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Endoscopy in gastro-oesophageal reflux disease

Jan G. Hatlebakk, MD, PhD, Professor *

Division of Gastroenterology, Department and Institute of Medicine, Haukeland University Hospital, NO-5021 Bergen, Norway

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Although gastro-oesophageal reflux disease is basically a clinical diagnosis, oesophago-gastroduodenoscopy is essential to assess the type and severity of tissue damage. The main role for endoscopy is to detect metaplastic or premalignant changes complicating gastro-oesophageal reflux, and allow for surveillance. Routine biopsies are potentially useful to increase the diagnostic precision in case of minimal mucosal abnormalities. Management algorithms should include endoscopy to be performed early in the course of disease in most patients, even in the absence of alarm symptoms. Routine use of the Los Angeles classification of oesophagitis and the Prague classification for metaplasia is necessary for a precise description and biopsy sampling. Magnification chromoendoscopy is particularly useful in the hands of experienced endoscopists, whereas novel technologies including confocal laser endomicroscopy may become an important method in specialised centres to optimise the surveillance of premalignant mucosa.

Introduction

Endoscopy has shaped our approach to upper gastrointestinal diseases, and particularly so to gastro-oesophageal reflux disease (GORD), which is a diagnosis with a short history, but with an increasing incidence in most parts of the world. GORD is essentially a clinical diagnosis, based on typical or atypical symptom profiles, and its response to therapy. [1] There is an important role for invasive procedures - including endoscopy - to clarify specific questions, such as the extent of tissue damage. Endoscopy of the oesophagus and the gastro-oesophageal junction is unique in its ability to visualise the gross anatomy as well as the more subtle changes in the mucosa of the area prone to

* Tel.: +47 55 97 29 00; fax: +47 55 97 29 50.
E-mail address: jan.hatlebakk@helse-bergen.no.

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injury from the action of gastroduodenal secretions. In patients with severe disease, endoscopy provides both the correct diagnosis, offers the endoscopist the possibility to take biopsies for routine diagnostic or research use, and rules out alternative conditions that could explain or contribute to the symptoms, such as malignant tumours or peptic ulcer disease. What has emerged as the most important reason to do oesophago-gastroduodenoscopy (OGD) in patients with GORD is to detect metaplasia and dysplasia, precursors for adenocarcinoma of the oesophagus. [2]

The role of endoscopy in GORD is changing. For the diagnosis of GORD, OGD is clearly a less sensitive method than oesophageal pH-metry or simply symptom evaluation and assessment of the effect of medication. [3] The importance of confirming the clinical diagnosis of GORD with endoscopy, and even verifying healing of reflux oesophagitis with a repeat examination may be overrated by many physicians and patients. A recent survey in primary care in six European countries showed considerable variation between countries in that between 42 and 68% of patients with GORD had been endoscoped at one time or other. [4] One explanation for repeated referrals for open access OGD is the limited confidence amongst primary care physicians in evaluating abdominal symptoms, and the fear for an underlying serious disease, including cancer, that makes the patient consult, even for longstanding, stable symptoms.

There is limited diagnostic value of a routine OGD in the typical patient with symptoms suggestive of GORD, since findings are most often normal, neither confirming nor excluding the diagnosis. The examination gives little useful information on the underlying dysfunction of the organs investigated. In several studies, 50–70% of GORD patients had non-erosive disease with a negative endoscopic examination. [5] This is important knowledge to communicate to referring physicians, to ensure proper therapy and adequate follow-up in case of an unsatisfactory response.

The important differences between countries in the use of OGD, [4] may possibly be due to local traditions and guidelines, as well as availability of endoscopic resources, since a waiting list restricts the options for investigations before empirical therapy. In some healthcare systems, a diagnosis of GORD confirmed by abnormal endoscopic findings gives reimbursement of costs for medication.

It is the aim of this review to discuss the optimal use of endoscopic methods and resources in the group of GORD patients and indicate the suitable timing of the initial investigation and follow-up.

