First Level Endoscopy in Barrett's Esophagus: Endoscopic Pictures, Praga Classification, and Biopsy Protocols

6

Massimo Conio, Antonella De Ceglie, and Mattia Crespi

6.1 Endoscopic Pictures

Endoscopy is considered the gold standard to diagnose Barrett's esophagus (BE). The term endoscopy is generally referred to as standard trans-oral endoscopy.

Trans-nasal endoscopy has shown a sensibility and specificity of 100% for endoscopic diagnosis of BE when compared with standard endoscopy; it was better tolerated and preferred by patients. However, standard endoscopy showed a better optical quality than that of trans-nasal endoscopy ($p < 0.0001$) [1].

The advent of high-resolution endoscopes (HRE) has significantly improved the quality of endoscopic images, making easier the identification of the landmarks. Better morphological details of the mucosa are obtained with magnification endoscopy and virtual chromoendoscopy [2].

At the time of endoscopy, three important landmarks must be recognized for a correct diagnosis of BE:

1. The gastro-esophageal junction (GEJ).
2. The diaphragmatic pinch.
3. The squamo-columnar junction (SCJ) or Z-line.

In Western guidelines, the upper end of the gastric folds (GF) is the landmark for the GEJ. The position of most proximal margin of the GF is assessed in deflate condition because air insufflation or deep inspiration may change its positions and mislead the diagnosis [3].

In Japanese guidelines, only the distal end of the lower esophageal palisade vessels (PVs) is considered as the endoscopic landmark of the GEJ [4]. PVs are longitudinal vessels running in the mucosal layer of the lower esophagus, descending into the submucosa once entering the cardia. PVs are most easily assessed when the

M. Conio (✉) · A. De Ceglie · M. Crespi
Department of Gastroenterology, General Hospital, Sanremo (IM), Italy

G. Galloro (ed.), *Revisiting Barrett's Esophagus*,
https://doi.org/10.1007/978-3-319-92093-1_6

lower esophagus is adequately distended. Their identification may be disturbed by several factors, such as mucosal inflammation, dysplastic changes, and a thick double muscularis mucosa [5].

In Scholvinck et al. study, PVs were located at a median of 1 cm distal of the GF in 63% of patients with BE and in 27% of cases, intestinal metaplasia was present in this discordant zone [6].

However, Amano et al. reported that PVs criteria showed an overall poor diagnostic reproducibility with a *k* value of 0.14 when compared with GF, and the level of agreement was independent of endoscopic experience [7].

The diaphragmatic pinch is the point at which the diaphragmatic crura constricts or "pinches" the esophagus; this landmark is important to denote the presence of a hiatal hernia.

The SCJ is the transitional point between stratified squamous and columnar epithelium of the esophagus and stomach, respectively. In normal esophagus, the GEJ and SCJ coincide [8] (Fig. 6.1).

BE has been traditionally defined as the presence of at least 1 cm of metaplastic columnar epithelium that replaces the stratified squamous epithelium normally lining the distal esophagus. Therefore, endoscopic presence of BE is suspected when the SCJ lies ≥1 cm above the GEJ at the level of its more proximal extension [9–11].

