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MENTORED REVIEW

Early Esophageal Cancer: A Gastroenterologist's Disease

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Abstract
Traditionally, early esophageal cancer (i.e., cancer limited to the mucosa or superficial submucosa) was managed surgically; the gastroenterologist's role was primarily to diagnose the tumor. Over the last decade, advances in endoscopic imaging, ablation, and resection techniques have resulted in a paradigm shift—diagnosis, staging, treatment, and surveillance are within the endoscopist's domain. Yet, there are few reviews that provide a focused, evidence-based approach to early esophageal cancer, and highlight areas of controversy for practicing gastroenterologists. In this manuscript, we will discuss the following: (1) utility of novel endoscopic technologies to identify high-grade dysplasia and early esophageal cancer, (2) role of endoscopic resection and imaging to stage early esophageal cancer, (3) endoscopic therapies for early esophageal cancer, and (4) indications for surgical and multidisciplinary management.

Keywords Early esophageal cancer · Esophageal adenocarcinoma · Esophageal squamous cell carcinoma · Endoscopic resection

Introduction

Esophageal cancer has a poor prognosis with an overall 5-year survival less than 20% [1, 2]. Advanced esophageal cancer patients typically present with symptoms of dysphagia and have an obvious mass on endoscopy. Imaging technologies including computed tomography (CT), positron emission tomography (PET), and endoscopic ultrasound (EUS) provide an accurate assessment of disease stage in advanced cancer [3, 4]. Once the diagnosis and depth of invasion have been ascertained, gastroenterologists play a peripheral role in the multidisciplinary management of advanced esophageal cancer.

In contrast, patients with early esophageal cancer are generally asymptomatic, and cross-sectional imaging technologies rarely identify the lesion. Even during endoscopy, the visible abnormality is often subtle. There has been a paradigm shift in treatment away from esophagectomy toward less morbid organ-sparing approaches, primarily endoscopic resection and ablation, with chemoradiation and surgery reserved for patients with high-risk features. Thus, early diagnosis, staging, and treatment of early esophageal cancer are within the purview of the gastroenterologist. Given the paucity of focused reviews on early esophageal cancer for gastroenterologists, our aim is to provide a practical, evidence-based summary that outlines approaches to early diagnosis, accurate staging, endoscopic treatments, and indications for multidisciplinary management in early esophageal cancer.

Diagnosis

About one-fifth of patients with esophageal cancer are diagnosed with localized disease found incidentally during upper endoscopy or screening and surveillance programs for Barrett's esophagus (BE)-associated esophageal adenocarcinoma (EAC) and squamous cell carcinoma (SCC) [2]. Careful inspection using high-definition white light endoscopy (HD-WLE) seems intuitive, but this strategy alone often misses subtle areas of high-grade dysplasia or cancer [5]. Random 4-quadrant biopsies at 1–2-cm intervals (i.e., the Seattle protocol) increases the yield for dysplasia and cancer in BE but lacks the precision to target an area of malignancy

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[5, 6]. Several commercially available endoscopic imaging technologies aim to increase the likelihood of identifying early esophageal cancer or high-grade dysplasia. These include electronic or dye-based techniques to highlight the mucosal surface pattern (chromoendoscopy) and technologies that enable real-time in vivo histology assessment (endomicroscopy and cystoscopy) or use infrared light to evaluate changes in tissue architecture (optical coherence tomography). Computer-aided diagnosis using deep learning may be adapted to automatically detect esophageal abnormalities [7, 8].

Machine learning is an artificial intelligence technique in which computers use data to improve their performance in a task without explicit instruction. In unsupervised learning, machines are given data inputs that are not explicitly paired to labels or outputs. The machine is tasked with finding its own structure and patterns from the set of objects. Pilot studies have shown computer-aided diagnosis with deep learning having the potential to detect early EAC; however, improved performance is needed before its implementation in the clinical setting [7, 8].

Adoption of any diagnostic test requires that it is accurate, practical, and cost-effective. In terms of accuracy, the American Society for Gastrointestinal Endoscopy (ASGE) recommends an imaging technology along with targeted biopsy must demonstrate a per-patient sensitivity of $\geq 90\%$, negative predictive value (NPV) $\geq 98\%$, and specificity $> 80\%$ for detecting high-grade dysplasia (HGD) or early EAC when compared to random biopsies [5]. The performance of commercially available technologies with regard to this threshold is summarized below.

1. Electronic chromoendoscopy: Electronic chromoendoscopy is a standard feature on most commercially available endoscopes. Fujinon gastroscopes are equipped with Fuji Intelligent Chromo Endoscopy (FICE), and Pentax gastroscopes include the I-scan feature. The most widely investigated electronic chromoendoscopy technology is narrow-band imaging (NBI), available on Olympus endoscopes. NBI works by filtering white light into specific wavelengths that are absorbed by hemoglobin and penetrate only the surface of human tissue. As a result, with NBI, capillaries on the mucosal surface are displayed in brown and veins in the submucosa are displayed in cyan (Fig. 1). Several prospective studies have compared the accuracy of NBI features of mucosal and vascular irregularity using differing classification schemes for high-grade dysplasia and cancer in the esophagus. A meta-analysis published by the ASGE Technology Committee reported that the pooled sensitivity, NPV, and specificity for electronic chromoendoscopy for HGD and cancer by using narrow-band imaging were 94.2% (95% CI 82.6–98.2), 97.5% (95% CI 95.1–98.7), and 94.4% (95% CI 80.5–98.6), respectively [5].
2. Dye-based acetic acid (AA) chromoendoscopy: When sprayed on Barrett's epithelium at low concentrations (1–3%), AA disrupts glycoprotein disulfide bonds, which eliminates the superficial mucus layer [9, 10]. The unbuffered acid then reversibly acetylates cellular proteins, leading to an acetowhitening reaction that highlights surface pattern (Fig. 2). After mucus layer disruption, AA reaches stromal capillaries causing vascular congestion leading to focal erythema. However, this is obscured beneath the acetowhite mucosa

