

Gastro Oesophageal Reflux Disease

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Highlights / Hoogtepunte

- How to diagnose GORD and identify high-risk patients.
- Who should be referred for endoscopy and how early?
- Algorithms for better management and referral of GORD patients.
- Hoe om die diagnose van GERS te maak en hoë risiko pasiënte te identifiseer.
- Wie moet vir endoskopie verwys word en hoe vroeg?
- Vloeciogramme vir beter behandeling en verwysing van GERS pasiënte.

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INTRODUCTION

Gastro oesophageal reflux disease (GORD) is one of the most common diagnoses made in general practice. This article will address some of the diagnostic features, investigations and treatment of this condition.

GASTRO OESOPHAGEAL REFLUX DISEASE (GORD)

Gastro oesophageal reflux disease usually presents with the classical symptom of heartburn. The accuracy of the diagnosis can be improved by first giving the definition of heartburn: "a burning pain that starts in the lower chest and rises towards the neck, usually occurring after food". However, if one relied only on heartburn as the diagnostic symptom of GORD, a large number of patients would be missed. It is important to seek the extra oesophageal symptoms of GORD. These include cough, asthma, recurrent sore throat, hoarseness and in some patients, dental problems.

The history should alert the doctor to the possibility of more serious underlying pathology, such as Barrett's oesophagus, oesophageal stricture or malignancy. These alarm symptoms should be sought, particularly in the older patients (greater than 45 years) with reflux symptoms. In patients with

severe reflux of more than 20 years duration a 44-fold increased risk oesophageal adenocarcinoma is reported.¹

ALARMS SYMPTOMS OF GORD

- Dysphagia.
- Chest pain, always excluding angina, MI's and other causes of chest pain.
- GI bleeding / anaemia.
- Choking.
- Unexplained weight loss.

EROSIVE OESOPHAGITIS

In various endoscopic trials in patients with reflux symptoms, about 50% will have evidence of erosive damage. The remaining 50% will show no signs of mucosal damage. It is not possible to separate these two groups by the severity of their symptoms, or by the impairment of quality of life scores.

A grading system currently in widespread use is the Los Angeles classification. Oesophagitis is graded on a scale A to D, with A and B being milder degrees of inflammation, and C and D showing more severe. Patients with erosive disease are at risk of complications of oesophagitis, including bleeding, stricture and Barrett's oesophagus.

NON EROSIIVE REFLUX DISEASE

From endoscopic data it is clear that a great proportion of patients undergoing examination for reflux symptoms, will have no endoscopic evidence of oesophagitis. The diagnosis of GORD cannot be rejected on the basis of negative endoscopic findings.² This group has been referred to as having non-erosive reflux disease (NERD). Patients with NERD experienced the same symptoms as those with erosive disease, and cannot be distinguished clinically from the latter.³ They suffer a similar impairment of quality of life as those with erosive disease. They do differ, however, in that they are unlikely to develop complications of reflux such as stricture, bleeding and Barrett's oesophagus. It is therefore important to recognise this group, as they frequently have need for less intensive therapy, requiring lower utilisation of their healthcare budget.

BARRETT'S OESOPHAGUS

Barrett's oesophagus is defined as intestinal metaplasia of the oesophagus. The diagnosis of Barrett's depends upon a histologic examination, with the finding of intestinal goblet cells in the oesophageal biopsies. Although the diagnosis is made histologically, one

must have a high index of suspicion for Barrett's oesophagus in patients with a long history of reflux symptoms. Middle-aged white men are at particularly high risk of developing Barrett's oesophagus. A further clue to the existence of Barrett's oesophagus is the patient who reports that they used to suffer from heartburn, but that the heartburn has become less severe or has disappeared over the recent months or years. This is because patients with Barrett's oesophagus often lose their sensitivity to acid and bile reflux, probably on the basis of damage to sensory nerves in the oesophageal mucosa. When Barrett's oesophagus is suspected patients must be referred for endoscopy, to enable biopsies to be taken to confirm the diagnosis of Barrett's oesophagus.

