Gastro-oesophageal reflux disease and hiatus hernia

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Abstract

Gastro-oesophageal reflux disease (GORD) is a common disorder with an increasing prevalence in th UK. The presence of a hiatus hernia is the strongest risk factor for developing GORD, although not essential. The most common symptoms experienced by patients with GORD are heartburn and acid regurgitation. Diagnosis of GORD is usually made from the clinical history. Endoscopy and ambulatory pH monitoring are adjunctive tests that can influence management decisions. The main goals of treatment are symptom control and the prevention of complications such as Barrett's oesophagus and peptic stricture. Treatment options include lifestyle interventions, proton pump inhibitors and, in selected patients, antireflux surgery.

Keywords Ambulatory reflux testing; gastro-oesophageal reflux disease; hiatus hernia; MRCP; proton pump inhibitors

Key points

- Gastro-oesophageal reflux is a physiological phenomenon; it becomes a disease when excess reflux causes symptoms or complications
- Endoscopy should be reserved for red flag symptoms and for screening for Barrett's oesophagus in individuals with higher risk
- Proton pump inhibitors are the most common treatment, but ambulatory reflux testing can help direct management in more difficult cases
- Antireflux surgery can be effective in well-chosen individuals

Definition

Gastro-oesophageal reflux occurs when there is movement of gastric contents into the oesophagus. A degree of gastro-oesophageal reflux is a normal physiological process, and in health the oesophagus can be exposed to acidic gastric contents up to 5% of the time. These episodes are usually brief and do not cause symptoms. Gastro-oesophageal reflux becomes a disease when the reflux becomes more prominent resulting in symptoms and/or complications, as stated in the Montreal Consensus definition[1]. Furthermore, this consensus document includes the associative syndromes and complications that can manifest secondary to both symptomatic and asymptomatic gastro-oesophageal reflux disease (GORD) (Figure 1).

Epidemiology

The global prevalence of GORD is increasing. In the UK, the incidence of GORD is approximately 5 per 1000 person−years, with an approximate prevalence of 10−20%[2]. There is a very small increase in incidence with age until 69 years, but thereafter the incidence decreases. There is no gender predilection to GORD (except in female patients during pregnancy).

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Pathophysiology

The gastro-oesophageal junction (GOJ) (and antireflux barrier) between the stomach and oesophagus is formed by the lower oesophageal sphincter (LOS) and the crural diaphragm. These usually lie at the same anatomical level. The LOS maintains a contractile tone to guard against reflux, and relaxes during swallowing to allow the passage of food and fluids. In addition to maintaining an anatomical barrier to reflux, the crural diaphragm contracts during inspiration, offering resistance to the reflux-favouring pressure gradient formed during inspiration.

Hiatus hernias are a common cause of reflux. In the presence of a hiatus hernia, the two key components of the GOJ are separated, and the mechanical and physiological antireflux barrier is disrupted[3] (Figure 2).

The extent of symptoms and mucosal injury depends on the interaction between aggravating factors (e.g. duration of contact, characteristic of refluxate, oesophageal hypersensitivity) and defensive factors (e.g. antireflux barrier integrity, chemical and mechanical oesophageal acid clearance, degree of oesophageal mucosal inflammation). Recent studies suggest that oesophagitis results not from the direct chemical effects of the refluxate on the oesophageal epithelium but via cytokine-triggered inflammation within the epithelium.

Risk factors associated with GORD

- Pregnancy.
- Obesity − the relative risk for symptoms has been reported as 1.43 for a body mass index (BMI) of 25−30 kg/m^2, increasing to 1.94 for a BMI >30 kg/m^2. However, waist circumference and waist-to-hip ratio have been shown to correlate more strongly than BMI.
- Cigarette smoking − several cross-sectional studies have shown a significant positive association with GORD and smoking (odds ratio 1.1−2.6).
- Drugs − anticholinergics, α/β-adrenoceptor blockers, calcium channel blockers, nitrates and theophylline reduce

