). There is a well-known association between Barrett's oesophagus and oesophageal adenocarcinoma. A study of patients with Barrett's oesophagus showed a 4% prevalence of oesophageal adenocarcinoma at initial endoscopy or within 6 months.[34] During the course of the study, over 4.8 years, the average risk for development of oesophageal adenocarcinoma in a patient with Barrett's oesophagus was one in 208 patient-years of follow-up, which was somewhat lower than had been found in previous studies.[35] Shaheen *et al.* have questioned whether there was publication bias in the reporting of cancer risk in Barrett's oesophagus in the earlier studies.[36] These authors reviewed all published estimates of cancer risk in Barrett's oesophagus between 1966 and 1998 and found a higher risk reported in smaller studies vs. larger studies. They concluded that the correlation between Barrett's oesophagus and oesophageal cancer may have been overestimated. A more recent study showed an incidence of one case of oesophageal adenocarcinoma in 285 patient-years of follow-up in a population of 136 patients with Barrett's oesophagus.[37]

With the rising incidence of oesophageal adenocarcinoma, some investigators have questioned whether patients with Barrett's oesophagus are the only individuals with chronic GERD who are at increased risk for its development. In recent years an association has been reported between chronic GERD and development of oesophageal adenocarcinoma (odds ratio 7.7).[38] The risk was proportional to the severity, frequency and duration of GERD symptoms.[38] Also suggested to contribute to the rise in oesophageal adenocarcinoma is the observation that *Helicobacter pylori (H. pylori)* infection is negatively associated with the development of Barrett's oesophagus and adenocarcinoma of the oesophagus.[39] However, there is little evidence that these observed phenomena of decreasing *H. pylori* prevalence and rising oesophageal adenocarcinoma are causally related. This observation may reflect the different epidemiology of *H. pylori* infection and GERD.[40]

Effect of H. pylori on GERD

Case control studies have shown little difference in the prevalence of *H. pylori* infection between patients with and without oesophagitis.[41] Furthermore, although infection with *H. pylori* has been inversely correlated with the risk of the development of severe or complicated GERD, there have been inconsistent results from studies around the world. These inconsistencies most likely stem from the fact that studies have not routinely controlled for the pattern of gastritis induced by *H. pylori* infection.[42] It is clear that there are multiple possible consequences of *H. pylori* infection, including an asymptomatic state (despite the presence of gastric inflammation), duodenal ulcer, gastric ulcer, noncardia gastric adenocarcinoma and gastric lymphoma of mucosa-associated lymphoid tissue.[43-45] Individuals from different parts of the world have varying presentations, with lower rates of gastric acid secretion among Africans than Caucasians.[46-49]

Among Caucasians, the antral-predominant form of *H. pylori*-induced gastritis produces hypergastrinaemia and, ultimately, relative hypersecretion of gastric acid,[47] and affected individuals are at increased risk of developing duodenal ulcer.[50] This should not influence an individual's risk of GERD unless there is also defective lower oesophageal sphincter function and/or hiatal hernia. Eradication of *H. pylori* infection from such individuals leads to a resolution of antral-predominant gastritis and, eventually, to the reduction of gastric acid secretion towards normal. This is associated with a reduced risk of the development or recurrence of duodenal ulcer;[51] reduced gastric acid output may even improve GERD symptoms in those who already had GERD. In those individuals who did not have GERD before the eradication of *H. pylori* infection, there is no reason to believe that it should develop post-eradication.

It is quite different for those with the corpus-predominant form of *H. pylori*-induced gastritis. Due to the involvement of the acid-secreting gastric corpus in the damaging inflammatory response to the infection, parietal cell mass is reduced and gastric acid secretion is correspondingly diminished.[50, 52] GERD is therefore unlikely in these individuals because of the low level of gastric acid secretion.[53] Some individuals may go on to develop gastric atrophy with hypochlorhydria, which is assumed to be an irreversible state. However, if the infection is eradicated before the development of atrophic gastritis, there may be recovery of gastric acid secretion towards normal.[54] For those individuals who have had defective lower oesophageal sphincter function, this increase in acid load may lead to the development of symptomatic GERD for the first time.[54]

