Rio de Janeiro Global Consensus on Landmarks, Definitions, and Classifications in Barrett's Esophagus: World Endoscopy Organization Delphi Study

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BACKGROUND AND AIMS: Despite the significant advances made in the diagnosis and treatment of Barrett's esophagus (BE), there is still a need for standardized definitions, appropriate recognition of endoscopic landmarks, and consistent use of classification systems. Current controversies in basic definitions of BE and the relative lack of anatomic knowledge are significant barriers to uniform documentation. We aimed to provide consensus-driven recommendations for uniform reporting and global application. **METHODS:** The World Endoscopy Organization Barrett's Esophagus Committee appointed leaders to develop an evidence-based Delphi study. A working group of 6 members identified and formulated 23 statements, and 30 internationally recognized experts from 18 countries participated in 3 rounds of voting. We defined consensus as agreement by ≥80% of experts for each statement and used the GRADE tool to assess the quality of evidence and the strength of recommendations. **RESULTS:** After 3 rounds of voting, experts achieved consensus on 6 endoscopic

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MEETING SUMMARY

landmarks (palisade vessels, gastroesophageal junction, squamocolumnar junction, lesion location, extraluminal compressions, and quadrant orientation), 13 definitions (BE, hiatus hernia, squamous islands, columnar islands, Barrett's endoscopic therapy, endoscopic resection, endoscopic ablation, systematic inspection, complete eradication of intestinal metaplasia, complete eradication of dysplasia, residual disease, recurrent disease, and failure of endoscopic therapy), and 4 classification systems (Prague, Los Angeles, Paris, and Barrett's International NBI Group). In round 1, 18 statements (78%) reached consensus, with 12 (67%) receiving strong agreement from more than half of the experts. In round 2, 4 of the remaining statements (80%) reached consensus, with 1 statement receiving strong agreement from 50% of the experts. In the third round, a consensus was reached on the remaining statement. **CONCLUSIONS:** We developed evidence-based, consensus-driven statements on endoscopic landmarks, definitions, and classifications of BE. These recommendations may facilitate global uniform reporting in BE.

Keywords: Barrett's esophagus; Definitions; Landmarks; Classifications; Delphi consensus; Reporting.

Barrett's esophagus (BE), the only known premalignant condition for esophageal adenocarcinoma (EAC), is characterized by columnar epithelium replacement of the normal esophageal squamous epithelium.[1] The impact of these 2 diseases is global; although there is a trend toward an increased prevalence of BE diagnosis in Asian countries,[2] in recent decades incidence and mortality of EAC have risen in the United States 6- and 7-fold, respectively.[3]

Despite the significant advances made in the diagnosing and treatment of BE, there is a need for standardized definitions, appropriate recognition of endoscopic landmarks, and consistent use of classifications.[4] Current controversies, including the exact location of the gastroesophageal junction (GEJ), residual and recurrent BE postendoscopic therapy, and relative lack of knowledge for anatomic landmarks, are significant barriers for uniform documentation. The endoscopist's perception of these shortcomings also constitutes a barrier to adopting current guidelines.

The World Endoscopy Organization Ad-hoc Barrett's Esophagus Committee conceived the need for a consensus on these essentials and nominated international experts to convene meetings and develop critical statements to provide consensus-driven recommendations for uniform, globally applicable reporting in research and clinical practice. The endorsed statements have been named the Rio de Janeiro global consensus on definitions, endoscopic landmarks, and classification systems in BE because they were first presented in a special session during the second World Congress of Endoscopy ENDO 2020, organized by the World Endoscopy Organization and held in Rio de Janeiro, Brazil, in March 2020.

Methods

We aimed to develop an evidence-based Delphi study throughout a series of in-person and virtual meetings.[5] Our first meeting occurred during Digestive Disease Week in May 2019. The World Endoscopy Organization Barrett's Esophagus Committee appointed 2 consensus leaders (F.E. and P.S.) based on their clinical expertise, leadership, and international recognition; using these same criteria, consensus leaders selected members for the working (C.H., D.A., H.M., and V.T.C.) and consensus groups and defined the timeline. Thirty internationally recognized experts from 18 countries comprised the consensus experts' panel.

The main steps in the process were to select the working and experts groups, identify relevant clinical areas, perform a systematic review of the literature to support the statements by a key-words search (Appendix 1), draft the statements, and anonymously vote for up to 3 rounds and provide feedback for each statement. From May 2019 to October 2019, consensus leaders and members of the working group collected the evidence to draft the initial statements based on literature review and experts' opinions throughout a series of virtual-based meetings. Experts received the statements and accompanying text, figures, and references in November 2019 and voted on the statements through an electronic 1-option questionnaire using a 5-point Likert scale: 1 = Strongly agree (A+), 2 = Agree (A), 3 = Neither agree nor disagree (U), 4 = Disagree (D), and 5 = Strongly disagree (D+) (Appendix 2).

We specified, a priori, that consensus would be achieved for a statement if ≥80% of experts were in agreement (A+ or A). Statements that did not achieve consensus were modified based on experts' anonymous comments for subsequent rounds of voting until consensus was achieved. After the third round of voting, statements not reaching an agreement were not eligible for endorsement. We used the GRADE tool to assess the quality of evidence and the strength of recommendations (Appendix 3).[6] Finally, during the second World Congress of Endoscopy, leaders and international experts gathered to debrief the study, present the main findings of the consensus, and develop a ready-to-use guide for practitioners.