The role of endoscopy in GORD

The role of OGD in the management of GORD depends to some extent on the setting - primary or specialist care - in addition to local availability of endoscopy services. Most patients are diagnosed and treated in primary care and in younger patients presenting with the typical reflux syndrome, OGD may not be justified, at least not as a first measure. This is particularly so when symptoms are mild and respond well to therapy. Several studies have only infrequently shown pathology except for reflux oesophagitis in such patients. In a community based study which recruited 593 patients in primary care, all with heartburn as the predominant symptom, we found no cases of cancer, and only few cases of peptic ulcer disease. [5] In this primary care population, reflux oesophagitis was mild (Los Angeles A and B) and Barrett's oesophagus was diagnosed in no more than 1.2%. Commonly, the symptom pattern is less unequivocal and referral for OGD is justified to rule out other disorders before a diagnosis of GORD can be made. Age above 50 may also be an indication for OGD, since malignant disease becomes more common, but this should not defer a trial of therapy. In low-prevalence areas for *Helicobacter pylori*, and for European or North American patients with classical symptoms of GORD, diagnostic tests for *H. pylori* are usually not justified.

When referred for evaluation in specialist or hospital care, patients are more likely to suffer debilitating symptoms, to have suffered symptoms for significantly longer time, and have fears of cancer. Patients are more likely to have failed OTC and prescription therapy, or have additional or atypical symptoms making the diagnosis of GORD less certain. In this context, OGD is more important to clarify the diagnosis, and alleviate worries of malignant disease, which may underlie the referral. Patients and primary care physicians are well aware of the ability of OGD to diagnose oesophago-gastric malignancy, and when a patient is referred with worries of cancer, performing OGD is always justified.

There are few absolute indications for OGD in patients with symptomatic GORD. There are so-called alarm symptoms which include haematemesis and newly developed dysphagia, indicating a tumour, peptic stricturing, or severe reflux oesophagitis, or pain on swallowing (Table 1). Reflux oesophagitis is a common cause for bleeding episodes from the oesophagus, although bleeding is usually self-limiting, and other sources of bleeding must be examined for, including peptic ulcers, cancer, or a tear at the cardia (Mallory-Weiss syndrome).

The diagnosis or exclusion of metaplasia or Barrett's oesophagus has been considered to be the main motivation for a well timed endoscopic examination in patients with symptoms of GORD. [6] Although true screening of the general population for Barrett's oesophagus is not useful, identification of those GORD patients who harbour Barrett's oesophagus, and are at risk for developing adenocarcinoma is an essential step in any program of surveillance. [7]

Recent surveys indicate that 20–30% of patients with GORD continue to have bothersome symptoms in spite of prescription medication, which includes PPIs and H2-receptor antagonists. [8,9] Medication does not take away episodes of gastro-oesophageal reflux, [10] just reduce the acidity of the refluxate, which means that a subgroup of patients may still have reflux-induced symptoms. [11] Many other patients suffer residual symptoms for other reasons which includes functional dyspepsia, gallstone disease, irritable bowel syndrome or chronic pancreatitis. It is reasonable to perform OGD to identify other disease in patients who do not respond as expected to adequate therapy for GORD, usually defined as double-dose PPIs. [12]

In the hands of an experienced endoscopist, who spends the necessary time to inspect the oesophageal mucosa closely on inserting the instrument, the diagnosis of reflux oesophagitis is a simple diagnosis leaving little doubt. [13] There are few differential diagnoses, which includes virus infections with Herpes simplex, Cytomegalovirus, or Varicella zoster virus, usually only seen in immunocompromised or multimorbid patients. [14]

Grading of reflux oesophagitis using a well validated classification is practically important, partly as an indication of the severity of disease, [15] partly as a means to compare observations in the case of a later control examination. The incidence of complications of reflux oesophagitis developing in future is closely related to grade of oesophagitis in the untreated patient. [16,17]

Grade of oesophagitis is also the way we communicate observations to referring physicians and amongst colleagues. The Los Angeles classification [18] is a reproducible and well adapted tool, and has gained widespread use between countries. There are also other classifications in use, some of which are also based on the recognition of the mucosal break, with or without fibrinous exudate, as the essential lesion. [19]

Complications of gastro-oesophageal reflux are not included in the Los Angeles classification and must be recorded separately. This includes the location and lengths of peptic strictures, hiatus hernia, the competence of the cardia, gastric retention, obstruction at the pylorus etc. Other significant findings such as peptic ulcers and erosions should be looked for and recorded (Tables 2 and 3).

