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AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review

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Abstract

DESCRIPTION: The purpose of this best practice advice (BPA) article from the Clinical Practice Update Committee of the American Gastroenterological Association is to provide an update on advances and innovation regarding the screening and surveillance of Barrett's esophagus.

METHODS: The BPA statements presented here were developed from expert review of existing literature combined with discussion and expert opinion to provide practical advice. Formal rating of the quality of evidence or strength of BPAs was not the intent of this clinical practice update. This expert review was commissioned and approved by the AGA Institute Clinical Practice Updates Committee (CPUC) and the AGA Governing Board to provide timely guidance on a topic of high clinical importance to the AGA membership, and underwent internal peer review by the CPUC and external peer review through standard procedures of *Clinical Gastroenterology and Hepatology*.

BEST PRACTICE ADVICE 1: Screening with standard upper endoscopy may be considered in individuals with at least 3 established risk factors for Barrett's esophagus (BE) and esophageal adenocarcinoma, including individuals who are male, non-Hispanic white, age >50 years, have a history of smoking, chronic gastroesophageal reflux disease, obesity, or a family history of BE or esophageal adenocarcinoma.

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2022.06.003.

BEST PRACTICE ADVICE 2: Nonendoscopic cell-collection devices may be considered as an option to screen for BE.

BEST PRACTICE ADVICE 3: Screening and surveillance endoscopic examination should be performed using high-definition white light endoscopy and virtual chromoendoscopy, with endoscopists spending adequate time inspecting the Barrett's segment.

BEST PRACTICE ADVICE 4: Screening and surveillance exams should define the extent of BE using a standardized grading system documenting the circumferential and maximal extent of the columnar lined esophagus (Prague classification) with a clear description of landmarks and the location and characteristics of visible lesions (nodularity, ulceration), when present.

BEST PRACTICE ADVICE 5: Advanced imaging technologies such as endomicroscopy may be used as adjunctive techniques to identify dysplasia.

BEST PRACTICE ADVICE 6: Sampling during screening and surveillance exams should be performed using the Seattle biopsy protocol (4-quadrant biopsies every 1–2 cm and target biopsies from any visible lesion).

BEST PRACTICE ADVICE 7: Wide-area transepithelial sampling may be used as an adjunctive technique to sample the suspected or established Barrett's segment (in addition to the Seattle biopsy protocol).

BEST PRACTICE ADVICE 8: Patients with erosive esophagitis should be biopsied when concern of dysplasia or malignancy exists. A repeat endoscopy should be performed after 8 weeks of twice a day proton pump inhibitor therapy.

BEST PRACTICE ADVICE 9: Tissue systems pathology-based prediction assay may be utilized for risk stratification of patients with nondysplastic BE.

BEST PRACTICE ADVICE 10: Risk stratification models may be utilized to selectively identify individuals at risk for Barrett's associated neoplasia.

BEST PRACTICE ADVICE 11: Given the significant interobserver variability among pathologists, the diagnosis of BE-related neoplasia should be confirmed by an expert pathology review.

BEST PRACTICE ADVICE 12: Patients with BE-related neoplasia should be referred to endoscopists with expertise in advanced imaging, resection, and ablation.

BEST PRACTICE ADVICE 13: All patients with BE should be placed on at least daily proton pump inhibitor therapy.

BEST PRACTICE ADVICE 14: Patients with nondysplastic BE should undergo surveillance endoscopy in 3 to 5 years.

BEST PRACTICE ADVICE 15: In patients undergoing surveillance after endoscopic eradication therapy, random biopsies should be taken of the esophagogastric junction, gastric cardia, and the distal 2 cm of the neosquamous epithelium as well as from all visible lesions, independent of the length of the original BE segment.

Endoscopic screening for Barrett's esophagus (BE) and subsequent surveillance is supported by current societal guidelines based on the potential for early detection of BE, dysplasia and neoplasia, and the option for endoscopic eradication therapy (EET), with an overarching goal of reducing the morbidity and mortality of esophageal adenocarcinoma (EAC).[1,2] However, less than 20% of patients diagnosed with EAC in the United States (US) have a preceding diagnosis of BE,[3] suggesting that current screening paradigms are inadequate.

The purpose of this best practice advice article from the Clinical Practice Update Committee of the American Gastroenterological Association (AGA) is to provide an update on advances and innovation regarding the screening and surveillance of BE. The target audience is all gastroenterologists and endoscopists, and the target patient population is adults with known or suspected BE.

Methods

This expert review was commissioned jointly by the AGA Institute Clinical Practice Updates Committee, the AGA Center for GI Innovation and Technology (CGIT), and the AGA Governing Board to provide timely guidance on a topic of high clinical importance to the AGA membership. The AGA CGIT Consensus Conferences bring together content experts, stakeholders (industry, regulatory, and payors), along with a patient advocate to discuss current needs and gaps in innovation relevant to the topic. This was a comprehensive didactic and discussion session created to provide a novel interactive environment to foster the AGA CGIT mission. The topic of this clinical practice update was thoroughly discussed by expert faculty contributors selected by AGA CGIT, industry representatives, and the patient advocate at the conference organized and hosted by AGA CGIT. The content of this expert review was generated, discussed, and voted upon by the expert faculty contributors at a closed-door meeting during the AGA CGIT conference. All faculty contributors provided up to date declaration of conflicts of interest to ensure credibility of this document, and signed off on the final manuscript, which underwent internal peer review by the Clinical Practice Updates Committee as well as external peer review through standard procedures of *Clinical Gastroenterology and Hepatology*.

