Adult GORD: advances and challenges in management

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Gastro-oesophageal reflux disease (GORD) is a common and often chronic condition that is associated with poor quality of life and significant complications. This review provides a summary of the pathophysiology, assessment and current management of GORD in adults.

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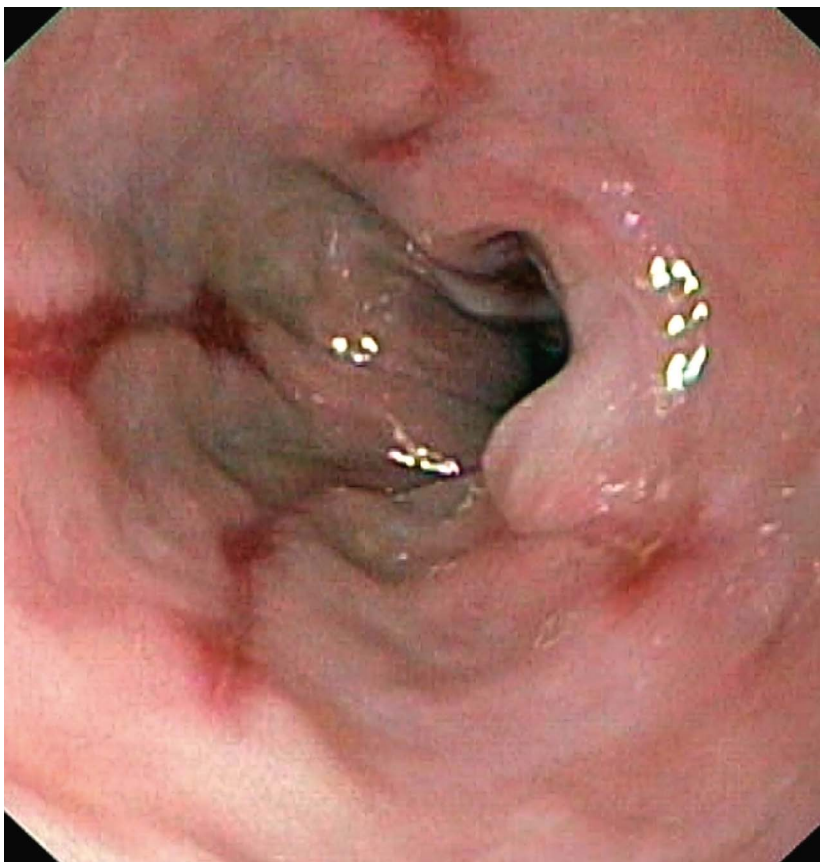

Gastro-oesophageal reflux disease (GORD) is common, with heartburn and regurgitation occurring at least weekly in up to 26 per cent of the European population.[1] Dyspepsia including reflux symptoms accounts for 5 per cent of primary care consultations and proton pump inhibitors (PPIs) are the most commonly prescribed gastrointestinal drugs.

GORD is often a relapsing or chronic problem resulting in poor quality of life and has significant complications including Barrett's oesophagus – a risk factor for oesophageal adenocarcinoma in a small percentage of patients. The increasing prevalence and incidence of reflux and oesophageal cancer is a worrying trend in the western world and is linked to the rise in obesity.[2] Recognition that extraoesophageal symptoms may be associated with reflux has opened up new questions about the diagnosis and management of chronic cough and globus.

Since the introduction of PPIs in the late 1980s, the GORD workload has evolved from healing of oesophagitis and peptic strictures, for which PPIs are extremely effective, to a high secondary care referral rate for nonerosive reflux (NERD) with failed PPI therapy. This reflects the issues of changing patient tolerance of symptoms, and nonacid and volume reflux (regurgitation) symptoms, which are less responsive to acid suppression therapy.[3]

Definition

The Montreal definition of GORD envelops the concepts of symptoms only *versus* tissue damage and extraoesophageal manifestations to more accurately describe the spectrum of GORD (see Figure 1).[4] This article will not address extraoesophageal disease management.