The essential part of OGD for GORD is an evaluation of the presence of metaplasia at the cardia, whether circumferential, as tongues, or islets. This implies locating (the most proximal part of) the z-line, and determining its position in relation to the cardia, with the proximal end of the gastric folds as the essential landmark for the cardia. Any distance between these two points is endoscopically suspected oesophageal metaplasia (ESEM), even if very short and asymmetrical. This requires some experience to determine with confidence and the observations should be recorded in the endoscopy files and expressed according to the Prague C and M classification. [20] ESEM must be confirmed with well directed biopsies. It is a common error to miss the level of the cardia and either include the length

Table 1
Suggested indications for oesophago-gastroduodenoscopy in patients with symptoms compatible with GORD.

1. Alarm symptoms, includes evidence of haemorrhage, weight loss and dysphagia
2. Age >45 years
3. Duration of symptoms > 5 years
4. Non-response to therapy with proton pump inhibitors
5. Relapse on proton pump inhibitor therapy

Table 2
The Los Angeles classification of reflux oesophagitis (see Ref. 18).

Grade A	One (or more) mucosal break no longer than 5 mm, that does not extend between the tops of two mucosal folds
Grade B	One (or more) mucosal break longer than 5 mm, that does not extend between the tops of two mucosal folds
Grade C	One (or more) mucosal break that is continuous between the tops of two mucosal folds, but which involves less than 75% of the circumference
Grade D	One (or more) mucosal break which involves at least 75% of the oesophageal circumference

of a hiatus hernia as metaplasia of the oesophagus, or conversely identify metaplastic mucosa as part of the hernia usually found in these patients.

It is furthermore a goal to limit resources used for control endoscopies. After a first endoscopy, OGD is often repeated, sometimes for unclear reasons. NERD does not develop into Barrett's oesophagus and reflux oesophagitis very infrequently, [17] which means there is no need to ascertain healing with a control endoscopy except in cases of severe reflux oesophagitis (Los Angeles grades C and D). Confirmed Barrett's oesophagus should be followed up according to guidelines developed in consensus by experts in the area, [21] which may at present include OGD every 3–5 years, in absence of any dysplastic histopathological changes. Repeat endoscopy is also indicated in patients developing new alarm symptoms during maintenance therapy, such as dysphagia or evidence of gastrointestinal bleeding. If a patient with GORD is considered for antireflux surgery, OGD is certainly indicated, which lets the surgeon inspect the anatomy of the area of interest around the cardia.

The timing of endoscopy in GORD

Routine endoscopy in younger patients with GORD symptoms of short duration may not be a good management strategy. Commonly, a negative endoscopy makes the patient and primary care physician insecure about the symptom-based diagnosis of GORD, leading to suboptimal therapy and symptom response. Some patients are anxious about undergoing OGD or even refuse. A subgroup of patients responds to lifestyle advice and a brief course of medication, and their symptoms disappear lastingly. An initial choice of acid-suppressive medication based on symptom severity and impact on daily life, takes well care of the patients' symptoms, quality of life, and productivity.

In a recent study, we saw a trend towards better clinical results of initial therapy based on a structured symptom evaluation using the GerdQ questionnaire [22] than of therapy based on severity of endoscopic findings (according to national guidelines). This is not a formal evaluation of treatment results in the shape of a controlled PPI test, which many investigators have found hard to document in a satisfactory way. PPIs are usually very effective as initial therapy for reflux symptoms, alleviating such symptoms as heartburn and regurgitation. The patient's satisfaction with symptom relief and consequent reassurance that the condition is correctly diagnosed and treated, is most important. Patients who do not improve as expected from PPI therapy, with recommended doses, should subsequently be referred for OGD.

It is recommended to taper or stop empirical medication after 3–6 months, which will lead to a symptom relapse in many patients. This is a suitable time for considering OGD, since the condition is confirmed to be chronic and the time is right for discussing future therapy, such as maintenance medication, usually with a PPI, or laparoscopic antireflux therapy.

From several studies, it seems that symptom duration of 5 years or more is a strong predictor of finding Barrett's oesophagus in white males. [23] Several studies suggest that most patients come to

Table 3
The Prague classification of Barrett's oesophagus (see Ref. 20).

C	Circumferential extent of metaplasia in cm
M	Maximum extent of metaplasia in cm

Both distances are measured from the gastro-oesophageal junction, represented by the proximal margin of the gastric mucosal folds.