Results

After 3 rounds of voting, all 23 statements achieved consensus. Experts achieved consensus on 6 endoscopic landmarks (palisade vessels [PVs], GEJ, squamocolumnar junction, lesion location, extraluminal compressions, and quadrant orientation), 13 definitions (BE, hiatus hernia, squamous islands, columnar islands, Barrett's endoscopic therapy [BET], endoscopic resection, endoscopic ablation, systematic inspection, complete eradication of intestinal metaplasia [CEIM], complete eradication of dysplasia [CED], residual disease, recurrent disease, and failure of endoscopic therapy), and 4 classification systems (Prague, Los

Abbreviations used in this paper: **BE, Barrett's esophagus; BET, Barretts endoscopic therapy; BING, Barrett's International NBI Group; CED, complete eradication of dysplasia; CEIM, complete eradication of intestinal metaplasia; EAC, esophageal adenocarcinoma; EMR, endoscopic mucosal resection; GEJ, gastroesophageal junction; HGD, high-grade dysplasia; IM, intestinal metaplasia; NBI, narrow-band imaging; PV, palisade vessels; RFA, radiofrequency ablation.**

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Angeles, Paris, and Barrett's International NBI Group [BING]). In round 1, 18 statements (78%) reached consensus, with 12 (67%) receiving strong agreement from more than half of the experts. In round 2, 4 remaining statements (80%), with 1 statement receiving strong agreement from 50% of experts. In the third round, consensus was reached on the remaining statement (Figure 1). Table 1 summarizes GRADE recommendations for quality of evidence and the strength of recommendation for each statement with supporting references.

Endoscopic Landmarks

PVs are longitudinal blood vessels in the lamina propria of the distal esophagus that communicate with the submucosal vessels in the gastric cardia and could be used to identify the GEJ endoscopically. *Agreement: A+, 20%; A, 63%; U, 10%; D, 7%; D+, 0%*

Evidence: Moderate

Recommendation: Strong

PVs are longitudinal veins located in the lamina propria of the lower esophagus that disappears from endoscopic view by becoming submucosal at the GEJ[7] (Figure 2). Although some Japanese guidelines consider the distal end of lower PVs as the landmark to identify the GEJ,[8] in a Japanese study, PVs had a significantly lower concordance to identify the GEJ than the proximal end of gastric folds when participant endoscopists were instructed in the Prague C&M criteria.[7] Endoscopic identification of PVs can be obscure in patients with BE or mucosal dysplasia, and their detection needs insufflation.[9] Western endoscopists' concerns relate to the variability, reproducibility, and difficulty in identifying PVs.

The GEJ is defined endoscopically as the anatomic border between the tubular esophagus and the proximal stomach defined by the proximal end of the gastric folds; the GEJ defines the distal extent of BE. *Agreement: A+, 60%; A, 27%; U, 0%; D, 3%; D+, 10%*

Evidence: Very low

Recommendation: Strong

Practitioners need to identify the GEJ landmark to define the distal extent of BE. Several definitions have been proposed for the GEJ, including the region where the tubular esophagus pinches before widening, the widening of the tubular esophagus into the stomach, and the distal end of longitudinal PVs.[8] However, it is difficult to localize the GEJ using the first 2 definitions, the PVs may be obscured in BE, and even among Japanese endoscopists concordance for the identification of the GEJ was lower when using the PVs than when using the proximal end of the gastric folds.[7] Thus, most experts and society guidelines recommend using the proximal extent of the gastric folds as the most suitable landmark to identify the GEJ[10–12] (Figure 2) with the caveat that the location of this landmark is affected slightly by excessive air inflation.[7]

The squamocolumnar junction is the transition zone between the stratified squamous mucosa of the esophagus and the metaplastic mucosa of BE or the columnar mucosa of the gastric cardia. *Agreement: A+, 63%; A, 37%; U, 0%; D, 0%; D+, 0%*

Evidence: Low

Recommendation: Strong

Identification of the squamocolumnar junction landmark or the Z-line is critical to determine the circumferential and maximal extents of BE. In an individual without BE, the GEJ and the squamous columnar junction should coincide[13] (Figure 2). BE is currently diagnosed when the squamous columnar junction is proximal to the GEJ by $\geq$1 cm with evidence of intestinal metaplasia (IM) on biopsy.[10] IM from a squamous columnar junction $<$ 1 cm above the GEJ has

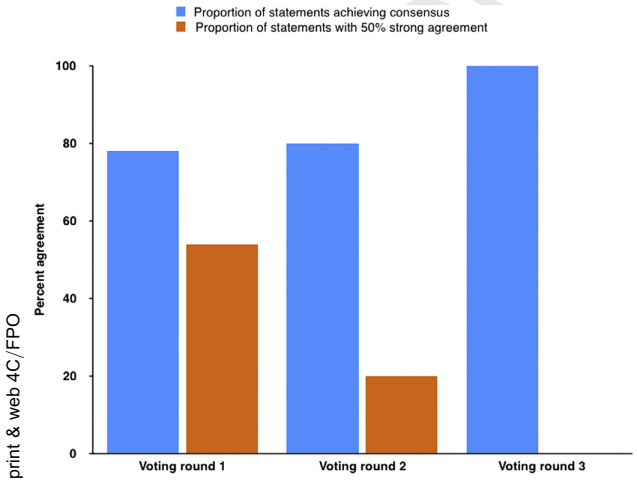

Figure 1. The proportion of statements achieving consensus and proportion of statements reaching strong agreement from >50% of experts with each round of voting.

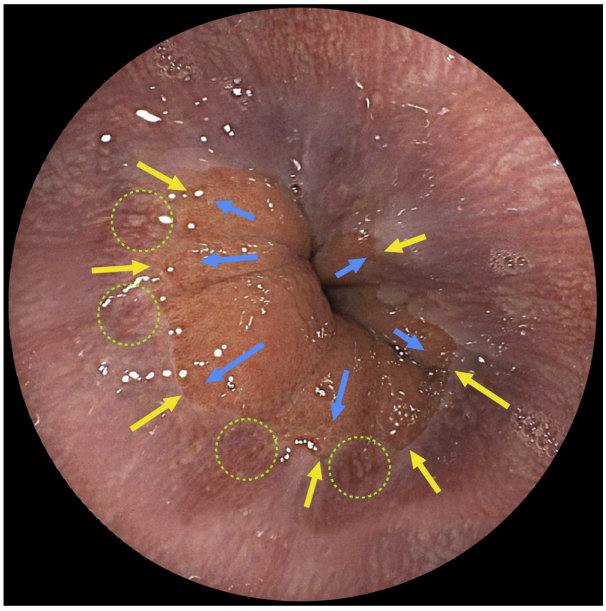

Figure 2. Normal endoscopic appearance of the GEJ. The proximal end of the gastric folds (*blue arrows*), the distal end of longitudinal palisade vessels (*green dotted circles*), and the squamous columnar junction (*yellow arrows*) coincide in patients with a normal appearance of the GEJ.

