Improving the diagnosis and management of GORD in adults

Hopper AD. Improving the diagnosis and management of GORD in adults. Practitioner 2015;259(1781):27-32

Dr Andrew D Hopper
MD FRCP
Gastroenterology Consultant,
Department of Gastroenterology,
Royal Hallamshire Hospital, Sheffield, UK
Improving the diagnosis and management of GORD in adults

How do patients with GORD present?

The prevalence of gastro-oesophageal reflux disease (GORD) is increasing worldwide. It is classically characterised by symptoms produced by the abnormal reflux of gastric contents into the oesophagus causing mucosal damage. Typical symptoms include heartburn and acid regurgitation that respond to therapy, however, they are now recognised as only a part of the disease spectrum. There are increasing numbers of atypical presentations of GORD and patients with proton pump inhibitor (PPI) treatment failure. These factors, and an increase in the recognised conditions associated with GORD, especially the rise in oesophageal adenocarcinoma, have led to new recommendations in practice for what is now considered to be a complex medical problem.

What are the potential complications?

PRESENTATION

Significant GORD symptoms are becoming more common and occur at least once a week in 8.8-26% of Europeans, which is 50% higher than studies before 1995, with equal prevalence of symptoms in men and women.1 Patients may present with classical symptoms, atypical symptoms or conditions associated with GORD, see table 1, p28.

What are the management options?

FIGURE

The many faces of gastro-oesophageal reflux disease. Using the history alone, it is very difficult to predict whether patients have a hiatus hernia and no mucosal damage (top left), oesophagitis (bottom left), oesophageal stricture (top right), Barrett’s oesophagus (bottom right) or oesophageal cancer (centre).

The classic presenting symptom of GORD is heartburn which gives the patient a familiar burning sensation, rising from the epigastrium upwards. It is worse lying flat, at night and after eating a large meal. However, these symptoms have a poor sensitivity for oesophagitis, when endoscopy is performed mucosal damage is found in only 55%. The frequency and severity of symptoms do not accurately predict the degree of oesophageal damage. If patients with GORD also describe symptoms of dyspepsia (localised burning pain in the epigastrium) this should be considered first with Helicobacter pylori testing or direct referral for gastroscopy if the patient is over 55 given the risk of gastric cancer in these patients. Chest pains secondary to oesophageal spasm and dysmotility from GORD can present as a symptom. Studies have shown that in patients where objective tests demonstrate GORD, chest pains improve, but not resolve, with PPI therapy, whereas without GORD there is little or no response. Non-objective testing using a history of heartburn with chest pain was not predictive of a response.

Oesophageal complications of GORD can present with dysphagia from peptic stricture and cancer development or even odynophagia which can be associated with medication-related oesophagitis. Waterbrash can sometimes be confused with reflux coming into the mouth but is a local saliva production response to reflux.

Lastly, there are a significant number of patients who do not have symptoms of GORD and undergo gastroscopy for other reasons when Barrett’s oesophagus or oesophagitis is found. Despite the lack of symptoms, treatment and follow-up is still required.

### POTENTIAL COMPLICATIONS

#### Health-related quality of life

About one-third of patients, and their doctors, classify GORD symptoms as disruptive as opposed to inconvenient. Patients with disruptive GORD have reduced physical and mental health, and 2.4 times higher levels of work absenteeism than those with non-disruptive GORD (2.8 hours vs 1.2 hours per week). Individuals with nocturnal GORD symptoms have been shown to have lower SF-36 summary scores for mental health than patients with type 2 diabetes, congestive heart failure and angina.

#### Peptic strictures

Peptic strictures are now much rarer, prevalence has fallen from 1% to 0.1% with the introduction of PPIs. Strictures develop from untreated erosive oesophagitis and present with dysphagia usually without weight loss. They are more common in men as an increased proportion of men develop erosive oesophagitis (60%) despite the male:female ratio of GORD symptoms being equal.