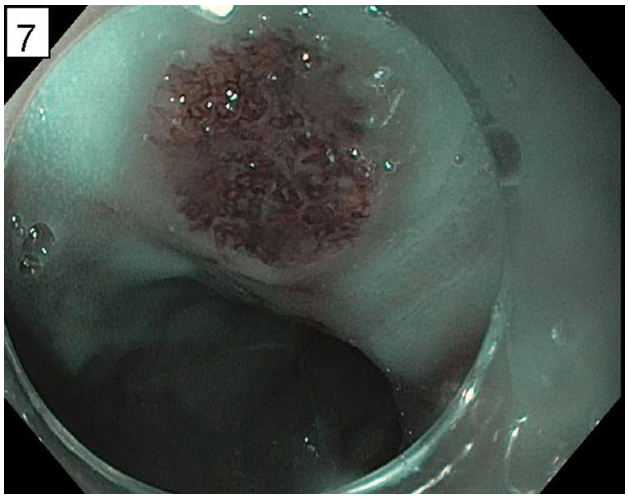

Fig. 1 Mucosal irregularity (irregular, dilated tortuous vessels and distorted pit pattern) visualized under narrow-band imaging—pathologic assessment of EMR specimen demonstrated high-grade dysplasia

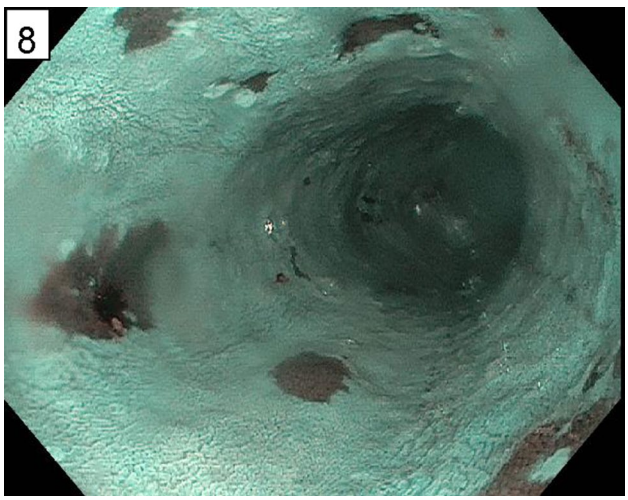

Fig. 2 Acetic acid chromoendoscopy combined with narrow-band imaging demonstrates several areas with early loss of acetowhitening reaction. Targeted biopsies were consistent with high-grade dysplasia

and only becomes visible after loss of acetowhitening (LAW) [10]. The low cytoplasmic content of neoplastic cells allows them to lose acetowhitening quicker than non-neoplastic cells; so, focal erythema is a pathognomonic sign for neoplasia [10]. In a meta-analysis of dye-based chromoendoscopy techniques in BE (acetic acid, methylene blue, and indigo carmine), only acetic acid met the accuracy threshold recommended by the ASGE [5]. Acetic acid itself is inexpensive (in our practice we dilute vinegar 1:1 to obtain a 2.5% AA solution), but AA chromoendoscopy requires use a spray catheter, which adds a small cost to the overall procedure (disposable catheter ~ $50.00).

3. Dye-based Lugol's iodine chromoendoscopy for SCC: Esophageal SCC has a higher prevalence in China, Eastern Asia, and Africa [4]. Some of these high-risk areas have implemented SCC screening and have reported their experience using Lugol's iodine to highlight neoplastic tissue [11]. Normal squamous tissue has abundant glycogen, which uptakes topically sprayed iodine and causes an intense brown–black mucosal discoloration. Dysplastic and malignant squamous cells do not contain glycogen and therefore exhibit lack of staining [12] (Fig. 3). In a systematic review that included 1911 patients, Morita et al. reported that sensitivity and specificity of Lugol's iodine for HGD and early SCC were 92% and 82%, while sensitivity and specificity of NBI were 88% and 88%, respectively [11]. Esophageal chromoendoscopy with Lugol's iodine solution increases HGD and SCC detection compared to white light esophagoscopy; however, the required use of a spray catheter, risks inherent with use (e.g., chest discomfort), and superior specificity with NBI while providing comparable diagnostic accuracy favor evaluation with electronic chromoendoscopy [11].
4. Confocal laser endomicroscopy (CLE): CLE uses a low-power laser to illuminate tissue at a selected depth and then detect reflected fluorescent light. A randomized trial that used an endoscope-based version of the technology (eCLE, Pentax Medical) reported higher rates of dysplasia and cancer identification using eCLE with targeted biopsies when compared to HD-WLE with random biopsies [13]. Unfortunately, eCLE is no longer commercially available. A version of the technology that uses a CLE probe passed through the working channel of the endoscope (pCLE) is commercially available (Cellvizio, Mauna Kea Technologies) (Fig. 4). Two prospective studies have compared pCLE to random biopsies. In both studies, pCLE demonstrated high specificity but low sensitivity for dysplasia and cancer [6, 14]. In its current iteration, pCLE requires dedicated capital equipment as well as a reusable probe (~ $10,000, 20 uses per probe), which is a significant barrier in an era of cost containment.
5. Optical coherence tomography (OCT): OCT is similar to ultrasound, except that reflection of infrared light rather than sound waves is used to generate high-resolution cross-sectional images of esophageal wall layers [15]. Unlike CLE, individual cells are not visualized. Instead, studies have used the presence or absence of glands and disruption in wall layers to define cancer (Fig. 5). Kohli et al. [15] conducted a systematic review of OCT for BE and cancer. They identified two prospective in vivo studies that assessed accuracy of OCT for dysplasia and early cancer. Diagnostic criteria differed in the two studies, and accuracy fell below recommended thresholds (sensitivity 68–83%, specificity 75–82%) [15]. Like CLE, the commercially available iteration of the technology (volumetric laser endomicroscopy, Nine Point Medical) requires capital equipment and a disposable through the scope balloon catheter (~ $1500–2000).

