UNITED EUROPEAN GASTROENTEROLOGY ueg education

Mistakes in the endoscopic diagnosis and management of Barrett's oesophagus and how to avoid them

Rehan J. Haidry and Cormac Magee

Barrett's oesophagus is the precursor to oesophageal adenocarcinoma, which carries a poor prognosis,[1] and it is likely that all endoscopists and gastroenterologists will encounter Barrett's oesophagus in their clinical practice. Careful assessment and management of patients who have Barrett's oesophagus with endoscopic surveillance and endoscopic endotherapy aims to reduce the risk of progression to invasive adenocarcinoma. Advances in endoscopic diagnosis and therapy should, therefore, help to reduce the risk of progression. As with all premalignant conditions and surveillance programmes,[2] careful multidisciplinary management of the patient is important to reduce the risk of causing them to become unduly concerned. Here, we present some mistakes that in our experience are commonly made in the endoscopic diagnosis and management of Barrett's oesophagus and give advice on how to avoid them.

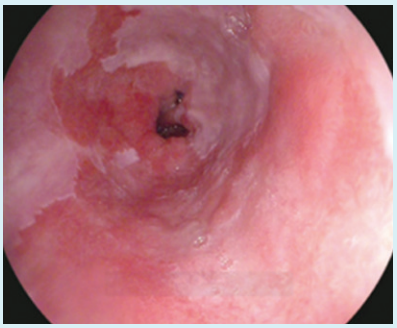

Image courtesy of R.J. Haidry and C. Magee.

Mistake 1 Overdiagnosis of Barrett's oesophagus

Overdiagnosis of Barrett's oesophagus can cause unneccesary endoscopic surveillance and many patients have a higher than accurate perception of their risk of cancer.[3] Barrett's oesophagus should be defined by accurately recognising the proximal limit of the gastric folds with moderate air insufflation at endoscopy.[4,5] Patients who have tongues of columnar epithelium that are shorter than 1 cm and no confluent columnar segment should not be given the diagnosis of Barrett's oesophagus, but instead be defined as having an irregular Z-line (figure 1). Patients who have an irregular Z-line should be reassured and should not enter into a surveillance programme.[2]

The extent of Barrett's oesophagus should be described using the Prague classification, and the maximal circumferential length (C) and maximal extent of tongues or islands (M) recorded (figure 2).[6] This allows determination of endoscopic intervals and, should dysplasia be found in a random biopsy sample, the area can be accurately relocated at repeat endoscopy.[7,8]

Mistake 2 Not allowing sufficient time for careful inspection of the oesophagus during endoscopy

16.4–38.0% of oesophageal adenocarcinomas are diagnosed within a year of surveillance endoscopy for Barrett's oesophagus.[9]

A systematic review has also shown that 25% of oesophageal adenocarcinomas are diagnosed within 12 months of the index endoscopy, highlighting the particular importance of the index endoscopy.[9] It is likely, given the natural progression of this disease, that most of these adenocarcinomas will have developed in missed lesions. As the time spent inspecting the Barrett's segment increases so the detection of neoplasia improves, and at least 1 minute should be spent inspecting each centimetre segment.[10]

Other factors are also known to improve the quality of the oesophageal inspection. The mucosa should be cleaned with a mucolytic agent and the patient made comfortable (sedation is often needed to achieve this) because retching can impair the endoscopist's view. We perform most of our Barrett's surveillance endoscopies under sedation rather than local anaesthetic throat spray to reduce artefact caused by motion if the patient is uncomfortable and to allow longer, comfortable inspection time. Particular attention should be paid to the right wall and proximal segment as this is where early cancers are most commonly found.[11–15] In addition, dedicated Barrett's surveillance lists seem to increase the rate of dysplasia detection when compared with nonspecialist lists.[16]

