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Guideline to Practice: Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline

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Implementation of information in guidelines can be fraught with difficulty. Although guideline recommendations generally provide straightforward pronouncements, given the complexities of patient care, in practice, implementing recommendations can be difficult. The purpose of this work was to demonstrate implementation of information in “Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline” (1). Below, we present 3 clinical vignettes that demonstrate the application of guidance to the bedside in commonly encountered situations.

VIGNETTE 1

A 55-year-old White man is referred by his primary care physician for an esophagogastroduodenoscopy (EGD) for screening for Barrett's esophagus (BE). The patient has a long history of proton pump inhibitor (PPI) use for daily heartburn and regurgitation, well controlled on omeprazole 20 mg daily. Of note, the patient smokes 1 pack of cigarettes daily. On physical examination, he has a body mass index of 35.

At the time of EGD, the esophageal landmarks are noted: diaphragmatic pinch at 40 cm, top of the gastric folds at 40 cm, and an irregular Z line at 40 cm (Figure 1). The remainder of the EGD was unremarkable. Per your routine practice, biopsies were obtained from

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the irregular Z line and read as “intestinal metaplasia that in the correct clinical setting is compatible with BE” (Figure 2). You now see the patient in the follow-up in clinic.

Comment

This patient has multiple risk factors for BE, including years of symptoms typical of gastroesophageal reflux, White race, age older than 50 years, smoking history, male sex, and obesity (2). Given these risk factors, screening EGD is recommended. While appropriate screening was performed, biopsies were obtained from an irregular-appearing Z line. The current definition of BE requires columnar mucosa of at least 1 cm in length in conjunction with intestinal metaplasia on biopsies. Neither patients with a normal-appearing Z line nor patients with a Z line demonstrating <1 cm of proximal displacement from the top of the gastric folds should undergo routine biopsies. The rationale for this recommendation comes from several lines of evidence. The Prague criteria used to measure BE demonstrate excellent reliability for segments >1 cm, but not for segments <1 cm (3). In addition, the risk of progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) is quite low for individuals with a normal or irregular Z line (<1 cm) (4,5). Unfortunately, biopsies of an irregular or normal Z line remain too common in clinical practice, representing a potential area for quality improvement (6). Because routine biopsy of the normal or irregular Z line leading to a false diagnosis of BE has unintended consequences (6,7), this practice should be avoided. This patient should be informed that he does not have BE and should not be enrolled in a surveillance endoscopy program. He can continue his effective PPI therapy and should only undergo further EGD should his clinical situation change.

VIGNETTE 2

A 56-year-old man with chronic heartburn controlled on daily PPI underwent an EGD. His endoscopy revealed suspected BE (Prague C2M4), and 4-quadrant biopsies were obtained every 2 cm. Histology was consistent with intestinal metaplasia with low-grade dysplasia (LGD) at a single level. He was referred for radiofrequency ablation (RFA). An expert pathology review of slides resulted in downgrading of diagnosis to BE without dysplasia. Repeat EGD was performed under maximal acid suppression using high-definition white light endoscopy and virtual chromoendoscopy. No visible lesions were identified, and 4-quadrant biopsies, obtained every centimeter, confirmed BE without dysplasia. Immunostaining of esophageal biopsies revealed no aberrant expression of p53. Repeat surveillance endoscopy in 3 years was recommended.

Comment

This case vignette highlights several management conundrums in patients with BE and LGD. The following questions arise in patients with BE and LGD:

1. Is the diagnosis of LGD accurate?
2. Is there prevalent HGD or EAC?
3. What is the role of adjunctive techniques to improve risk stratification?
4. What is the appropriate management in patients with confirmed LGD?

Professional society guidelines recommend that biopsies demonstrating dysplasia undergo a second expert pathology review, given significant interobserver variability, especially for the diagnosis of indefinite for dysplasia and LGD. A meta-analysis demonstrated that the expert pathology review resulted in a change in diagnosis in 55% of cases (8). Patients with confirmed LGD are at higher risk of progression to HGD or EAC than those not confirmed, with increasing risk based on the number of pathologists agreeing with the diagnosis (9).