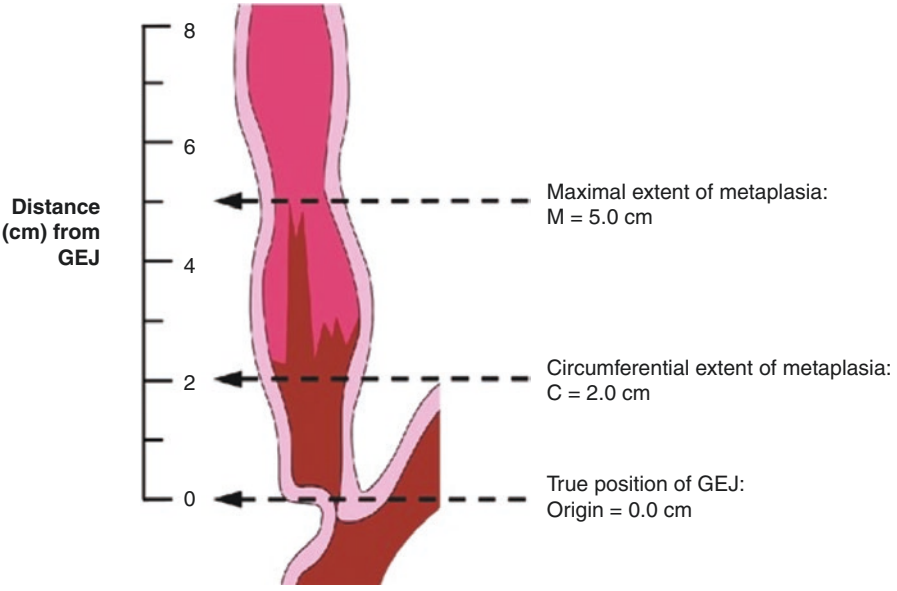

Fig. 6.1 Diagrammatic representation of endoscopically identified Barrett's esophagus showing an area classified as C2M5 according to Prague classification. *GEJ* gastroesophageal junction, *M* maximal extent of the metaplasia, *C* extent of circumferential metaplasia. (Adapted from *Sharma P* et al. [3] by permission from Elsevier and Copyright Clearance Center. License number 4233801225643-Nov 21, 2017)

Upward displacement of the SCJ is concealed if severe esophagitis is present, and the correct diagnosis of BE may be difficult [12].

BE should only be diagnosed when there is a clearly endoscopically visible change from squamous to columnar epithelium in the distal esophagus, starting at GEJ. In patients with esophagitis (Los Angeles Classification B, C, D), endoscopic examination should be repeated after 8–12 weeks of therapy with PPI [9].

Metaplastic columnar epithelium is characterized by the typical salmon color and coarse texture. Histologically, three distinct types of cells are involved: gastric fundic type, cardiac type, and specialized intestinal metaplasia (SIM) characterized by the presence of goblet cells [13].

Disagreement remains in guidelines as to the histological features of the columnar mucosa necessary to define BE: pathologists in Europe and the United States require intestinal metaplasia within columnar-lined mucosa (CLM) in the tubular esophagus to diagnose BE, whereas in the United Kingdom and Japan only the presence of CLM is required [9–11, 14].

However, intestinal metaplasia has been considered as the most biologically instable type of metaplastic columnar epithelium with the greatest risk of neoplastic progression through dysplasia to adenocarcinoma [15].

An irregular Z-line/columnar-lined esophagus <1 cm (ultra-short BE) should be ignored because of the lack of an established cancer risk of intestinal metaplasia at this level and, being a common finding especially in patients with reflux disease, the excessive demands if they were put under surveillance [16–18].

Endoscopists should also avoid to take biopsies from the gastric cardia or at GEJ when there is no visible columnar epithelium, as the presence of IM is a common pathological finding, occurring up to 18% of people undergoing elective endoscopic examination, irrespective of indication, without an increased risk of developing cancer [19].

Also islands of columnar metaplasia in the proximal esophagus should not be confused with BE; these are cervical inlet patches that very rarely have intestinal metaplasia and more rarely develop cancer [20].

6.2 Prague Classification

In the presence of BE, endoscopic evaluation should be carried out using the Prague criteria which considers circumferential (C) and maximum (M) extent of endoscopic visible columnar-lined esophagus in centimeters (Fig. 6.2).

"C" is considered as the difference in endoscope insertion distance between the positions recorded for the GEJ and the proximal margin of the circumferential Barrett's epithelium; "M" is considered as the difference in endoscope insertion distance between the positions recorded for the GEJ and the proximal margin of the longest tongue-like segment of Barrett's epithelium.

The presence and location of visible lesions should also be reported according to the Paris classification [10, 11, 21] (Fig. 6.3).

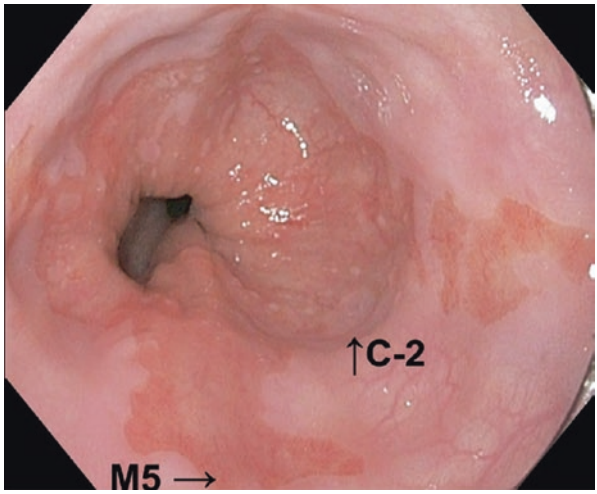

Fig. 6.2 Endoscopic aspect of Barrett's esophagus (Praga C2 M5)