The significance of Barrett's oesophagus is that it is a pre-malignant condition leading in some individuals to adenocarcinoma of the oesophagus.⁴ This is a devastating complication, as these patients often present late in the course of the illness, making surgical cure impossible. In the patient with Barrett's oesophagus a surveillance program is advised, with periodic endoscopic examinations being performed to detect dysplasia. The presence of high-grade dysplasia would require intervention, either in the form of an oesophagectomy, or some other form of ablative therapy. The latter is not being routinely performed in South Africa.

Oesophageal adenocarcinoma is one of the most rapidly increasing forms of malignancy in the western world, and generally has a poor prognosis. Whilst detecting Barrett's oesophagus and dysplasia may have some impact on these numbers, it is clear that many patients present with established malignancy never having consulted a doctor about reflux, and never having had an endoscopy. A greater awareness on the part of patients and medical practitioners may impact on this disease in future.

Who should be referred for an endoscopy and how early?

The risk of development of oesophageal adenocarcinoma in association with Barrett's oesophagitis is so small in

unselected individuals presenting with typical symptoms of reflux disease, that the risk alone should not be the primary determinant of whether endoscopy is done. The individual at highest risk is the middle-aged white male with a long history of reflux symptoms.

However, in patients without alarm symptoms who have not been endoscoped, prompt endoscopy is the best clinical strategy in those who have experienced reflux symptoms *at least twice a week for at least six months*. In chronic heartburn patients, most patients will be endoscoped at some stage or another and it may be best to accept this, and do the endoscopy as early as possible.

The following GORD patients should be referred to a gastro-enterologist:

- Patients with any alarm symptom(s).
- Chronic heartburn patients (at least two times a week for at least six months).
- Those who fail on standard or high dose PPI's.
- Those who have recurrent symptoms after 4-6 weeks of successful initial therapy. (Trial of withdrawal.)
- Patients with odynophagia.
- Patients with extra-oesophageal symptoms.
- Non-cardiac chest pain.
- Those requiring continuous (long term) therapy.

GORD THERAPY

Pharmacological therapy

The hierarchy of the efficacy of primary drug therapy treatments, which should be used to guide the choice of step-down (or step-up) therapy, is depicted in **figure 1**. Drug cost within the applicable practice setting should also guide the choice of step-down therapy. Combination H2 receptor antagonist and prokinetic drug therapy are not included as primary therapies because of compelling evidence from RCT's suggesting that:

- For initial and maintenance therapy of reflux esophagitis there is an ascending level of efficacy from either H2 receptor antagonist or a prokinetic drug, to a combination of the latter, to a proton pump inhibitor^{6,7,8}.
- For initial therapy of NERD patients there is an ascending level of efficacy from either a H2 receptor antagonist or prokinetic drug to a proton pump inhibitor^{9,10,11}.
- There are minimal or no gains in efficacy from doubling of the dose of H2 receptor antagonists therapy.
- Maintenance combination therapy with a pro-kinetic drug and an H2 receptor antagonist is more efficacious than monotherapy with an H2 receptor antagonist or a pro-kinetic drug alone⁷.

Figure 1: Hierarchy of the efficacy of primary drug therapies

(Full acknowledgement to the source: **Figure 5** Dent J, Brun J, Febricke AM, Fennerty MB, Janssens, Kabrilas PJ et al. An evidence based appraisal of reflux disease management- the Genval Workshop Report. *Gut* 1999;44(suppl 2):S1-S16.)