Screening for Barrett's Esophagus

Best Practice Advice 1: Screening with standard upper endoscopy may be considered in individuals with at least 3 established risk factors for BE and EAC, including individuals who are male, non-Hispanic white, age >50 years, have a history of smoking, chronic gastroesophageal reflux disease (GERD), obesity, or a family history of BE or EAC.

Current guidelines suggest endoscopic screening for an "at-risk" population.[2] The vast majority of patients (up to 90%) with EAC have never had a diagnosis of BE. A recent meta-analysis of 49 studies suggests that the prevalence of BE in the GERD population is 3%, and this increases with each additional risk factor.[4] These risk factors for BE include the presence of chronic GERD and at least 2 of the following: age >50 years, male gender, Caucasian race, smoking, obesity, family history of BE or EAC.[1] The highest prevalence was seen with family history along with GERD at 23.4%.[4] Chronic GERD is defined as >5 years or symptoms (heartburn or regurgitation) occurring frequently (weekly or greater).

However, the requirement of GERD symptoms has significantly limited the impact of screening on detection of EAC.

The panel discussed the limitations of chronic GERD symptom as a mandatory prerequisite for endoscopic screening. A recent study of prevalent EAC assessed societal guidelines in the US (n = 663) and United Kingdom (UK) (n = 645) to determine the sensitivity of current screening recommendations.[1,5,6] In these cohorts, 54.9% of the US patients and 38.9% of the UK patients would not have been identified by current screening guidelines. Furthermore, the reason most patients (US, 86.5%; UK, 61.4%) did not meet screening guidelines was the lack of symptomatic GERD. Furthermore, a second study of US veterans also identified that >50% of patients with EAC did not have frequent GERD symptoms and would not have met current screening guidelines.[7]

Multiple predictive tools have been developed identify patients at risk of BE. These tools not only use GERD symptoms, but also multiple other clinical and demographic factors implicated in BE and EAC.[8] These predictive indices have been developed for real-time risk assessment without a prerequisite of GERD through patient assessment and questionnaires. From the available tools, the HUNT (Nord-Trondelag Health Study), M-BERET (Michigan BE pREdiction Tool), and Kunzmann tools were found to be more sensitive for predicting BE than GERD symptoms alone.[8] Although further validation of these tools is needed, they can be considered in the clinical evaluation of patients for endoscopic screening.

The optimal number of risk factors for screening remains to be well-defined and inclusion of GERD remains fraught with several limitations. The threshold number of risk factors is largely based on expert opinion. These factors provided the impetus to propose a screening approach that is not restricted to patients with GERD and considers all defined risk factors for BE and EAC. Therefore, screening with standard upper endoscopy may be considered in individuals with at least 3 established risk factors for BE and EAC, including individuals who are male, non-Hispanic white, age >50 years, have a history of smoking, chronic GERD, obesity, or a family history of BE or EAC. The reduction of the valuation of GERD in this paradigm is felt to significantly improve detection of BE and more accurately identify the “at-risk” population. Future studies should assess the impact of this approach (benefits and harms) in screening for BE.

Best Practice Advice 2: Nonendoscopic cell-collection devices can be considered as an option to screen for BE.

Although upper endoscopy with biopsies remains the gold standard for the diagnosis of BE, there is a significant need for noninvasive screening tools that are easy to administer, patient friendly, and cost-effective for the detection of BE. Transnasal endoscopy offers the use of an ultrathin endoscope that can be performed in the office setting without sedation. Although guidelines have acknowledged this as an alternative to sedated endoscopy, it remains costly, expert-dependent, and not desirable to patients.[2] This gap has led to the development of multiple novel cell collection devices which offer a nonendoscopic alternative for screening. Current nonendoscopic cell collection devices include Cytosponge (Medtronic GI Solutions), EsoCheck (Lucid Diagnostics), and EsophaCap (Capnostics) (See Supplementary Appendix). All 3 nonendoscopic devices have demonstrated excellent

tolerability, safety, and sensitivity for the diagnosis of BE. Further data is needed to validate patient selection and the optimal setting for administration of these novel devices in the US.

Endoscopic Examination of Barrett's Esophagus

Best Practice Advice 3: Screening and surveillance endoscopic examination should be performed using high-definition white light endoscopy (HD-WLE) and virtual chromoendoscopy (VC), with endoscopists spending adequate time inspecting the Barrett's segment.

