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# Treatment of High-Grade Dysplasia and Early Stage Esophageal Adenocarcinoma with an Endoscope: The Ultimate in Minimally Invasive, Curative Therapy

**Wayne L. Hofstetter · Marta L. Davila**

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**Abstract** There has been a radical paradigm shift away from esophagectomy as the standard of therapy for high-grade dysplasia and early esophageal cancer. A number of organ-sparing endoscopic procedures including endoscopic resection, radiofrequency ablation and cryoablation are emerging as viable and preferable options for the treatment of early esophageal neoplasia. This review article will discuss ideal candidates for endoscopic therapies, current treatment modalities, clinical and safety outcomes, and specific management recommendations.

**Keywords** Dysplasia · Early stage esophageal adenocarcinoma · Radiofrequency ablation · Cryotherapy · Endoscopic resection · Esophagectomy · Intramucosal cancer · Endoscope · Treatment

## Introduction

Within the past two decades, the treatment of esophageal high grade dysplasia (HGD) and early esophageal cancer has undergone radical transformation. The previous gold standard of resection has long been challenged by ablative therapies, for the most part unsuccessfully, but recent technological advances have brought about a change in the treatment paradigm that is disruptive to previous therapies and represents a clear advance in therapy. Organ-sparing therapy is now accepted to be definitive and effective management of selected cases of HGD and intra-mucosal cancer (IMC) of the esophagus [1•, 2–4].

In the United States, the incidence of esophageal adenocarcinoma (EAC) has been increasing disproportionately to other disease sites [5]. In fact, the rise in incidence of EAC is inconsistent with most other cancers which are either stable or declining. The reasons for this are not completely clear, but what known is this is an insidious disease. Symptoms occur late in the disease process leaving most cases of EAC diagnosed at an advanced stage; a point where the disease is lethal in the majority of patients. Therefore, it is imperative that we make an early diagnosis and institute appropriate treatment in the hopes of impacting survival.

### Etiology, Risk and Endoscopic Surveillance of BE

First and foremost is a discussion on the etiology of the disease and who is at risk to develop HGD or esophageal adenocarcinoma. Increased body mass index (BMI), hiatal hernia, and gastroesophageal reflux disease (GERD) are all considered to be contributors to the formation of Barrett's esophagus (intestinal metaplasia) [6]. Barrett's is one of the most important risk factors and is considered to be a precursor for esophageal adenocarcinoma (EAC) [3–5]. However, it is also recognized that many patients presenting with a new diagnosis of HGD or IMC have never had symptoms of reflux. Whether that is because "silent" reflux is present in this subgroup of patients, or there are other variables driving the progression to neoplasia is not

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W. L. Hofstetter (✉)
Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, 1400 Pressler Ave Unit 1489, Houston, TX 77030, USA
e-mail: whofstetter@mdanderson.org

M. L. Davila
Department of Gastroenterology, Hepatology and Nutrition, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 146, Houston, TX 77030, USA

fully understood. There is, however, a better comprehension about disease progression once Barrett's esophagus is present. Through a series of genetic alterations-BE can progress from non-dysplastic intestinal metaplasia to low-grade dysplasia (LGD), high-grade dysplasia (HGD), and invasive esophageal adenocarcinoma [7]. But, an orderly progression through the metaplasia-dysplasia-cancer sequence may not be present in every patient; even those undergoing close surveillance. One explanation is that we are missing those events in real-time, another being that the disease has the ability to skip intermediate stages. Nonetheless, guidelines on who to screen and how often are one of the most important elements in discovering early, curable disease that can be treated without surgery, chemotherapy or radiation. Because it is rare that patients present with symptoms of early disease, other clues should be used to set into motion the need for a screening endoscopy. Unfortunately, current recommendations by expert consensus panels lack sufficient evidence to support routine screening for BE. According to the AGA report "well-established risk factors for Barrett's esophagus include advanced age, male sex, white ethnicity, GERD, hiatal hernia, elevated body mass index, and a predominantly intra-abdominal distribution of body fat. [However], despite the considerable published data available on risk factors for Barrett's esophagus, few attempts have been made to apply this information systematically in the design of guidelines on who to screen for the condition" [1•].