Several adjunctive techniques are available to aid in the diagnosis of dysplasia and to improve risk stratification in patients with nondysplastic BE and LGD. The addition of p53 immunohistochemistry to the histopathologic assessment of dysplasia has been recommended by the British Society of Gastroenterology to improve dysplasia diagnosis (10). Its use to predict progression was not endorsed in the current guidelines because of insufficient evidence. WATS3D (CDx Diagnostics, Suffren, NY) is a computer-aided analysis of brush samples which, when used as an adjunct to biopsies, may increase the yield of dysplasia detection (11) while TissueCypher, a tissue systems pathology test, may better prognosticate risk of progression in BE than the traditionally used dysplasia grade (12). Insufficient evidence exists to allow a general recommendation for the use of either of these technologies, and more work is needed to define the role of adjuncts in risk stratification of BE and LGD. Regarding the management of patients with confirmed LGD, current guidelines suggest a patient-centered approach in deciding between endoscopic eradication therapy (EET) and endoscopic surveillance. EET is suggested in patients with confirmed LGD to reduce the risk of progression to HGD or EAC; however, patients who place a high value on avoiding adverse events related to EET may choose surveillance instead.

VIGNETTE 3

A 70-year-old man underwent EET with endoscopic mucosal resection and RFA for BE with HGD and achieved complete eradication of intestinal metaplasia (CEIM) after 3 EET sessions. He underwent surveillance endoscopy for 2 years after achieving CEIM, with no endoscopic or histologic evidence of recurrence. On presentation for his year 2 surveillance endoscopy after CEIM, he denied any alarming symptoms, and heartburn was well controlled on twice-daily PPI therapy. Endoscopy revealed no endoscopic evidence of BE but an area of nodularity at the gastroesophageal junction (GEJ) (Figure 3a,b). This lesion was biopsied, revealing HGD. Dysplasia was confirmed by the expert pathology review. He was referred to a tertiary care center where the lesion was endoscopically resected by cap-assisted endoscopic mucosal resection. Pathology revealed HGD without EAC and negative lateral and deep margins. During follow-up endoscopy, given the presence of HGD, the GEJ and gastric cardia were ablated with RFA. Biopsies at 3 and 6 months after ablation did not reveal any intestinal metaplasia, and the patient was referred to his local gastroenterologist for continuing endoscopic surveillance.

Comment

Recurrence of intestinal metaplasia is well described after successful EET. Meta-analyses and cohort studies (Table 1) have reported the incidence of recurrent intestinal metaplasia, dysplasia, and HGD/EAC after successful EET of dysplastic BE to be 8–10, 2, and 1

per 100 patient-years, respectively. Given the considerable risk of recurrent BE and the possibility of EAC, endoscopic surveillance is recommended after successful EET to detect recurrence. Surveillance is suggested at year 1 after CEIM and after every 2 years thereafter in patients with LGD pre-EET, and at 3, 6, 12 months, and annually thereafter in patients with HGD/intramucosal EAC pre-EET. Careful inspection of the esophagus and the gastric cardia (in antegrade and retroflexed views) using high-definition endoscopy and virtual chromoendoscopy is recommended. Surveillance biopsies should target the distal 2–5 cm of the esophagus and GEJ, with targeted sampling from any visible lesions. In the presence of visible lesions, endoscopic resection for precise histological assessment is recommended, in addition to ablation of any residual flat columnar mucosa. Studies have reported that endoscopic therapy of recurrent BE is successful in achieving CEIM in over 90% of cases.

CONCLUSION

The above vignettes illustrate the application of recommendations from the updated guidelines for care of patients with BE to common clinical scenarios. These scenarios highlight either guidance that has changed since the last iteration (for instance, surveillance intervals in BE after successful EET) or situations where data suggest that common clinical practice deviates from best practice recommendations (e.g., the errant diagnosis of BE due to biopsies of a normal Z line). Adherence to the evidence-based recommendations in the guidelines should improve outcomes and provide cost-effective care for your patients with BE.