OGD only several years after symptoms first appeared. [24] This may be the reason why it is not often that metaplasia is seen to develop after an initial normal endoscopy, or that the extent of metaplastic mucosa has increased under observation. It is possible that metaplasia tends to develop during childhood or during the healing of the earliest bouts of oesophagitis. No more than 50% of patients who develop adenocarcinoma of the oesophagus have ever had OGD. This fact favours early endoscopy even for the purpose of diagnosing Barrett's oesophagus, shortly (within a year or two) after the patient first consults.

This first endoscopy might ideally serve to stratify patients for risk of developing oesophageal adenocarcinoma, and thus their need for endoscopic follow-up. Many patients with Barrett's oesophagus have little symptoms, likely due to hyposensitivity in both the columnar and squamous epithelium, and they are important to identify. In many patients with GORD who have no major complications, this may be their 'once in a lifetime' examination, which needs consideration for its optimal timing.

It is an important practical question whether OGD should be performed on or off medical therapy with PPIs, since these are effective to heal oesophagitis in more than 80% of patients, [25] depending on its severity. In order to optimise the possibility to diagnose reflux oesophagitis and other erosive mucosal disease, ongoing therapy should be tapered or stopped at least 10–14 days prior to the procedure. There is little data available to say that even this is adequate, since gastric pH may not be fully back to normal, and it is essentially unknown how long it takes for healed oesophagitis to recur. Symptoms are however likely to recur in patients with GORD of any severity, and the endoscopist is likely to obtain more realistic information about GORD symptoms after stopping medication, since long-term PPI use will often modify not only the severity, but also the type and pattern of symptoms. The recent experience of symptom relapse can give useful information about the initial effect of therapy, which can be years ago.

If we accept the diagnosis of suspected metaplasia and the taking of optimal biopsies for histopathological diagnosis of Barrett's oesophagus as the main indication for OGD, this can be best achieved in a GORD patient on stable therapy with a PPI, most often healed of reflux oesophagitis. Metaplastic mucosa is then usually well demarcated from squamous epithelium and any residual inflammatory changes of reflux oesophagitis. This makes it easier to evaluate and measure the changes endoscopically. Should extensive reflux oesophagitis still be present, this might indicate further therapeutic measures. Furthermore, suppressing reactive, inflammatory changes in the metaplastic mucosa makes it also easier for the pathologist to diagnose dysplasia with confidence.

Recent advances in endoscopic imaging in GORD

Amongst patients diagnosed with GORD, no more than 30–60% show the classical signs of reflux oesophagitis, as defined in the Los Angeles classification. [3,5] Improvements in technology that would increase the sensitivity of endoscopy to recognise minor signs of injury to the squamo-columnar mucosal junction, would allow for a more confident diagnosis of GORD, and reduce the need for further diagnostic procedures, including (impedance) pH-metry, and repeat OGD.

Standard white-light endoscopy with a 140–170° view is what is used for routine endoscopy, despite the introduction of several new diagnostic modalities. It is important to spend time for inspection of the cardia both on introduction and withdrawal of the endoscope, since the experienced endoscopist can recognise many of the structures pinpointed as suspect by more resource-demanding methods. Endoscopic therapy for GORD has been developed using different methods, none of which are in extensive use at present, but are likely to be developed further, giving the endoscopist an important role in therapy.

Magnification endoscopy based on both optical and electronic image magnification in combination with improved CCD technology with up to 1.1 million megapixels, has given better picture quality with a wealth of details. This has led to a search for minor signs predictive of reflux action on the mucosa of the gastro-oesophageal junction, in absence of mucosal breaks. [26] From a longer candidate list, three signs were documented to have the required specificity >95%: pin-point vessels, serrated z-line, and obscured palisade vessels. [27] Still, inter-observer variation even amongst very experienced endoscopists was found to be highly insufficient, with merely obscured palisade vessels

showing a satisfactory kappa value. It could be shown that proton pump inhibitor therapy led to an improvement of these endoscopic changes.

Transnasal endoscopy with an instrument with a small diameter of 4–5 mm could make it easier to do both first-time investigations to detect metaplasia, and follow-up patients with repeat biopsies in case of Barrett's oesophagus. Studies have confirmed the adequacy of transnasal endoscopy for diagnosing the condition.