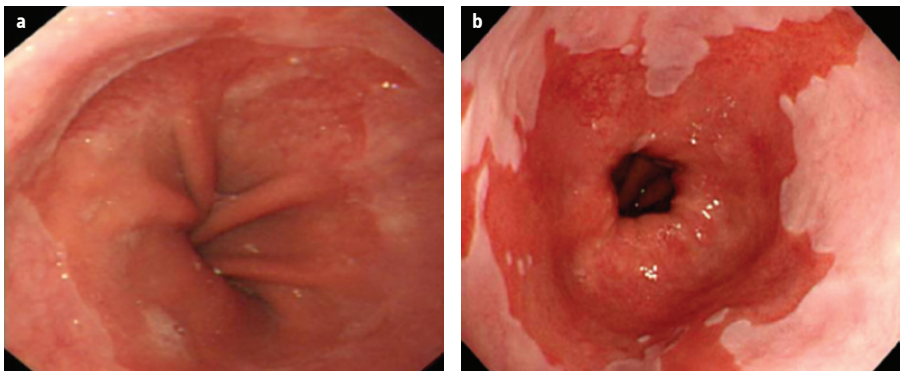

Figure 1 | Diagnosing Barrett's oesophagus. **a** | An irregular Z-line only. **b** | Barrett's oesophagus.

Cite this article as: Haidry RJ and Magee C. Mistakes in the endoscopic diagnosis and management of Barrett's oesophagus and how to avoid them. *UEG Education* 2018; 2018: 12–14.

Rehan J. Haidry is at the Department of Gastroenterology at University College London Hospitals and the Division of Surgery and Interventional Sciences at University College London, UK. Cormac Magee is at the Department of Gastroenterology at University College London Hospitals and the Department of Metabolism and Experimental Therapeutics, University College London, UK.

All images courtesy of: R. J. Haidry and C. Magee

Correspondence to: r.haidry@ucl.ac.uk

Conflicts of interest: CM declares no conflicts of interest. RJH has received research grant support from Pentax Medical, to support research infrastructure.

Published online: March 29, 2018

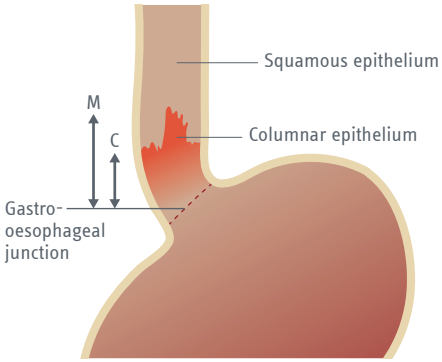

Figure 2 | Illustration of the Prague C + M criteria for grading endoscopic Barrett's oesophagus. According to the Prague criteria,[6] the area of endoscopic Barrett's oesophagus is defined by the maximal length of circumferential columnar epithelium (C) and the maximal extent of columnar epithelium (M) proximal to the gastro-oesophageal junction. For example, C3M5 represents circumferential columnar epithelium of 3 cm and a maximal extent of columnar epithelium of 5 cm.

Mistake 3 Failing to use available imaging adjuncts to detect neoplasia

The detection of early neoplasia is the rationale for endoscopic assessment of Barrett's oesophagus. Therefore, available adjuncts to aid neoplasia detection should be considered by the endoscopist, in particular high-definition endoscopes, as advised by the ESGE.[7] Most endoscopes now available have image enhancement modes with virtual chromoendoscopy that can help to detect neoplasia (e.g. narrow-band imaging [NBI; Olympus], i-scan [Pentax], blue light imaging [BLI; Fujinon]).[17–19] Endoscopists should familiarise themselves with these techniques and use them during Barrett's oesophagus endoscopies. In addition, acetic acid 1.5–3.0% sprayed onto the mucosa via a spray catheter is a safe method to detect areas of rapid loss of aceto-whitening, which can be a sign of dysplastic tissue (figure 3), in some analyses improving the diagnostic yield by over 14-fold.[20,21]

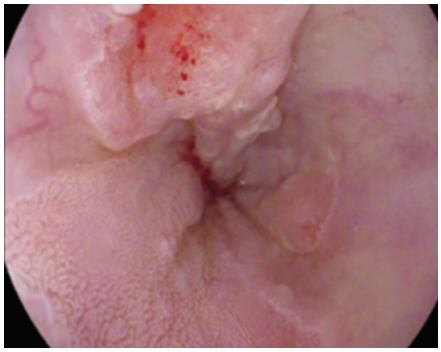

Figure 3 | A visible dysplastic lesion demonstrating rapid loss of aceto-whitening following application of acetic acid.

Mistake 4 Not following biopsy protocols correctly

Following careful inspection of the oesophagus, targeted biopsy samples should be taken from areas identified as potentially dysplastic, with which the above-mentioned techniques can help. The location of these areas should be marked and the samples sent to the histopathology laboratory in separate pots, so that if dysplasia is identified in a sample the location it was taken from can be found more easily at a later endoscopy if therapy is to be considered.