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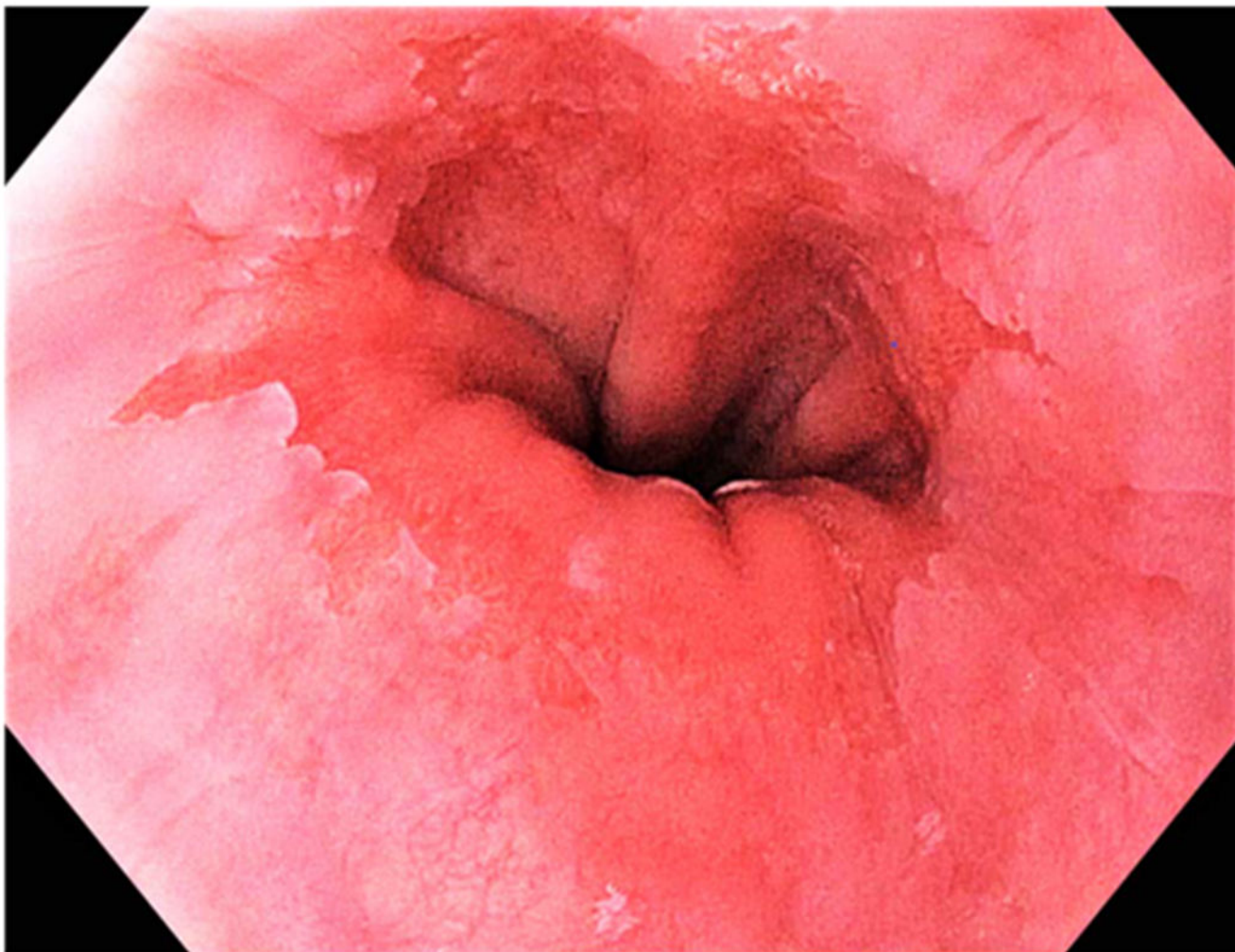


Figure 1.
Endoscopic photograph of an irregular Z line. Note the relatively small displacement from the top of the gastric folds to the most proximal extent of the Z line.