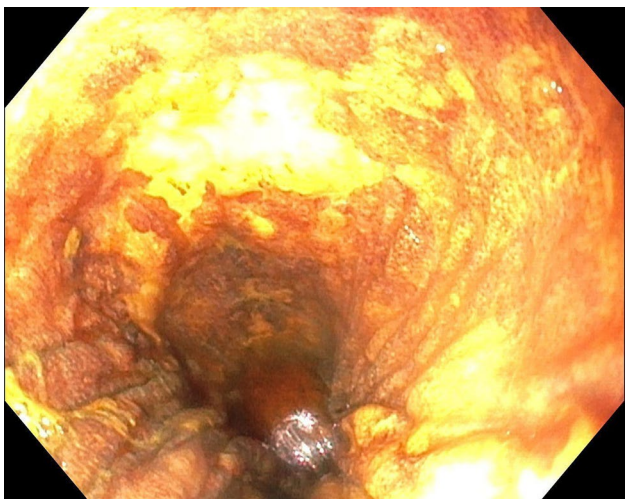

Fig. 3 Lugol's iodine chromoendoscopy identified non-staining areas, endoscopic resection demonstrated intra-mucosal SCC

Staging

Whereas imaging technologies (PET-CT and EUS) are required to stage advanced esophageal cancer, the cornerstone of staging early esophageal cancer is endoscopic resection (ER). Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are methods of ER used to most accurately identify depth of invasion. EMR is an acceptable method for lesions less than 15 mm in size, whereas ESD is preferred for larger lesions to acquire an *en bloc* specimen. Unlike imaging, ER also provides information about degree of differentiation and lymphovascular (LV) invasion. Depth of invasion [16–21], histologic grade [19–22], and LV invasion [11, 16–18, 20] all predict risk of

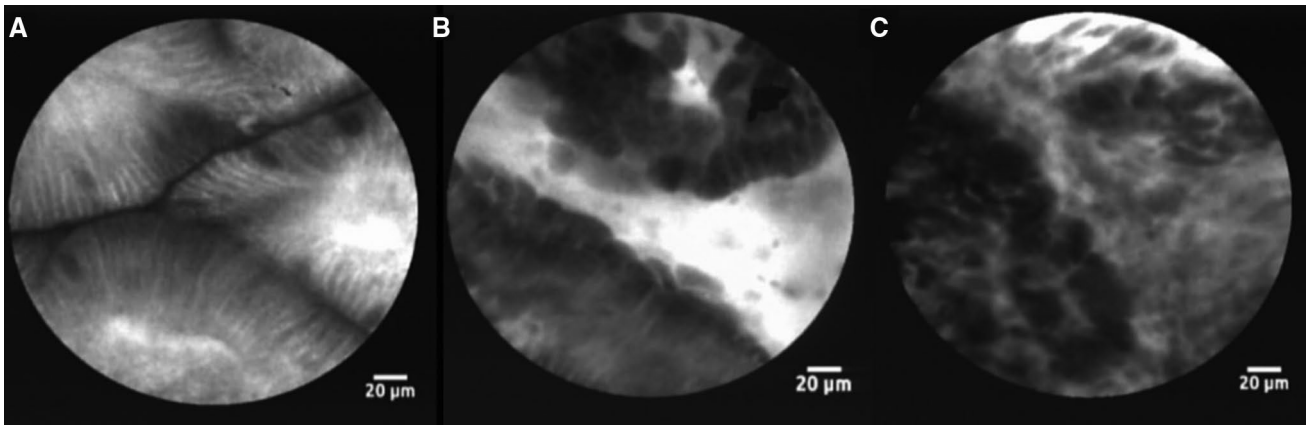

Fig. 4 Probe-based confocal laser endomicroscopy (pCLE): **a** non-dysplastic Barrett's esophagus with goblet cells easily identified, uniform columnar epithelium with equidistant glands and cells, **b** dysplastic Barrett's esophagus with dark, irregular, villiform structures with thick borders, and **c** early esophageal adenocarcinoma with disorganized/loss of villiform architecture, dark columnar cells with inability to identify goblet cells, and dilated irregular vessels