Table 1. GRADE Recommendations for Quality of Evidence and Strength of Recommendation for Each Statement With Supporting References

Statements	Quality of Evidence	Strength of Recommendation	References
PVs refer to longitudinal blood vessels in the lamina propria of the distal esophagus that communicate with the submucosal vessels in the gastric cardia and could be used to identify the GEJ endoscopically.	Moderate	Strong	7–9
The GEJ is defined endoscopically as the anatomic border between the tubular esophagus and the proximal stomach defined by the proximal end of the gastric folds; the GEJ defines the distal extent of BE.	Very low	Strong	7, 8, 10–12
The squamous columnar junction is the transition zone between the stratified squamous mucosa in the esophagus and the metaplastic mucosa of BE or the columnar mucosa of the gastric cardia.	Low	Strong	10, 13–15
The distance from the incisors is a simple and accurate measure to determine the longitudinal location of esophageal lesions.	Low	Strong	16, 17
Extraluminal compressions on the anterior esophageal wall caused by the left main bronchus and left atrium can facilitate the location of esophageal lesions.	Low	Strong	16, 18–21
Quadrant identification at the GEJ is facilitated by instilling 3–4 mL of water through the endoscope's working channel, which identifies the left quadrant by gravity in the left lateral decubitus position.	Very low	Weak	16, 21
BE is defined as a columnar-lined esophagus confirmed with IM on biopsy, extending at least 1 cm above the GEJ.	Low	Strong	12, 14, 22–24
A hiatus hernia is a gastric pouch that extends from the diaphragmatic pinch distally to the GEJ proximally.	Low	Weak	25–27
Squamous islands are discrete areas of whitish or pale-colored squamous epithelium, seen at endoscopy, that are surrounded by columnar Barrett's epithelium.	Low	Strong	28–30
Columnar islands are discrete areas of columnar BE, seen at endoscopy, surrounded by paler-colored squamous esophageal epithelium and discontinuous from the circumferential and maximal extent of Barrett's segment.	Low	Strong	10, 31
BET is the eradication of dysplastic BE or intramucosal EAC by tissue resection and/or ablation during endoscopy.	Very low	Strong	10, 32–36
Endoscopic resection in BE is the removal of visible neoplastic lesions using EMR or endoscopic submucosal dissection techniques.	Very low	Strong	32, 33, 37–39
Endoscopic ablation is the destruction of dysplastic or neoplastic tissue by heating or freezing; this may be performed in non-nodular or residual BE after endoscopic resection of visible lesions.	Very low	Strong	35, 40–45
Systematic inspection of Barrett's mucosa with high-definition white-light endoscopy should be performed to identify any discrete lesions or areas of mucosal abnormality, which should be biopsied, in addition to routine, 4-quadrant biopsies every 1–2 cm.	Low	Weak	10, 46–48
CEIM is the presence of only neosquamous epithelium and absence of columnar-lined epithelium or IM on surveillance biopsies.	Very low	Strong	49–51
CED is the absence of dysplasia or intramucosal EAC on surveillance biopsies of the treated BE segment with or without neosquamous epithelium.	Very low	Strong	10, 51, 52

Table 1. Continued

Statements	Quality of Evidence	Strength of Recommendation	References
Residual disease in BE is the presence of columnar-lined esophagus or columnar islands and IM and or dysplasia in biopsies during surveillance endoscopies after BET without achieving CEIM.	Very low	Strong	53–54
Recurrent BE is the presence of columnar-lined esophagus or columnar islands at endoscopy with confirmed IM and/or dysplasia in biopsies when CEIM has been achieved after BET.	Very low	Strong	10, 49, 50, 55–57
Failure of BET is defined as persistent columnar-lined esophagus with an inadequate response after at least 4 ablation sessions (after resection of focal lesions).	Very low	Weak	40, 56–61
The Prague criteria should be used to document the circumferential and maximal extent of BE above the GEJ.	Low	Strong	11, 12, 23, 62–64
The Los Angeles classification should be used to describe the appearance and the grade of severity of erosive esophagitis during endoscopy.	Moderate	Strong	65–67
The Paris endoscopic classification should be used to describe all visible lesions suspicious of neoplasia during BE endoscopic examination.	Very low	Strong	68–69
The BING criteria is a validated system used to identify and describe HGD/EAC endoscopically in BE patients with the use of NBI.	Very low	Weak	70, 71

demonstrated a very low risk of progression to EAC,[14] and authorities have described this as specialized IM at the GEJ.[10,15]

The distance from the incisors is a simple and accurate measure to determine the longitudinal location of esophageal lesions. *Agreement: A+, 40%; A, 57%; U, 0%; D, 3%; D+, 0%*

Evidence: Low

Recommendation: Strong

Measurement of the distance from the incisors, using the insertion depth markings of the endoscope, is a simple method to determine the longitudinal location of esophageal lesions and estimate the extent of BE.[16,17] A precise location facilitates interventions by a second therapeutic endoscopist, documents lesion eradication during surveillance, and determines the extent of biopsies when using the Seattle protocol.[16] Although the GEJ can also be used to determine the location of a lesion, it is influenced by breathing, insufflation, and presence of a hiatus hernia.