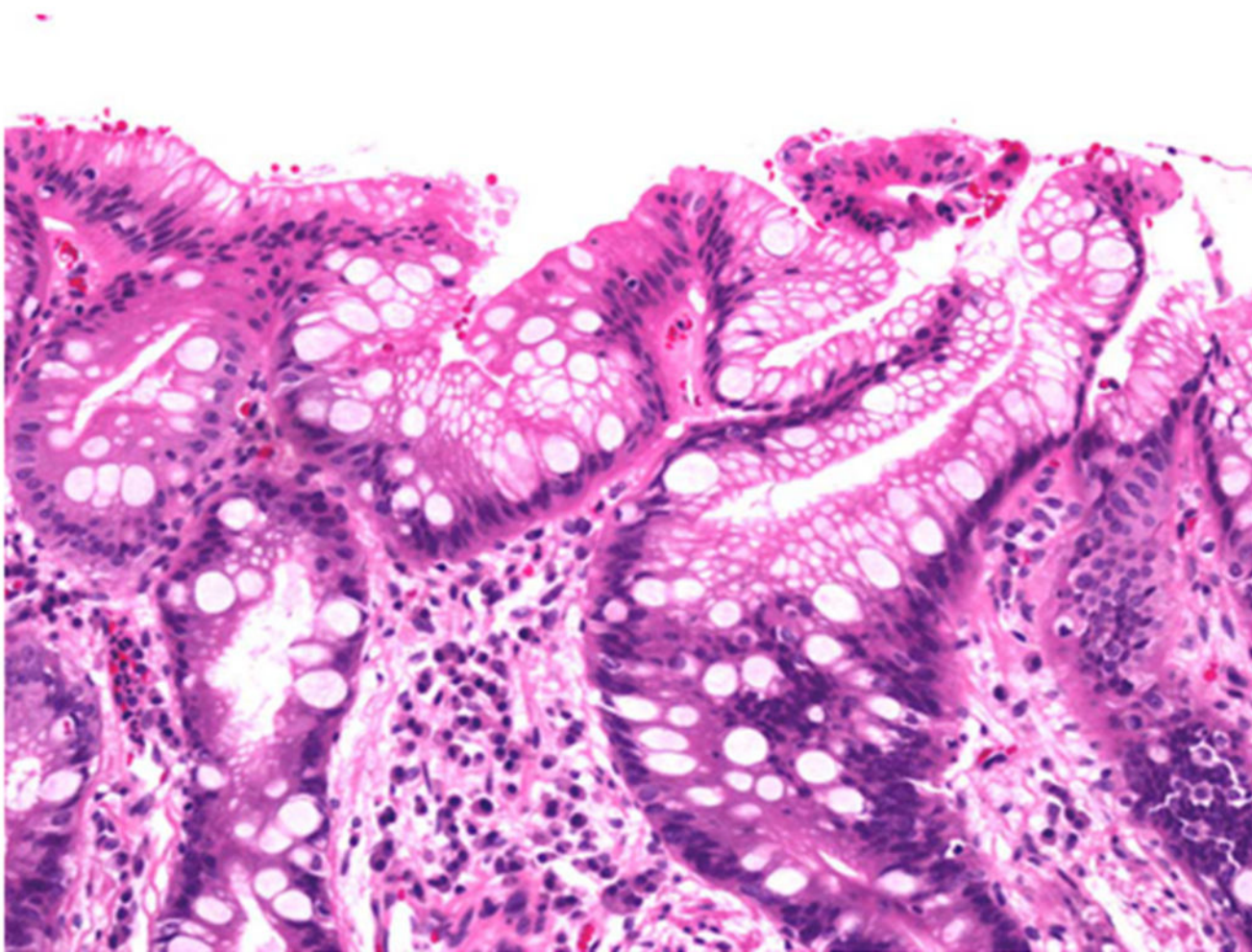


Figure 2.
Hematoxylin and eosin staining of endoscopic biopsy of the irregular Z line, demonstrating intestinal metaplasia with goblet cells. Courtesy of John Goldblum, MD.

