

Diagnosis and management of gastro-oesophageal reflux disease

N.P. Dinamithra, N.M.M. Nawarathne

Gastro-enterology and Hepatology Unit, National Hospital of Sri Lanka

Introduction

Gastro-oesophageal reflux disease (GORD) is a common disease encountered by both gastroenterologists and generalists alike. This article will provide an overview of GORD and its presentation, extra oesophageal manifestations, complications and recommendations for an approach to the diagnosis and management of this important disease.

Epidemiology

Epidemiologic estimates of the prevalence of GORD are based primarily on the typical symptoms of heartburn and regurgitation. A systematic review found the prevalence of GORD to be 10–20 percent in the Western world [2]. Community prevalence of GORD in Sri Lanka is not known but a single study done by Nawarathne et al found it closer to 15% [1]. While clinically troublesome heartburn is seen in about 6 percent of the population [3], chest pain may be the sole presenting complaint of GORD [4,5]. It is imperative to distinguish cardiac from non-cardiac chest pain, before considering GORD as the cause of chest pain. Although the symptom of dysphagia can be associated with uncomplicated GORD, its presence warrants investigation for a potential complication including motility disorders, ring, stricture or malignancy [6]

A systematic review found that 38 % of the general population has dyspepsia. Dyspepsia was more frequent in patients with GORD than those without. The symptoms of epigastric pain, early satiety, belching and bloating were more likely to be PPI-responsive compared to nausea. In general, these symptoms can be considered to be a part of GORD if they respond to a PPI trial [7]. Symptoms at night have a greater impact on quality of life (QOL) when compared to day symptoms.

Therefore, nocturnal symptoms and sleep disturbances are important to elucidate when dealing with GORD patients [8]. Aging increases the prevalence of erosive oesophagitis, i.e. Los Angeles (LA) grades C and D [9]. Barrett's oesophagus increases in prevalence after age 50, especially in Caucasian males [10]. The patients with erosive oesophagitis are more likely to be men. Women are more likely to have non erosive reflux disease (NERD). Barrett's oesophagus is more frequent in men compared to women [11]. The male to female, gender ratio for oesophageal adenocarcinoma is estimated to be 8:1 [10].

There is a definite link between GORD and obesity. Several meta-analysis found an association between body mass index (BMI), waist circumference, weight gain and the presence of symptoms and complications of GORD including erosive reflux disease (ERD) and Barrett's oesophagus [12,13].

Establishing the diagnosis of GORD

The diagnosis of GORD is mainly clinical but it is made using a combination of symptom presentation, objective testing with endoscopy, ambulatory reflux monitoring, and response to a trial of anti-secretory therapy. The symptoms of heartburn and regurgitation are the most reliable to arrive at a presumptive diagnosis based on history alone. However, these are not as sensitive as most believe. Empiric PPI therapy (a PPI trial) is a reasonable approach to confirm GORD when it is suspected in patients with typical symptoms. It has a sensitivity of 78 percent and specificity of 54 percent. Dysphagia has historically been an alarm symptom and an indication for early endoscopy. Based on retrospective case control studies respiratory symptoms have been associated with GORD. In addition, dental erosions, sinusitis, chronic laryngitis and voice disturbance have similarly been associated with GORD.

Endoscopic findings of GORD include erosive

Correspondence: N.P. Dinamithra
E-mail: npdinamithra@yahoo.com

oesophagitis, strictures, and a columnar lined oesophagus or Barrett's oesophagus. As such, endoscopy has excellent specificity for the diagnosis of GORD especially when erosive oesophagitis is seen. In a study done on Sri Lankan patients who had symptoms suggestive of GORD, hiatus hernia (HH), columnar lined oesophagus (CLO) and reflux oesophagitis (RO) were found in 14.3%, 9.5% and 13.3% respectively [1]. Based on current literature the use of routine biopsy of the oesophagus to diagnose GORD cannot be recommended in a patient with heart-burn and a normal endoscopy. In addition, the practice of obtaining mucosal biopsies from a normal appearing gastro-oesophageal junction (GOJ) has not been demonstrated to be useful in GORD patients [14].