Extraluminal compressions on the anterior esophageal wall caused by the left main bronchus and left atrium can facilitate the location of esophageal lesions. *Agreement: A+, 17%; A, 67%; U, 13%; D, 3%; D+, 0%*

Evidence: Low

Recommendation: Strong

Endoscopic, anatomic, and radiologic studies have confirmed the existence of extraluminal compressions in the esophagus.[16,18,19] Using high-definition white-light endoscopy, the left main bronchus and left atrium compressions were consistently identified at 25.8 cm (standard deviation, 2.3) from the incisors in 99% of patients and at 31.4 cm (standard deviation, 2.4) from the incisors in 100% of patients. Endoscopic ultrasound confirmed that both landmarks were at the anterior esophageal wall.[16] Identification of these extraluminal compressions facilitates the location of lesions[16] and photodocumentation of the esophagus.[20,21]

Quadrant identification at the GEJ is facilitated by instilling 3–4 mL of water through the endoscope's working channel, identifying the left quadrant by gravity in the left lateral decubitus position. *Agreement: A+, 20%; A, 60%; U, 13%; D, 7%; D+, 0%*

Evidence: Very low

Recommendation: Weak

Clockwise orientation–based GEJ quadrant identification, which relies on the examiners' endoscopic field, may not identify quadrants accurately. Instilling 3–4 mL of water or indigo carmine dye[16] through the endoscope's working channel when the patient is in the left lateral position identifies the left quadrant by gravity and locates the right quadrant at the opposite side[21] (Figure 3). In addition, identifying the left main bronchus and left atrium landmark on the anterior esophageal wall facilitates recognizing the anterior quadrant at the GEJ and locates the posterior quadrant at the opposite side.[16] After achieving accurate anatomic quadrant identification, a clock-face distribution with 12 o'clock on top precisely locates abnormalities in the esophageal circumference.[21]

Definitions

BE is defined as a columnar-lined esophagus confirmed with IM on biopsy, extending at least 1 cm above the GEJ. *Agreement: A+, 47%; A, 40%; U, 3%; D, 3%; D+, 7%*

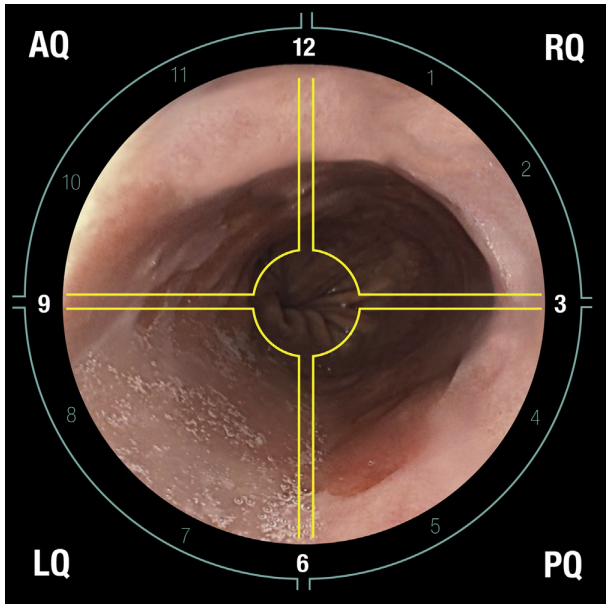

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Figure 3. Quadrant orientation at the GEJ. In the left lateral position, water instilled through the endoscope's working channel falls by gravity identifying the left quadrant (*LQ*). The right quadrant (*RQ*) locates at the opposite side, from 12 to 3 o'clock; the anterior quadrant (*AQ*) locates from 9 to 12 o'clock; and the posterior quadrant (*PQ*) locates from 3 to 6 o'clock. A clock-face distribution with 12 o'clock on top can be used to correctly pinpoint superficial lesions and biopsy sites in the esophageal circumference.

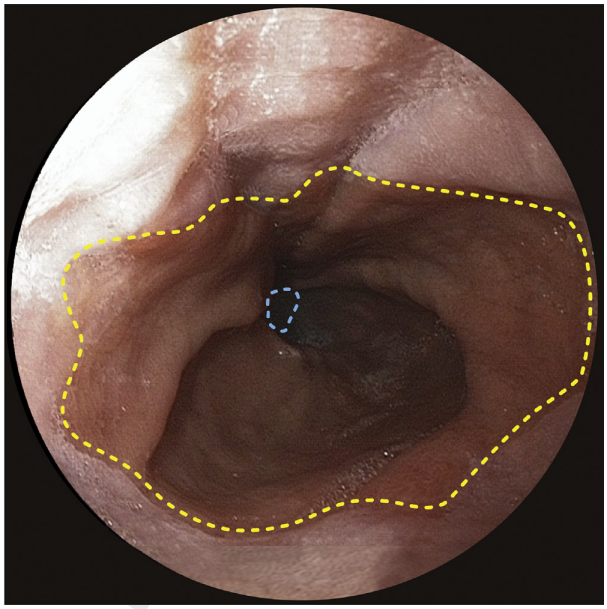

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Figure 4. Endoscopic appearance of a hiatus hernia. The gastric pouch that extends from the diaphragmatic pinch (*blue dashed line*) distally to the upper end of the gastric folds (*yellow dashed line*) proximally relates to a hiatus hernia.