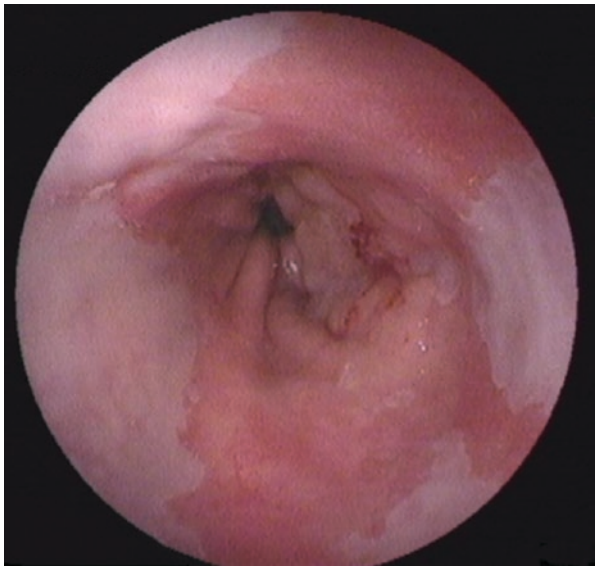

Fig. 6.3 C0M4 Barrett's esophagus containing a 15 × 13 mm (Paris 0-IIa) lesion at 4 o'clock in white light

The presence or absence of erosive esophagitis using the Los Angeles classification should also be reported [11].

The Prague C&M classification is based on validated, explicit, consensus-driven criteria developed by The International Working Group for Classification of Oesophagitis (IWGCO) [3].

Video recordings were scored by an international panel of 29 endoscopists, and the overall reliability coefficients for endoscopic recognition of BE ≥1 cm was 0.72 (0.91 for C and 0.66 for M), whereas for BE ≤1 cm, it was 0.22. These results demonstrated that the C&M grading system could be easily understood; it has been validated by endoscopists with different experience levels [22, 23].

This classification uses the top of GF as landmark for the distal BE segment because in the most patients with BE, the PVs are not visible with the standard endoscopic imaging and may be less clear if esophagitis is present [3].

All guidelines recommend to describe the extent of BE using the Prague criteria avoiding to define endoscopic segment of BE as "long," "short," and "ultra-short" without an established cut-off for any of these categories [9–11].

In this classification, segments of Barrett's epithelium shorter than 1 cm are not considered, due to inability of endoscopists to reliably measure it.

Epstein A et al. analyzing data coming from two prospective patient cohorts found metaplastic-appearing mucosa in islands in 40.7% of entire cohort, specialized intestinal metaplasia confirmed in 10.8% of cases, and 18% of island extended farther than the Prague M segments by a mean distance of 2.3 cm. The prevalence of dysplasia in these islands was 3.4%, so the authors concluded that excluding columnar islands from Prague endoscopic classification could lead to an underestimation of the presence of BE as well as a falsely low-grade dysplasia [22].

British Society of Gastroenterology guidelines suggest a modification of the Prague classification in future, providing an easier system for recording columnar-lined epithelium not continuous with the GEJ [10].

6.3 Biopsy Protocol

The diagnosis of BE requires both endoscopic findings and histologic confirmation; it becomes necessary to adopt a standard bioptic sampling protocol. SIM and dysplasia have a patchy distribution into the columnar epithelium, and, Eloubeidi et al. study, reported that the diagnostic yield of SIM decreased with the declining length of BE: >65% (>5 cm), 50% (3–5 cm), 25% (<3 cm) [24].

Therefore, diagnostic yield increases with an increased number of biopsies and an aggressive biopsy protocol of four quadrant biopsies every 1–2 cm has been recommended.

The Seattle Protocol involves 4-quadrant biopsy sampling every 2 cm throughout the columnar-lined esophagus. Furthermore, every mucosal irregularity should be sampled since it is more likely to hide dysplastic tissue [25, 26].

Target biopsy samples from visible lesions should be taken before random biopsies; distal area should be biopsied first starting 1–2 cm above GEJ and advancing proximally to minimize obscure view from bleeding [10]. This method is actually recommended by the American Gastroenterological Association [27].

In patients with previous diagnosis of dysplasia history, a 4-quadrant biopsies every 1 cm protocol should be performed, due to the "mosaic pattern" with which dysplasia is manifested [9].

A prospective study demonstrated a significant increase in the detection of early lesions when the Seattle bioptic protocol was applied [28].

However, this protocol only samples up to 5% of BE epithelium and can miss up to 40% of treatable neoplasia [29].