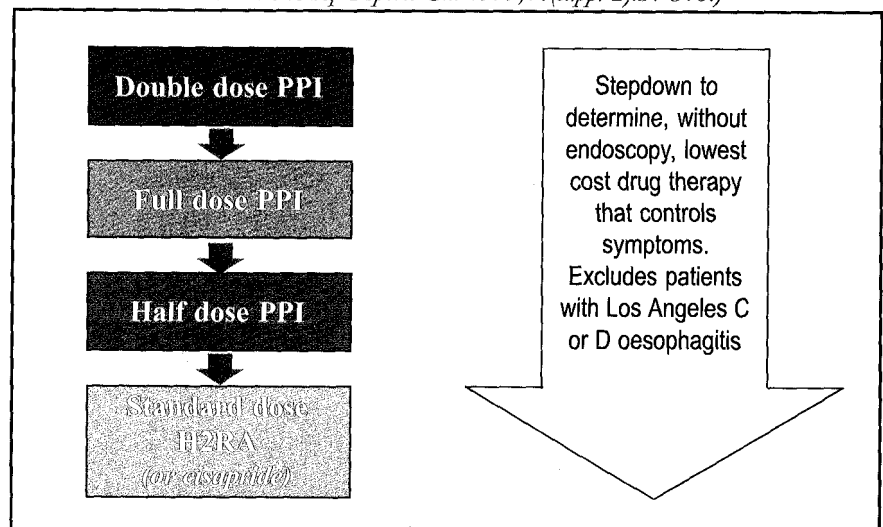


Figure 2: Major management pathways for initial management of patients who have not been endoscoped and for endoscopy negative or mild (Los Angeles A or B) oesophagitis patients.
 (Full acknowledgement to the source: **Figure 3:** Dent J, Brun J, Febricke AM, Fennerty MB, Janssens, Kabrillas PJ et al. An evidence based appraisal of reflux disease management- the Genval Workshop Report. Gut 1999;44(suppl 2):S1-S16.)