Oesophageal manometry is of limited value in the primary diagnosis of GORD. Neither a decreased lower oesophageal sphincter pressure, nor the presence of a motility abnormality is specific enough to make a diagnosis of GORD. Manometry should be used to aid placement of the transnasal pH-impedance probes and is also recommended before consideration of antireflux surgery, primarily to rule out achalasia or severe hypomotility. Ambulatory reflux monitoring (pH or impedance-pH) is the only test that allows for determining the presence of abnormal oesophageal acid exposure, reflux frequency and symptom association with reflux episodes. GORD is common during pregnancy and manifests as heartburn, and may begin in any trimester. One study found its onset to be around 50 percent in the first trimester, 40 percent in the second trimester, and 10 percent in the third trimester [15]. Severity also increased throughout pregnancy. Despite its frequent occurrence during pregnancy, heartburn usually resolves after delivery [16]. In the occasional pregnant patient who does require testing, upper GI endoscopy is the test of choice, but should be reserved for patients whose symptoms are refractory to medical therapy or who have suspected complications. If possible however, upper GI endoscopy should be delayed until after the first trimester.

Management of GORD

Lifestyle interventions are part of therapy for GORD. Counseling is often provided regarding weight loss, elevation of head end of bed, tobacco and alcohol cessation, avoidance of late-night meals, and cessation

of foods that can potentially aggravate reflux symptoms including caffeine, coffee, chocolate, spicy foods, highly acidic foods such as oranges and tomatoes, and foods with high fat content. There was an increase in oesophageal acid exposure times with tobacco and alcohol consumption in addition to ingestion of chocolate and fatty foods. However, tobacco and alcohol cessation (4 trials) were not shown to raise lower oesophageal sphincter pressure (LOSP), improve oesophageal pH, or improve GORD symptoms. A recent systematic review concluded that there was lack of evidence that consumption of carbonated beverages causes or provokes GORD [17].

Weight gain even in subjects with a normal BMI has been associated with new onset of GORD symptoms [18]. Multiple cohort studies have demonstrated reduction in GORD symptoms with weight loss [19, 20]. A large case control study based on a Nurses Health Cohort demonstrated a 40 percent reduction in frequent GORD symptoms for women who reduced their BMI by 3.5 or more compared with controls [18]. Assumption of the recumbent position has been associated with worsening of oesophageal pH values and GORD symptoms. Three randomized controlled trials have demonstrated improvement in GORD symptoms and oesophageal pH values with head end elevation of the bed [21, 22].

Medical options for patients failing lifestyle modifications include antacids, histamine-receptor antagonists (H2RA), or PPI therapy. PPI therapy has been associated with superior healing rates and decreased relapse rates compared with H2RAs and placebo for patients with erosive oesophagitis [24]. A 1997 meta-analysis demonstrated superior healing rates for all grades of erosive oesophagitis using PPI therapy compared with H2RAs, sucralfate, or placebo [25]. PPIs showed a significantly faster healing rate (12%) vs. H2RAs (6%) and placebo (3%). A Cochrane systematic review in patients with non-erosive reflux disease demonstrated superiority for PPI therapy compared with H2RAs and prokinetics for heartburn relief [26]. There are seven PPIs available in the market at present. Meta-analyses fail to show significant difference in efficacy for symptom relief between PPIs [27]. All of the PPIs with the exception of omeprazole- sodium bicarbonate

and dexlansoprazole, should be administered 30–60 minute before meals to assure maximal efficacy. It would be expected that 70 – 80 percent of patients with ERD and 60 percent of patients with NERD would demonstrate complete relief on PPI therapy. Risk factors for lack of symptom control have included patients with longer duration of disease, presence of hiatal hernia, extra oesophageal symptoms, and lack of compliance [28]. Maintenance PPI therapy should be administered for GORD patients who continue to have symptoms after PPI is discontinued and in patients with complications including erosive oesophagitis and Barrett's oesophagus (BO). In patients found to have any length of BO, retrospective studies have suggested a decreased risk for dysplasia in patients continuing PPI usage [29].

