

# Mistakes in gastro-oesophageal reflux disease diagnosis and how to avoid them

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According to the Montreal definition, “[gastro-oesophageal reflux disease (GORD)] is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications.”<sup>1</sup> GORD has a negative effect on quality of life and is frequently encountered in clinical practice, with an estimated prevalence of around 24% in Europe.<sup>2</sup> In the US, GORD-related healthcare costs account for \$9 billion per year.<sup>3</sup> A variety of symptoms are associated with GORD—heartburn and regurgitation are typical symptoms, while chest pain, cough and sore throat are considered atypical symptoms—but none is pathognomonic.

In case of a typical presentation of GORD in a young patient, and in the absence of alarm signs (e.g. bleeding, dysphagia, weight loss), it is common practice to treat the GORD without investigation. In other cases, upper gastrointestinal endoscopy is usually the first-line examination, more to rule out mucosal complications than to make a positive diagnosis of GORD. Although the presence of erosive oesophagitis is specific to GORD, most patients in whom GORD is suspected based on their clinical presentation have normal endoscopy findings. In this situation, ambulatory reflux monitoring (either pH or pH-impedance monitoring) may be required to identify reflux episodes, to link them with symptom occurrence and then to confirm the clinical diagnosis of GORD. Another common clinical presentation is a patient with symptoms suggestive of GORD that persist despite proton pump inhibitor (PPI) therapy. Indeed 20–60% of patients with GORD-suggestive symptoms are not satisfied with PPI therapy.<sup>4,5</sup> After evaluating a patient’s compliance with their treatment, complementary examinations are indicated to determine if resistance to treatment is secondary to persistent GORD, to reflux hypersensitivity or to an erroneous diagnosis of GORD.

Here, we report 10 conditions that clinicians should be aware of to avoid making an erroneous diagnosis of GORD. The discussion draws on a combination of published data and clinical experience.

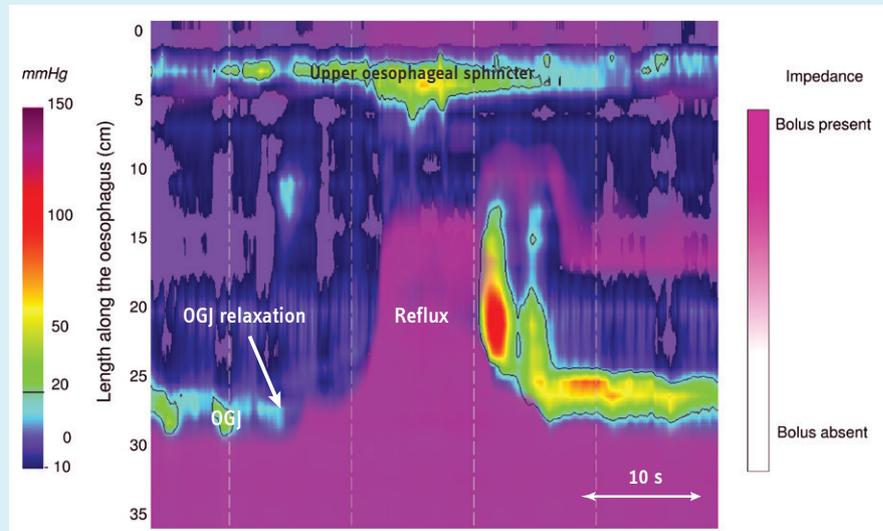


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## Mistake 1 Not considering a diagnosis of achalasia in patients who have nocturnal regurgitation

Achalasia is a rare oesophageal motility disorder that is characterized by incomplete relaxation of the oesophagogastric junction during swallowing and the absence of normal oesophageal peristalsis.<sup>6</sup> Dysphagia and chest pain are the most frequent symptoms of achalasia and regurgitation can occur as a consequence of poor oesophageal clearance.<sup>6</sup> In some patients who have achalasia, nocturnal regurgitation is the only clinical manifestation.<sup>7</sup> As the symptoms of achalasia can mimic the symptoms of GORD, it is recommended that oesophageal manometry be performed in patients who have GORD symptoms that are resistant to PPI therapy and before antireflux surgery to rule out achalasia.<sup>8</sup>

## Mistake 2 Missing a diagnosis of rumination syndrome in patients with pre-prandial and post-prandial regurgitation

Rumination syndrome is a functional gastrointestinal disorder that is characterized by the effortless regurgitation of food from the stomach to the oral cavity, followed by either reswallowing or spitting. Patients with rumination syndrome often report so-called reflux symptoms.<sup>9</sup> Taking a careful history from the patient is important for the diagnosis of rumination syndrome. Symptoms usually begin within 10 minutes of finishing a meal and end when the refluxate is becoming acidic; they do not occur when the patient is asleep.<sup>9</sup> There is little or no improvement of symptoms with antireflux or antiemetic medication.<sup>9</sup> A correct diagnosis of rumination syndrome is

often delayed (by 21 to 27 months from presentation) and patients might be reluctant to accept the diagnosis. Objective testing (oesophageal manometry alone or combined with impedance monitoring) may

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not be necessary for the diagnosis, but can be useful to help explain the disorder to the patient.