Pathophysiology

It is now accepted that GORD results from multiple factors that cause dysfunction of the lower oesophageal sphincter, with

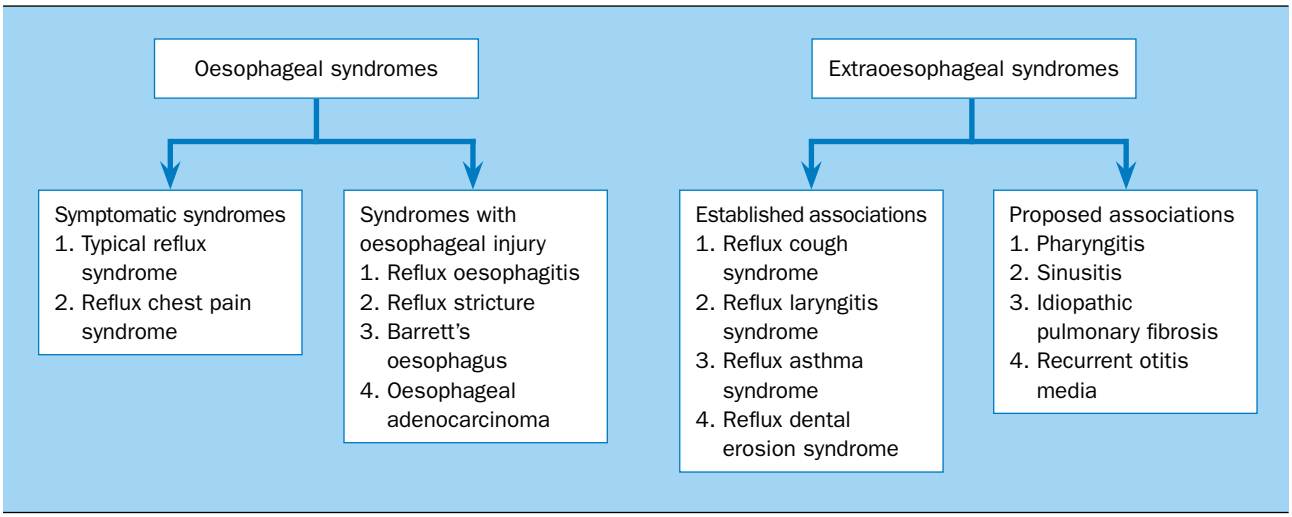

Figure 1. Montreal classification of GORD

Lower oesophageal sphincter factors
• Increased transient lower oesophageal sphincter relaxations • Hiatus hernia • Hypotensive lower oesophageal sphincter
Oesophageal factors
• Poor clearance • Mucosal sensitivity • Mucosal resistance • Reduced saliva
Intra-abdominal and gastric factors
• Increased pressure • Acid pocket • Posture • Delayed gastric emptying • Pregnancy
Hyperacidity
• Lifestyle • Rebound after prolonged PPI therapy • Hypercalcaemia • Zollinger-Ellison syndrome

Table 1. Multifactorial aetiology of GORD

obesity and the development of a hiatus hernia being central concepts (see Table 1).[5] A relatively new concept of the postprandial 'acid pocket' – an area of pooling of acid in the proximal stomach – explains the paradox of increased heartburn after eating despite the buffering effect of food and supports the concept of using alginate preparations after meals to control these symptoms.

Diagnosis

Primary care diagnosis is reliant on symptom assessment and response to PPI therapy, although validated patient symptom scoring tools have been developed to improve sensitivity of diagnosis and differentiate from dyspepsia and functional disease, for example the GerdQ tool (see Figure 2).[6]

Endoscopy

Endoscopy remains the tool of choice for assessing tissue damage but will be normal in up to 70 per cent of patients, is invasive, costly and carries a risk of morbidity and small risk of mortality.

NICE guidance[7] for diagnosis of oesophageal cancer recommends a two-week wait endoscopy referral for those with dysphagia or who are over 55 years of age with weight loss plus one or more of the following: upper abdominal pain, reflux or dyspepsia symptoms. Nonurgent endoscopy is recommended for treatment-resistant dyspepsia; upper abdominal pain and low haemoglobin; raised platelet count plus one or more of nausea, vomiting, weight loss, reflux/dyspepsia, upper abdominal pain; or nausea and vomiting plus one or more of weight loss, reflux/dyspepsia, upper abdominal pain.

Ongoing symptoms can be managed according to a previous endoscopy finding without the need for repeat endoscopy, unless new alarm symptoms have occurred. Barium swallow is not recommended as a primary investigation for the diagnosis of reflux disease due to its poor sensitivity and specificity.

Barrett's oesophagus screening and surveillance

There is no routine recommendation for endoscopic screening for Barrett's oesophagus due to the low evidence base for improving outcomes from population screening. However, the NICE guideline for GORD and dyspepsia in adults[8] suggests it could be considered in those patients with individual risk factors, including long duration of symptoms, known previous oesophagitis, hiatus hernia, oesophageal stricture or ulcers, male gender or worsening frequency of symptoms.