The Seattle protocol should then be used to take samples around the four quadrants of the mucosa, starting at the gastro-oesophageal junction and then every 2cm to the proximal limit of the Barrett's segment (figure 4).[3,22] However, it should be noted that this probably represents sampling of only 3.5% of the mucosa.[23] Large capacity forceps may help to sample a larger area. Newer techniques including 'Watts-3D' may also, in future, aid sampling a larger area.[24]

Mistake 5 Taking biopsy samples from an inflamed segment of Barrett's oesophagus

If, on inspection, the Barrett's segment appears inflamed, there is a risk of misdiagnosing a patient with dysplasia if biopsy samples are taken. Such a misdiagnosis clearly has the potential to distress the patient and also risk unnecessary intervention. Patients should not have biopsy samples taken when an inflamed Barrett's segment is found, but instead they should be placed on maximal acid suppression. A repeat endoscopy should be performed at a later date and biopsy samples should then be taken. In our experience, we would usually double the current dose of acid suppression and perform a repeat endoscopy in 2–3 months.

Mistake 6 Commencing endotherapy without confirming the presence of dysplasia

If low-grade dysplasia (LGD) is identified in biopsy samples, the patient should have a second endoscopy to confirm its presence before endotherapy is commenced. This second endoscopy avoids exposing patients unnecessarily to the risks of endotherapy, which include bleeding and stricture formation. The identification of LGD should be carefully considered as there is significant intraobserver and interobserver variability in its pathological diagnosis, with one series demonstrating a 73% downgrading of LGD at expert histological review.[25] In complex cases, the histology findings and the patient's case should ideally be discussed in a multidisciplinary team meeting with expert pathologists and endoscopists to help decide on the course of action. Patients should have the opportunity to discuss the potential benefits and risks of therapy with an experienced health professional, ideally in an outpatient-clinic-based setting.

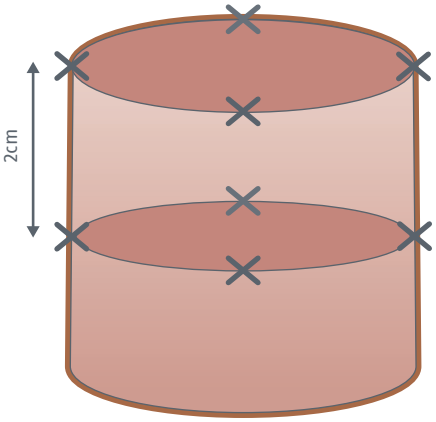

Figure 4 | Schematic representation of the Seattle protocol for taking biopsy samples.

Mistake 7 Performing endotherapy inconsistently

Endotherapy should be undertaken by those with sufficient experience to select the correct treatment modality and to deal with potential complications. Visible lesions should be identified and removed by endoscopic mucosal resection (EMR). Careful staging should be performed by an experienced endoscopist to assess the lesion and consider endoscopic ultrasound (EUS) or cross-sectional imaging if there is any concern regarding the presence of invasive carcinoma (figure 5). All visible lesions should be removed and at subsequent endoscopies radiofrequency ablation (RFA) used to treat the remaining Barrett's mucosa. Argon plasma coagulation (APC) can also be

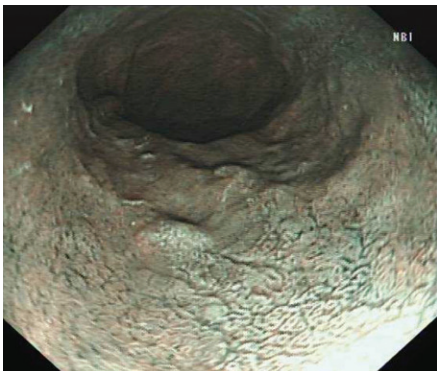

Figure 5 | Visible, nodular dysplasia in a segment of Barrett's oesophagus under narrow band imaging.

used to treat areas of Barrett's mucosa.[26–28] Newer techniques including cryoablation have shown promise as alternative therapies.[29] Following the completion of therapy, biopsy samples should be taken at least 3 months afterwards to confirm eradication of dysplasia and metaplasia.[26–28] Biopsy samples taken too soon after intervention may not yield a reliable pathology report due to acute changes in tissue caused by interventions.