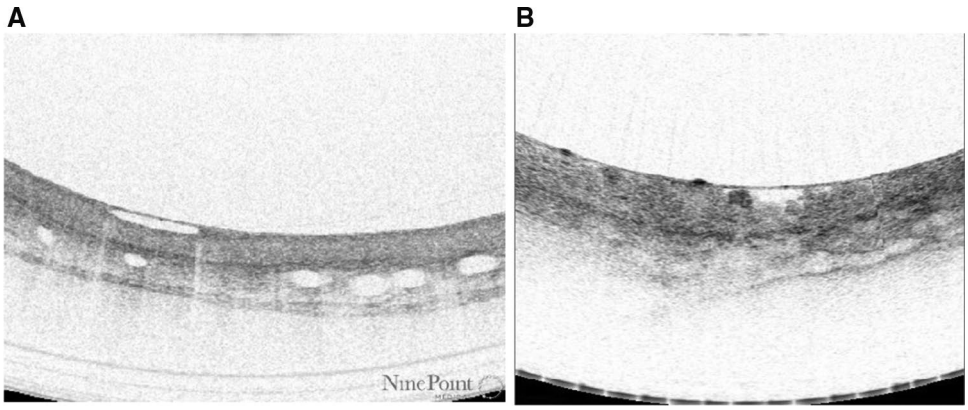

Fig. 5 Optical coherence tomography (OCT) pictures showing: **a** non-dysplastic Barrett's esophagus with well-defined layered structure including regular crypt-like glandular structures in the mucosa and submucosa without disruption, and surface intensity is equal or less compared to the subsurface, and **b** high-grade dysplastic Barrett's esophagus with loss of layering and irregular glands including irregular mucosal surface, and reduced light scattering with greater surface intensity compared to the subsurface

malignant locoregional adenopathy; therefore, it is critical to determine whether an organ-sparing approach is reasonable. In many cases, ER also serves as a curative procedure (Fig. 6).

Utility of cross-sectional imaging and EUS is unclear in early esophageal cancer. Few published studies evaluated the correlation between locoregional adenopathy and depth of submucosal tumor invasion. The risk of locoregional adenopathy and metastasis was reported only as high as 8% for intra-mucosal and 33% for SM1 esophageal cancer (Table 1) [16–19, 22–27]. Notably these studies have low sample sizes [16, 26]. Mildly hypermetabolic lymph nodes identified on PET-CT are more likely to be reactive than malignant, yet their identification may inappropriately dissuade physicians from an organ-sparing approach to treatment. EUS is less invasive to ER; however, a diagnostic accuracy of 65% in tumor staging [23] limits its ability to establish a defined role distinguishing intra-mucosal to submucosal involvement.

In a nationwide survey conducted by our group, only 56% and 38% recommended EMR to stage a 10-mm EAC and SCC, respectively. For a 10-mm cancer, approximately 25% did not recommend any cross-sectional imaging [28]. This suggests that education initiatives utilizing ER in staging and further investigation regarding the accuracy and cost–benefit of EUS and cross-sectional imaging in early esophageal cancer are warranted.

Treatment and Surveillance

Prior to the introduction of endoscopic techniques, esophagectomy was the treatment of choice for early esophageal cancer. Esophagectomy provides precise pathologic

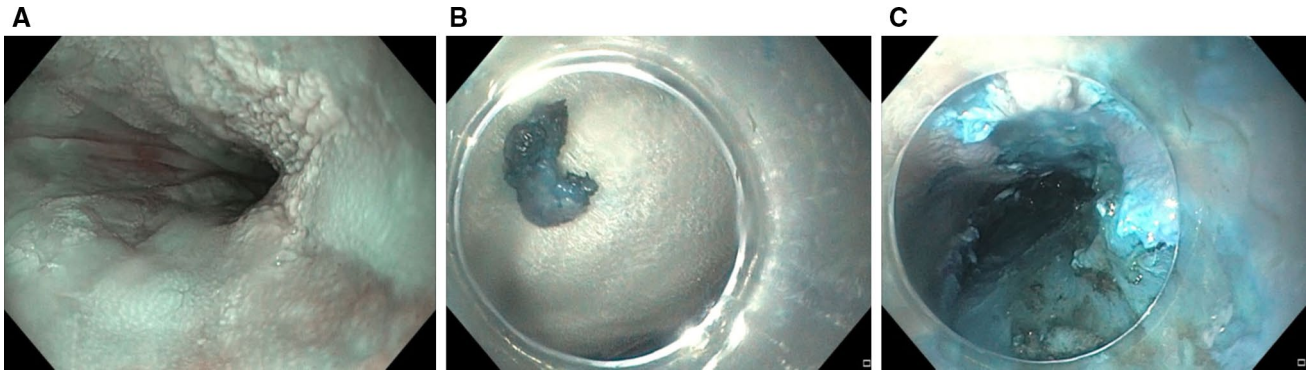

Fig. 6 Images of a 3-cm squamous cell cancer. **a** Identification of lesion on narrow-band imaging, **b** *en bloc* specimen after endoscopic submucosal dissection, **c** post-inspection following endoscopic submucosal dissection. Pathology revealed SCC with positive deep margin and lymphovascular invasion; after multidisciplinary discussion patient underwent chemoradiation and achieved a clinical complete response

Table 1 Risk of regional adenopathy and metastasis based on depth of invasion [16–19, 22–27]