The most serious long-term consequences of GERD, namely Barrett's oesophagus and oesophageal adenocarcinoma, are encountered most frequently in industrialized Western nations.[55, 56] Obesity, an independent risk factor for oesophageal adenocarcinoma, may be a contributor. However, the different phenotypical manifestations of *H. pylori*-related gastritis may also have a role. Because hypochlorhydria from corpus-predominant gastritis is most common in developing nations, and hyperchlorhydria from antral-predominant gastritis is typical in industrialized nations, there may be differing disease burdens. In the case of corpus-predominant gastritis, there will be an excess of noncardia gastric adenocarcinoma and relatively little GERD and oesophageal adenocarcinoma. Studies of patients infected with more inflammatory strains, such as *cagA* positive *H. pylori*, support this. These patients have been shown to be less prone to severe oesophagitis and Barrett's change.[57, 58] These strains are more likely to cause more severe corpus gastritis with atrophy and hypochlorhydria. However, these patients are at very much greater risk of developing gastric cancer as a result of this adverse histology.[59]

In antral-predominant gastritis, gastric adenocarcinoma will be less prevalent but there should be more cases of duodenal ulcer and, by extension, the relative hypersecretion of acid will increase the disease burden from GERD and its complications. The conclusion that *H. pylori* infection protects against GERD and its complications is likely to be an oversimplification. It may not be *H. pylori per se* that protects against GERD, but rather the pattern of gastritis that it induces and, more importantly, the consequence that gastritis has for gastric acid secretion.[42]

An initial observational report suggested that duodenal ulcer patients who have been cured of *H. pylori* infection were more likely to develop *de novo* GERD than those with untreated infection or those who had failed eradication.[60] Identifiable risk factors for the apparent development of GERD included the presence of some corpus gastritis before eradication.[60] This is consistent with the above hypotheses; presumably, those patients who had corpus gastritis experienced increased gastric acid output after successful cure of the infection, which tipped the balance in favour of developing GERD.[52] Also consistent with the above hypotheses is that eradication of *H. pylori* infection from patients in the USA (where the antral-predominant form of gastritis is dominant) has generally not been associated with the new development of GERD.[61] However, the observation has not been confirmed by subsequent prospective studies and was inconclusive because of methodological issues.[62] Reports of GERD symptoms improving after *H. pylori* infection has been cured are presumably due to reduced gastric acid load.[53, 63]

Obesity has also been thought to have a link to oesophageal adenocarcinoma. Investigators have found that obesity is a significant risk factor for hiatal hernia. Through this increased hiatal hernia incidence, obesity can be significantly associated with oesophagitis.[64-66] For more on the relationship between GERD and obesity, see the article by Orr *et al.* in this supplement.[67]

The pharmacodynamic effect of proton pump inhibitors is enhanced in the presence of *H. pylori* infection. Healing rates of erosive oesophagitis may be higher among *H. pylori*-positive than among *H. pylori*-negative patients.[68] However, the eradication of *H. pylori* infection from GERD patients has not been associated with a need for an increase in proton pump inhibitor dose to maintain patients in remission.[69, 70] This contradicts observations that a period of prolonged gastric acid hypersecretion may be triggered by the concomitant eradication of *H. pylori* infection and the withdrawal of proton pump inhibitor therapy, which is not found in patients in whom *H. pylori* is not eradicated.[71] At present, the gastric acid hypersecretion that has been observed after proton pump inhibitor withdrawal is not of proven clinical consequence. Although not all clinicians feel it is mandatory to check GERD patients for *H. pylori* infection, physicians should consider eradicating infection from such patients. The benefits of *H. pylori* eradication are likely to outweigh any theoretical risks. Furthermore, long-term proton pump inhibitor therapy in the presence of *H. pylori* infection increases the rate at which gastric mucosal atrophy and intestinal metaplasia develop.[72] This is not seen when proton pump inhibitors are used in uninfected subjects or in those in whom eradication therapy has been given successfully before proton pump inhibitor use.[73] Although the consequences of this are not yet known, eradication of *H. pylori* before long-term therapy has been advocated in recent consensus statements.[74]