Esophageal capsule endoscopy has also been seen as a method to make endoscopic examinations more acceptable to the patients, particularly as a tool for screening, since biopsies cannot be obtained. It is a problem that the observation time in the oesophagus can be very short, and that the sensitivity for diagnosing ESEM is less than desirable, but the negative predictive value of the examination is good. [28]

Chromoendoscopy – particularly with methylene blue, indigo carmine or acetic acid - has seen a new era of interest and potential in combination with magnification endoscopy. The visualisation of the mucosa with any associated nodules is facilitated and allows for more targeted biopsies, as well as a preliminary consideration of dysplasia. Endo et al. were able to define five different pit patterns using methylene blue and compared with histological findings. Magnifying chromoendoscopy could discern between the tubular or villous patterns of intestinal metaplasia, the dot or straight patterns of gastric epithelium, and a long, oval pattern being intermediate. [29] Acetic acid has similarly been employed to better define the pit patterns associated with specialised or incomplete intestinal metaplasia in patients with Barrett's oesophagus, and may be the preferred staining for several reasons. [30,31] Sharma et al. investigated the utility of chromoendoscopy with indigo carmine to recognise abnormal mucosal patterns in 56 patients with suspected og established Barrett's oesophagus. [32] An irregular or distorted mucosal pattern was relatively sensitive and specific for high-grade dysplasia, so that taking biopsies guided by this finding took shorter time than taking the usual four-quadrant biopsies (Figs. 1 and 2).

Colour filtering has been developed by manufacturers of endoscopic equipment, including Narrow-Band Imaging (NBI®) from Olympus, Spectral Estimation Technology (MBI®) from Fujinon, and I-Scan® from Pentax to study the mucosal morphology. Like chromoendoscopy, this may improve the detection of abnormal surface pit patterns and guide the taking of biopsies, in both gastric and oesophageal mucosa, especially in areas of metaplastic mucosa. The principle behind these systems is filtering by post-processing after which only specific wavelengths of light, which penetrate to different depths in the mucosa (red deepest, blue most shallow) remain, to improve detectability of abnormal vessels and

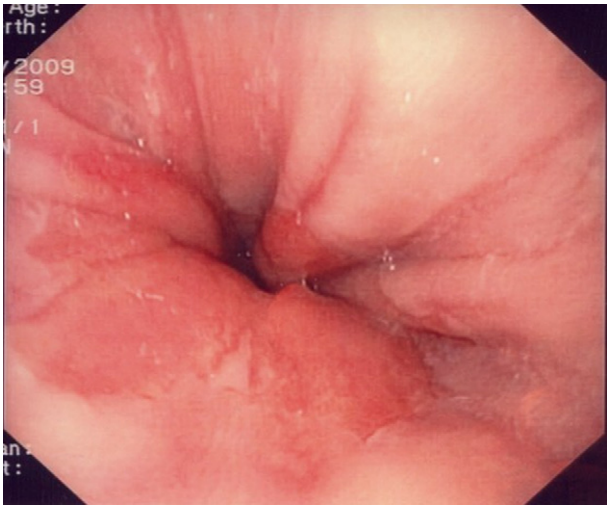

Fig. 1. Reflux oesophagitis grade A according to the Los Angeles classification, with a mucosal break at one o'clock.