Evidence: Low

Recommendation: Strong

Three columnar-lined epithelial types are associated with BE: gastric fundic, cardia, and intestinal types, the latter characterized by the presence of goblet cells. The lack of high-quality data supporting an elevated risk of EAC in patients with columnar metaplasia without IM[22] supports current guidelines requiring IM on biopsy as a sine qua non to diagnose BE.[10,11] Others recommend the basic histologic definition of BE by using any of the described 3 types of epithelia, precluding confirmation of IM on biopsy.[23] The risk of cancer appears to be higher in patients with long-segment disease than those with a short-segment disease.[24] Authorities currently recommend at least 1 cm of extent above the GEJ to diagnose BE based on the substantially lower cancer progression risk and the poor interobserver agreement for IM < 1 cm.[10,12,14]

A hiatus hernia is a gastric pouch that extends from the diaphragmatic pinch distally to the GEJ proximally. *Agreement: A+, 37%; A, 60%; U, 3%; D, 0%; D+, 0%*

Evidence: Low

Recommendation: Weak

Hiatus hernia refers to a condition in which elements of the abdominal cavity, most commonly the stomach, herniate through the esophageal hiatus into the mediastinum[25] (Figure 4). Determining hiatus hernia prevalence is challenging because of the inherent subjectivity in diagnostic criteria, and estimates vary widely from 10% to 80% in the adult population of North America.[26] Hiatus hernia is associated with an increased risk of BE, even after adjusting for significant confounders such as gastroesophageal reflux disease and body mass index and is strongly associated with long-segment BE.[27]

Squamous islands are discrete areas of whitish or pale-colored squamous epithelium, seen at endoscopy, surrounded by columnar Barrett's epithelium. *Agreement: A+, 47%; A, 53%; U, 0%; D, 0%; D+, 0%*

Evidence: Low

Recommendation: Strong

Squamous islands are areas of neosquamous epithelium that have developed in the metaplastic columnar-lined esophagus. Squamous islands are observed in patients receiving high-dose proton pump inhibitor therapy after antireflux surgery and after endoscopic ablation and photodynamic therapy.[28] Biopsy-induced regrowth of squamous epithelium is presumed to be the origin of squamous islands found frequently in BE during endoscopic surveillance.[29] After staining with Lugol's iodine solution, squamous islands have been reported in up to 78% of patients with BE.[30]

Columnar islands are discrete areas of columnar BE seen at endoscopy, surrounded by paler-colored squamous esophageal epithelium, and discontinuous from the circumferential and maximal extent of Barrett's segment. *Agreement: A+, 43%; A, 57%; U, 0%; D, 0%; D+, 0%*

Evidence: Low

Recommendation: Strong

A retrospective study in patients who underwent esophagogastroduodenoscopy for known BE or BE-associated neoplasia demonstrated metaplastic-appealing

mucosa in columnar islands in 34% of patients; histologically, IM was confirmed in 59% of patients who underwent biopsy.[31] Although excluding columnar islands from a formal assessment of BE extent may underestimate the maximal extent of BE and overlook the highest grade of dysplasia,[31] currently data are limited the clinical importance of these islands, which are discontinuous from the BE segment. Because columnar island mucosa were not included in the Prague classification, authorities recommend reporting them separately in the endoscopy report.[10]

BET is the eradication of dysplastic BE or intramucosal cancer by tissue resection and/or ablation during endoscopy. *Agreement: A+, 70%; A, 23%; U, 7%; D, 0%; D+, 0%*

Evidence: Very low

Recommendation: Strong

BET aims to eradicate nodular dysplasia/EAC and achieve CEIM, decreasing the likelihood of recurrent dysplasia. Methods of tissue removal for visible lesions include endoscopic mucosal resection (EMR)[32] and endoscopic submucosal dissection.[33] In patients with low-grade dysplasia, histologic confirmation by an expert gastrointestinal pathologist is recommended, as is a repeat examination with high-definition white-light endoscopy under maximal acid suppression to rule out the presence of visible lesions.[34] For patients with confirmed nonvisible low-grade dysplasia and without life-limiting comorbidity, radiofrequency ablation (RFA) is considered the preferred treatment modality, although endoscopic surveillance every 12 months is an acceptable alternative.[10,35,36]

Endoscopic resection in BET is the removal of visible neoplastic lesions using EMR or endoscopic submucosal resection techniques. *Agreement: A+, 77%; A, 20%; U, 3%; D, 0%; D+, 0%*

Evidence: Very low

Recommendation: Strong

Visible lesions should be resected en bloc to facilitate an accurate histologic assessment. Methods of tissue removal include EMR,[32] multiband EMR,[37] and endoscopic submucosal direction.[33] Based on a Western retrospective study, endoscopic submucosal dissection results in a more definitive treatment of early BE neoplasia, with significantly lower recurrence and residual disease rates and less need for repeat endoscopic treatments than with EMR.[38] Endoscopic resection modifies the diagnosis in at least 30% of patients with Barrett's neoplasia given the larger tissue sample available for histologic analysis, and therefore authorities recommend resection of nodular dysplasia before ablation.[39]

Endoscopic ablation is the destruction of dysplastic or neoplastic tissue by heating or freezing; this may be performed in non-nodular or residual BE after endoscopic resection of visible lesions. *Agreement: A+, 67%; A, 23%; U, 0%; D, 10%; D+, 0%*

Evidence: Very low

Recommendation: Strong

Endoscopic resection of visible lesions without ablation yields unacceptably high recurrence rates of high-grade dysplasia (HGD) and EAC.[40] The main ablative therapies are RFA,[35,41] cryotherapy,[42] and argon plasma coagulation.[43] Although histologic outcomes of cryoballoon ablation and RFA seem to be comparable,[44] RFA is currently the most commonly used ablative therapy with demonstrated safety and efficacy for both CEIM and CED.[35,41] Cryotherapy demonstrated similar rates of CED but lower rates of CEIM when compared with RFA.[43] For patients in whom RFA therapy failed, cryotherapy is frequently used as a second-line option.[45] Argon plasma coagulation seems to be a cost-effective approach often used as a secondary therapy when scattered islands or small tongues of residual columnar tissue are encountered after RFA.[43]

Systematic inspection of Barrett's mucosa with high-definition white-light endoscopy should be performed to identify any discrete lesions or areas of mucosal abnormality, which should be biopsied, in addition to routine, 4-quadrant biopsies every 1–2 cm. *Agreement: A+, 53%; A, 37%; U, 3%; D, 7%; D+, 0%*