Medical options for GORD patients with incomplete response to PPI therapy are limited. The addition of bedtime H2RA has been recommended for patients with symptoms refractory to PPI. Prokinetic therapy with metoclopramide in addition to PPI therapy is another option often considered for these patients. Combination therapy of Metoclopramide with H2RA has not been shown to be more effective compared with H2RA or prokinetic therapy alone [30]. The other option is to use baclofen for refractory GORD patients. Baclofen, a GABA (b) agonist, has been demonstrated to be effective in GERD by its ability to reduce transient LOS relaxations [31], and reflux episodes [32]. Potential surgical options for GORD include laparoscopic fundoplication or bariatric surgery in the obese. Reasons to refer GORD patients for surgery may include desire to discontinue medical therapy, non-compliance, side-effects associated with medical therapy, the presence of a large hiatal hernia, oesophagitis refractory to medical therapy, or persistent symptoms documented to be caused by refractory GORD. With the introduction of oesophageal pH-impedance monitoring, patients found to have abnormal amounts of non-acid reflux on PPI therapy with good symptom correlation may be considered for surgery [34]. Refractory dyspeptic symptoms including nausea, vomiting and epigastric pain are less likely to demonstrate symptomatic response. The highest surgical responses are seen in patients with typical symptoms of heartburn and/or regurgitation that demonstrate good response to PPI therapy. Surgical options, its recommendation and

evidence are shown in table 1.

1. Surgical therapy is a treatment option for long-term therapy in GORD patients. (Strong recommendation, high level of evidence)
2. Surgical therapy is generally not recommended in patients who do not respond to PPI therapy. (Strong recommendation, high level of evidence)
3. Preoperative ambulatory pH monitoring is mandatory in patients without evidence of erosive oesophagitis. All patients should undergo preoperative manometry to rule out achalasia or scleroderma-like esophagus. (Strong recommendation, moderate level of evidence)
4. Surgical therapy is as effective as medical therapy for carefully selected patients with chronic GORD when performed by an experienced surgeon. (Strong recommendation, high level of evidence)
5. Obese patients contemplating surgical therapy for GORD should be considered for bariatric surgery. Gastric bypass would be the preferred operation in these patients. (Conditional recommendation, moderate level of evidence)
6. The usage of current endoscopic therapy or transoral incisionless fundoplication cannot be recommended as an alternative to medical or traditional surgical therapy. (Conditional recommendation, moderate level of evidence)

Table 1. Surgical options for GORD [33]

Extra oesophageal presentations of GORD

The spectrum of clinical presentations attributed to GORD has expanded from typical oesophageal symptoms of heartburn and regurgitation, to an assortment of extra oesophageal manifestations including respiratory and laryngeal symptoms. A number of epidemiological studies have identified an association between GORD and these extra oesophageal symptoms, but causality cannot be concluded from these studies. A systematic review of 28 studies found that symptoms of GORD and abnormal 24-hour pH monitoring were present in 59 and 51% of asthma patients, but concluded that there was little data to clarify the direction of causality [35]. Cohort studies suggest that GORD may be the cause in 21–41 percent of chronic nonspecific cough [36].

GORD refractory to treatment with PPIs

We are seeing increasing numbers of patients treated empirically with PPIs for symptoms that are suspected to be due to GORD, but who do not respond to these medications. The term refractory GORD encompasses

a heterogeneous group of patients that may differ in symptom frequency and severity, PPI dosing regimen (once or twice daily), and response to therapy (from partial to absent). Dealing with this category of patients is shown in table 2 and figure 1 [33] with the level of evidence and degree of recommendation.