### Mistake 3 Assuming an isolated sore throat and pharyngeal pain are related to GORD

The role of GORD in ear, nose and throat (ENT) symptoms is difficult to establish. Some laryngoscopic signs such as erythema, vocal fold oedema, diffuse laryngeal oedema, posterior commissure hypertrophy, granuloma, thick endolaryngeal mucus, pseudosulcus vocalis (mucous membrane on the vocal fold) and ventricular obliteration can be related to GORD. However, the specificity of these signs for GORD is poor and some can be encountered in up to 70% of asymptomatic subjects.<sup>10</sup> Thus, the presence of ENT symptoms even when there are endoscopic laryngeal signs is not sufficient for the diagnosis of GORD. In addition, the response to PPI therapy is not reliable in this group of patients because of a large placebo effect.<sup>10</sup> Therefore, reflux detection with pH or pH-impedance monitoring should be recommended in patient with ENT symptoms to confirm the diagnosis of GORD.

### Mistake 4 Basing the diagnosis of GORD on the response to PPI therapy alone

Performing a PPI test is a pragmatic approach to the diagnosis of GORD. The Diamond study, a multinational trial that compared the ability of a systematic questionnaire with clinical symptom-based diagnosis and ambulatory reflux testing in primary care patients who had frequent upper gastrointestinal symptoms, observed a positive response to a 2-week trial of PPI therapy in 69% of patients with GORD and 51% of those without GORD. Thus, the PPI test is not reliable for the diagnosis of GORD.<sup>11</sup> While it is common to initiate PPI treatment empirically, the response to PPI treatment does not necessarily mean that the patient has pathological GORD (they could have another diagnosis [e.g. functional symptoms, rumination, achalasia...]).

### Mistake 5 Referring all patients with GORD symptoms resistant to PPI therapy for antireflux surgery

Up to 60% of patients with symptoms suggestive of GORD are not satisfied with PPI therapy.<sup>4,5</sup> The reasons for this dissatisfaction might be persistent abnormal oesophageal acid exposure despite therapy, reflux hypersensitivity or functional symptoms. At least one

third of patients who do not respond to PPI therapy have functional symptoms.<sup>4,5</sup> These patients should not be referred for antireflux surgery.

Ambulatory reflux testing is recommended in patients with symptoms suggestive of GORD to confirm the diagnosis.<sup>8</sup> pH monitoring alone or combined with impedance monitoring is performed off PPI therapy in patients who have no previous history of proven GORD (i.e. no oesophagitis, no Barrett's mucosa).<sup>8</sup> By contrast, pH-impedance monitoring on PPI therapy is preferred in patients with previous proven GORD (i.e. oesophagitis grade C or D, Barrett's mucosa >1cm, pathological oesophageal acid exposure on pH monitoring performed off PPI therapy).<sup>8</sup>

### Mistake 6 Missing a diagnosis of GORD because oesophageal acid exposure is absent on pH monitoring performed in the absence of PPI therapy

Ambulatory oesophageal pH monitoring consists of measuring the oesophageal pH with either a catheter introduced transnasally into the oesophagus or a capsule clipped in the distal oesophagus (wireless pH monitoring). Reflux episodes are defined as an oesophageal pH <4. As reflux occurrence is physiological, the absence of a period during which the oesophageal pH is <4 is unlikely, even in a patient without pathological GORD. Thus, an oesophageal pH constantly >4 might be secondary to inhibition (e.g. PPI therapy), the absence of acid secretion (e.g. Biermer disease [pernicious anaemia], autoimmune gastritis)<sup>12</sup> or misplacement of the pH probe. Some patients describe having major discomfort during the test and a significant reduction of their daily routine, which may also produce a false-negative test result. Repeat pH monitoring or performing other complementary tests (e.g. taking gastric biopsy samples) may be useful in these cases.<sup>8</sup>

### Mistake 7 Not assessing symptom reflux association test results with caution, especially in the absence of significant reflux

During ambulatory reflux testing, patients are requested to record their symptoms, usually by pressing a button on the data recorder. The most frequently used symptom-reflux association parameters are the symptom index ([SI] the percentage of symptom events related to reflux episodes, pathological if >50%) and the symptom association probability ([SAP] statistical parameter corresponding to a Fisher exact test exploring the strength of the

relationship between the symptoms and reflux, pathological if >95%).<sup>8</sup> Overall, only a minority of reflux episodes (around 10%) are perceived as symptomatic by the patient.<sup>13</sup> A high or low number of reported symptoms increase the risk of discordance between these two tests. Thus, the diagnosis of functional symptoms might be considered instead of the diagnosis of reflux hypersensitivity, even if SI or SAP is positive.