The mechanism for this shift is unknown but is amplified further when the complications of Barrett’s oesophagus (70% male) and oesophageal adenocarcinoma (80% male) develop. Thus, male gender is a major risk factor for oesophageal complications of reflux in addition to Caucasian ethnicity and obesity.

#### Barrett’s oesophagus and oesophageal cancer

GORD is a risk factor for both Barrett’s oesophagus and oesophageal adenocarcinoma. The risk increases with duration, severity and frequency. Barrett’s oesophagus is a change in the epithelium of the oesophagus from squamous to columnar mucosa known as intestinal metaplasia. This is caused by injury and inflammation related to GORD. Barrett’s oesophagus affects about 1.6% of the population and is found in 15-19% of people undergoing endoscopy for reflux symptoms.

#### Extra-oesophageal presentations

Laryngo-pharyngeal reflux (LPR) disease defines GORD beyond the oesophagus up to the laryngeal and pharyngeal level, thus causing extra-oesophageal damage and includes asthma, chronic cough, laryngeal inflammation (hoarse voice), chronic sinusitis, otitis media, and dental erosions.

### Table 1

<table>
<thead>
<tr>
<th>Presentations of gastro-oesophageal reflux disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical symptoms</strong></td>
</tr>
<tr>
<td><strong>Atypical symptoms</strong></td>
</tr>
<tr>
<td><strong>Non-gastrointestinal conditions</strong></td>
</tr>
</tbody>
</table>

Oesophageal GORD presentations

The classic presenting symptom of GORD is heartburn which gives the familiar burning sensation, rising from the epigastrium upwards. It is worse lying flat, at night and after eating a large meal. However, these symptoms have a poor sensitivity for oesophagitis, when endoscopy is performed mucosal damage is found in only 55%. The frequency and severity of symptoms do not accurately predict the degree of oesophageal damage. If patients with GORD also describe symptoms of dyspepsia (localised burning pain in the epigastrium) this should be considered first with Helicobacter pylori testing or direct referral for gastroscopy if the patient is over 55 given the risk of gastric cancer in these patients. Chest pains secondary to oesophageal spasm and dysmotility from GORD can present as a symptom.
Barrett’s oesophagus is a precursor and risk factor for adenocarcinoma with a recently revised lower risk of 0.1-0.33% per year.\textsuperscript{24,25} Therefore a diagnosis is generally followed by endoscopic surveillance to identify cancer at an early stage, when treatment gives longer survival.\textsuperscript{26}

Performing endoscopy on patients with GORD solely as an indicator to check for Barrett’s oesophagus or adenocarcinoma is now considered very inefficient. GORD accounts for 30% of referrals for gastroscopy.\textsuperscript{27} However, less than 5% of patients with oesophageal adenocarcinoma have a previous diagnosis of Barrett’s oesophagus\textsuperscript{28} and more than one-third of patients with adenocarcinoma have no history of reflux disease.\textsuperscript{29}

**MANAGEMENT**

NICE has recently produced guidance on the investigation and management of dyspepsia and GORD.\textsuperscript{29} The key recommendations are summarised in table 2, below.

### Table 2

**Summary of NICE recommendations**

**Management**

- Offer patients with GORD a full-dose PPI for 4 or 8 weeks
- If symptoms recur after initial treatment, offer a PPI at the lowest dose possible
- If initial treatment for healing oesophagitis fails, consider switching to another PPI
- Offer a full-dose PPI long-term as maintenance treatment for severe oesophagitis
- Offer endoscopy to diagnose Barrett’s oesophagus if individual risk factors are high

**Indications for referral**

- Patients of any age with gastro-oesophageal symptoms that are non-responsive to treatment
- Those with suspected GORD who are thinking about surgery
- Patients with *H. pylori* that has not responded to second-line eradication therapy