Evidence: Low

Recommendation: Weak

High-definition white-light endoscopy is superior to standard-definition white-light endoscopy for detecting dysplastic lesions in BE.[46] A meta-analysis reported the rate of HGD/EAC defined as a neoplasia detection rate of 7% in patients undergoing index endoscopy for screening for BE of 3.5-cm average length.[47] A post-hoc study in which all procedures were performed by experienced endoscopists at academic centers reported that after excluding patients with overtly suspicious lesions, patients with a Barrett's inspection time of at least 1 min/cm were more likely to be reported as having endoscopically suspicious lesions and HGD/EAC.[48] Random 4-quadrant biopsies every 1–2 cm is currently the accepted biopsy protocol for surveillance of BE.[10]

CEIM is the presence of only neosquamous epithelium and absence of columnar-lined epithelium or IM on surveillance biopsies. *Agreement: A+, 57%; A, 40%; U, 0%; D, 0%; D+, 3%*

Evidence: Very low

Recommendation: Strong

After ablation therapy, CEIM is achieved histologically by the presence of neosquamous epithelium and the absence of columnar-lined epithelium or IM in biopsies from the esophageal body and the GEJ.[49,50] In patients with HGD/EAC, focal EMR followed by RFA is as safe and effective as step-wise EMR to achieve CEIM with a lower rate of adverse effects.[51] The long-term durability after CEIM is not well characterized. A study with 2.8 years of follow-up reported recurrent BE in 25% of patients achieving CEIM by RFA, with 75% of recurrences located at the GEJ.[49]

CED is the absence of dysplasia or intramucosal cancer on surveillance biopsies of the treated Barrett's segment with or without neosquamous epithelium. *Agreement: A+, 53%; A, 43%; U, 0%; D, 0%; D+, 3%*

Evidence: Very low

Recommendation: Strong

Although the ultimate goal of BET is to achieve CEIM, frequently CED is achieved without CEIM. Persistent IM after BET increases the risk of dysplasia recurrence,[52] and all efforts to achieve CEIM are critical. In patients with

non-nodular dysplastic BE, RFA is associated with a higher CED rate than other endoscopic alternatives and is currently the preferred treatment method.[10] In patients with nodular HGD/EAC, focal EMR followed by RFA is as safe and effective as stepwise EMR with a lower rate of adverse effects.[51]

Residual disease in BE is the presence of columnar-lined esophagus or columnar islands and IM and/or dysplasia in biopsies during surveillance endoscopies after endoscopic treatment, without achieving CEIM. *Agreement: A+, 43%; A, 47%; U, 3%; D, 7%; D+, 0%*

Evidence: Very low

Recommendation: Strong

Residual disease refers to failure to achieve CEIM and CED after BET. A study reported residual IM in 57% of short-segment BE patients with visible lesions after the first single session of EMR followed by RFA. After the second RFA session, residual IM presented in 5% of patients after a median follow-up of 19 months when using an intention-to-treat analysis.[53] Treatment of residual BE is similar to dysplastic BE and includes endoscopic resection of any visible abnormalities followed by ablation of the remaining residual nondysplastic and dysplastic BE.[54]

Recurrent BE is the presence of columnar-lined esophagus or columnar islands at endoscopy with confirmed IM and/or dysplasia in biopsies when CEIM has been achieved after BET. *Agreement: A+, 43%; A, 43%; U, 7%; D, 7%; D+, 0%*

Evidence: Very low

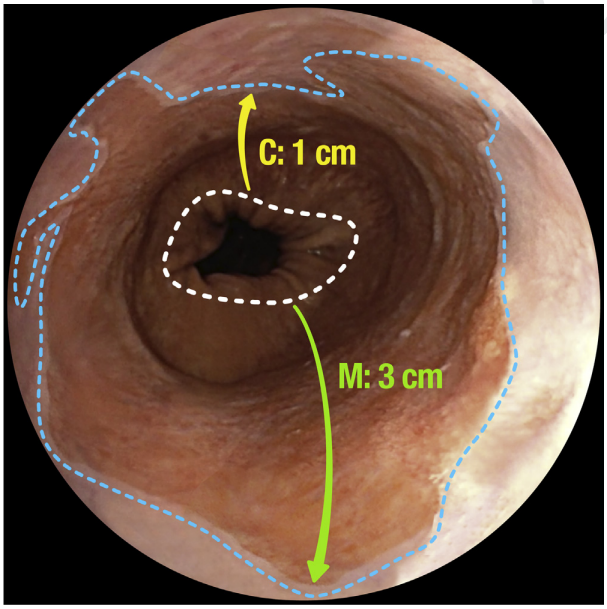

Figure 5. Estimation of the circumferential and maximal extents of BE. BE extends from the proximal end of the gastric folds distally (*white dashed line*) to the squamous columnar junction proximally (*blue dashed line*). The distance from the proximal end of the gastric folds to the shortest circumferential extent and the maximal extent of Barrett's segment are 1 (*yellow arrow*) and 3 cm (*green arrow*), resulting in a C1M3 BE.

Recommendation: Strong

After CEIM and CED, authorities recommend sampling the neosquamous mucosa and the GEJ with 4-quadrant biopsies.[10,55] Although IM limited to the GEJ does not warrant additional ablation therapy,[55] surveillance studies reported dysplasia rates at the GEJ in 24%–28% of all recurrent BE,[49,50] prompting careful surveillance of the esophageal body and the GEJ after ablation. After CEIM, the recurrence rate for IM is substantial, with some studies demonstrating rates of up to 33% within 2 years, with dysplasia and EAC being 22% of the total recurrence cases.[50] Meta-analyses have demonstrated that age, long-segment BE, and prior baseline dysplasia are predictors of high-risk recurrence after ablative therapy.[56,57] It is noteworthy that centers performing >10 ablation procedures per year have a reduced BE recurrent risk compared with centers performing <3 procedures.[56]