Screening to detect Barrett's oesophagus and oesophageal adenocarcinoma

Current guidelines from the American College of Gastroenterology recommend that patients with chronic GERD be screened for Barrett's oesophagus, especially those older than 50 years of age, in whom GERD is most prevalent.[22] Other experts recommend that screening may not alter outcomes. However, assessment of symptoms alone does not distinguish patients with Barrett's oesophagus from those with uncomplicated GERD. Many patients

with Barrett's oesophagus are clinically indistinguishable from other patients with GERD or they may even under-report symptoms or be asymptomatic.[26, 75] In an effort to improve identification of patients at increased risk for Barrett's oesophagus, Gerson *et al.* outlined the following parameters that indicate a higher risk: male sex, symptoms of heartburn, odynophagia and nocturnal symptoms.[76] Dysphagia was not predictive of Barrett's oesophagus.

The goal of endoscopic surveillance in this population is to identify patients who are at increased risk for cancer due to the presence of Barrett's oesophagus. Macdonald *et al.* evaluated the findings from more than 29 000 endoscopies performed at a university hospital[77, 78] and found Barrett's oesophagus in 1.4% of cases. Approximately one-third of the patients with Barrett's oesophagus were entered into a yearly surveillance programme over a 10-year period (average surveillance time of 4.4 years), and the length of involved oesophagus did not vary. During that time, only one patient had oesophageal adenocarcinoma identified through the surveillance programme and four others developed oesophageal adenocarcinoma that was detected during endoscopy. The authors suggested that routine surveillance should be limited to patients with risk factors including stricture, ulceration or long-segment (> 80 mm) Barrett's oesophagus.

Although there is no single guideline that is universally accepted in practice for performing surveillance in Barrett's oesophagus, some professional societies, including the American College of Gastroenterology, have made recommendations for such surveillance. The American College of Gastroenterology guidelines recommend surveillance endoscopy for patients with Barrett's oesophagus as determined by endoscopic findings, such that a 3-year interval is considered appropriate in the absence of dysplasia on two consecutive endoscopic biopsies.[79] The cost-effectiveness of this strategy was evaluated by Inadomi *et al.*,[80] who used a decision analysis model to evaluate the cost of screening and surveillance of a high-risk group of individuals consisting of men > 50 years old with GERD symptoms. They concluded that performing a single screening examination in the high-risk group and then limiting surveillance to patients with Barrett's oesophagus with dysplasia is cost-effective, whereas surveillance of patients with Barrett's oesophagus without dysplasia is not, even if conducted at 5-year intervals. However, screening and surveillance remains a very controversial topic of discussion among the experts and further examination is warranted.[81]

CONCLUSIONS

The oesophageal complications of persistent or inadequately treated GERD cause a significant amount of morbidity. With the increased use of proton pump inhibitors, the incidence of oesophageal strictures has been reduced, but there have not been significant differences in the cases of upper GI bleeding and Barrett's oesophagus, and therefore they remain problematic. These complications may be related to nocturnal reflux. To reduce the morbidity associated with these oesophageal complications, an increased awareness among primary care providers and the general public of risk factors for persistent GERD is needed. It is troubling that in spite of the increased use of diagnostic endoscopy and effective treatment strategies, the incidence of oesophageal adenocarcinoma continues to rise. There is no convincing evidence that the negative association with *H. pylori* has a major role in this

increase. The world-wide increase in obesity may be more important. Screening and surveillance strategies have been proposed that maximize the identification of patients who may progress from Barrett's oesophagus to oesophageal adenocarcinoma. In some decision analysis models, the cost-effectiveness of these programmes is disputed. Further research should help identify those patients with chronic GERD who are at highest risk for progression to oesophageal adenocarcinoma, and who could benefit most from surveillance efforts.

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Table 1.

Potential oesophageal complications of persistent GERD

Erosive oesophagitis
Ulceration
Oesophageal strictures
Oesophageal haemorrhage
Barrett's oesophagus
Oesophageal adenocarcinoma

Table 2.

Ratios of oesophageal adenocarcinoma in white males

Age (years)	1974–80	1981–87	1988–94
< 55	1.0	1.4	2.3
55–64	1.0	1.3	2.3
65–74	1.0	2.4	4.5
75+	1.0	2.0	3.8

Adapted from Devesa S.S. *et al. Cancer* 1998; 83: 2049–53;[33] with permission.