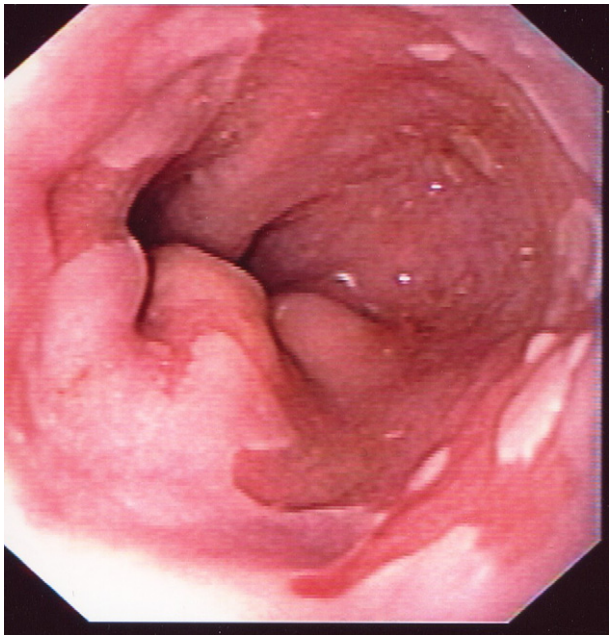

Fig. 2. Barrett's oesophagus observed with routine white-light endoscopy. There are areas of metaplasia proximal to the gastro-oesophageal junction (the upper margins of the gastric folds), but only posteriorly. According to the Prague classification of Barrett's oesophagus, therefore, this is a C0M3 (no circumferential, but 3 cm maximum extent).

pit patterns, including those seen in metaplastic and dysplastic mucosa. As an example, the NBI system uses green light of wavelength 540 nm to visualise vascular patterns, and blue light of 415 nm for surface evaluation (Fig. 3). [33] In a recent study the investigators looked at patients with GORD with or without Barrett's oesophagus and compared with controls. NBI demonstrated microerosions as well as increased vascularity in patients compared with controls. [34] Hoffman et al. could show that I-Scan was as effective as chromoendoscopy with acetic acid to guide the taking of biopsies in patients with Barrett's oesophagus, and thus saved time and cost by reducing the number of biopsies needed. [35] In a more recent multicentre study, inter-observer agreement was evaluated for regularity of mucosal and vascular patterns, and found to be moderately good. [36]

Optical coherence tomography is a novel imaging technique based on low-coherence interferometry. Resolution is in the order of 10–20 μm, which gives the possibility of discerning the wall layers from each other, as shown by Sivak et al. in a preliminary study from several parts of the gastrointestinal tract. [37]

Confocal laser endomicroscopy is a method for *in vivo* fluorescence microscopy that can visualise the mucosa up to 250 μm into the wall of the oesophagus, using either a specialised endoscope with a built-in glassfibre bundle (Pentax) [38] or a mini-probe system (Mauna Kea). [39] In the oesophagus, this method has been employed for studying abnormalities of the squamous epithelium in erosive and non-erosive GORD, demonstrating the increased density of the papillae with their dilated capillary loops, increased leakage of fluorescein, as well as dilated intercellular spaces. [40,41] In Barrett's oesophagus, endomicroscopy can visualise the goblet cells with dark spots of mucin typical of intestinal metaplasia, but also abnormal subepithelial capillaries and the dark, irregular cells of intramucosal neoplasia. [42] Kiesslich et al. have proposed a set of criteria for the endomicroscopic evaluation. In being a histopathological method, confocal laser endomicroscopy is a new field for most endoscopists, requiring close cooperation with pathologists for a considerable period of time to build up experience in evaluating the findings. Confocal laser endomicroscopy is likely to be reserved for evaluating premalignant disorders at specialised referral centres (Fig. 4).