Failure of BET is defined as persistent columnar-lined esophagus with an inadequate response after at least 4 adequate ablation sessions (after resection of focal lesions). *Agreement: A+, 23%; A, 63%; U, 3%; D, 7%; D+, 3%*

Evidence: Very low

Recommendation: Weak

Long-segment BE, especially when >10 cm, is considered the strongest predictor of endoscopic treatment failure for CED and CEIM; greater age is also a factor associated with failure to achieve CEIM.[58] Although patients with a more extended baseline BE might need more than 4 RFA sessions,[59] most studies show that patients with non-nodular dysplastic BE ≤ 8 cm in length had ≥87% CEIM when receiving up to 4 RFA sessions.[60,61] Other factors associated with failure of BETinclude piecemeal resection, baseline HGD, no ablative therapy after endoscopic resection, >10 months until achieving a complete response, presence of multifocal neoplasia, and poor control of acid reflux.[40,56,57]

Classification Systems

The Prague criteria should be used to document the circumferential and maximal extent of BE above the GEJ. *Agreement: A+, 70%; A, 23%; U, 7%; D, 0%; D+, 0%*

Evidence: Moderate

Recommendation: Strong

The Prague classification is a consensus-driven, internationally validated set of criteria to uniformly report the C and M extent of BE during endoscopy.[12] Accurate measurement and description of the extent of BE are clinically relevant because the length of BE determines the risk of progression to HGD/EAC[62,63] and surveillance intervals for nondysplastic BE patients[11,23] (Figure 5). When practitioners comply with documenting endoscopic landmarks and the Prague classification, a significant increase in dysplasia detection rate is observed.[64]

The Los Angeles classification should be used to describe the appearance and grade of severity of erosive esophagitis during endoscopy. *Agreement: A+, 50%; A, 47%; U, 3%; D, 0%; D+, 0%*

Evidence: Moderate

Recommendation: Strong

The Los Angeles classification of reflux-associated endoscopic changes in the esophageal mucosa has been recommended for uniform reporting of erosive esophagitis severity and was validated in patients with both pH monitoring and on acid suppression therapy.[65] In the presence of severe erosive esophagitis, authorities recommend against taking biopsies to rule out BE. In patients who have suspected BE and erosive esophagitis of Los Angeles grades B, C, or D, repeat endoscopy is recommended after 8–12 weeks of proton pump inhibitor therapy to ensure healing of the esophagitis and exclude the presence of BE and dysplasia.[66] Studies have shown a prevalence of 9%–27% of BE on repeat endoscopy after proton pump inhibitor therapy.[66,67]

The Paris endoscopic classification should be used to describe all visible lesions suspicious of neoplasia during Barrett's endoscopic examination. *Agreement: A+, 53%; A, 43%; U, 3%; D, 0%; D+, 0%*

Evidence: Very low

Recommendation: Strong

The Paris endoscopic classification of superficial neoplastic lesions proposes a general framework to classify the macroscopic appearance of superficial esophageal, stomach, and colon lesions. The classification distinguishes 3 lesion types: polypoid (type 0-I); nonpolypoid, nonexcavated (type 0-II); and nonpolypoid, excavated (type 0-III). In addition, type 0-II lesions are subdivided into 2 based on the absence (type 0-IIa and 0-IIb) or presence of depression (type 0-IIc).[68] In the columnar epithelium, a cutoff height of 2.5 mm is recommended to differentiate polypoid from nonpolypoid lesions. The clinical relevance of the different subtypes relates to the risk of submucosal invasion and lymph node metastases.[69]

The BING criteria is a validated system used to identify and describe HGD and adenocarcinoma endoscopically in BE using narrow-band imaging modality. *Agreement: A+, 27%; A, 57%; U, 13%; D, 3%; D+, 0%*

Evidence: Very low

Recommendation: Weak

The BING developed an international, consensus-driven narrow-band imaging (NBI) classification to identify HGD and EAC based on a simple classification of mucosal and blood vessel patterns.[70] In the study, a subset of NB images was internally validated by experts blinded to the medical history of the patients and related pathology. When observers suspected dysplasia with a high degree of confidence, the BING criteria had an accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of 92%, 91%, 93%, 89%, and 95%, respectively, with a high level of interobserver agreement. However, the current BING criteria are based only on still images and do not include low-grade dysplasia surface changes. Although the use of the BING criteria is appropriate if NBI is available, further studies are required to evaluate whether NBI or similar electronic technologies should be routinely used during BE surveillance and to define the competency of nonexperts to identify subtle mucosal changes.[71]

Discussion

The lack of agreement on basic definitions, landmarks, and classifications has hampered our ability to build

Table 2. Ready-to-use Guide for Practitioners

Endoscopic documentation
1. Identify the GEJ by recognizing the proximal end of the gastric folds.
2. Identify the squamous columnar junction by recognizing the transition zone between the stratified squamous mucosa of the esophagus and the metaplastic mucosa of BE.
3. Estimate the distance (if any) between the GEJ and the squamous columnar junction by measuring their distances from the incisors.
4. If the above distance is ≥1 cm, use the Prague C & M criteria to determine and report BE's circumferential and maximal extents.
5. Determine the presence of a hiatus hernia by recognizing a gastric pouch between the diaphragmatic pinch and the proximal end of the gastric folds.
6. Describe the presence and grade of erosive esophagitis using the Los Angeles classification. If BE is suspected, repeat endoscopy after healing erosive esophagitis grades B, C, and D.
7. Determine the location of visible lesions using the distance from the incisors and the quadrant of the circumference where the lesion is located.
8. Document the macroscopic appearance of visible suspicious lesions using the Paris classification.
9. Report the type of endoscopic resection (EMR or endoscopic submucosal dissection) used to remove visible lesions.
Inspection and biopsies
1. Identify the 4 quadrants of the GEJ by instilling 3–4 mL of water; recognize the left quadrant by gravity.
2. Inspect the BE segment systematically using high-definition white-light endoscopy.
3. If NBI is available, use the BING criteria to identify and describe HGD/EAC.
4. Perform and document target biopsies of visible lesions followed by 4-quadrant biopsies every 1–2 cm of the BE segment.
5. Perform biopsies of columnar islands and document separately from biopsies of the BE segment.
6. For histologic assessment, the presence of IM on biopsy is a sine qua non for BE diagnosis.
Surveillance
1. Report CEIM and CED or residual or recurrent disease or failure of BET.
2. Report CEIM with at least 1 proven negative biopsy on surveillance endoscopy 3–6 months after therapy.