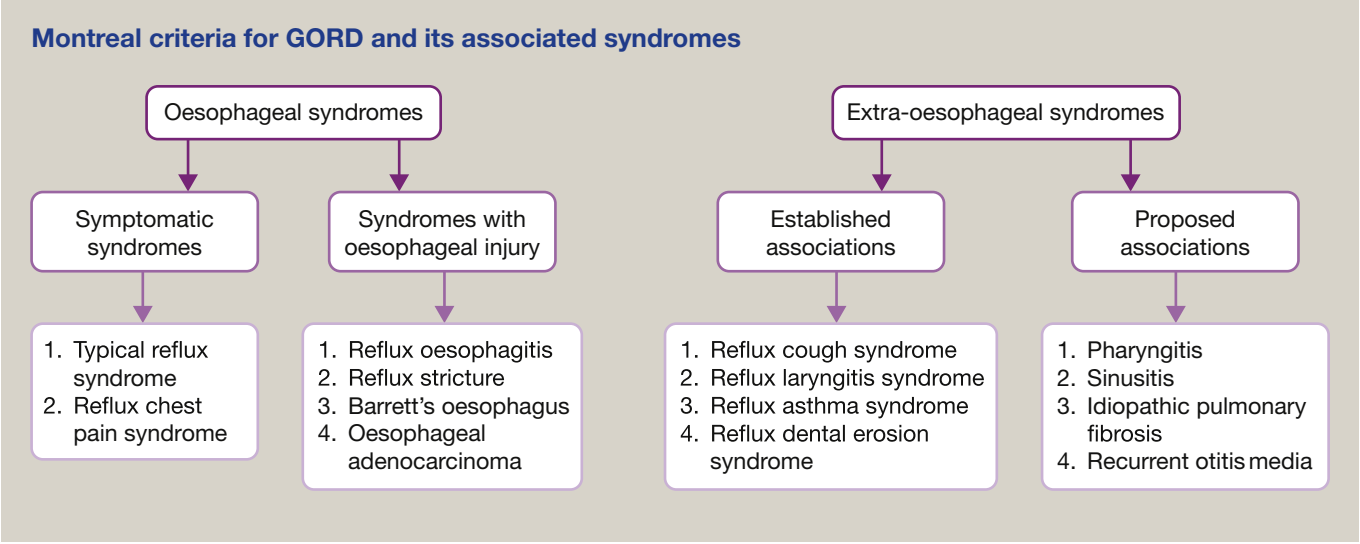

Figure 1 Reproduced from Nimish Vakil, Sander van Zanten, Peter Kahrilas et al. The Montreal Definition and Classification of Gastroesophageal Reflux Disease: A Global Evidence-Based Consensus. *American Journal of Gastroenterology* 2006; **101**: 1900–1920 with permission from Wolters Kluwer Health, Inc.

LOS pressure through smooth muscle and neuronal mechanisms.

- Hiatus hernia – anatomical changes associated with hiatus hernias can facilitate reflux by reducing the competence of the LOS as well as by inhibiting clearance of oesophageal acid after reflux.
- Family history of heartburn or GORD – an immediate family history increases the likelihood of having symptoms by a factor of 3. This could in part be driven by a genetic risk of hiatus hernias.
- Psychological stress –a higher score on a psychosomatic symptom checklist is associated with a higher risk of GORD symptoms (although not increased reflux per se).
- Foods and meal portions – although no study has demonstrated a clinical association between certain foods and reflux, it is known that certain dietary components (e.g. caffeine, alcohol) can reduce LOS tone. Individuals eating in the 1–2 hours before sleep are more likely to experience excess nocturnal symptoms.

Clinical features

The most common symptoms of GORD are heartburn and acid regurgitation. Heartburn is defined as a retrosternal burning sensation. Acid regurgitation is defined as the perception of flow of refluxed gastric content into the mouth or hypopharynx. Symptoms are often worse after eating, on bending or on lying down.