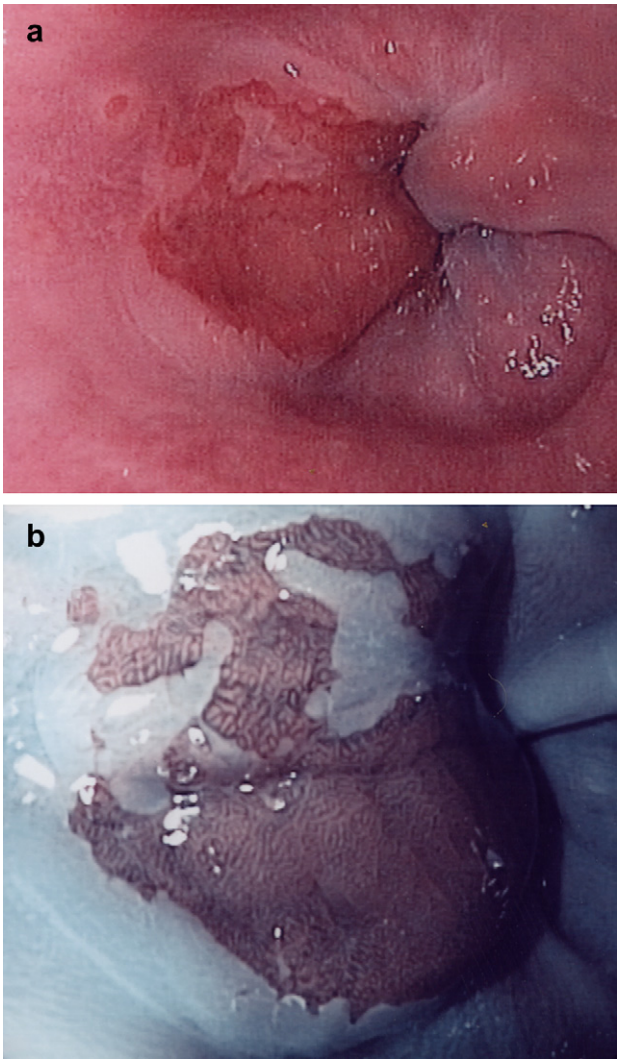

Fig. 3. Short-segment Barrett's oesophagus visualised with (a) standard white-light endoscopy, and (b) narrow-band imaging. Notice how the light filtering accentuates the mucosal pit pattern of the metaplastic mucosa.

Magnification endoscopy with acetic acid may be an excellent method in the hands of experienced endoscopists doing surveillance in groups of patients with Barrett's oesophagus. Light filtering technology such as NBI may be particularly useful for less experienced endoscopists performing the routine endoscopies, to facilitate the observation of mucosal abnormalities. Cost-effectiveness has yet to be demonstrated in routine OGD in patients with GORD.

The role of biopsies in GORD

The unique opportunity for taking biopsies from the oesophagus during upper gastrointestinal endoscopy in patients with symptomatic GORD, even in the absence of suspicion of metaplasia, has not been explored sufficiently in adults. [43] Paediatric gastroenterologists have used histopathology more routinely to exclude alternative pathology even when endoscopy of the oesophagus has been normal.

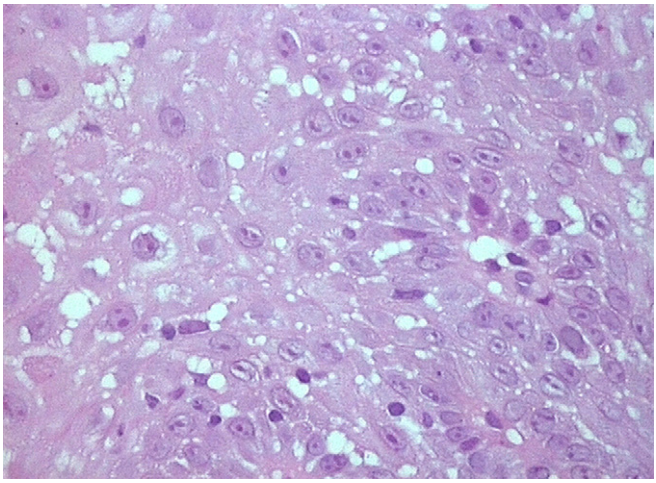

Fig. 4. Dilated intercellular spaces in oesophageal squamous mucosa. To the right there is a papilla with a vessel.

Recent studies suggest that oesophageal mucosal biopsies are of considerable interest in patients with unexplained symptoms and no or only minor endoscopic changes. Given the suboptimal sensitivity of routine endoscopy for diagnosing GORD, information from histological examinations may imaginably contribute to a correct diagnosis, with no further use of invasive procedures.

Histopathological examination of the squamous epithelium in patients with reflux oesophagitis may show signs compatible with microscopic oesophagitis, including neutrophilic leucocytes. This is however an infrequent finding except in cases of severe oesophagitis. [44] The classical findings described in the early studies by Ismail-Beigi et al.: increased height of mucosal papillae, and hyperplasia of the basal epithelial layer, [45] have recently been confirmed even in mild oesophagitis. [43] Until now, the full spectrum of histological findings, as well as their diagnostic precision in GORD have not been studied in well characterised patient populations.