uniform reporting and quality metrics in BE. In practice, these drawbacks result in misdiagnosis and inappropriate surveillance intervals and explain, in part, the poor compliance with established management protocols. We developed an evidence-based Delphi international consensus to provide clinically relevant recommendations and a ready-to-use guidance for practitioners worldwide. We concentrated on statements that address disparities in global reporting of BE as definitions and terminologies rather than management strategies. In numerous ways, our consensus is remarkable. First, the overall consensus process involved 37 leaders from 18 countries, indicating that these agreements can be applied globally. Second, the statements addressed 4 critical components of BE management, yielding 23 statements with a high level of agreement. Third, several statements focused on the Achilles heel of BE, which is the variability of definition and recognition of endoluminal landmarks that can lead to an incorrect diagnosis, sampling, and surveillance, if inappropriately recognized. Fourth, even though most statements were developed based on the assumption that well-designed, large, randomized trials may never be done, the relevance of our study is demonstrated by the fact that 18 statements (78%) reached consensus in the first round of voting. Finally, because all of our findings are clinically applicable, we developed a ready-to-use guide to help practitioners recognize, diagnose, classify, and report BE (Table 2).

Establishing quality measures in BE is critical to improving clinical practice and is therefore a research priority. Although neoplasia detection rate,[48] Barrett's inspection time,[49] and close compliance with follow-up intervals are known as potential quality indicators in BE, there are no established relationships between former indicators and relevant patient outcomes (eg, postendoscopy neoplasia detection).[4] We believe that adopting these practical and straightforward statements lays the groundwork for standardized reporting in BE and implementing quality measures globally.

Our study has several drawbacks. First, data are scarce and of relatively poor quality relating to landmarks, definitions, surveillance, and classifications in BE, highlighted by 20 statements with low or very low levels of evidence. As a result, we gathered the evidence to formulate the statements primarily from limited randomized controlled trial data, cohort studies, and expert opinions, potentially limiting their clinical adoption. Second, our panel of experts was not composed of a multidisciplinary group but of expert gastroenterologists and educators who regularly manage patients with BE. Thus, the lack of input from other disciplines might have influenced the results and that most statements reached consensus in the first round of voting. Finally, we did not apply a format to standardize experts' comments, resulting in the diverse presentation of clinical viewpoints.

In the future, these statements could serve as the foundation for standardizing endoscopic examination and establishing quality indicators, given the necessity for systematic and uniform reporting and the need to generate benchmarks for quality assessment.[72] Future studies could report their findings using these consensus-driven definitions and landmarks, enabling comparison between cohorts and populations.

In conclusion, we have developed evidence-based, consensus-driven statements on endoscopic landmarks, definitions, and classifications of BE. These recommendations may facilitate global uniform reporting in BE and constitute a foundation for a standardized endoscopic examination and a template for physicians when documenting their quality of care in patients with BE. Implementing this standardized nomenclature further facilitates benchmarking and comparison of outcomes in BE across academic centers and regions around the world.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2022.03.022.

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Conflicts of interest
This author discloses the following: Fabian Emura received a loan of endoscopic equipment from Jomedical SAS. The remaining authors disclose no conflicts.

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Appendix 1

Key Terms for Literature Search

An electronic literature search was performed in PubMed, EMBASE, and Google Scholar from the inception of the databases to October 1, 2019 using the following key words: "BE," "Barrett's esophagus," "Barrett's oesophagus," "BO," "landmarks," "GEJ," "gastro esophageal junction," "SCJ," "squamo-columnar junction," "PV," "palisade vessels," "incisors," "left main bronchus," "left atrium," "quadrants," "HH," "hiatus hernia," "squamous islands," "columnar islands," "low-grade dysplasia," "LGD," "high-grade dysplasia," "HGD," "esophageal adenocarcinoma," "EAC," "EMR," "endoscopic mucosal resection," "multiband EMR," "MB-EMR," "ESD," "endoscopic submucosal dissection," "RFA," "radio frequency ablation," "esophagectomy," "cryotherapy," "HDWLE," "high definition white light endoscopy," "Seattle protocol," "Seattle," "complete eradication of intestinal metaplasia," "CEIM," "complete remission of intestinal metaplasia," "complete eradication of dysplasia," "CED," "complete remission," "residual Barrett esophagus," "recurrent Barrett's esophagus," "EET," "Endoscopic eradication therapy," "BET," Barrett's endoscopic therapy," "failure of Barrett's treatment," "Prague criteria," "Los Angeles classification," "Paris classification," "Paris," "NBI," "narrow band imaging."

Q16 **Appendix 2.** Five-point Likert scale

Point	Description
A+	Strongly agree
A	Agree
U	Neither agree nor disagree
D	Disagree
D+	Strongly disagree

Appendix 3. Overview Of The Grading Of Recommendation Assessment, Development And Evaluation Systems tool

Quality of Evidence	Strength of Recommendation
High: Further research is unlikely to change our confidence in the estimate of the effect • Several high-quality studies with consistent results • In some special cases: one large, high-quality multicenter trial	Strong: When the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Moderate: Further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate • One high-quality study • Several studies with some limitations	Weak: When the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced
Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate • One or more studies with several limitations	
Very low: Any estimate of effect is very uncertain • Expert opinion • No direct research evidence • One or more studies with very severe limitations	