The goal of endoscopic screening and surveillance in BE is early detection of BE-related dysplasia and early EAC. Consistent with recent guidelines,[2,9] the panel agrees with the routine use of HD-WLE *and* VC during screening and surveillance endoscopy in patients with BE. In an updated meta-analysis that included 504 patients, virtual chromoendoscopy with HD-WLE was associated with a higher detection rate of HGD/EAC compared with HD-WLE alone (14.7% vs 10.1%; relative risk, 1.44).[10] Although available data suggest comparable rates of dysplasia detection between virtual and traditional chromoendoscopy techniques, VC is the preferred approach as this imaging platform is available in most endoscopes, requires no additional costs, and circumvents the problems associated with dye-based chromoendoscopy such as the need for dye spraying equipment, additional time required, cumbersome nature of the procedure, difficulty in achieving uniform coating of the mucosal surface with the dye, and inability to detect superficial vascular patterns.[2] Incorporation of training in virtual and traditional chromoendoscopy during fellowship and training programs for the practicing endoscopists will be important for widespread routine implementation in clinical practice.[10] The clinical use of VC is suggested regardless of endoscope manufacturer, but is should be clear that majority of data supporting this is for narrow-band imaging only. There are limited data addressing the impact of inspection time on detection of BE-associated neoplasia in patients undergoing screening and surveillance endoscopy.[11-13] Conceptually, there was agreement that adequate inspection time would lead to more careful examination of the BE mucosa and potentially increased detection of BE-associated neoplasia. Future studies need to define the optimal threshold for inspection time per cm of the BE segment. Although the panel purposefully did not name a time period comprising an adequate exam due to lack of data on this issue, the European Society for Gastrointestinal Endoscopy and United European Gastroenterology recommend a procedure time of ≥7 minutes for upper endoscopy and inspection time of ≥1 minute/cm of the circumferential extent of the Barrett's mucosa.[14]

Although screening and surveillance upper endoscopy may be effective in detecting dysplasia and curable EAC, it is imperfect. Similar to post-colonoscopy colorectal cancer,[15] BE-associated high-grade dysplasia (HGD) and EAC can be diagnosed before the next recommended endoscopic evaluation after an upper endoscopy that was negative for HGD or EAC.[16,17] Meta-analyses and cohort studies suggest that a high proportion of HGD or EAC are missed within the first year following the index endoscopy that diagnosed BE.[18,19] To address the importance of the quality of endoscopic examination, using an evidence-based approach, an international working group recently standardized terminology and definitions for post-endoscopy esophageal adenocarcinoma and post-endoscopy esophageal neoplasia;

EAC and HGD/EAC detected before the next recommended surveillance endoscopy in a patient with nondysplastic BE (NDBE), respectively.[10] A conceptual 10-step approach to a high-quality endoscopic examination in patients with BE is highlighted in Table 1.

Best Practice Advice 4: Screening and surveillance endoscopic examinations should define the extent of BE using a standardized grading system documenting the circumferential and maximal extent of the columnar lined esophagus (Prague Classification) with a clear description of landmarks and location and characteristics of visible lesions (nodularity, ulceration), when present.

The panel acknowledged that the impact of use of standardized grading criteria for BE length (Prague classification) and visible lesions (Paris classification) (Figure 1, A) on critical outcomes such as improved detection of BE-associated neoplasia has not been assessed. The panel suggested the routine use of these classification practices as surrogates for performance of a high-quality endoscopy exam.

Best Practice Advice 5: Advanced imaging technologies may be used as adjunctive imaging techniques to identify dysplasia.

The panel were supportive of the need to have improved imaging technologies to better identify areas of dysplasia and early cancer. Technologies considered for this discussion included confocal (CLE) or volumetric laser endomicroscopy. A meta-analysis of 14 studies of 789 patients with 4047 lesions found CLE had a per-lesion analysis pooled sensitivity and specificity of 77% (95% confidence interval [CI], 0.73–0.81) and 89% (95% CI, 0.87–0.90), respectively.[20] A separate meta-analysis of 5 studies involving 251 patients assessing within-patient comparisons of narrow band imaging and CLE found the pooled additional detection rate of CLE for per-lesion detection of neoplasia in patients with BE was 19.3% (95% CI, 0.05–0.33), but a comparable per-patient pooled sensitivity and specificity.[21] Volumetric laser endomicroscopy, though not currently available commercially, has introduced several new advances with regards to imaging in BE, including laser marking and the interpretation of imaging using artificial intelligence.[22,23] The panelists felt strongly this was an important area where further innovation is needed, but that the use of these techniques was not required for a high-quality exam and the data to date did not support its routine use. However, the panel felt these technologies were promising and carried potential benefits in select cases and currently might be best utilized in expert centers.

Best Practice Advice 6: Sampling during screening and surveillance endoscopic examinations should be performed using the Seattle biopsy protocol (4-quadrant biopsies every 1–2 cm and target biopsies from any visible lesion).