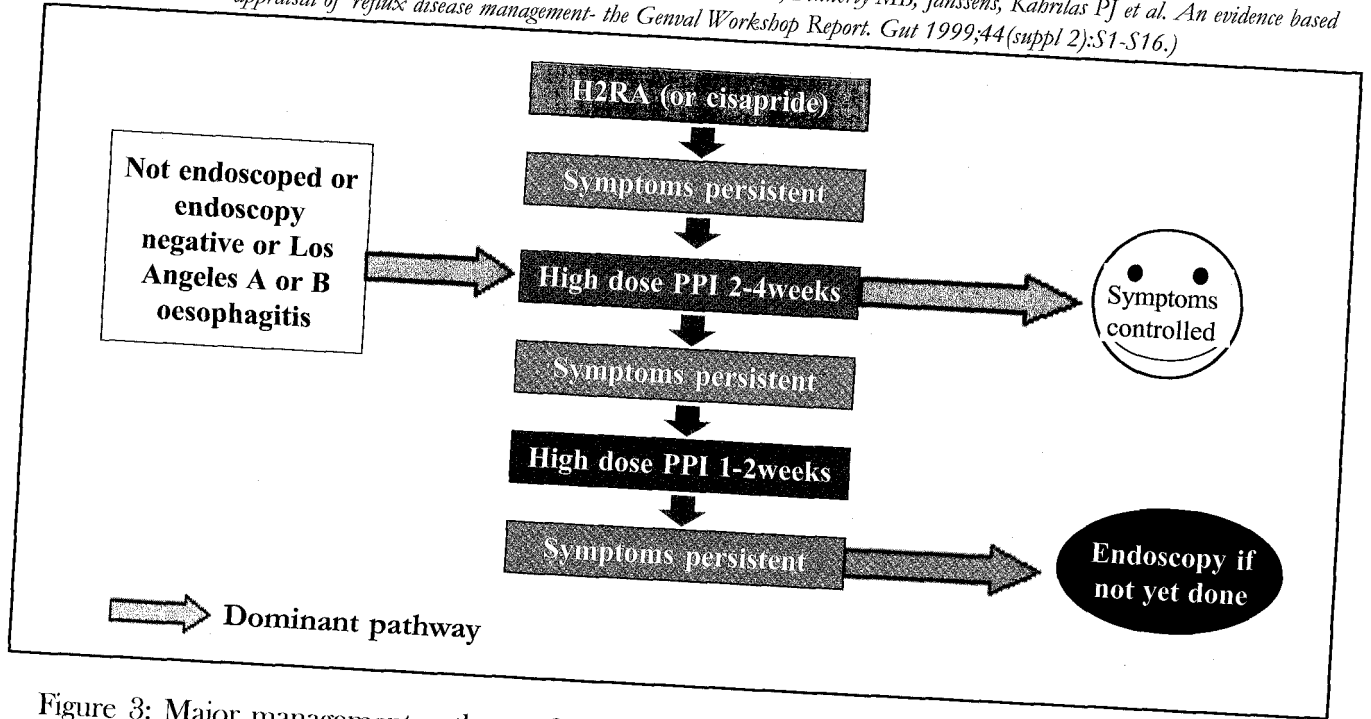
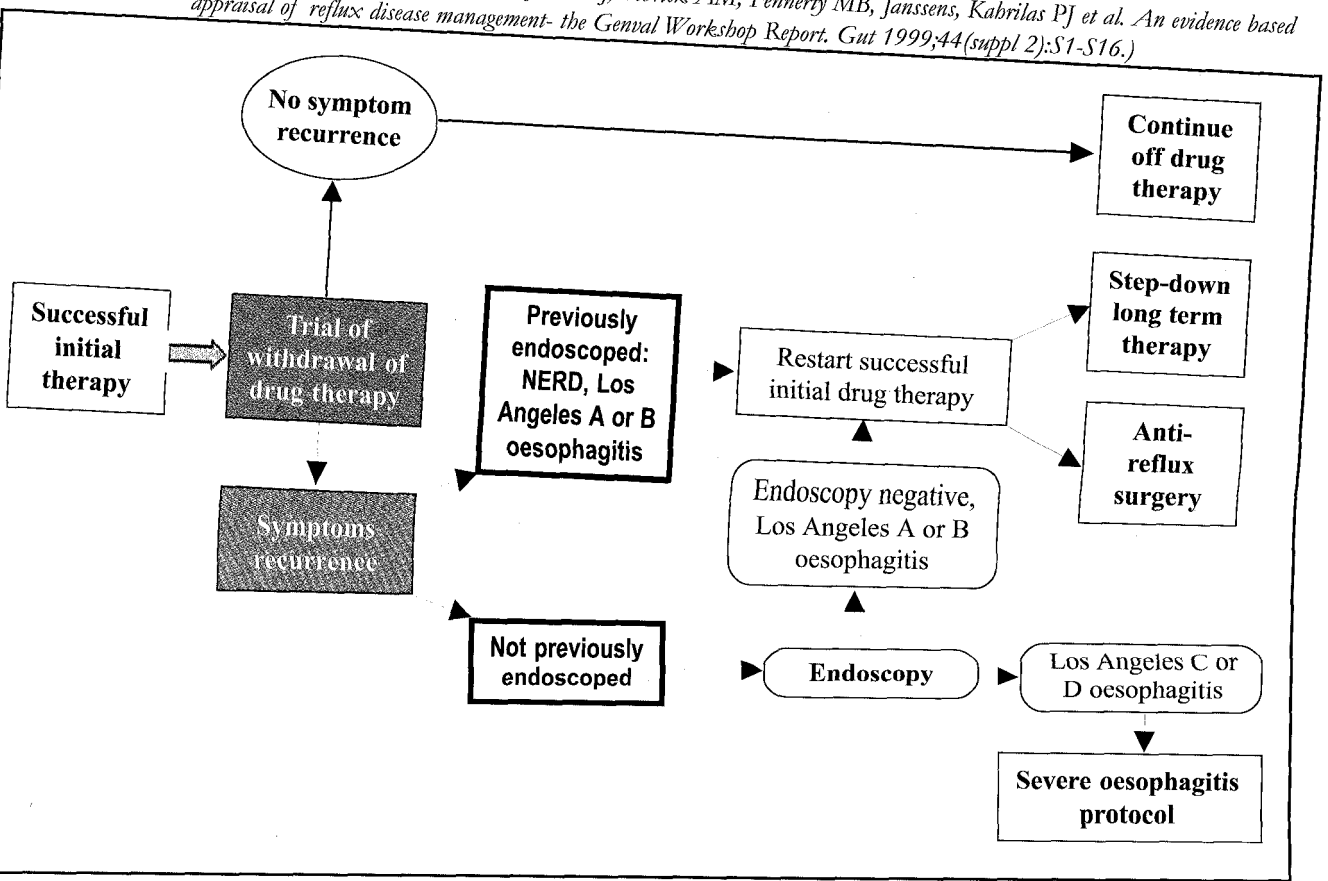