Some individuals also report dysphagia, which can occur in the presence of oesophageal stricturing. Atypical symptoms reported include cough, laryngitis, asthma (wheeze) and dental erosions. The presence of alarm symptoms (anaemia, dysphagia, haematemesis, melaena, persistent vomiting, involuntary weight loss) raises the possibility of oesophagitis, peptic stricturing or cancer. Physical examination is generally normal.

Diagnosis

GORD can be diagnosed using a combination of clinical history, endoscopy, pH monitoring and response to an antisecretory drug. In the majority of patients a careful history and empirical

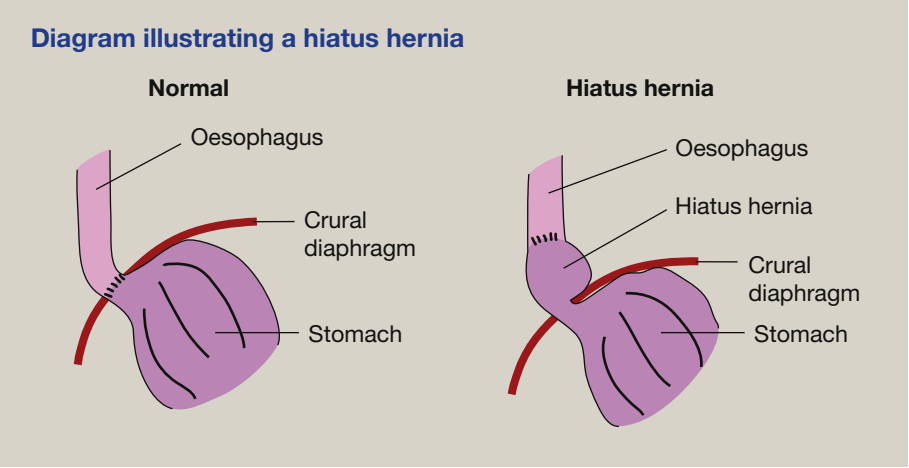

Figure 2

use of proton pump inhibitors (PPIs) is enough, but in more difficult cases adjunctive testing can be used.

Proton pump inhibitor (PPI) trial

A short (4–8-week) trial of PPI and lifestyle interventions is often the first step in patients <45 years old who have typical symptoms. Although pragmatic and cost-effective, symptomatic relief does not equate to a diagnosis of GORD. PPI trial has a sensitivity of 71% but a specificity of only 44% compared with formal diagnostic testing.

Oesophago-gastro-duodenoscopy (OGD)

OGD is indicated for patients with alarm symptoms or atypical, persistent (>5 years) or relapsing symptoms. It is advised to evaluate complications of GORD and alternate diagnoses. High-grade oesophagitis (Table 1), biopsy-proven Barrett's oesophagus (BO) and/or peptic stricturing is considered confirmatory evidence of GORD. At high grades of oesophagitis (C, D), BO can be obscured by erosion; repeat endoscopy is therefore recommended after a minimum 8-week course of PPI.

Endoscopy is completely normal in 60–70% of patients with true GORD. As such, a negative endoscopy cannot exclude GORD. If endoscopy is performed to diagnose GORD, current literature suggests performing OGD off PPI medication to maximize diagnostic potential. Where patients already have a diagnosis or presence of complications, endoscopy can be performed while the patient is on PPI medication.

It should be noted that an important minority of patients with heartburn and normal endoscopy do not have reflux disease, but instead have so-called functional heartburn. In functional heartburn, heartburn occurs in the absence of excess reflux or association with reflux episodes. It is more common in patients with other functional disorders and psychological comorbidity. Diagnosis can be confirmed with ambulatory reflux monitoring (see below), and treatment is most often with e.g. fluoxetine/amitriptyline.

In individuals with predominant dysphagia, it is important to perform oesophageal biopsies to exclude eosinophilic oesophagitis (which can be associated with refractory heartburn).

Routine testing for *Helicobacter pylori* for reflux is currently not recommended by guidelines.

Ambulatory reflux monitoring

Patients with no or a partial response to PPI therapy and with normal endoscopy can be assessed using ambulatory reflux monitoring. This should also be performed before considering antireflux surgery, even when there is a complete PPI response.