The adherence to this protocol is limited, especially in long segment of BE; many practicing gastroenterologists take a smaller number of biopsies at

unspecified intervals. Ishaq et al. in a study involving 228 gastroenterologists in the United Kingdom indicated that the average number of biopsies taken was four [30].

Harrison et al. evaluated the number of biopsies needed to identify SIM in 125 patients (BE mean length: 4.9 cm; range: 1–11 cm). Their data pointed out that at least eight random biopsies were required to diagnose SIM. In contrast, if only four biopsies were obtained, goblet cells were diagnosed in only 34.7% of cases [31].

When it is not possible to perform eight biopsies, given the small length of columnar epithelium, four biopsies per cm of circumferential BE (one on each quadrant) and one biopsy per cm in tongues of BE should be obtained [32].

It has been demonstrated that BE without dysplasia was more frequently located in the posterior wall of the esophagus (38.4%) rather than in the right (28.8%), anterior and left wall (22.6% vs. 10.2%, respectively). Dysplastic lesions were more commonly detected in the posterior (39.3%) than in the anterior (35.8%), right (21.4%), and left wall (3.5%).

Thus, during endoscopic assessment of BE, more attention should be focused at the right hemisphere and at the posterior wall of the lower esophagus where advanced lesions may occur with higher frequency [33–37].

When endoscopic findings are suggestive for BE but histology doesn't confirm the diagnosis, it is recommended to repeat biopsies after 1–2 years, since about 30% of these patients are going to get a BE diagnosis at one of the following exams [38].

In order to help pathologists to distinguish between true BE and IM of the cardia, the endoscopist should label the site from which the samples are taken (esophagus, proximal stomach/cardia) [10, 39].

The development of advanced endoscopic imaging techniques that increase the detection of both IM and dysplasia in BE has been the focus of intense research. The aim of such imaging modalities is the possibility to identify dysplasia without the need for biopsy or with the ability to focus biopsies to areas most likely to contain dysplastic epithelium.

Modern endoscopes with a high-resolution charged-coupled device (CCD), combined with high-definition television monitors, provide excellent image quality, having a high number of pixels (up to one million). HRE are also equipped with an electronic zoom system that provides magnification, allowing the identification of mucosal patterns and microvessels. The maximal efficiency of these systems is in combination with chromoendoscopy (CE) [40, 41].

Dyes are used in CE to enhance endoscopic detection. Methylene blue (MB) is a vital dye absorbed by columnar intestinal-type cells and has been used to improve the yield of MI and dysplasia in BE. Its absorption is reduced in areas of high-grade dysplasia (HGD) and early cancer due to the paucity of goblet cells in the setting of dysplasia, while the behavior of low-grade dysplasia is unpredictable. Biopsies could be targeted on suspicious areas only. Conflicting data come from literature regarding the utility of MB in detecting MI and dysplasia when compared with conventional 4-quadrant random biopsy [42]. In addition, the combination of methylene blue and white-light illumination has recently been reported to increase the genetic damage in Barrett's tissue [43].

Indigo carmine (IC) is a contrast agent not absorbed by cells. It enhances the mucosal irregularities of the mucosa and can help in the identification of BE. Sharma et al. used indigo carmine combined with high-magnification endoscopy to identify and described three patterns of BE: ridged/villous, circular, and irregular/distorted. The ridged/villous pattern had a sensitivity of 71% for IM, while the distorted pattern had a specificity of 88% in the identification of HGD/early cancer [44].

Instillation of acetic acid (AA) on the esophageal mucosa, in conjunction with high-resolution and magnifying endoscopy has been investigated to identify IM and dysplasia in BE.

AA results in reversible alterations of the proteins in the cell, modifying their optical properties, allowing the clear demarcation of BE and the identification of mucosal pit-patterns. When 1–3% AA is sprayed on BE epithelium, there is an initial aceto-whitening reaction for a few minutes, improving the examination of BE epithelium: dysplastic areas tend to lose aceto-whitening faster than non-dysplastic areas.

Guelrud et al. were the first to describe this method in BE patients, and they identified four pit-patterns: type I-round pits, type II-reticular, type III-villous, type IV ridged with a cerebriform appearance of the mucosa. Only types III and IV were highly predictive of the presence of SIM [45].

Data coming from literature about the usefulness of AA in predicting the presence of SIM in BE are conflicting.