1. The first step in management of refractory GORD is optimization of PPI therapy. (Strong recommendation, low level of evidence)
2. Upper endoscopy should be performed in refractory patients with typical or dyspeptic symptoms principally to exclude non-GORD etiologies. (Conditional recommendation, low level of evidence)
3. In patients in whom oextraesophageal symptoms of GORD persist despite PPI optimization, assessment for other etiologies should be pursued through concomitant evaluation by ENT, pulmonary, and allergy specialists (Strong recommendation, low level of evidence)
4. Patients with refractory GORD and negative evaluation by endoscopy (typical symptoms) or evaluation by ENT, pulmonary, and allergy specialists (extra oesophageal symptoms), should undergo ambulatory reflux monitoring (Strong recommendation, low level of evidence)
5. Reflux monitoring off medication can be performed by any available modality (pH or impedance-pH) (Conditional recommendation, moderate level of evidence). Testing on medication should be performed with impedance-pH monitoring in order to enable measurement of nonacid reflux. (Strong recommendation, moderate level of evidence)
6. Refractory patients with objective evidence of ongoing reflux as the cause of symptoms should be considered for additional anti reflux therapies that may include surgery. (Conditional recommendation, low level of evidence). Patients with negative testing are unlikely to have GORD and PPI therapy should be discontinued. (Strong recommendation, low level of evidence)

Table 2. Management of "refractory" GORD [33]

Complications associated with GORD

Numerous “complications” have been associated with GORD including erosive oesophagitis, stricture, and Barrett's oesophagus (BO). Obesity has been demonstrated to be a risk factor for symptoms, ERD, BO, and adenocarcinoma. It may be that the presence of an abnormal waist-to-hip ratio is the greatest risk factor for the presence of BO [37].

There are limited data to suggest that a columnar lined

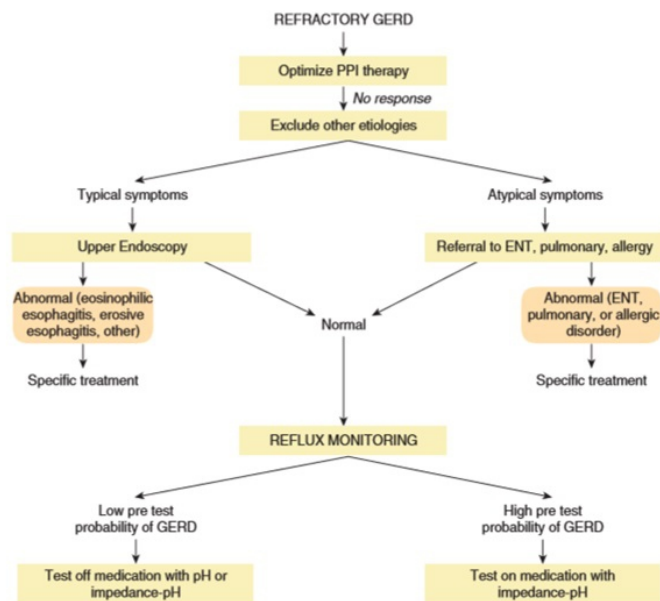


Figure 1. Algorithm for the evaluation of refractory gastroesophageal reflux disease (GORD) [33].

oesophagus (Barrett's oesophagus) can be obscured by any grade of erosive oesophagitis, most commonly it is obscured by grades C and D [38,39] . On the basis of these data, a repeat endoscopy after a minimum 8-week course of PPI therapy is recommended in patients with grades C and D oesophagitis but also can be considered in lower grades.

Peptic strictures are infrequent in practice, and are likely related to the widespread use of anti-secretory therapy. Strictures tend to occur most often in Caucasians, older patients with a longer duration of untreated symptoms, and in the setting of abnormal oesophageal motility. Intra lesional corticosteroids (40 mg of triamcinolone injected in four 1 ml aliquots) in a four quadrant pattern can be considered in peptic strictures refractory to dilation.

Barrett's oesophagus is the only complication of GORD with malignant potential. BO can be found in 5 to 15 percent of patients who undergo endoscopy for symptoms of GORD [40] and tends to be seen at the higher end of this range in patients with long duration of symptoms, who are over the age of 50, male, and Caucasian.

Conclusion

In summary, refractory GORD remains a difficult clinical challenge. Many pathological mechanisms have

been proposed as causes of refractory symptoms but, in most cases, data supporting the hypotheses remain equivocal. The work-up of a refractory patient should clearly include a careful history, and the consideration of alternative diseases that require alternative treatments is paramount. Reflux monitoring studies are helpful in determining the presence or absence of GORD, and reflux-symptom analysis is a very important tool that presently requires further refinement and better outcome studies to aid our interpretation.

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