Despite a lack of consensus, we would recommend that any patient who has had long standing reflux requiring therapy, or continues to be symptomatic with GERD despite therapy, has a family history of esophageal neoplasia, or unexplained anemia should strongly consider screening for Barrett's esophagus. Furthermore, longitudinal studies have shown that initial presentation with erosive esophagitis (LA Grade C/D) and regular intake of PPI were independently associated with progression to Barrett's esophagus, warranting screening in these populations [8]. If BE has been discovered, the purpose of surveillance is to detect the presence of esophageal lesions that are at high risk of progressing to EAC. Although the benefit of surveillance has not been conclusively proved, several studies have shown that patients who contracted EAC while under surveillance presented at a lower stage of disease and had improved survival when compared to those not undergoing surveillance [9–11]. In fact, a number of gastroenterological societies have developed surveillance guidelines under the assumption that the practice will reduce deaths.

As the risk of EAC varies depending upon the degree of dysplasia, surveillance guidelines also vary (Table 1). Patients with non-dysplastic BE (NDBE) should consider endoscopic surveillance every 3–5 years [11]. Careful inspection of the Barrett's segment with white light high-resolution endoscopy remains the standard of care, with 4-quadrant biopsies taken every 2 cm (Seattle protocol); any degree of dysplasia should be confirmed by an expert pathologist [12]. Moreover, if mucosal irregularities are identified these should be biopsied (with multiple bites taken to increase accuracy) and submitted in separate specimen containers for expert review. Patients with low-grade dysplasia (LGD) should have two expert pathologists review the biopsy specimens and may undergo repeat surveillance within 6 months to confirm the diagnosis. There is level 1 evidence to support endoscopic treatment of LGD with radiofrequency ablation given a natural history toward increased risk of progression to high grade dysplasia or cancer [13•]. Patients who opt not to treat LGD should undergo surveillance yearly.

**Table 1** Guidelines for patients with Barrett's esophagus with and without dysplasia

| Diagnosis | Recommendations |
|---|---|
| Non-dysplastic BE | EGD every 3–5 years |
| | Four-quadrant biopsies every 2 cm |
| | Focused biopsy on areas of abnormality |
| Low-grade dysplasia | Confirm results with expert pathologist |
| | Follow-up EGD with biopsies in 6 months |
| | Consider endoscopic resection and/or ablation |
| | Surveillance after therapy is necessary |
| High-grade dysplasia | Confirm results with expert pathologist |
| | Refer for endoscopic resection and/or ablation |
| | Consider esophagectomy in refractory cases |
| | Surveillance after endoscopic therapy is necessary |

Despite older literature that advocated for surveillance, patients with confirmed high-grade dysplasia (HGD) should always be referred for treatment [12, 14•, 15]. There are several strong indications for this recommendation. First, without intervention, the risk of progression from *flat* HGD to EAC is high, ranging from 6 to 19 % per year. Patients with macroscopically visible lesions, such as a nodular esophagus, have a much higher risk of progression [15, 16••]. Second, there is a risk of concomitant adenocarcinoma in patients diagnosed with BE-HGD. For patients undergoing esophagectomy whose indication was BE-HGD, surgical literature consistently reported the risk of harboring invasive cancer as ±50 % [14•]. Given better endoscopy techniques and better equipment, more recent literature suggests that the rate of undiagnosed cancer may be as low 11 % in patients with visible lesions [17].

The only patients who should consider surveillance in the presence of HGD are those who are unfit or unwilling to undergo therapy. In this case endoscopy should be scheduled every 3 months with random 4-quadrant

biopsies every 1 cm with focused biopsies on any mucosal irregularity.

## Diagnosis and Staging

A very careful exam of the Barrett's segment is recommended using high-definition white light endoscopy. In fact, a study by Gupta et al. [18] shows that the longer the time spent inspecting the Barrett's segment, the higher the likelihood of detecting suspicious lesions. In that study 112 patients underwent surveillance by 11 different endoscopists. Those who had an average inspecting time greater than 1 min per centimeter BE, detected more suspicious lesions than those who spent a minute or less, and there was a trend towards higher detection of HGD/EAC.