Mistake 8 Not following up patients who have Barrett's oesophagus

Patients with Barrett's oesophagus will often have long intervals (3–5 years) between endoscopies and it is important not to lose them to follow up. Having a database to record patients on a surveillance programme is crucial, and accurate communication with the patient and their general practitioner can help reduce the risk of losing them. Surveillance should follow guidelines on intervals.[4,5,30,31]

Mistake 9 Continuing surveillance in patients for whom it is no longer appropriate

Patients with Barrett's oesophagus may develop other comorbidities during a surveillance programme that make them less suitable to continue with surveillance. Consideration of the patient as a whole at each interaction with health professionals and informed discussion with the patient is important to avoid surveillance in patients for whom it is no longer suitable, due to life-limiting illness or a condition that would make endoscopy unsafe or very uncomfortable for the patient.

References

1. Howlader N et al. *SEER Cancer Statistics Review, 1975-2013* 2016; National Cancer Institute. Bethesda, MD.
2. Wilson JMG and Jungner G, Principles and Practice of Screening for Disease. *WHO Public Health Papers* 1968.
3. Shaheen NJ, et al. The perception of cancer risk in patients with prevalent Barrett's esophagus enrolled in an endoscopic surveillance programme. *Gastroenterology* 2005; 129: 429–436.
4. Fitzgerald RC, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus, *Gut* 2014; 63: 7–42.
5. Shaheen NJ, et al. ACG Clinical Guideline: Diagnosis and management of Barrett's esophagus, *Am J Gastroenterol* 2016; 111: 30–50.
6. Sharma P, et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. *Gastroenterology* 2006; 131: 1392–1399.
7. Weusten B, et al. Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. *Endoscopy* 2017; 49: 191–198.
8. Sampliner RE. Practice guidelines on the diagnosis, surveillance, and therapy of Barrett's esophagus. *Am J Gastroenterol* 1998; 93: 1028–1032.
9. Visrodia K, et al. Magnitude of missed esophageal adenocarcinoma after Barrett's esophagus diagnosis: a systematic review and meta-analysis. *Gastroenterology* 2016; 150: 599-607.e7.
10. Gupta N, et al. Longer inspection time is associated with increased detection of high grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus. *Gastrointest Endosc* 2012; 76: 531–538.
11. Kariyawasam VC, et al. Circumferential location predicts the risk of high-grade dysplasia and early adenocarcinoma in short-segment Barrett's esophagus. *Gastrointest Endosc* 2012; 75: 938–944.
12. Pech O, et al. Prospective evaluation of the macroscopic types and location of early Barrett's neoplasia in 380 lesions. *Endoscopy* 2007; 39: 588–593.
13. Edebo A, et al. Circumferential and axial distribution of esophageal mucosal damage in reflux disease. *Dis Esophagus* 2007; 20: 232–238.
14. Enestvedt BK, et al. Location, location, location: does early cancer in Barrett's esophagus have a preference? *Gastrointest Endosc* 2013; 78: 462–467.
15. Cotton, CC et al. Spatial predisposition of dysplasia in Barrett's esophagus segments: a pooled analysis of the SURF and AIM – dysplasia trials. *Am J Gastroenterol* 2015; 110: 1412–1419.
16. Ooi J et al. Dedicated Barrett's surveillance sessions managed by trained endoscopists improve dysplasia detection rate. *Endoscopy* 2017; 49: 524–528.
17. Sharma P, et al. Development and validation of a classification system to identify high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus using narrow-band imaging. *Gastroenterology* 2017; 150: 591–598.
18. Lipman G, et al. Systematic assessment with I-SCAN magnification endoscopy and acetic acid improves dysplasia detection in patients with Barrett's esophagus. *Endoscopy* 2017; 49: 1219–1228.
19. Subramaniam S, et al. OC-068 Blue light imaging for Barrett's neoplasia classification (blinc): the development and validation of a new endoscopic classification system to identify barrett's neoplasia. *Gut* 2017; 66: A36–A37.
20. Coletta M, et al. Acetic acid chromoendoscopy for the diagnosis of early neoplasia and specialized intestinal metaplasia in Barrett's esophagus: a meta-analysis. *Gastrointest Endosc* 2016; 83:57–67.e1.
21. Kandiah K, et al. International development and validation of a classification system for the identification of Barrett's neoplasia using acetic acid chromoendoscopy: the Portsmouth acetic acid classification (PREDICT). *Gut* Epub ahead of print 28 September 2017. DOI: 10.1136/gutjnl-2017-314512.
22. Levine DS, et al. Safety of a systematic endoscopic biopsy protocol in patients with Barrett's esophagus. *Am J Gastroenterol* 2000; 95: 1152–1157.
23. Tschanz ER. Do 40% of patients resected for Barrett's esophagus with high-grade dysplasia have unsuspected adenocarcinoma? *Arch Pathol Lab Med* 2005; 129: 177–180.
24. Johanson JF, et al. Computer-assisted analysis of abrasive transepithelial brush biopsies increases the effectiveness of esophageal screening: a multicenter prospective clinical trial by the EndoCDx Collaborative Group. *Dig Dis Sci* 2011; 56: 767–772.
25. Duits LC, et al. Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel. *Gut* 2015; 64: 700–706.
26. Haidry RJ, et al. Radiofrequency ablation and endoscopic mucosal resection for dysplastic barrett's esophagus and early esophageal adenocarcinoma: outcomes of the UK National Halo RFA Registry. *Gastroenterology* 2013; 145: 87–95.
27. Shaheen NJ, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. *N Engl J Med* 2009; 360: 2277–2288.
28. Phoa KN, et al. Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial. *JAMA* 2014; 311: 1209–1217.
29. Visrodia K, et al. Cryotherapy for persistent Barrett's esophagus after radiofrequency ablation: a systematic review and meta-analysis. *Gastrointest Endosc* Epub ahead of print 21 February 2018. DOI: 10.1016/j.gie.2018.02.021.
30. El-Serag HB, et al. Surveillance endoscopy is associated with improved outcomes of oesophageal adenocarcinoma detected in patients with Barrett's oesophagus. *Gut* 2016; 65: 1252–1260.
31. Kastelein F, et al. Impact of surveillance for Barrett's oesophagus on tumour stage and survival of patients with neoplastic progression. *Gut* 2016; 65: 548–554.