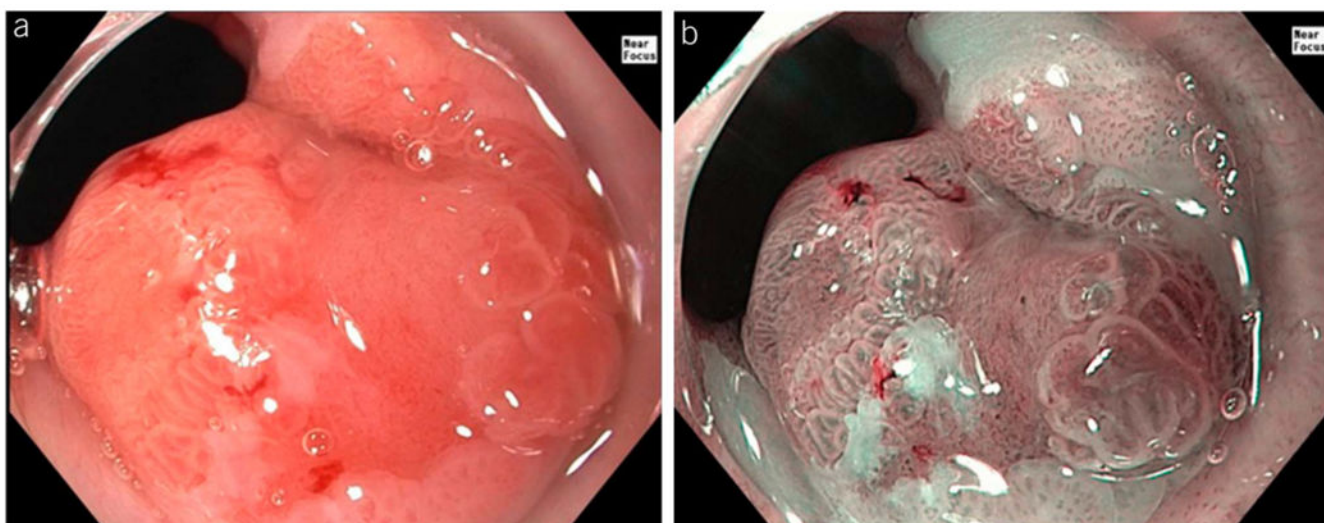


Figure 3. (a and b) Nodular recurrence of BE with HGD at the gastroesophageal junction in a patient with initially successful EET, on white light (a) and narrow band (b) imaging. BE, Barrett's esophagus; EET, endoscopic eradication therapy; HGD, high-grade dysplasia.

Recurrence rates of intestinal metaplasia and neoplasia after endoscopic eradication therapy of dysplastic BE and intramucosal adenocarcinoma

Table 1.

Study	CEIM patients (N)	Incidence of IM per 100 PY, (95% CI)	Incidence of any dysplasia per 100 PY, (95% CI)	Incidence of HGD/EAC per 100 PY, (95% CI)
Krishnamoorthi et al. (13)	3,186	9.5	2.0	1.2
Fujii-Lau et al. (14)	3,213	8.6	1.9	NA
Tan et al. (15)	337	10.8	2.2	0.3
Sami et al. (16)	594	9.6	2.8	1.6
Wani et al. (17)	807	5.2	1.6	NA
van Munster et al. (18)	1,154	4.9	1.0	0.7

BE, Barrett's esophagus; CEIM, complete eradication of intestinal metaplasia; CI, confidence interval; EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia. Adapted from Kolb et al. (19)