Hoffman et al. evaluated the diagnostic yield of magnifying endoscopy with AA targeted biopsies compared with random biopsies in patients with BE greater than 2 cm. The authors simplified the Guelrud's classification: type I–II (gastric epithelium) and type III–IV (BE). Magnifying endoscopy predicted BE with a sensitivity and specificity of 100% and 66%, respectively. AA biopsies allowed a diagnosis of SIM in 78% of patients, while in the random group was 57%. The number of biopsies needed to confirm BE was half when AA was used. Only types III and IV were predictors of BE with a sensitivity of 100%, specificity of 64%, and accuracy rate of 83%. However, the authors stated that the combined approach cannot be recommended in daily clinical practice [46].

Pech et al. in their prospective study showed similar positive results: when AA (balsamic vinegar) without magnification endoscopy was used to study surface pattern in 20 patients with BE, the reliability of predicting the presence of specialized columnar epithelium was high [47].

Coletta et al. meta-analysis evaluating 13 prospective studies showed that AA had a high sensitivity for SIM characterization, but a poor specificity, suggesting that histological confirmation is necessary when AA is positive.

In contrast, non-magnification AA chromoendoscopy had an overall high diagnostic accuracy for detecting HGD/early cancer, comparable to that of more advanced imaging techniques such as narrow-band imaging with magnification [48].

Similar data have been reported in ASGE Technology Committee systematic review and meta-analysis: the pooled sensitivity, NPV, and specificity for AA chromoendoscopy (96.6%, 98.3%, and 84.6%, respectively), as well as for

narrow-band imaging and confocal laser endomicroscopy, into detection of dysplasia in BE met the thresholds set by the American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) initiative on imaging in BE, who recommends that a new imaging technology with target biopsy should have a per-patient sensitivity ≥90%, specificity ≥80%, and a NPV ≥98% in order to eliminate the need for random biopsy during surveillance [49, 50].

Bhandari et al. have showed that histology on AA-target biopsies was more cost-effective than the Seattle protocol in high-risk population [51] (Figs. 6.4 and 6.5).

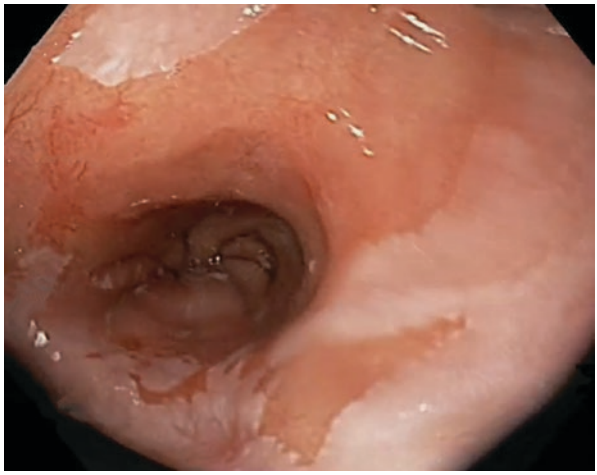

Fig. 6.4 Barrett's esophagus on white-light endoscopy

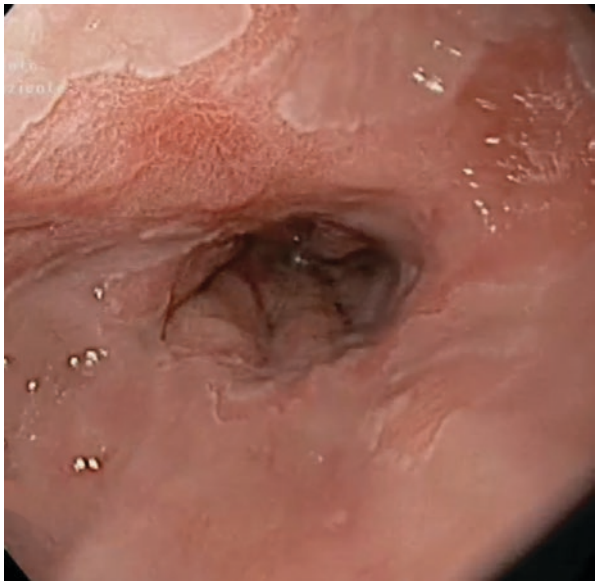

Fig. 6.5 Same patient as Fig. 6.4 after acetic acid chromoendoscopy showing normal Barrett's esophagus with an area of HGD highlighted by differential loss of aceto-whitening

Recently, a new classification system known as PREDICT (the Portsmouth acetic acid classification) for the diagnosis of Barrett's neoplasia using AA has been developed and validated.