The support for this structured biopsy protocol is based on observational data suggesting that the use of the Seattle biopsy protocol (Figure 1, B) is associated with a higher dysplasia detection rate (relative risk, 2.75).[10] The panel acknowledged that endoscopists can meet this criterion if they prefer not to sample a visible lesion and refer the patient for endoscopic resection. Unfortunately, several studies have consistently demonstrated suboptimal adherence rates to the Seattle biopsy protocol.[24-26] The odds of detecting dysplasia significantly decreased with nonadherence to the Seattle biopsy protocol (odds ratio [OR], 0.53; 95% CI, 0.35–0.82).[24] A recent analysis using a national quality

benchmarking registry that included 58,709 endoscopies showed that nearly 20% of endoscopies were not adherent to the Seattle biopsy protocol, and that endoscopists were less adherent with increasing BE length; with the odds of nonadherence increasing by 31% with every 1-cm increase in length.[26]

Best Practice Advice 7: Wide-area transepithelial sampling (WATS-3D) may be used as an adjunctive technique to sample the suspected or established Barrett's segment (in addition to the Seattle biopsy protocol).

WATS-3D is a novel method that uses an abrasive brush to sample larger surface areas of the esophagus. These specimens allow for analysis of large sheets of cells while maintaining the 3-dimensional aspects of the tissue. The tissue is analyzed by software that uses convoluted neural networks to identify abnormal cells, which are confirmed by an expert pathologist. A recent systematic review and meta-analysis of 7 studies demonstrated an incremental yield for dysplasia detection of 7.2%.[27] In addition, pathologic interpretation of these specimens has been shown to have less interobserver variability with kappa of 0.86.[28] As such, the recent ASGE guidelines supported the use of WATS-3D in addition to Seattle protocol in select patients (eg, indeterminate for dysplasia or clinically high-risk NDBE) undergoing surveillance.[2] Further prospective studies directly comparing WATS-3D and Seattle protocol are needed to understand if WATS-3D sampling might be as or more effective.

Best Practice Advice 8: Patients with erosive esophagitis may be biopsied when concern of dysplasia or malignancy exists, with the caveat that a repeat endoscopy after 8 weeks of twice-daily proton pump inhibitor (PPI) is performed.

The panel discussed the importance of preventing delays in diagnosing dysplasia and malignancy when concerning endoscopic findings are encountered in the setting of esophagitis. Although the potential for overcalling dysplasia (especially low-grade dysplasia [LGD]) in the setting of active inflammation exists, the panel felt that this should not preclude obtaining biopsies as expert pathologists have been shown to be able to distinguish inflammation from true LGD.[29] When such samples are obtained, documentation should be included regarding the presence and severity of the esophagitis visualized. Although once a day PPI may be sufficient for healing some patients, given the potential for an incomplete response in a subset of patients with severe esophagitis, twice a day therapy was suggested to maximize efficacy, especially given the limited downside to such a short treatment course. Treatment for 8 weeks was suggested, as this has been the typical duration of most trials of PPI for the healing of esophagitis and has been recommended by prior guidelines.[30-32] The panel noted that a relook endoscopy is only needed for those with Los Angeles Grade C and D esophagitis.[33] The indication for repeat endoscopy is to document healing of esophagitis and to assess for any features of malignancy. Furthermore, follow-up esophagogastroduodenoscopy may reveal underlying Barrett's in up to 10% to 12% of patients.[34-36]

Risk Stratification of Barrett's Esophagus

Best Practice Advice 9: Tissue systems pathology-based prediction assay may be utilized for risk stratification of patients with NDBE.

Risk stratification among patients with NDBE has been limited to clinical scoring systems. Recently, a tissue systems pathology assay (Tissue Cypher), commercially available in the US, has been validated and demonstrated to accurately risk stratify patients with NDBE (low, intermediate, high) for progression to HGD/EAC with a 4.7-fold increased risk in patients stratified as high risk.[37] The assay is performed on routine biopsies from the Barrett's segment and quantifies 9 protein-based biomarkers (p16, p53, AMACR, HER2, Cytokeratin 20, CD68, COX-2, HIF-1alpha, and CD45Ro), along with nuclear morphology and tissue architecture. It is performed on formalin-fixed, paraffin-embedded biopsies. The result is a numeric score from 1 to 10 that corresponds to a patient's risk for progression. To date, there have been 5 independent studies including 239 progressors and 656 nonprogressors across the US and Europe. The sensitivity and specificity for Tissue cypher for detecting progression in patients with NDBE is 30.4% and 95%, respectively, with the sensitivity increasing to 50% if multiple levels are examined.[38] A recent spatial-temporal analysis of progressors and nonprogressors demonstrated that a high-risk score was associated with a rate of progression of 6.9%, similar to LGD.[38] In addition, a study using Markov modeling suggesting that Tissue Cypher-based risk stratification becomes cost-effective after 5 years, with an incremental cost-effectiveness ratio of $52,483/quality-adjusted life years. Finally, a recent pooled analysis of international studies in 472 patients with NDBE demonstrated that a high Tissue Cypher risk score was a strong independent predictor for progression to HGD/EAC (OR, 14.2; 95% CI, 5–39; $P < .001$).[39] Based on these data, the panel agreed that the Tissue Cypher assay may be of benefit for risk stratification of patients with NDBE.

Best Practice Advice 10: Risk stratification models may be utilized to selectively identify individuals at risk for Barrett's associated neoplasia.