Recent changes to Barrett's surveillance guidelines support decreased endoscopic surveillance intervals for non-dysplastic Barrett's based on new data showing a lower than previously thought risk of adenocarcinoma. Dysplastic, high-risk Barrett's has new guidance including the endoscopic management of high-grade dysplasia as a first-line therapy rather than oesophagectomy, representing a major change in practice.[9]

Oesophageal ambulatory pH studies

For patients refractory to treatment and where the diagnosis is in doubt or for those patients requesting antireflux surgery, 24-hour catheter-based pH studies have been the gold standard, allowing quantification of reflux and proving causality between symptoms and reflux events.

New advances have included the development of a multichannel impedance combined pH catheter, which allows the measurement of both acid and nonacid reflux by recording changes in electrical resistance caused by reflux rather than changes in pH, allowing identification of additional patients who may benefit from increased reflux therapy or surgery. These investigations can divide patients into different phenotypic subgroups, defining a group of patients with reflux-type symptoms but no actual reflux (functional heartburn or alternative diagnosis), allowing the withdrawal of inappropriate PPI therapy and use of alternative management strategies such as low-dose tricyclic antidepressants, SSRIs or psychological interventions (see Figure 3).

A wireless pH system, *eg* BRAVO capsule, Diagmed Healthcare, is also available for those patients unable to tolerate an indwelling 24-hour nasal catheter and has the advantages of measuring acid reflux events for up to 96 hours with fewer restrictions on the patient. Another advantage of 96-hour recording is that it allows recording to be done on and off a PPI to judge efficacy. However, the potential extra pick up of reflux with prolonged monitoring may not justify the added expense of this test (which requires endoscopic placement) over conventional studies in most patients. In difficult diagnostic situations, there is the disadvantage that only pH, *ie* acid events, can be measured and reflux events can be variable from day to day.

Treatment

Initial emphasis is placed upon lifestyle advice, including weight reduction, avoidance of precipitating factors, elevation of the head of the bed (approximately 20cm or eight inches), not eating within two to three hours of lying down, stopping smoking and reducing alcohol intake. Drugs that may contribute to reflux or cause dyspeptic symptoms should be reviewed. Examples include theophylline, calcium-channel blockers, bisphosphonates, NSAIDs, nitrates, steroids and tetracyclines. Although poorly evidence based, some individuals may benefit from dietary restrictions including caffeine, chocolate, fried foods and fizzy drinks, although the emphasis should be on promoting healthy eating and weight reduction in the overweight patient. Modification of lifestyle or medicines review may prevent the need for maintenance PPI therapy.

When you think of the symptoms you have had in the last seven days, how did you experience the following:
Answer the questions by setting a cross in one square in each row

	No. of days			
	0	1	2-3	4-7
1. How often did you have a burning feeling behind your breastbone (heartburn)?	☐ (0)	☐ (1)	☐ (2)	☐ (3)
2. How often did you have stomach contents (liquid or food) moving upwards to your throat or mouth (regurgitation)?	☐ (0)	☐ (1)	☐ (2)	☐ (3)
3. How often did you have a pain in the middle of the upper stomach?	☐ (3)	☐ (2)	☐ (1)	☐ (0)
4. How often did you have nausea?	☐ (3)	☐ (2)	☐ (1)	☐ (0)
5. How often did you have difficulty getting a good night's sleep because of your heartburn and/or regurgitation?	☐ (0)	☐ (1)	☐ (2)	☐ (3)
6. How often did you take additional medication for your heartburn and/or regurgitation other than what the physician told you to take?	☐ (0)	☐ (1)	☐ (2)	☐ (3)

GerdQ symptom scores:
< 8: low probability for GORD
≥ 8 and ≤ 3 on questions 5 and 6 (impact questions): GORD with low impact on daily life
≥ 8 and ≥ 3 on questions 5 and 6 (impact questions): GORD with high impact on daily life

Figure 2. The GerdQ tool for diagnosis and management of GORD in primary care

Medical therapy

Mild symptoms can be managed with an antacid or H_2-receptor antagonists, but the mainstay of therapy for moderate and severe symptoms and for healing of oesophagitis remains PPIs. NICE recommendations[8] are for an initial four to eight-week course to settle symptoms with maintenance therapy being the lowest effective dose, preferably with as-needed dosing thereafter. Severe oesophagitis, especially if there has been previous dilatation of a stricture, requires full-dose PPI for eight weeks with long-term full-dose maintenance therapy to prevent recurrence. Barrett's patients also require long-term maintenance PPI therapy, but at the lowest dose sufficient to control symptoms.