Your Barrett's oesophagus briefing

BORN module

- Barrett's Oesophagus Related Neoplasia (BORN) interactive web-based training module for endoscopists developed and validated by members of the International Working Group for the Classification of Oesophagitis [https://mediamotor.academy/born/index.php].

UEG Week

- "Case finding and surveillance of Barrett's oesophagus" session at 25th UEG Week 2017 [https://www.ueg.eu/education/session-files/?session=1900&conference=149].
- "Management of early Barrett's neoplasia: When and how to resect or ablate?" session at 25th UEG Week 2017 [https://www.ueg.eu/education/session-files/?session=1846&conference=149].
- "Update on Barrett's oesophagus" session at UEG Week 2016 [https://www.ueg.eu/education/session-files/?session=1555&conference=144].
- "Management of Barrett's oesophagus: The gold standard" session at UEG Week 2016 [https://www.ueg.eu/education/session-files/?session=1617&conference=144].
- "Barrett's and oesophageal cancer" presentation in the "Bringing molecular tests to GI cancer clinics" session at UEG Week 2016 [https://www.ueg.eu/education/document/barrett-s-and-oesophageal-cancer/131295/].

Society Conferences

- ESGE & ESDO Quality in Endoscopy 2016 - Upper GI Endoscopy & Neoplasia [https://www.ueg.eu/education/conference-files/?conference=143].

Standards and Guidelines

- Weusten BLAM, et al. Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. *Endoscopy* 2017; 49: 191–198. [https://www.ueg.eu/education/document/endoscopic-management-of-barrett-s-esophagus-european-society-of-gastrointestinal-endoscopy-esge-position-statement/147393/].
- di Pietro M, et al. Revised British Society of Gastroenterology recommendation on the diagnosis and management of Barrett's oesophagus with low-grade dysplasia. *Gut* 2018; 67: 392–393 [https://www.ueg.eu/education/document/revised-british-society-of-gastroenterology-recommendation-on-the-diagnosis-and-management-of-barrett-s-oesophagus-with-low-grade-dysplasia/174755/].
- di Pietro M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. *Gut* 2014; 63: 7–42 [https://www.ueg.eu/education/document/british-society-of-gastroenterology-guidelines-on-the-diagnosis-and-management-of-barrett-s-oesophagus/141808/].