The panel agreed on the value of using risk stratification models to stratify surveillance intervals and influence the decision on whether to perform EET. However, at present, the only validated clinical risk stratification model for predicting progression to HGD/esophageal cancer in patients with known BE is the Progression in Barrett's Esophagus score.[40] This score was developed from 2697 patients, of whom 154 (5.7%) developed HGD or esophageal cancer. Factors significantly associated with progression included baseline confirmed LGD, male sex, smoking, and BE length. Scores assigned identified patients with BE that progressed to HGD or EAC with a c-statistic of 0.76 (95% CI, 0.72–0.80; $P < .001$), with the high-risk group progressing at a rate of 2.1% compared with 0.73% for the intermediate group and 0.13% for the low-risk group. Of note, this score is heavily influenced by the presence of LGD but was found to perform better in predicting progression than LGD alone in a separate BE cohort.[41] Other nonvalidated models using clinical variables have included the presence of esophagitis, lack of PPI use, being overweight, increasing age, and a known duration of BE of ≥10 years.[42-46] The panelists noted that several additional models were currently in development and noted that

models incorporating both clinical and biomarker parameters would likely ultimately be needed to optimize predictive accuracy.

Provider Expertise in Managing BE

Best Practice Advice 11: Given the significant interobserver variability among pathologists, the diagnosis of Barrett's-related neoplasia should be confirmed by an expert pathology review.

The panelists acknowledged the significant interobserver variability in the interpretation of dysplasia among pathologists and the importance of high-quality expert pathology review in the diagnosis of BE-related neoplasia.[2,47] An accurate diagnosis of dysplasia is critical for clinical decision-making and risk stratification, including the selection of endoscopic eradication therapy vs intensive surveillance. A systematic review and meta-analysis showed that expert pathology review resulted in a change in the pathologic diagnosis (upgrading or downgrading) in 55% (95% CI, 31%–77%) of all patients.[47] Available data suggests LGD, as confirmed by expert pathology review, is associated with a higher rate of disease progression to HGD/EAC.[47] P53 immunohistochemistry can help confirm dysplasia and improve consistency of reporting.[48,49] This Best Practice Advice is consistent with GI guidelines that recommend confirmation of dysplasia of any grade by a second pathologist with expertise in GI pathology.[9,47]

Best Practice Advice 12: Patients with BE-related neoplasia should be referred to endoscopists with expertise in advanced imaging, resection, and ablation.

Physicians with expertise in Barrett's neoplasia management have been shown to identify more visible lesions compared with nonexperts.[50] The panelists strongly felt that physicians performing endoscopic eradication therapy for BE-related neoplasia should either perform or work in centers that can offer both resection and ablation techniques, as recommended by prior quality metrics.[51] Expert centers should ideally be defined based on adequate volume, availability of needed technology, procedural expertise, and exceeding established quality metrics.

Follow-up and Surveillance of BE

Best Practice Advice 13: Patients with BE should be placed on at least daily PPI therapy.

Epidemiologic evidence from observational studies that have demonstrated a significant decrease in the risk of progression to HGD and EAC in patients with BE with PPI therapy. A systematic review and meta-analysis showed that PPI therapy was associated with a 71% reduction in the risk of HGD or EAC (adjusted OR, 0.29; 95% CI, 0.12–0.79).[52] In 4 cohort studies that reported the time to progression to HGD or EAC, PPI users were also significantly less likely to progress to HGD or EAC (adjusted hazard ratio, 0.32; 95% CI, 0.15–0.67). The AspECT trial demonstrated that high-dose PPI was superior to low-dose PPI for lengthening the time to reach the combined end point of death from any cause, EAC, or HGD. However, several study limitations prevent these conclusions to be generalizable. The trial was not double-blinded, the event rate was low, and only a small effect size was noted. The overall benefit was skewed towards all cause-mortality rather than cancer-related

mortality, most relevant to the BE population.[53] As such, there was insufficient information in these studies on whether taking PPI twice daily would provide any added benefit over once daily administration. The panel also considered the potential harms of long-term PPI therapy and the suggested associations between PPI therapy and the risk of several outcomes.[54,55] Evidence is inadequate to establish causal relationships between PPI and any of these proposed associations, with the exception of enteric infection.[55] Given the unclear benefit of higher doses of PPI on oncogenesis, the panel suggested at least daily dosing, with higher doses considered for those requiring them for symptom control and among patients with BE-related neoplasia undergoing endoscopic eradication therapy.

Best Practice Advice 14: Patients with NDBE should undergo surveillance endoscopy in 3 to 5 years.

Endoscopic surveillance in patients with known BE remains the gold standard for dysplasia and neoplasia detection. Current guidelines recommend endoscopic surveillance every 3 to 5 years[1] based on a low risk of progression to HGD/EAC in patients with NDBE. Surveillance intervals are shortened significantly in patients with dysplasia but should remain 3 to 5 years for patients with NDBE. The interval allows for gastroenterologists some flexibility to individualize intervals for each patient. Most recently, the American College of Gastroenterology guidelines for 2022 recommended consideration of the segment length when determining surveillance interval, with longer intervals for segments <3 cm.[9] Careful discussions and assessments of the value of endoscopic surveillance, given other comorbidity and risks, should be a part of the management of all patients with BE.