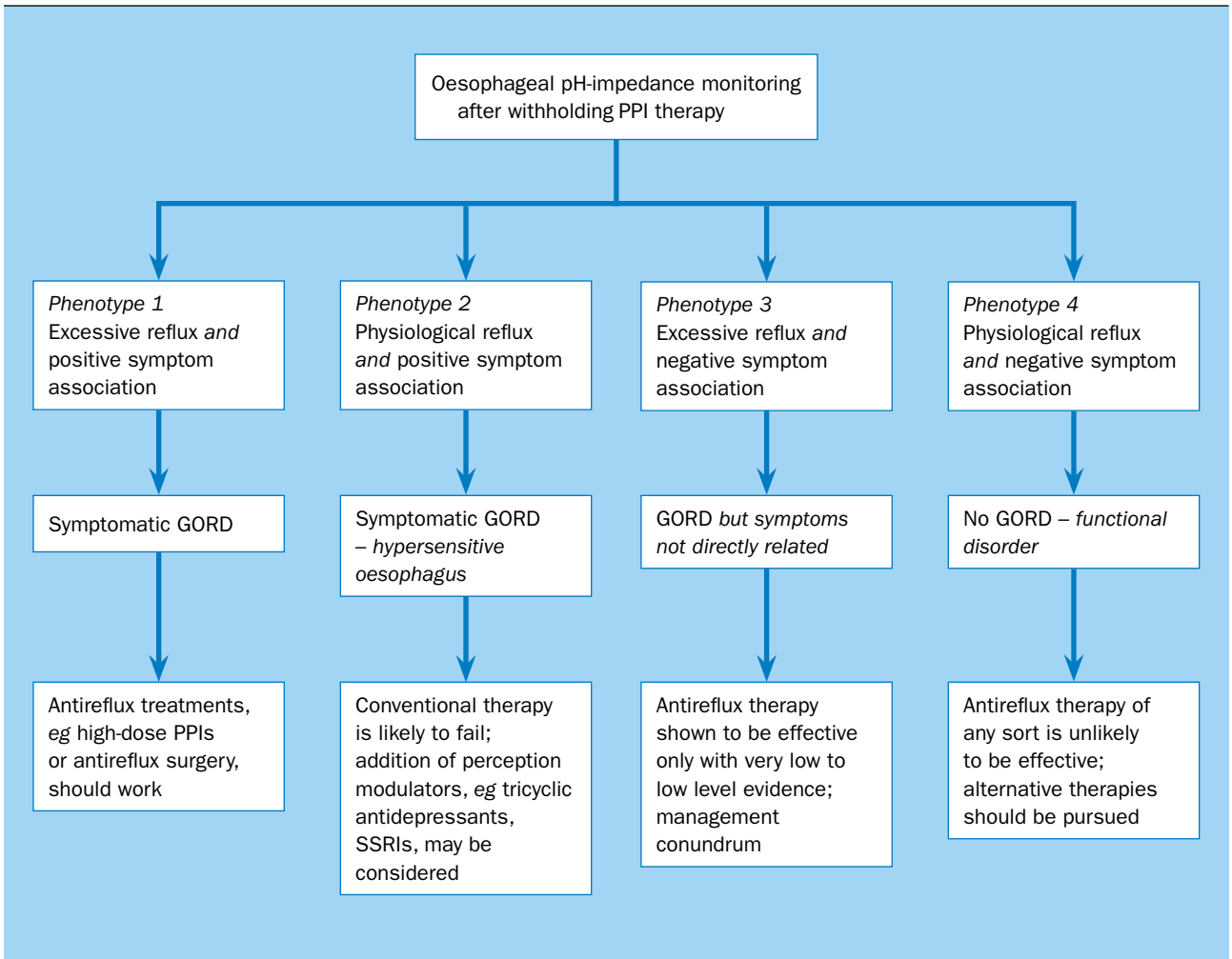

Figure 3. Using impedance to define the reflux problem

Rebound hyperacidity

It is recognised that PPIs may be a cause of recurrent reflux symptoms due to acid suppression causing hypergastrinaemia, which leads to an increased parietal cell mass in the stomach resulting in hypersecretion of acid after PPI therapy is stopped. This can last for many weeks resulting in resumption of PPI use and dependence.[10] It can be prevented by weaning patients off PPI therapy slowly with reducing doses and the use of alginates and H_2-receptor antagonists. Audits suggest that up to 85 per cent of patients on long-term PPI therapy for GORD or nonulcer dyspepsia could be stepped down to lower dose PPI or alginate therapy alone, resulting in clinical and cost benefits.[11,12]