This classification is based on two criteria: focal loss of aceto-whitening and surface patterns of Barrett's mucosa. The application of PREDICT improved the sensitivity and NPV for the identification of Barrett's neoplasia [52].

Although chromoendoscopy, in comparison to other endoscopic imaging modalities, is relatively inexpensive, requiring only a spray catheter and contrast agent, it has not gained widespread clinical use because it is considered time consuming, requiring careful execution of the all necessary steps, and it is strictly dependent on the operator, with high inter-observer and intra-observer variability, as reported by Meining et al. [53]

Except for PREDICT classification, published in September 2017, no previous standardized classification criteria of mucosal patterns have been established for dye-based chromoendoscopy. Therefore, advanced imaging modalities have been considered not superior to standard white-light endoscopy in BE surveillance and not recommend for routine use [10, 28, 32].

The unquestionable advantage of CE is that it obliges endoscopists to spend more time inspecting the esophagus, improving the detection of tiny mucosal abnormalities [12].

Gupta et al. study reported that endoscopists with an average inspection time lasting more than 1 min/cm on BE were more likely to detect HGD/EAC than endoscopists with shorter inspections times, suggesting that high quality BE examination should incorporate inspection of the mucosa at a rate of 1 min/cm or slower [54].

Conclusions

During index endoscopy when BE is suspected or in known BE endoscopic surveillance, a careful inspection of the BE mucosa is recommended, cleaning the mucosal surface of mucus, saliva, and food debris using mucolytic agents or antifoaming agent. Endoscopic characteristic of the metaplastic epithelium must be described according to the Praga C&M criteria, reporting the site of the landmarks and the presence and location of visible lesions according to the Paris classification. The Seattle biopsy protocol and target biopsy samples from visible lesions are recommended at the time of diagnosis and at subsequent surveillance.

In our Unit, we perform the endoscopic surveillance of BE patients using HRE under deep sedation with propofol in order to perform an adequate inspection.

In addition, we use an EMR or ESD cap on the tip of the scope that allows a better examination of cardia region, smoothing GF.

References

1. Shariff MK, Varghese S, O'Donovan M, et al. Pilot randomized crossover study comparing the efficacy of transnasal disposable endosheath with standard endoscopy to detect Barrett's esophagus. Endoscopy. 2016;48:110–6.

2. Bennett C, Vakil N, Bergman J, et al. Consensus statements for management of Barrett's dysplasia and early-stage esophageal adenocarcinoma, based on a Delphi process. Gastroenterology. 2012;143:336–46.
3. Sharma P, Dent J, Armstrong D, Bergman JJ, et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. Gastroenterology. 2006;131:1392–9.
4. Aoki T, Hanyu N, Mukai H. Gastroesophageal reflux disease and Barrett's esophagus: inspection in Japan. Sogo Rinsho. 2005;50:2005–8. (in Japanese).
5. Ishimura N, Amano Y, Kinoshita Y. Endoscopic definition of esophagogastric junction for diagnosis of Barrett's esophagus: importance of systematic education and training. Dig Endosc. 2009;21:213–8.
6. Schölvinck DW, Goto O, Seldenrijk CA, et al. Detection of palisade vessels as a landmark for Barrett's esophagus in a western population. J Gastroenterol. 2016;5:682–90.
7. Amano Y, Ishimura N, Furuta K, et al. Which landmark results in a more consistent diagnosis of Barrett's esophagus, the gastric folds or the palisade vessels? Gastrointest Endosc. 2006;64:206–11.
8. Tan WK, di Pietro M, Fitzgerald RC. Past, present and future of Barrett's oesophagus. Eur J Surg Oncol. 2017;43:1148–60.
9. Shaheen NJ, Falk GW, Iyer PG, Gerson LB, American College of Gastroenterology. ACG clinical guideline: diagnosis and management of Barrett's esophagus. Am J Gastroenterol. 2016;11:30–50.
10. Fitzgerald RC, di Pietro M, Ragunath K, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Gut. 2014;63:7–42.
11. Weusten B, Bisschops R, Coron E, et al. Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2017;49:191–8.
12. Conio M. Esophageal chromoendoscopy in Barrett's esophagus: "cons". Gastrointest Endosc. 2006;64:9–12.
13. Paull A, Trier JS, Dalton MD, Camp RC, Loeb P, Goyal RK. The histologic spectrum of Barrett's esophagus. N Engl J Med. 1976;295:476–80.
14. Salimian KJ, Waters KM, Eze O, et al. Definition of barrett esophagus in the United States: support for retention of a requirement for goblet cells. Am J Surg Pathol. 2018;42(2):264–8.
15. Bhat S, Coleman HG, Yousef F, et al. Risk of malignant progression in Barrett's esophagus patients: results from a large population-based study. J Natl Cancer Inst. 2011;103:1049–57.
16. Ishimura N, Amano Y, Appelman HD, et al. Barrett's esophagus: endoscopic diagnosis. Ann N Y Acad Sci. 2011;1232:53–75.
17. Dickman R, Levi Z, Vilkin A, Zvidi I, Niv Y. Predictors of specialized intestinal metaplasia in patients with an incidental irregular Z line. Eur J Gastroenterol Hepatol. 2010;22:135–8.
18. Kim JB, Shin SR, Shin WG, et al. Prevalence of minimal change lesions in patients with nonerosive reflux disease: a case-control study. Digestion. 2012;85:288–94.
19. Spechler SJ, Zeroogian JM, Antonioli DA, Wang HH, Goyal RK. Prevalence of metaplasia at the gastro-oesophageal junction. Lancet. 1994;344:1533–6.
20. Chung CS, Lin CK, Liang CC, Hsu WF, Lee TH. Intentional examination of esophagus by narrow-band imaging endoscopy increases detection rate of cervical inlet patch. Dis Esophagus. 2015;28:666–72.
21. Endoscopic Classification Review Group. Update on the Paris classification of superficial neoplastic lesions in the digestive tract. Endoscopy. 2005;37:570–8. Review.
22. Epstein JA, Cosby H, Falk GW, Khashab MA, et al. Columnar islands in Barrett's esophagus: do they impact Prague C&M criteria and dysplasia grade? J Gastroenterol Hepatol. 2017;32:1598–603.
23. Vahabzadeh B, Seetharam AB, Cook MB, et al. Validation of the Prague C & M criteria for the endoscopic grading of Barrett's esophagus by gastroenterology trainees: a multicenter study. Gastrointest Endosc. 2012;75:236–41.