### Table 3

**Urgent endoscopy referral criteria\textsuperscript{29,60,61}**

- Chronic gastrointestinal bleeding
- Dysphagia
- Progressive unintentional weight loss
- Persistent vomiting
- Iron-deficiency anaemia
- Epigastric mass
- Suspicious barium meal result
- Unexplained upper abdominal pain and weight loss, with or without back pain
- Obstructive jaundice
- In patients with unexplained worsening of their dyspepsia and known cancer risk factors:
  - Barrett’s oesophagus
  - Atrophic gastritis or intestinal metaplasia
  - Peptic ulcer surgery more than 20 years ago

**Endoscopy**

Endoscopy should not be routinely offered at initial presentation unless the patient has dysphagia or other symptoms suggestive of upper gastrointestinal cancer, see table 3, below. This is because GORD symptoms have a low predictive value for oesphagitis and Barrett’s oesophagus, especially in patients under the age of 50. However, as detailed above discussion regarding risks for Barrett’s oesophagus including duration and frequency of symptoms, obesity, male gender and age should be considered.

**Lifestyle and self-help**

Weight loss advice is a standard part of GORD management. The effect has been shown to be reversible with a dose-dependent relationship between weight reduction and improvement in reflux symptoms, as well as increased treatment success rates.\textsuperscript{30, 31} However, there have been some studies that have shown no benefit with weight loss even after bariatric surgery.\textsuperscript{32} Abdominal obesity causes GORD by elevating intra-abdominal pressure, which promotes reflux and the development of hiatus hernia. Central obesity, localised to the abdomen, is increasing in most regions affected by the increase in GORD. Obesity is more common in men than women and abdominal obesity is also more likely in men than women.\textsuperscript{33}

‘**Stopping or reducing smoking results in an almost two-fold improvement in severe symptoms**’

GORD symptoms are increased by 70% among daily smokers who have been smoking for more than 20 years.\textsuperscript{34} The effect is reversible as stopping or reducing smoking results in an almost two-fold improvement in severe symptoms, compared with those who continue to smoke.\textsuperscript{35}

Although changing dietary constituents such as fatty foods, alcohol, chocolate and citrus products has been shown to affect oesophageal pH in trials the effect seems not to be great enough to change patients’ symptoms.\textsuperscript{36} Other interventions such as small meals, early meals and elevation of the head of the bed and sleeping on the left side may be difficult. However, there is some evidence regarding their efficacy and these measures should be advised if patients are willing to try them.\textsuperscript{36}

Most over the counter medication is effective and fast acting with ranitidine and alginates showing a 40-60% symptom benefit over placebo. However, antacids only show a small benefit of 11%.\textsuperscript{37}

**PPI treatment trial**

If there is a clear history of GORD then empirical treatment with full dose PPI therapy for 4-8 weeks is recommended. If symptoms return a PPI is then restarted at the lowest dose possible to control symptoms.\textsuperscript{38} It is important to note the possibility of a 2 week phase of rebound hyperacidity in some patients upon cessation or reduction of PPI before increasing dosages.\textsuperscript{39} Although PPIs are generally safe the lower dose minimises any long-term side effects.
including a two-fold increased risk of Clostridium difficile in hospitalised patients.40

Patients with oesophageal complications of peptic stricture or Barrett’s oesophagus require long-term PPI therapy to prevent recurrence or reduce cancer progression risk.

Specific GORD presentations

For LPR disease symptoms the clinical response is slower for respiratory symptoms than for symptoms typical of reflux and high doses of PPIs for long periods, up to eight weeks, are often required.41 Affected patients may not have typical reflux symptoms or mucosal injury on endoscopy because the pharynx and larynx are exquisitely sensitive to acid and heal slowly.