T-stage	Definition	Risk of lymph node metastasis	
		EEAC (%)	EESCC (%)
Tis	High-grade dysplasia or cancer limited to epithelium (T1aM1)	0	0
T1a	Cancer limited to lamina propria (M2) or muscularis mucosa (M3)	0–4.5	0–8
T1bSM1	Cancer limited to superficial one-third or ≤ 200 µm of submucosa)	0–22	8–33
T1bSM2	Cancer extending to middle one-third of submucosa	0–36	17–30
T1bSM3	Deep invasion into the distal one-third of submucosa	20–78	36–70

EEAC early esophageal adenocarcinoma, *EESCC* early esophageal squamous cell carcinoma

staging and permanently removes the entire Barrett's mucosa at risk of progression to recurrent cancer. However, the surgery requires several days of intensive inpatient postoperative care and carries a substantial risk of mortality and morbidity [23]. Major complications risks include: death (1–8.4% in high-volume centers, and as high as 20% in low-volume centers), recurrent laryngeal nerve paralysis (29.3%), anastomotic leaks and fistulas (3–16.6%), atrial fibrillation (9.8–19%), delayed gastric emptying (10–50%), dumping syndrome (5–68%), anastomotic strictures (9–66%), and gastroesophageal reflux (60–80%) [22, 23, 32–34, 40–45].

Endoscopic eradication therapy (EET), primarily ER, can achieve complete eradication (i.e., R0 resection in the case of ER) in ≥ 90% of T1a esophageal cancers [29–31]. When compared to surgical resection of T1a esophageal cancer, EET is associated with a similar cancer-free survival and a substantially lower morbidity rate [23, 24, 32–35]. However, EET is associated with a shorter procedure and anesthesia duration, less cost, and a shorter hospital stay [23]. Given these favorable data, the National Comprehensive Cancer Network (NCCN) recommends endoscopic therapy (ET) as "preferred" when compared to surgery for Tis, T1a EAC, and SCC [3]. Esophagectomy is listed as an acceptable option. The NCCN also lists EET as a feasible option for T1bSM1 EAC and SCC without high-risk features. These high-risk features include poorly differentiated cancer (grade 3 or 4), lymphovascular or perineural invasion, and a positive deep margin [3, 16, 17, 19, 25, 36]. The rationale for EET in T1bSM1 cancer is that risk of malignant locoregional adenopathy is relatively low (0–8.7%) if high-risk features are absent [16, 17, 19, 36].

Analysis of the Surveillance Epidemiology and End Results (SEER) database from 1998 to 2009 found that only 21% of patients with stage Tis and T1 esophageal cancer were treated with EET [35]. Even among elderly patients with in situ and T1a esophageal cancer, only 12% underwent endoscopic management, while 41% underwent esophagectomy [37]. In a more recent nationwide survey of US gastroenterologists, only 12% and 23% recommended surgery for a 10-mm EAC and SCC, respectively [28]. This suggests a paradigm shift over the past decade with widespread acceptance of EET as first line therapy for T1a esophageal cancer. However, for T1bSM1 EAC and SCC, there was more disagreement. Approximately 55% of respondents selected surgery as the preferred therapy for T1bSM1 EAC as well as for SCC [28]. Thus, optimal therapy for superficial submucosal esophageal cancer is yet undefined

as evidence does not allow a consensus on treatment meriting further investigation.

Endoscopic resection: ER forms the cornerstone of EET. As described earlier, ER is ideally performed as part of staging. *En bloc* resection is preferred as it allows the pathologist to accurately assess depth of invasion as well as to determine whether residual tumor is present at the deep or lateral margins. Several endoscopic resection techniques have been described (Table 2). EMR techniques are usually less time-consuming than ESD; however, ESD may be necessary for lesions > 15 mm in size to acquire an *en bloc* specimen. Curative resection rates are as high as 100% [24]. Although substantially less morbid that esophagectomy, complications occur far more frequently than with diagnostic upper endoscopy and include bleeding (6.7%), perforation (up to 4.6%), and stricture formation (13.4%) [23, 24, 30, 31, 38].

Endoscopic ablation: Endoscopic ablation plays an adjunctive role in EET as it is used to treat residual BE after ER of early-stage EAC. In a multidisciplinary setting, ablation may be used for lesions that are endoscopically unresectable (e.g., due to fibrosis), for positive lateral margins following ER, and for multifocal early esophageal cancer [3, 39]. Ablation techniques that have been described in these settings include radiofrequency ablation (RFA), liquid nitrogen spray cryoablation (Fig. 7), photodynamic therapy (PDT), and argon plasma coagulation (APC) (Table 3). Stricture formation is a potential complication of all ablative modalities, particularly PDT. The reported risk of stricture formation after endoscopic ablation of cancer ranges from 0 to 30% (highest in PDT) [24, 39].

Indications for multidisciplinary management: A multidisciplinary discussion is warranted in patients with early esophageal cancer who have high-risk features identified from the ER specimen (positive deep margin, invasion past the superficial submucosa, lymphovascular invasion, or poorly differentiated histology). Options in these patients include an esophagectomy versus definitive chemoradiation. Salvage endoscopic ablation is an option for patients who decline or are not fit for surgery or chemoradiation, provided they are medically fit to undergo multiple sedated endoscopic procedures.

Surveillance after organ-sparing therapy: Following complete eradication of cancer and underlying BE with EET or chemoradiation, the NCCN recommends surveillance endoscopy at the following intervals: every 3 months for the first year, every 6 months for the second year, and then annually thereafter [3]. In patients who undergo surgical resection, surveillance is recommended.

Our Approach

Suggested approaches to diagnose, stage, and treat early EAC and esophageal squamous cell carcinoma (ESCC) and patients with a visible lesion are outlined in Figs. 8 and 9.