Best Practice Advice 15: In patients undergoing surveillance after endoscopic eradication therapy (EET), 4-quadrant random biopsies should be taken of the esophagogastric junction, gastric cardia, and the distal 2 cm of the neosquamous epithelium, as well as from all visible lesions, independent of the length of the original BE segment.

Traditionally, 4-quadrant random post-EET surveillance biopsies have been recommended in the cardia, at the esophagogastric junction and every 1 cm in entire prior BE segment. Three studies have reported on the anatomic location of recurrent BE after EET.[56-58] In total, they evaluated 1235 patients achieving complete eradication of intestinal metaplasia and observed 233 recurrences, for an aggregate recurrence rate of 18.9%. The majority of nonvisible recurrence of intestinal metaplasia occurred at the esophagogastric junction, whereas most recurrences in the tubular esophagus were visible. Using the aforementioned best practice statement post-EET surveillance biopsy strategy, 98% (228/233) of all recurrences could be identified. The panelists felt that for a BE length of <2 cm, such an approach was still reasonable given the potential for subsquamous/tangential extension up to 1 cm beyond the proximal end of the squamocolumnar junction. The panelists also recognized the value of obtaining cardia biopsies to assess for dysplasia (Figure 1, C).

Best Practice Advice (BPA) Statements

Screening for Barrett's Esophagus (BE)

Best Practice Advice (BPA) Statements
BPA #1. Screening with standard upper endoscopy may be considered in individuals with established risk factors for BE and esophageal adenocarcinoma – presence of at least 3 risk factors (individuals who are male, non-Hispanic white, age >50 years, have a history of smoking, chronic gastrointestinal reflux disease, obesity, or a family history of BE or esophageal adenocarcinoma).
BPA #2. Nonendoscopic cell collection devices can be considered as an option to screen for BE.
Endoscopic Examination of BE
BPA #3. Screening and surveillance exams should be performed using high-definition white light endoscopy and virtual chromoendoscopy, with endoscopists spending adequate time inspecting the Barrett's segment.
BPA #4. Screening and surveillance exams should define the extent of BE using a standardized grading system documenting the circumferential and maximal extent of the columnar lined esophagus (Prague classification) with a clear description of landmarks and the location and characteristics of visible lesions (nodularity, ulceration), when present.
BPA #5. Advanced imaging technologies such as endomicroscopy may be used as adjunctive imaging techniques to identify dysplasia.
BPA #6. Sampling during screening and surveillance exams should be performed using the Seattle biopsy protocol (4-quadrant biopsies every 1–2 cm and target biopsies from any visible lesion).
BPA #7. Wide area transepithelial sampling may be used as an adjunctive technique to sample the suspected or established Barrett's segment (in addition to the Seattle biopsy protocol).
BPA #8. Patients with erosive esophagitis may be biopsied when concern of dysplasia or malignancy exists, with the caveat that a repeat endoscopy after 8 weeks of twice a day proton pump inhibitors is performed.
Risk Stratification of BE
BPA #9. Tissue systems pathology-based prediction assay may be utilized for risk stratification of patients with nondysplastic BE.
BPA #10. Risk stratification models may be utilized to selectively identify individuals at risk for Barrett's associated neoplasia.
Provider Expertise in Managing BE
BPA #11. Given the significant interobserver variability among pathologists, the diagnosis of BE-related neoplasia should be confirmed by an expert pathology review.
BPA #12. Patients with BE-related neoplasia should be referred to endoscopists with expertise in advanced imaging, resection, and ablation.
Follow-up and Surveillance of BE
BPA #13. Patients with BE should be placed on at least daily proton pump inhibitor therapy.
BPA #14. Patients with nondysplastic BE should undergo surveillance endoscopy in 3 to 5 years.
BPA #15. In patients undergoing surveillance after endoscopic eradication therapy, 4-quadrant random biopsies should be taken of the esophagogastric junction, gastric cardia, and the distal 2 cm of the neosquamous epithelium as well as from all visible lesions, independent of the length of the original BE segment.

Conclusion

Targeted BE screening and surveillance using existing methodologies, as well as use of emerging and novel screening technologies, have the potential to improve early detection of dysplasia, neoplasia, and EAC within populations at risk for BE (Figure 2).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of interest

The authors disclose the following. V. Raman Muthusamy reports consultant for Medtronic, Boston Scientific, research support from Boston Scientific; Advisory Board: Endogastric Solutions; honoraria from Torax Medical/Ethicon; and stock from Capsovision. Sachin Wani reports consultant for Exact Sciences advisory board for Cernostics; and research support from Lucid Diagnostics and CDx Diagnostics. Prakash Gyawali reports consultant for Medtronic. Srinadh Komanduri reports consultant for Medtronic, Boston Scientific, Castle Biosciences, and Johnson & Johnson.