Given the significant effect GORD has on quality of life and that exposure to PPI therapy during pregnancy seems to predispose the fetus to minimal risk, PPI use is felt to be acceptable if symptomatically necessary during pregnancy.42

Refractory GORD

Patients with no response to PPIs should be referred for further investigation of alternative causes other than GORD, see table 4, above. However, a partial response to PPI therapy can be improved in a number of ways. Given the short action of PPIs, increasing the dose is beneficial if given twice a day with, or up to 60 minutes before, meals (at the time of acid production). Compliance with this regimen has been shown to be difficult (46% optimal compliance) and should be addressed before further changes are made.43

Switching to an alternative PPI is an evidence-based step in the NICE recommendations, although specific PPIs are not mentioned the evidence supports esomeprazole.44,45 If there are nocturnal symptoms additional H2-receptor antagonists at night (ranitidine 300 mg or famotidine 40 mg) have been shown to be beneficial in more than 70% of patients. However, tolerance has been reported in a minority of cases, therefore it might be advisable to recommend use on an as required basis.46

Prokinetics improve oesophageal peristalsis but although there is some benefit to quality of life there is no benefit to symptoms.47,48 Therefore, with the recent safety concerns addition of domperidone or metoclopramide to PPI treatment is not recommended.

H. pylori eradication

Helicobacter pylori may inhibit or make GORD symptoms worse depending on how the infection affects the stomach. However, there has been either little or no overall effect on GORD shown from H. pylori eradication.49,50 Given the overlap in symptoms of GORD and dyspepsia and the association with peptic ulceration and gastric cancer current guidelines recommend H. pylori testing and eradication.51

Anti-reflux surgery

Only carefully selected patients should undergo fundoplication for reflux disease. Laparoscopic Nissen fundoplication is currently considered the standard procedure. The procedure involves wrapping the gastric fundus around the lower end of the oesophagus and stitching it in place, reinforcing the lower oesophageal sphincter and preventing the stomach slipping up through the diaphragm so reducing the hiatus hernia.

Comparisons of surgery with PPI therapy have found that dysphagia and flatulence were more common in the surgical group but prevalence and severity of symptoms were lower with surgery e.g. heartburn (16% PPI vs 8% surgery) and regurgitation (13% PPI vs 2% surgery).52

Complications of fundoplication include dysphagia which usually resolves within 3 months but persists in 5% of cases, which may require dilation or, rarely, revision surgery. Early satiety, weight loss, discomfort with large meals, hiccups and difficulty burping or vomiting can also occur. GORD symptoms can recur in 10% of patients 5-10 years after surgery and as many as 50% of patients who undergo anti-reflux surgery may become PPI users 10-15 years after surgery.53 This emerging data has now shifted the cost-benefit model back in favour of medical treatment.54

Therefore, careful surgical selection is required.

NICE recommends referral for patients with symptom control with PPIs, but who do not wish to continue with this therapy long term, or those who are unable to tolerate PPIs because of side effects such as diarrhea or cough. The patients that benefit most are those with proven oesophagitis, some but incomplete response to PPIs or anatomical defects such as a hiatus hernia.

Chronic cough and extra-oesophageal complications of GORD can be treated with fundoplication. A response to medical therapy is a predictor of surgical response which has been shown to be complete in 51% of patients with chronic cough55 and also successful as a treatment for asthma.56

A complete lack of response to acid inhibition should raise doubts about the diagnosis of GORD and surgery is unlikely to be of benefit and may even worsen pre-existing symptoms. Full assessment with oesophageal pH monitoring and symptom correlation is required in nearly all patients where a surgical option is considered.