Recently, the finding of dilated intercellular spaces between cells in the squamous mucosa, has been found to correlate with the severity of gastro-oesophageal reflux. This was shown with electron microscopy by Tobey et al., [46] and by Solcia et al., [47] it has more recently been confirmed also with light microscopy that more than 2–3 times wider spaces exist between squamous epithelial cells in the granular layer of the mucosa. [48,49] The finding of dilated intercellular spaces has been more consistent than most other histopatholological markers for GORD, being found in 40–100% of patients with non-erosive disease, but in few controls (<20%). [43]

In studies by Vieth et al., various parameters of inflammation have been evaluated for their usefulness in diagnosing GORD. It was found that lymphocyte infiltrates in the epithelium were more common than intraepithelial neutrophilic or eosinophilic granulocytes, but still much less common that elongated papillae and a thickened basal layer. [50] In a different study involving GORD patients with or without reflux oesophagitis, abnormal histopathologic findings were made in 98% of patients with erosive and 76% of patients with non-erosive disease. [51] Zentilin et al. have in addition developed a sum score for rating the severity of microscopic oesophagitis, compensating for the varying appearance of inflammation and also for inter-observer variability, incorporating the following parameters: basal cell hyperplasia, papillary elongation, intercellular space dilatation, intraepithelial eosinophils, neutrophils, and necrosis. [51] This sum score, ranging 0–22, was found to have a cut-off of 2 that reliably discriminated GORD patients from controls. In biopsies taken from the z-line and 2 cm proximal to it, the authors could relate the sum score to the severity of reflux oesophagitis, and follow the improvement in these parameters, as well as the sum score, during 3 years of therapy for GORD. [52] Improvement on therapy was shown both during medical therapy with esomeprazole 20–40 mg daily, or after laparoscopic antireflux surgery, but with a surprising slow normalisation of some

inflammatory parameters (including dilated intercellular spaces and basal cell hyperplasia) particularly at the distal site in the oesophagus. [52] The taking of routine biopsies from the distal oesophagus, 1–2 cm proximal to the z-line, and quantifying single parameters or a sum score in the evaluation of oesophageal biopsies would add diagnostic sensitivity to endoscopic examination of the oesophagus, in patients suspected of GORD.

All observations of suspected metaplastic mucosa need to be confirmed by histopathology in well directed biopsies. It is extremely important to confirm the origin of biopsies from the tubular oesophagus and the anatomic relationship to the cardia. It is at present practically impossible for the pathologist to reliably discern between the mucosa of a hiatus hernia at the cardia and that from metaplastic oesophageal mucosa. The description of the biopsy sites related to the Prague classification, and often with a diagram of the gross anatomy may be useful for the consultant pathologist.

Another important use of histopathology in the patient with oesophageal symptoms with or without endoscopic abnormal findings, has been to exclude alternative pathology. Although the endoscopic aspect of reflux oesophagitis is relatively specific, there are cases when viral pathology including Cytomegalovirus or Herpes simplex should be excluded, both giving rise to lesions that can be confused. Eosinophilic oesophagitis, increasingly often diagnosed in the adult patient, gives rise to symptoms and motility abnormalities not incompatible with GORD. Biopsies taken from both the proximal and distal oesophagus usually distinguish between GORD and eosinophilic oesophagitis, although, as stated above, there are cases when the density of eosinophils in the distal oesophageal mucosa may overlap. [52]

Endoscopy has contributed greatly to our vision and understanding of GORD and will continue to play an important role. New technology and better use of available resources such as more extensive and well informed use of histopathology and chromoendoscopy is likely to yield better clinical results.

Practice points

- Initial therapy for GORD should, in the absence of alarm symptoms, be symptom-based, with a trial of effective acid-suppressive medication
- There is usually an indication for OGD within the first 1–2 years after diagnosis, and this could be done without stopping medication
- Biopsies should be taken from the distal oesophagus in GORD patients with no obvious endoscopic abnormalities
- Magnification chromoendoscopy with acetic acid or optical light filtering such as narrow-band imaging, is useful to improve the yield of bioptic material in patients suspected of having metaplastic mucosa

Research agenda

- Outcome studies are needed to better define the concept of an early OGD to stratify patients for risk for developing metaplasia and adenocarcinoma of the oesophagus
- Prospective studies are needed to investigate if routine biopsies from the distal oesophagus can replace more extensive diagnostic workup for the diagnosis of GORD, such as 24-h (impedance) pH-metry
- Outcome studies are needed to decide whether novel technology such as confocal laser endomicroscopy can replace the traditional four-segment biopsies in surveillance of Barrett's oesophagus
- Endoscopic interventions for treating GORD are needed to offer alternatives to life-long potent acid suppression with proton pump inhibitors

Conflict of interest statement

None.

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