24. Eloubeidi M, Provenzale D. Does this patient have Barrett's esophagus? The utility of predicting Barrett's esophagus at the index endoscopy. Am J Gastroenterol. 1994;94:937–43.
25. Levine DS, Blount PL, Rudolph RE, et al. Safety of a systematic endoscopic biopsy protocol in patients with Barrett's esophagus. Am J Gastroenterol. 2000;95:1152–7.
26. Spechler SJ, Sharma P, Souza RF, Inadomi JM, Shaheen NJ. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology. 2011;140:1084–91.
27. Reid BJ, Blount PL, Feng Z, et al. Optimizing endoscopic biopsy detection of early cancers in Barrett's high-grade dysplasia. Am J Gastroenterol. 2000;95:3089–96.
28. Fitzgerald RC, Saeed IT, Khoo D, Farthing MJ, Burnham WR. Rigorous surveillance protocol increases detection of curable cancers associated with Barrett's esophagus. Dig Dis Sci. 2001;46:1892–8.
29. Kariv R, Plesec TP, Goldblum JR, et al. The Seattle protocol does not more reliably predict the detection of cancer at the time of esophagectomy than a less intensive surveillance protocol. Clin Gastroenterol Hepatol. 2009;7:653–8.
30. Ishaq S, Harper E, Brown J, et al. Survey of current clinical practice in the diagnosis, management and surveillance of Barrett's metaplasia: a UK national survey. Gut. 2003;53:A32.
31. Harrison R, Path FRC, Perr I, et al. Detection of intestinal metaplasia in Barrett's esophagus: an observational comparator study suggests the need for a minimum of eight biopsies. Am J Gastroenterol. 2007;102:1154–61.
32. Abela JE, Going JJ, Mackenzie JF, McKernan M, O'Mahoney S, Stuart RC. Systematic four-quadrant biopsy detects Barrett's dysplasia in more patients than nonsystematic biopsy. Am J Gastroenterol. 2008;103:850–5.
33. Pera M. Trends in incidence and prevalence of specialised intestinal metaplasia, Barrett's esophagus and adenocarcinoma of the gastroesophageal junction. World J Surg. 2003;27:999–1008.
34. Csendes A, Smok G, Burdiles P, et al. Prevalence of intestinal metaplasia according to the length of specialised columnar epithelium lining the distal esophagus in patients with gastroesophageal reflux. Dis Esophagus. 2003;16:24–8.
35. Spechler SJ. Intestinal metaplasia at the gastroesophageal junction. Gastroenterology. 2004;126:567–75.
36. Bibbò S, Ianiro G, Ricci R, et al. Barrett's oesophagus and associated dysplasia are not equally distributed within the esophageal circumference. Dig Liver Dis. 2016;48:1043–7.
37. Savarino E, Villanacci V. Barrett's esophagus detection: multiple biopsies are useful, even better if you have an "X" on your map. Dig Liver Dis. 2016;48:1041–2.
38. Khandwalla HE, Graham DY, Kramer JR, et al. Barrett's esophagus suspected at endoscopy but no specialized intestinal metaplasia on biopsy, what's next. Am J Gastroenterol. 2014;109:178–82.
39. Srivastava A, Odze RD, Lauwers GY, Redston M, Antonioli DA, Glickman JN. Morphologic features are useful in distinguishing Barrett esophagus from carditis with intestinal metaplasia. Am J Surg Pathol. 2007;31:1733–41.
40. Kara MA, Peters FP, Rosmolen WD, Krihnadath KK, ten Kate FJW, Fockens P, Bergman JJGHM. High-resolution endoscopy plus chromoendoscopy or narrow-band imaging in Barrett's esophagus: a prospective randomized crossover study. Endoscopy. 2005;37:929–36.
41. Elta GH, Wang KK. Enhanced endoscopic imaging. Preface. Gastrointest Endosc Clin N Am. 2009;19:xiii–xiv.
42. Ngamruengphong S, Sharma VK, Das A. Diagnostic yield of methylene blue chromoendoscopy for detecting specialized intestinal metaplasia and dysplasia in Barrett's esophagus: a meta-analysis. Gastrointest Endosc. 2009;69:1021–8.
43. Olliver JR, Wild CP, Sahay P, et al. Chrmoendoscopy with methylene blue and associated DNA damage in Barrett's oesophagus. Lancet. 2003;362:373–4.
44. Sharma P, Marcon N, Wani S, et al. Non-biopsy detection of intestinal metaplasia and dysplasia in Barrett's esophagus: a prospective multicenter study. Endoscopy. 2006;38:1206–12.