Table 2 Endoscopic resection techniques [24, 46]

Technique	Description	Pros and cons
Injection-assisted EMR	Submucosal injection facilitates capture and removal with a snare	Pro—Does not require specialized equipment; within most endoscopist's skill set Con—Flat or mildly raised tissue may be difficult to ensnare despite injection
Cap-assisted EMR	Following submucosal injection, lesion is suctioned into a distal plastic cap. Snare fits into a groove at the distal portion of the cap ("suck and cut" technique)	Pros—Cap facilitates capture of tissue, and reduces likelihood of a positive deep margin Cons—Despite submucosal injection, higher risk of resecting muscularis propria (i.e., perforation)
Band ligation EMR	Most common technique in the USA. Lesion sucked into a cap and ligated with a rubber band to create a "pseudopolyp," which is then resected using snare cautery	Pros—Submucosal injection not required; dedicated devices allow for a snare to pass through the device and for multiple band resections without scope exchange Con—Smaller outer diameter (11–14 mm) ligating cap compared to cap-assisted EMR
ESD	Submucosal injection to expand submucosal space, followed by mucosal incision and submucosal dissection using dedicated knives	Pros—allows for *en bloc* resection irrespective of the size and shape. High curative resection rates even for tumors > 2.5 cm Cons—Requires specialized training and equipment; high stricture rates (15–60%).

EMR endoscopic mucosal resection, *ESD* endoscopic submucosal dissection

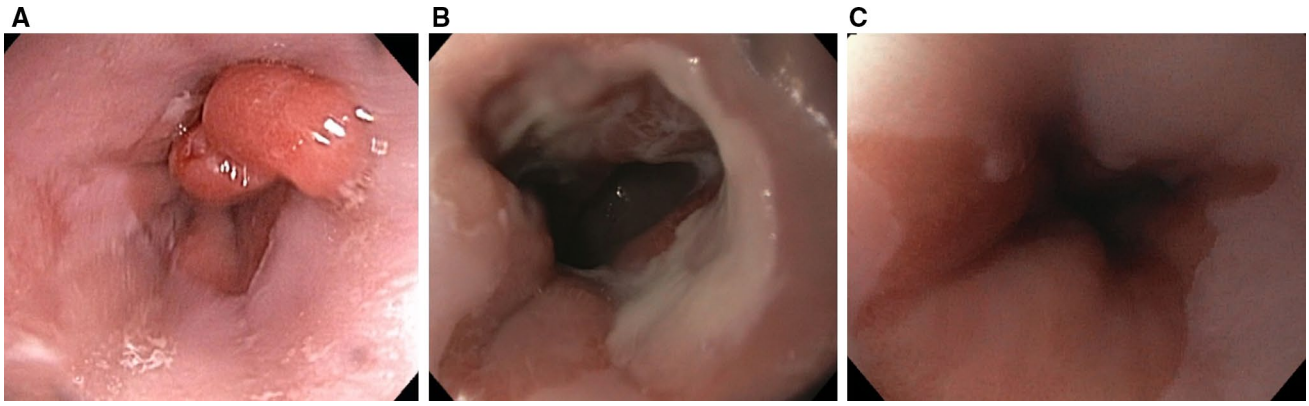

Fig. 7 **a** 25-mm esophageal mass, T1bSM2 on EUS, in a patient whose comorbidities precluded surgery and who declined chemoradiation, **b** visible ulcer but no mass seen after three sessions of liquid nitrogen spray cryotherapy, and **c** 2-year follow-up with no evidence of recurrence

Table 3 Endoscopic ablation techniques [24]

Ablation technique	Description
RFA	Bipolar energy delivered to the epithelium, which leads to water vaporization, protein coagulation, and tissue necrosis. Depth of injury is superficial, so not always suitable as a primary cancer treatment
LNSC	Uses liquid nitrogen to deliver thermal energy causing repeat cycles of freezing and thawing leading to tissue necrosis. Safe, well tolerated, and effective in BE and early EAC; limited data in ESCC
PDT	Utilizes laser therapy to activate a photosensitizer causing tissue ischemia and necrosis. Mostly used as palliative treatment. High adverse events including stricture and photosensitivity
APC	Uses argon gas to conduct electrical current inducing tissue necrosis

RFA radiofrequency ablation, *LNSC* liquid nitrogen spray cryotherapy, *PDT* photodynamic therapy, *APC* argon plasma coagulation, *EAC* esophageal adenocarcinoma, *ESCC* esophageal squamous cell carcinoma

In patients with BE, we perform HD-WLE, NBI, acetic acid chromoendoscopy along with Seattle protocol biopsies (4-quadrant biopsies at 1–2-cm intervals) to assess for dysplasia and neoplasia. In patients without BE and with a mid- to proximal esophageal lesion, we often consider chromoendoscopy with Lugol's iodine as an adjunct to NBI. If we identify a lesion < 15 mm in size, we perform band ligation EMR during the same session using snare cautery below the band without submucosal injection. If histology is interpreted as HGD or T1a cancer, we do not routinely obtain cross-sectional imaging if the lateral and deep margins are negative and there are no high-risk features. In patients with BE, we ablate the remaining segment of intestinal metaplasia. Following complete eradication, we perform surveillance at intervals recommended by the NCCN as follows: upper endoscopy (EGD) every 3 months for 1 year, every 6 months for the following year, and then annually thereafter.