Figure 3: Major management pathways following drug therapy that produces successful control of symptoms in the patient groups shown. The pathways ensure that reflux disease is a recurrent problem before long term therapy or surgery are considered. The option on-demand therapy merits a trial in patients with NERD.
 (Full acknowledgement to the source: **Figure 4:** Dent J, Brun J, Febricke AM, Fennerty MB, Janssens, Kabrillas PJ et al. An evidence based appraisal of reflux disease management- the Genval Workshop Report. Gut 1999;44(suppl 2):S1-S16.)



- Maintenance therapy with either a pro-kinetic drug or an H2 receptor antagonist is significantly less effective than therapy with a proton pump inhibitor^{7,12}.

In all of the above studies, cisapride was used as the prokinetic drug and it was subsequently included in the Genval guidelines. The role of cisapride as a prokinetic agent is currently being re-evaluated because of safety issues. Cisapride is metabolised in the liver by cytochrome p450 CYP 3A4. When cisapride is co-administered with other drugs utilising the same metabolic pathway, the metabolism of cisapride may be reduced. This can lead to higher than normal blood levels of cisapride, with potential ventricular arrhythmias resulting. **The use of cisapride in the treatment of GORD is therefore not recommended at present.**

One generally advocates a "stepped down" approach to the treatment of GORD. This strategy would have one using a Proton Pump Inhibitor (PPI) at full dose, and then stepping down to the lowest effective dose and form of treatment. The goals of treatment are to relieve symptoms, and to maintain a healed oesophageal mucosa. In patients with NERD, an "on demand" strategy may be effective. It had been demonstrated that such patients could control their symptoms by taking a maintenance dosage of a PPI every third day, on average.⁵

Two other management pathways from the *Genval report 1999* give very practical guidelines for physicians on duration of therapy, referral for endoscopy and are designed to ensure that long term therapy or surgery are only considered in recurrent, persistent disease. (See figure 2 and 3)

Patients with Barrett's oesophagus have a more severe form of reflux disease, and may require a higher than normal dose of PPI. Similarly patients with extra oesophageal manifestations of GORD often require double dose PPI for 3 months to get control of troublesome symptoms such as cough, hoarseness, etc.

The "PPI test" is a useful strategy in the younger (less than 45 years of age) patients with reflux symptoms and without alarm symptoms. A 14-day

course of PPI in standard dose will in most cases relieve symptoms. Should symptoms recur after stopping treatment, further investigation is usually required.

Life-style changes

Evidence to prove that life style changes have a significant role in the initial and long-term management of GORD is lacking. Most evidence come from case reports or flawed clinical trials. However, most clinicians accept that life style changes have a positive role to play. Lifestyle changes include: the avoidance of particular foods and/or alcoholic drinks, which provoke reflux induced symptoms, smoking cessation and weight loss.

Surgery

The role of surgery in GORD should be individualised, after a thorough discussion with the patient. A minority of GORD patients may be candidates for antireflux surgery. Firm indications for surgery include large volume refluxers, patients with large hiatal hernias, patients with paraoesophageal hernias, and at times those presenting with complications such as bleeding. Surgery does not seem to confer any additional benefit in patients with Barrett's oesophagus. These patients would in any case need ongoing surveillance, whether treated medically or surgically. A full and frank discussion should be held with the surgeon, and this should include the complications of surgery, with details of morbidity and mortality. The outcome of surgery usually depends upon proper patient selection, and perhaps more importantly, proper surgeon selection. It must be remembered that a significant number of patients end up on anti-secretory therapy following antireflux surgery. One must beware of advising surgery in patients who have failed to respond to adequate medical therapy. It is rare given the effective medication available today, to have a patient fail medical therapy. Medical therapy achieves the same goal as surgery i.e. reduction of oesophageal acid exposure, so that failure of drug treatment will often predict failure of surgical therapy. □

Please refer to CPD Questionnaire on page 55.

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