Optimising medical therapy

In patients with refractory reflux symptoms (defined as a suboptimal response to PPI therapy), optimisation of medical therapy includes reinforcing compliance, timing PPIs to 30 minutes before a meal and using twice daily dosing (more effective blocking of activated proton pump receptors). The addition of an H_2-receptor antagonist at night such as ranitidine 300mg may help with nocturnal symptoms, but to avoid tachyphylaxis developing, a regimen of two weeks on and two weeks off is recommended. Additional adjuvant therapy with an alginate preparation may also be useful after meals and at night. Changing to an alternative PPI can be tried but the evidence base for this is low.

Other drugs

There is a limited role for prokinectic agents, which work by increasing gastric emptying, promoting oesophageal clearance and improving lower oesophageal sphincter tone. Evidence suggests poor efficacy in GORD and issues with safety restricting courses to five days, which is not helpful for chronic symptoms, so these agents cannot be recommended for general use.

Baclofen, a $GABA_B$-receptor agonist, reduces transient lower oesophageal relaxations by up to 50 per cent and is a potential add-on therapy to PPIs, but its use is limited by significant side-effects including sedation.

Visceral pain modulators such as low-dose tricyclic antidepressants, trazodone and SSRIs have been shown to reduce noncardiac chest pain and may have an increasing role in func-

tional heartburn and reflux-induced pain in terms of improving quality of life through pain desensitisation rather than reflux reduction.[13]

Nonmedical therapy

Endoscopic therapy

The Stretta device involves using a radiofrequency ablation catheter endoscopically delivered to induce a controlled mucosal injury to the lower oesophageal sphincter resulting in remodelling. Ten-year data demonstrates improvements in quality of life, reduction in symptoms and PPI use, and decreased acid reflux. This is an attractive day case procedure as an alternative to traditional antireflux surgery, but is not widely available.[14] In general, endoscopic techniques such as suturing devices and injection techniques have a smaller evidence base to support their use compared with traditional surgery but, after redesign from an earlier model, the Stretta device has now accumulated several years' worth of data and has the potential to become a standard therapy in the future.

Surgery

Antireflux surgery, usually laparoscopic fundoplication, is effective at reducing all forms of reflux[15] and is the best treatment for patients with marked anatomical abnormalities. It works best in those with documented reflux and a PPI response. It is important to make a secure diagnosis as symptoms such as gas bloat, nausea, dysphagia and pain are likely to be exacerbated in patients with pre-existing functional symptoms post-surgery. Long-term efficacy and patient satisfaction are likely to be equivalent to PPI usage, although a substantial percentage of patients will be back on medication within five years.

New surgical interventions

New, less invasive surgical techniques may become established in the near future including laparoscopic insertion of an expandable titanium bead necklace (LINX) around the lower oesophagus sphincter to augment it[16] or the laparoscopic implantation of neurostimulator electrodes onto the lower oesophageal sphincter (EndoStim).[17] Both techniques have the advantages of being less invasive, reversible, with good side-effect profiles and initial good short-term results, but have limited long-term data. They may offer an approach for patients with co-morbid limitations to more traditional surgical techniques and those who wish to avoid the potential side-effects of antireflux surgery.

The future

The increasing workload of GORD and difficulties in assessing the increasing burden of patients not responsive to PPIs without the use of invasive tests remains a challenge. Therapies have been largely restricted to acid suppression alone because of the success of PPIs in healing oesophagitis, but PPIs do not address the primary causes of reflux or treat nonacid reflux. New drug developments to improve oesophageal function, gastric emptying, oesophageal mucosal resilience and sensitivity are required. Noninvasive methods for detecting the presence of Barrett's oesophagus and risk stratification for cancer will reduce the need for endoscopy, *eg* Cytosponge. New techniques to avoid fundoplication surgery and address PPI failures may also have an increasing role in the future.

In the meantime, optimisation of lifestyle and PPI use first with selective secondary care referral for the accurate identification of true reflux and its complications in PPI nonresponders defines the GORD management pathway.

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Declaration of interests

Dr Basu has received lecture and chairman fees for symposia in 2014 and 2015 from Reckitt Benckiser.

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