For a visible esophageal lesion ≥ 15 mm in size, we perform EUS despite its limitations to assess for deep submucosal invasion or invasion into the muscularis propria. If the muscularis propria is intact, we generally attempt ESD rather than piecemeal EMR with the rationale to obtain a single *en bloc* specimen allowing the pathologist to assess lateral and deep margins. If submucosal invasion or high-risk features including a positive deep margin are present, a PET-CT is obtained, and the case is discussed in a multidisciplinary tumor board setting. A high proportion of our patients are elderly with several comorbid conditions, so definitive chemoradiation is often selected over esophagectomy [12]. We perform repeat EGD at least 6 weeks after chemoradiation to minimize sampling non-viable tumor [47] and offer ablation for persistent or recurrent intestinal metaplasia. Patients with multifocal early esophageal cancer are also discussed in tumor board. Options for these patients include ablation, chemoradiation, or surgery.

Summary

1. NBI and acetic acid may be useful as low-cost adjuncts to increase identification of HGD and early EAC during a carefully performed HD-WLE examination; Lugol's iodine may increase identification of HGD and early SCC.

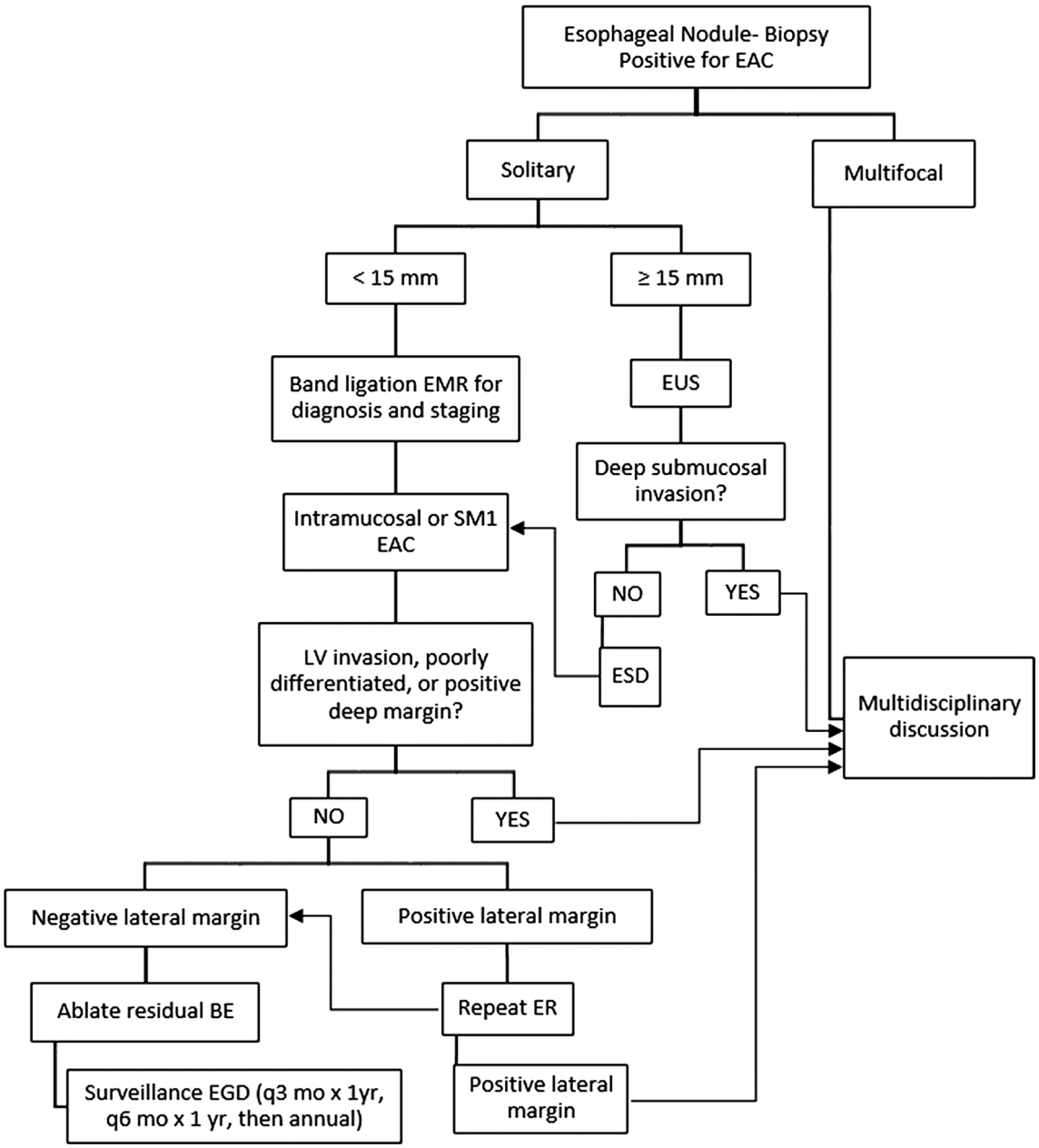

Fig. 8 An approach to diagnose, stage, and treat early esophageal adenocarcinoma. *EAC* esophageal adenocarcinoma, *EMR* endoscopic mucosal resection, *EUS* endoscopic ultrasound, *LV* lymphovascular, *ESD* endoscopic submucosal dissection, *BE* Barrett's esophagus, *ER* endoscopic resection, *EGD* esophagogastroduodenoscopy, *mo* months, *yr* year