### Mistake 8 Neglecting supragastric belching as a possible cause of excessive belching

Excessive belching is frequently associated with GORD symptoms or dyspepsia.<sup>14</sup> Two mechanisms of excessive belching have been described—the gastric belch and the supragastric belch.<sup>14</sup> The gastric belch results from a reflex that leads to the relaxation of the oesophagogastric junction and venting of gastric air. There is a behavioural component to supragastric belching, which is the sucking of air into the oesophagus and then expelling it immediately before it has reached the stomach. Most patients with excessive belching are suffering with supragastric belching and do not have GORD. The phenomenon of supragastric belching usually stops when the patient has their mouth open (e.g. when biting a pen); this simple test might be used during an office visit if such a diagnosis is suspected. The diagnosis of supragastric belching can be confirmed by pH-impedance monitoring. A typical feature of supragastric belching is the rapid increase in impedance level that progresses from the proximal to the distal oesophagus, followed by a rapid decrease that progresses from the distal to the proximal oesophagus.<sup>14</sup>

### Mistake 9 Differentiating between GORD and eosinophilic oesophagitis based on the response to PPI therapy

Eosinophilic oesophagitis (EOE) is an emerging disease that is characterized by the infiltration of eosinophils within the oesophageal mucosa.<sup>15,16</sup> In adults, the most frequent clinical presentation of EOE is dysphagia and food impaction.<sup>15,16</sup> However, some patients report regurgitation and heartburn.<sup>15,16</sup> Thus, GORD and EOE can have a similar clinical presentation. Furthermore, eosinophils might also be encountered in the oesophageal mucosa of patients who have GORD. Data have demonstrated that PPI therapy might be effective in patients who have EOE in the absence of associated GORD.<sup>15,16</sup> This feature is called PPI-responsive

eosinophilia and might represent a subgroup of EOE. Thus, the response to PPI therapy is not a reliable way to differentiate GORD from EOE.

### Mistake 10 Not considering obstruction as a cause of reflux symptoms after oesophago-gastric surgery

Reflux symptoms can occur after antireflux or bariatric surgery.<sup>17</sup> They might be secondary to an obstruction at the level of the oesophago-gastric junction or at the level of the anastomosis. In the case of obstruction, ingested food might stay above the obstruction and induce reflux into the oesophagus. After ruling out a mucosal lesion or stenosis with endoscopy, high-resolution impedance manometry might be useful in patients who have reflux symptoms after surgery to demonstrate the presence of an obstruction and reflux above the level of the obstruction. In patients who have undergone previous sleeve gastrectomy, an increased intragastric pressure is frequently associated with reflux occurrence.<sup>16</sup>

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### Your GORD briefing

#### Online courses

- ‘Gastro-Oesophageal Reflux Disease’ from ESPCG [<https://www.ueg.eu/education/online-courses/gastro-oesophageal-reflux/>].

#### UEG Week

- ‘Does my patient really have GORD?’ session at UEG Week 2016 [<https://www.ueg.eu/education/session-files/?session=1614&conference=144>].
- ‘GORD’ presentation in the ‘Oesophageal diseases: What’s new in 2016?’ session at UEG Week 2016 [<https://www.ueg.eu/education/session-files/?session=1662&conference=144>].
- ‘Dilemmas in GORD’ session at UEG Week 2015 [<https://www.ueg.eu/education/session-files/?session=1450&conference=109>].
- ‘Challenges in GORD’ session at UEG Week 2014 [<https://www.ueg.eu/education/session-files/?session=1255&conference=76>].
- ‘New options in gastro-oesophageal reflux disease’ session at UEG Week 2014 [<https://www.ueg.eu/education/session-files/?session=1127&conference=76>].
- ‘Therapy Update: GORD’ session at UEG Week 2014 [<https://www.ueg.eu/education/session-files/?session=1188&conference=76>].
- ‘Mechanisms of refractory GORD symptoms’ session at UEG Week 2013 [<https://www.ueg.eu/education/document/non-compliance-with-medical-therapy-in-gastro-oesophageal-reflux-disease/104109/>].

#### Society conferences

- ‘Translational developments in gastroesophageal reflux disease (GERD)’ session at NeuroGASTRO Meeting 2015 [<https://www.ueg.eu/education/session-files/?session=1683&conference=105>].

#### Standards & Guidelines

- Bishop D, et al. NICE Quality Standard 112: Gastro-oesophageal reflux in children and young people. January 2016 [<https://www.ueg.eu/education/document/nice-quality-standards-gastro-oesophageal-reflux-in-children-and-young-people/141818/>].
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