45. Guelrud M, Herrera I, Essenfeld H, Castro J. Enhanced magnification endoscopy: a new technique to identify specialized intestinal metaplasia in Barrett's esophagus. Gastrointest Endosc. 2001;53:559–65.
46. Hoffman A, Kiesslich R, Bender A, et al. Acetic acid-guided biopsies after magnifying endoscopy compared with random biopsies in the detection of Barrett's esophagus: a prospective randomized trial with crossover design. Gastrointest Endosc. 2006;64:1–8.
47. Pech O, Petrone MC, Manner H, et al. One-step chromoendoscopy and structure enhancement using balsamic vinegar for screening of Barrett's esophagus. Acta Gastroenterol Belg. 2008;71:243–5.
48. Coletta M, Sami SS, Nachiappan A, Fraquelli M, Casazza G, Ragunath K. 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.
49. ASGE Technology Committee, Thosani N, Abu Dayyeh BK, Sharma P, et al. ASGE Technology Committee systematic review and meta-analysis assessing the ASGE preservation and incorporation of valuable endoscopic innovations thresholds for adopting real-time imaging-assisted endoscopic targeted biopsy during endoscopic surveillance of Barrett's esophagus. Gastrointest Endosc. 2016;83:684–98.
50. Sharma P, Savides TJ, Canto MI, et al. ASGE Technology and Standards of Practice Committee. The American Society for Gastrointestinal Endoscopy PIVI (preservation and incorporation of valuable endoscopic innovations) on imaging in Barrett's esophagus. Gastrointest Endosc. 2012;76:252–4.
51. Bhandari P, Kandaswamy P, Cowlishaw D, Longcroft-Wheaton G. Acetic acid-enhanced chromoendoscopy is more cost-effective than protocol-guided biopsies in a high-risk Barrett's population. Dis Esophagus. 2012;25:386–92.
52. Kandiah K, Chedgy FJQ, Subramaniam S, 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. 2017. https://doi.org/10.1136/gutjnl-2017-314512. pii: gutjnl-2017-314512 [Epub ahead of print] PubMed PMID: 28970288.
53. Meining A, Rosch T, Kiesslich R, et al. Inter- and intra-observer variability of magnification chromoendoscopy for detecting specialized intestinal metaplasia at the gastroesphageal junction. Endoscopy. 2004;36:160–4.
54. Gupta N, Gaddam S, Wani SB, Bansal A, Rastogi A, Sharma P. Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus. Gastrointest Endosc. 2012;76:531–8.