2. ER is the best test to diagnose early esophageal cancer and to stage a visible lesion on endoscopy, particularly if the lesion is < 15 mm in size.
3. ER is preferred to surgery for T1a EAC or SCC without high-risk features (i.e., negative deep margin, no lymphovascular invasion, and not poorly differentiated).
4. EMR techniques are generally less time-consuming than ESD and allow for *en bloc* resection if the lesion is < 15 mm; ESD may be necessary to obtain an *en bloc* specimen if the lesion is ≥ 15 mm in size.
5. Endoscopic ablation is an important adjunct to eradicate residual BE, and in select settings to ablate multifocal early esophageal cancer, or solitary lesions not amenable to ER.
6. Endoscopic surveillance after successful eradication of cancer and intestinal metaplasia is recommended at the following intervals: every 3 months for the first year, every 6 months for the 2nd year, and then annually thereafter.

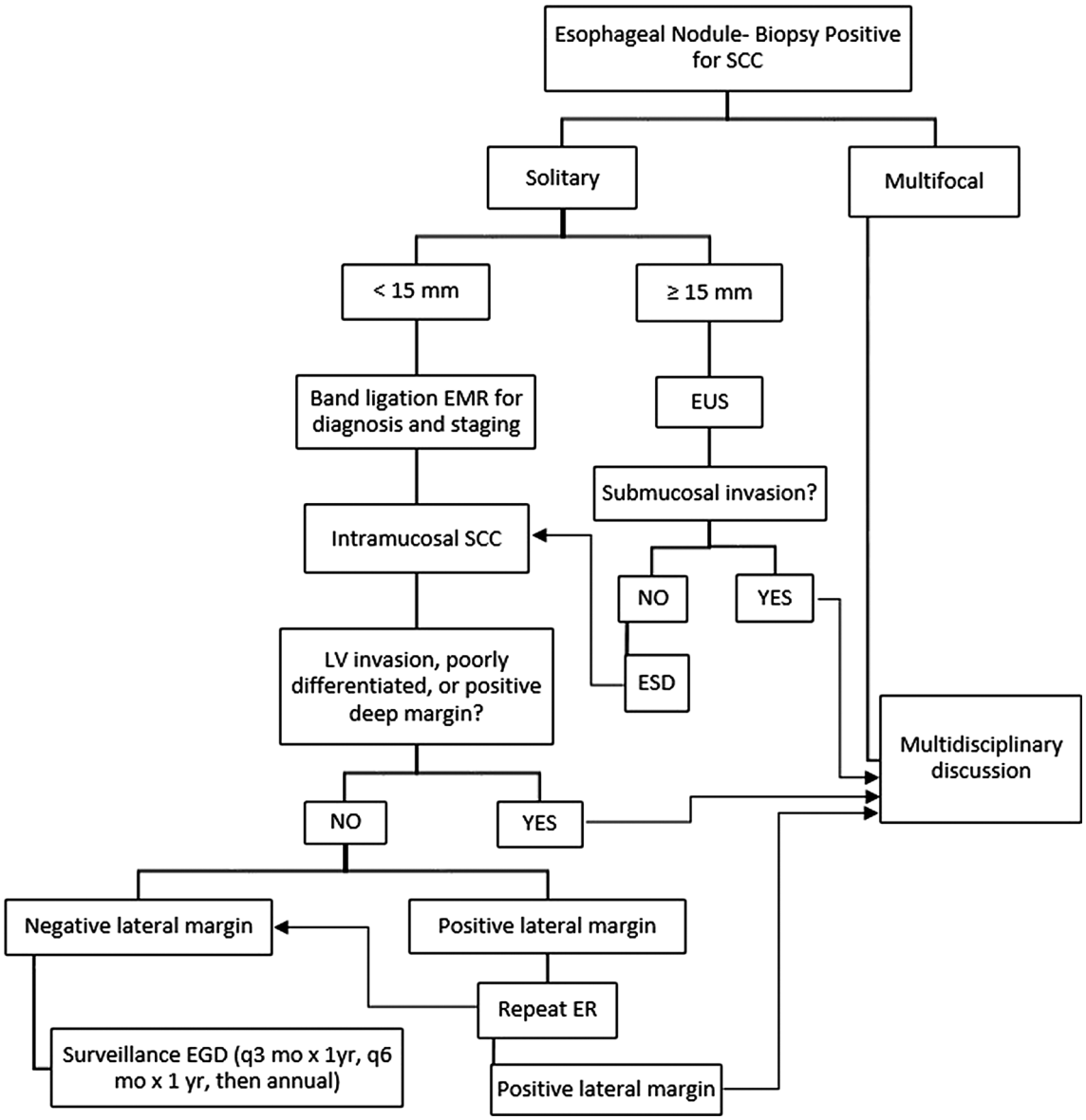

Fig. 9 An approach to diagnose, stage, and treat early esophageal squamous cell carcinoma. *SCC* squamous cell carcinoma, *EMR* endoscopic mucosal resection, *EUS* endoscopic ultrasound; *ESD* endoscopic submucosal dissection, *ER* endoscopic resection, *EGD* esophagogastroduodenoscopy, *mo* months, *yr* year

7. A multidisciplinary discussion is warranted for early esophageal cancer patients who have high-risk features. Options for these patients include surgery, chemoradiation, or salvage endoscopic ablation.

Compliance with Ethical Standards

Conflict of interest Dr. Shah served on a research advisory board for CSA Medical, Inc.

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