24-hour ambulatory pH monitoring: ambulatory monitoring can objectively assess oesophageal acid exposure. The number of reflux episodes and the oesophageal acid exposure time are measured. Patients also record symptom episodes, allowing a temporal association between symptoms and reflux symptoms to be established.

Where there is pathological acid exposure (Table 2), a diagnosis of GORD can be made. Where there is physiological acid exposure, a diagnosis of hypersensitive oesophagus (normal acid exposure but a positive reflux–symptom association) or functional heartburn (normal acid exposure, no reflux–symptom association) can be made (Figure 3). Ambulatory reflux monitoring usually uses a transnasal catheter connected to a portable receiver device. More recently, wireless recording via intra-oesophageal devices placed during endoscopy has allowed wire-free ambulatory recording.

The addition of impedance to pH monitoring enables further evaluation of non-acid reflux and gas movement, which are associated with symptoms in some patients.

Oesophageal manometry

Although not a diagnostic test for GORD, oesophageal manometry can accurately diagnose hiatus hernias and is required to exclude major oesophageal motility disorders (e.g. aperistalsis, achalasia) before antireflux surgery.

Treatment

The main goals of treatment are symptom control and prevention of complications[4].

Lifestyle interventions

Most interventions are based on physiological data suggesting that certain lifestyle changes can influence the content or amount of reflux and/or the frequency of LOS relaxation. Encouraging avoidance of food in the 2 hours before bed and elevating the head at night has been shown to have some benefit in symptom relief. Although outcome data regarding weight loss are lacking, a

The Los Angeles classification of oesophagitis

Grading depends on the degree of mucosal disruption in the distal oesophagus on endoscopy:

- Grade A – breaks of ≤5 mm
- Grade B – breaks of >5 mm
- Grade C – breaks extending between the tops of ≥2 mucosal folds, but <75% of circumference
- Grade D – circumferential breaks >75%

Table 1

pH monitoring metrics

Acid exposure time – this is reliably extracted from automated analysis and predicts the response to medical and surgical reflux therapy:

- <4% is physiological
- 4–6% is inconclusive
- >6% is pathological

Number of reflux episodes – this is an adjunctive measure to acid exposure time when the result is borderline or inconclusive:

- >80 reflux episodes in 24 hours is abnormal
- <40 reflux episodes in 24 hours is physiological

Symptom-reflux association – a metric of the temporal association between symptom episodes (recorded by button presses on data recorder) and reflux episodes

- Symptom index (SI, proportion of symptoms preceded by reflux events)
- Symptom associated probability (SAP, statistical analysis of association of symptoms and reflux events)