Abbreviations used in this paper:

AGA	American Gastroenterological Association
BE	Barrett's esophagus
BPA	Best Practice Advice
CGIT	Center for GI Innovation and Technology
CI	confidence interval
CLE	confocal laser endomicroscopy
EAC	esophageal adenocarcinoma
EET	endoscopic eradication therapy
GERD	gastroesophageal reflux disease
HD-WLE	high definition-white light endoscopy
HGD	high-grade dysplasia
LGD	low-grade dysplasia
NDBE	nondysplastic Barrett's esophagus
OR	odds ratio
PPI	proton pump inhibitor
UK	United Kingdom
US	United States
VC	virtual chromoendoscopy

WATS-3D	wide-area transepithelial sampling

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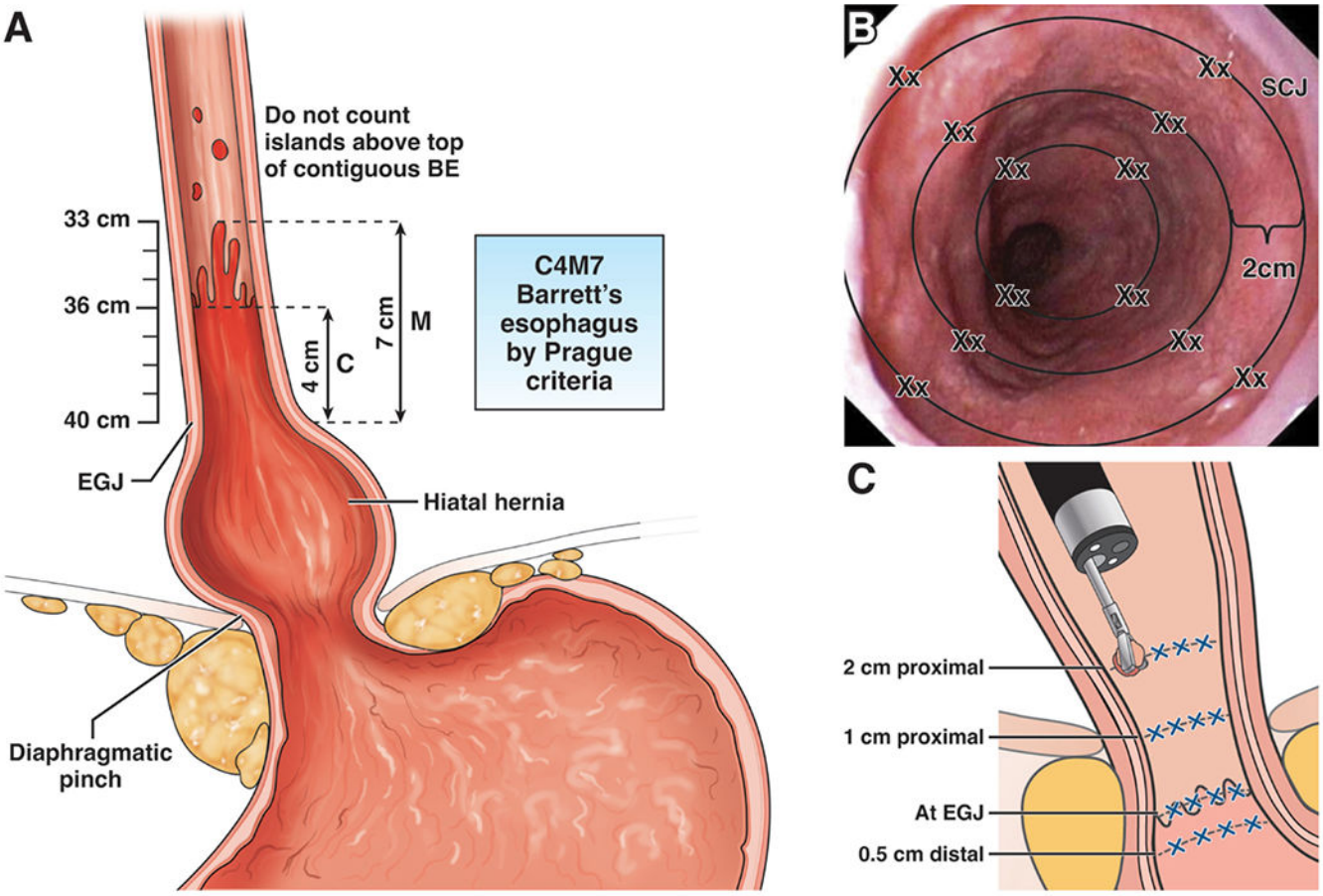

Figure 1.

A, The Prague classification for BE. *B*, Illustration of the Seattle biopsy protocol for performing surveillance in patients with NDBE.[59] *C*, Illustration of a simplified protocol for performing random surveillance biopsies in patients status post EET. Of note, all visible lesions in the cardia and tubular esophagus should be biopsied separately.[57] EGJ, Esophagogastric junction.