Studies have shown no change in the prevalence of Barrett’s oesophagus or in the incidence of adenocarcinoma when patients treated surgically were compared with patients treated with medical therapy. Therefore on its own cancer protection is not an indication for fundoplication.57

The increase in obesity prevalence is considered a major factor in the increased prevalence of GORD therefore bariatric surgery, particularly gastric bypass, should be considered in appropriate patients as it can effectively reduce GORD symptoms.58

FUTURE DIRECTIONS

New treatment modalities are gaining evidence and being developed. There are a number of endoscopic procedures using radiofrequency energy to the gastro-oesophageal junction, injection of bulking agents, or implantation of a bioprosthesis into the lower oesophageal sphincter, and suturing of the proximal gastric folds. Variations in fundoplication surgical techniques are also being developed along with laparoscopic implantable rings of magnets around the gastro-oesophageal junction which has shown successful long-term data but is without a comparative trial.59

The prevalence of GORD is increasing and is likely to be a further burden to healthcare caused by the...
GORD is defined as a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications. Many patients with GORD complications such as oesophagitis, and up to a third of patients with Barrett’s oesophagus have no reflux or heartburnsymptoms. Conversely, patients can be symptomatic even when normal reflux levels are found and there is an absence of mucosal damage. Significant GORD symptoms are becoming more common and occur at least once a week in 8.8-26% of Europeans, with equal prevalence of symptoms in men and women.

The frequency and severity of symptoms do not accurately predict the degree of oesophageal damage. If patients with GORD also describe symptoms of dyspepsia this should be considered first with Helicobacter pylori testing or direct referral for gastroscopy if the patient is over 55 given the risk of gastric cancer in these patients.

Extra-oesophageal GORD should be considered for chronic cough. Oesophageal disease can account for up to 20% of cases of chronic cough. Guidelines on chronic cough suggest use of empirical treatment for GORD including a therapeutic trial of three to six weeks with omeprazole at the lowest dose possible to control symptoms. Patients are recommended. If symptoms return a PPI is then restarted with a PPI and the lowest dose possible.

GORD is a risk factor for both Barrett’s oesophagus and oesophageal adenocarcinoma. The risk increases with duration, severity and frequency. Endoscopy should not be routinely offered at initial presentation unless the patient has dysphagia or other symptoms suggestive of oesophageal adenocarcinoma. The risk increases with 45% of patients with asthma, and erosive oesophagitis on endoscopy has a 50% higher likelihood of a diagnosis of asthma.

Smoking cessation and weight loss are beneficial in reducing GORD symptoms. Weight loss advice is a standard part of GORD management. Abdominal obesity causes GORD by elevating intra-abdominal pressure, which promotes reflux and the development of hiatus hernia. GORD symptoms are increased by 70% among daily smokers who have been smoking for more than 20 years.

If there is a clear history of GORD then empirical treatment with full dose PPI therapy for 4-8 weeks is recommended. If symptoms return a PPI is then restarted at the lowest dose possible to control symptoms. Patients with oesophageal complications of peptic stricture or Barrett’s oesophagus require long-term PPI therapy to prevent recurrence or reduce cancer progression risk. Patients with no response to PPIs should be referred for further investigation of alternative causes other than GORD.

Only carefully selected patients should undergo fundoplication for reflux disease. Obesity is a major factor in the increased prevalence of GORD. Bariatric surgery, particularly gastric bypass, should be considered in appropriate patients.

Special interest sections and newsletters

● Special interest sections collating editorials, clinical reviews, symposium and special report articles in that area
● Some sections appear with direct links to the current evidence base. e.g. Cancer, Women’s health, Children and young people, Urology

Special Interest: Cancer
All articles on cancer in the journal online appear with direct links to the current evidence base:
● Results of pre-defined search requests made to PubMed
● The US National Cancer Institute’s database of peer-reviewed, regularly updated, evidence-based summaries
● Results of pre-defined search requests made to NHS Evidence

Subscriptions
Individual: £85 INDIVIDUAL
Individual overseas: £138 INDIVIDUAL
Online only individual: £110 INDOL

Telephone from UK: 0844 815 5934
Telephone from overseas: +44 1795 418 670
Fax: +44 (0) 1795 414 555
Email: thepractitioner@servicehelpline.co.uk

The Practitioner, Subscriptions Department,
800 Guillat Avenue, Kent Science Park,
Sittingbourne, Kent, ME9 8GU