Table 2

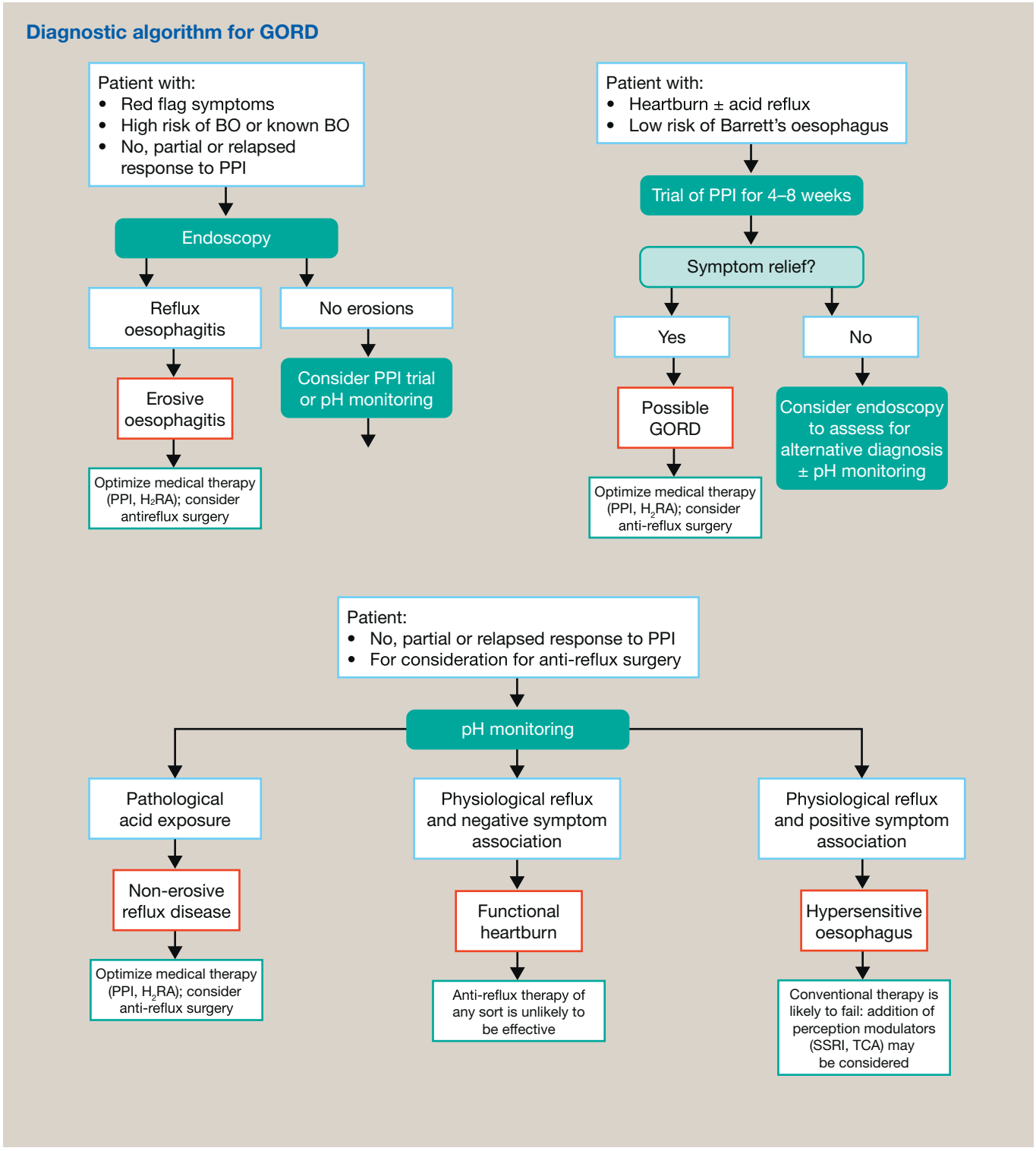

Figure 3

multitude of studies demonstrate a correlation between obesity and GORD; therefore weight reduction should be encouraged. Smoking cessation has also shown some benefit in symptom relief.

Antacids and alginate preparations

Antacids and alginates are often used as initial treatment for mild to moderate GORD (with alginate preparations having superior efficacy). They also have a role as add-on treatment in refractory disease.

Histamine-2 receptor antagonists (H_2RAs)

H_2RAs act by blocking gastric production in parietal cells; at peak activity, H_2RAs reduce acid production by 60–70%. They also promote healing of low-grade oesophagitis. Overall, H_2RAs are

well tolerated, although they are cytochrome CYP450 inhibitors and can cause clinically significant drug interactions. A further limitation of H_2RAs is tachyphylaxis. Fackler et al. showed that the addition of a night-time H_2RA to PPI therapy improved nocturnal symptom control; however, the effect significantly decreased after 1 week of regular use, and no benefit was seen at 1 month.

Proton pump inhibitors

PPIs are currently the most efficacious medical therapy for GORD, reducing gastric acid production by up to 90%. PPIs prevent gastric acid secretion by inhibiting H^+/K^+-ATPase membrane channels. All PPIs are weak bases and therefore accumulate and bind to actively secreting pumps where the pH is lowest. Because they bind to active pumps, PPIs should be taken 30–60 minutes before a meal. PPIs have proven benefits over H_2RAs in terms of healing of oesophagitis and symptom relief.