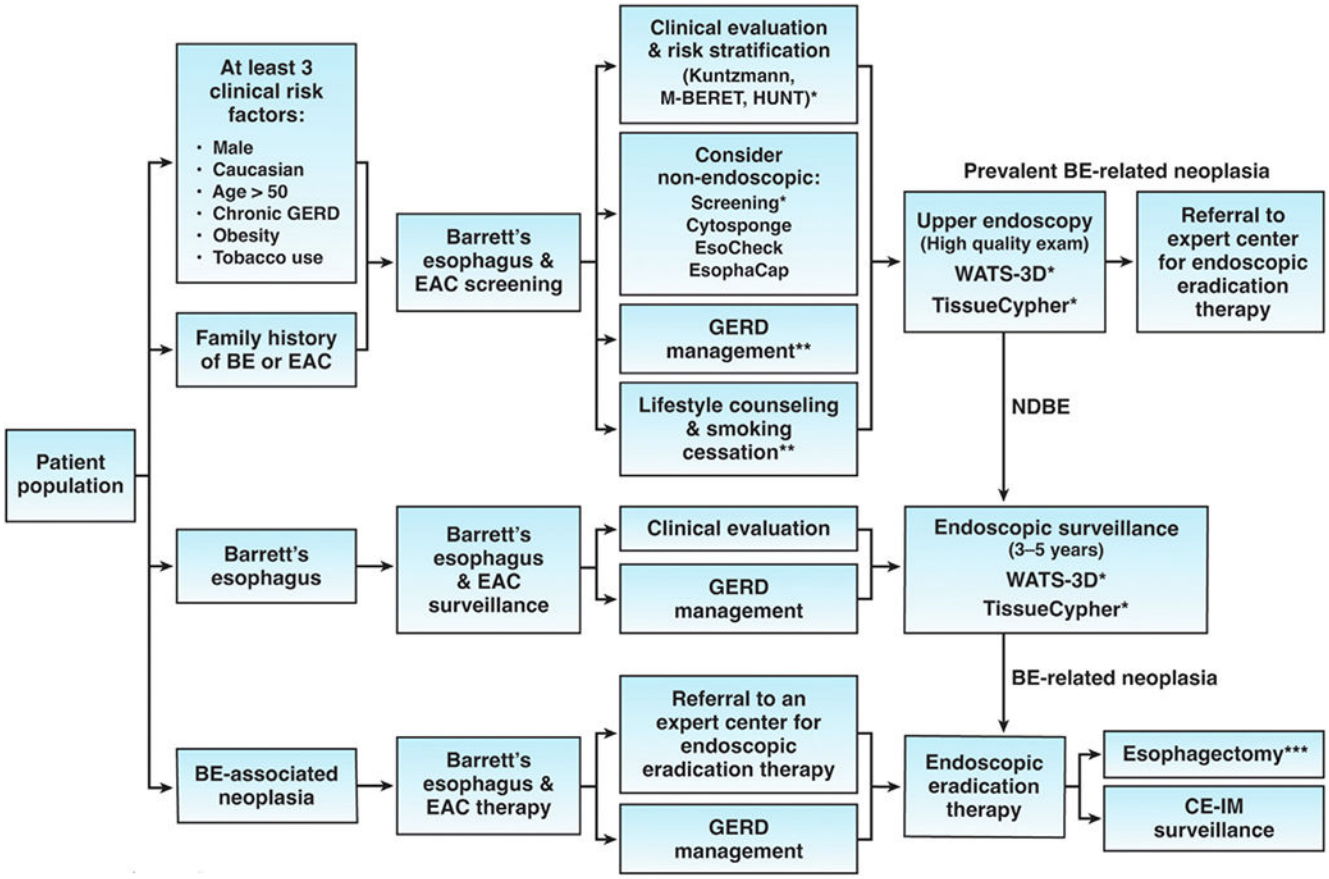

Figure 2.

Suggested BE care pathway.

*May be utilized as per BPA in this document

**When clinically appropriate

***For T1b or higher stage cancers by EMR or neoplastic disease refractory to EET

Table 1.

Ten-step Approach to Endoscopic Examination of Barrett's Esophagus (BE)

Approach	Rationale
1. Identify esophageal landmarks, including the location of the diaphragmatic hiatus, gastroesophageal junction, and squamocolumnar junction	1. Critical for future exams
2. Consider use of a distal attachment cap (especially in patients with prior diagnosis of dysplasia)	2. Facilitate visualization
3. Clean mucosa well using water jet channel and carefully suction the fluid	3. Remove any distracting mucus or debris and minimize mucosal trauma
4. Utilize insufflation and desufflation	4. Fine adjustments to luminal insufflation can help with detection of subtle abnormalities
5. Spend adequate time inspecting the Barrett's segment and gastric cardia in retroflexion	5. Careful examination increases dysplasia detection
6. Examine the Barrett's segment using HD-WLE	6. Standard of care
7. Examine the Barrett's segment using chromoendoscopy (including virtual chromoendoscopy)	7. Enhances mucosa pattern and surface vasculature
8. Use the Prague classification to describe the circumferential and maximal Barrett's segment length	8. Standardized reporting system
9. Use the Paris classification to describe superficial neoplasia	9. Standardized reporting system
10. Use the Seattle protocol (in conjunction with virtual chromoendoscopy) with a partially deflated esophagus to sample the Barrett's segment	10. Increases dysplasia detection

Adapted from Kolb J, Wani S. Curr Opin Gastroenterol 2020;36:351–358.[60]

HD-WLE, High-definition white light endoscopy.