It is recommended to start with the lowest efficacious dose of PPI and titrate up until symptoms are relieved, as there are risks associated with long-term use. Maintenance PPI is recommended for individuals whose symptoms return when the PPI is stopped and for those with erosive oesophagitis or BO.

Long-term PPI use is generally safe. There is increased risk of gastrointestinal infections (e.g. *C. difficile*), and possibly bone density reduction in post-menopausal women. Concerns about interactions with antiplatet drugs, role in heart disease, dementia etc are thus far unfounded.

New agents

PPIs with extended half-lives, PPIs with immediate and modified-release action, and combination drugs where additives enhance acid suppression are some of the newer drugs in trial phases. New agents such as potassium competitive acid blockers have been shown to have a faster onset than traditional PPIs and are more stable at a lower pH.

Surgery

Surgical fundoplication returns the GOJ to the abdominal cavity, mobilizes the gastric fundus and closes the diaphragmatic crura through a short tension-free fundoplication. Patient selection is key, with success depending on symptom profile, manometry and reflux study findings, and prior response to PPI (PPI responders are more likely to obtain symptom relief). Excellent outcomes are seen in carefully selected populations[5], but surgical outcomes are modest if selection is less rigorous.

The most commonly performed surgical procedure is the Nissen's fundoplication. More recently, magnetic sphincter augmentation (LINX® reflux system) has shown similar efficacy. An interesting concept under evaluation is LOS pacing (EndoStim®) via laparoscopic placement of electrodes. This increases resting LOS tone and reduces frequency of transient LOS relaxation. Uncontrolled trials have shown promising results.

Endoscopic approaches

Endoscopic antireflux techniques include endoscopic fundoplication (EsophyX®) and radiofrequency-induced sphincter augmentation (Stretta®). Uncontrolled studies show modest benefit, and there might be a limited role for these procedures.

Complications

Erosive oesophagitis

Erosive oesophagitis is classified using the Los Angeles Classification (Table 1). It occurs when excessive refluxate results in necrosis of the surface mucosa, causing erosions and ulcers. The condition responds well to PPI therapy.

Oesophageal stricturing

Peptic stricturing is a result of the fibrotic healing process of erosive oesophagitis, with increased occurrence at the squamocolumnar junction. Stricturing occurs more often in older white males with a longer duration of untreated symptoms. Regular PPI therapy is required, and strictures can require endoscopic dilatation.

Barrett's oesophagus

BO is defined as the partial replacement, from the GOJ proximally, of stratified squamous epithelium with metaplastic columnar epithelium that is clearly visible endoscopically and confirmed histopathologically. Annually, 0.1–0.5% of individuals with BO develop oesophageal adenocarcinoma. Risk factors for the development of oesophageal adenocarcinoma include age >50 years, male gender, Caucasian ethnicity, positive smoking history and central obesity.

Current guidelines recommend against screening the general GORD population, instead focusing on individuals with risk factors or a first-degree relative with confirmed BO or oesophageal adenocarcinoma. In the absence of dysplasia, surveillance depends on the length of BO: individuals in whom segments are <3 cm with intestinal metaplasia should undergo endoscopic surveillance every 3–5 years, whereas those with segments ≥3 cm should receive surveillance every 2–3 years. Where dysplasia is present, endoscopic therapy and more intensive surveillance is indicated.

Prognosis

Most patients achieve symptom relief from PPI therapy; however, the relapse rate off medication is high. Patients with more severe oesophagitis (grades C and D) are at higher risk of complications such as strictures and BO. ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the question below. The answer can be found at the end of the issue or online here.

Question 1

A 25-year-old man presented with intermittent retrosternal burning pain after meals, on and off over the past 6 months. There was occasional dysphagia, and he had had one episode of self-resolving food bolus obstruction. He occasionally experienced an acid taste in the mouth.
Clinical examination was normal.

What is the most appropriate next step?

A No further investigation is required; reassure him
B Lifestyle measures (address alcohol, smoking, weight)
C Empirical trial of proton pump inhibitor (PPI)
D Upper gastrointestinal endoscopy with mucosal biopsy
E 24-hour pH monitoring