A number of recent imaging technologies such as chromoendoscopy, narrow band imaging (NBI-Olympus TM), autofluorescence imaging, and confocal laser endomicroscopy, have become available for detailed visualization and characterization of mucosal and cellular architecture. Although the use of chromoendoscopy is not well defined in routine surveillance of BE, we advocate using either electronic imaging or vital staining to facilitate the examination of patients suspected of having HGD. These modalities may be helpful in guiding focused biopsies [11, 19].

In cases of large and obviously invasive EAC, endoscopic ultrasound (EUS) is routinely used to estimate the depth and nodal status of the disease. In contrast, EUS has a limited role in the evaluation of patients with BE-HGD and early EAC. Most experts would not recommend EUS in patients with a flat Barrett's segment and HGD detected by biopsy. In the evaluation of superficial lesions, the accuracy of EUS staging is modest at best [20]. In a study comparing the accuracy of endoscopy to EUS, the sensitivity of EUS staging for mucosal tumors was 90 % and for submucosal tumors 46 %, which was not significantly different from the sensitivity of high-resolution endoscopy in experienced hands [21]. A systematic review compared EUS staging to endoscopic mucosal resection (EMR) or surgical pathology for early (T1–T2) tumors, EUS predicted the T-stage of the target lesion with 67 % accuracy (12 studies, $n = 132$). As some patients had multiple lesions, on an individual patient analysis the accuracy of staging was only 56 % [22•]. There are several factors that may predispose to poor prediction of stage using EUS in early EAC including: wall thickening due to inflammation, presence of a duplicated muscularis mucosa, anatomical changes at the level of the GE junction/cardia, and endoscopist's experience [22•]. Despite the inaccuracies in determining depth, we would continue to advocate for EUS-guided fine needle aspiration (FNA) in select cases where there is a possibility of detecting malignant lymphadenopathy. In a study of 25 patients referred for EUS evaluation (12 diagnosed with BE-HGD and 13 with intra-mucosal adenocarcinoma), 7 patients were found to have suspicious lymphadenopathy. Fine-needle aspiration confirmed malignancy in 5 of these 7 patients. Therefore EUS identified 5 patients (20 %) who were unsuitable candidates for endoscopic therapy [23]. Studies like this one highlight the importance of a careful approach to individual patients with BE and mucosal lesions.

Endoscopic mucosal resection (EMR) has emerged as a diagnostic and therapeutic tool for patients with BE-related early adenocarcinoma. EMR allows for removal of mucosal and superficial submucosal lesions and is superior to EUS for the assessment of depth of invasion. In comparison to EGD-EUS, EMR will change the clinico-pathologic assessment in 30–49 % of cases [24, 25]. In a prospective study of 75 patients with biopsy proven HGD or early cancer, pathology from an EMR changed the grading or staging in 48 % of patients (downgrading in 28 % and upgrading in 20 %) [24]. In another study of 293 EMR procedures for focal lesions, the final histology led to a change in treatment in 30 % [25]. Imagine altering the recommended therapy of an individual patient from combined multimodality therapy with chemoradiation and surgery to an organ-sparing, curative EMR.

In summary, optimal staging is key to the management of BE-associated mucosal lesions. Endoscopic resection can play a large role in the work up and treatment of patients with early disease.

## Endoscopic Treatment of HGD/IMC

- Endoscopic therapy can be divided into therapies that ablate or destroy tissue and therapies that resect tissue.
- Endoscopic resection can supply a large piece of tissue to pathology for interpretation.
- Ablation therapies do not provide a pathologic specimen and are considered suboptimal to resection therapies. However, ablation therapies can be applied to larger surface areas.
- Ablative therapies include photodynamic therapy, thermal laser, APC (argon plasma coagulation), multipolar electrocoagulation, radiofrequency ablation (RFA) and cryoablation. Of those, we will focus on describing radiofrequency ablation and cryoablation given their effectiveness, ease of application, and low risk of adverse effects.

## Radiofrequency Ablation

Radiofrequency ablation (Covidien, Sunnyvale, CA, USA) achieves direct tissue destruction through a system that

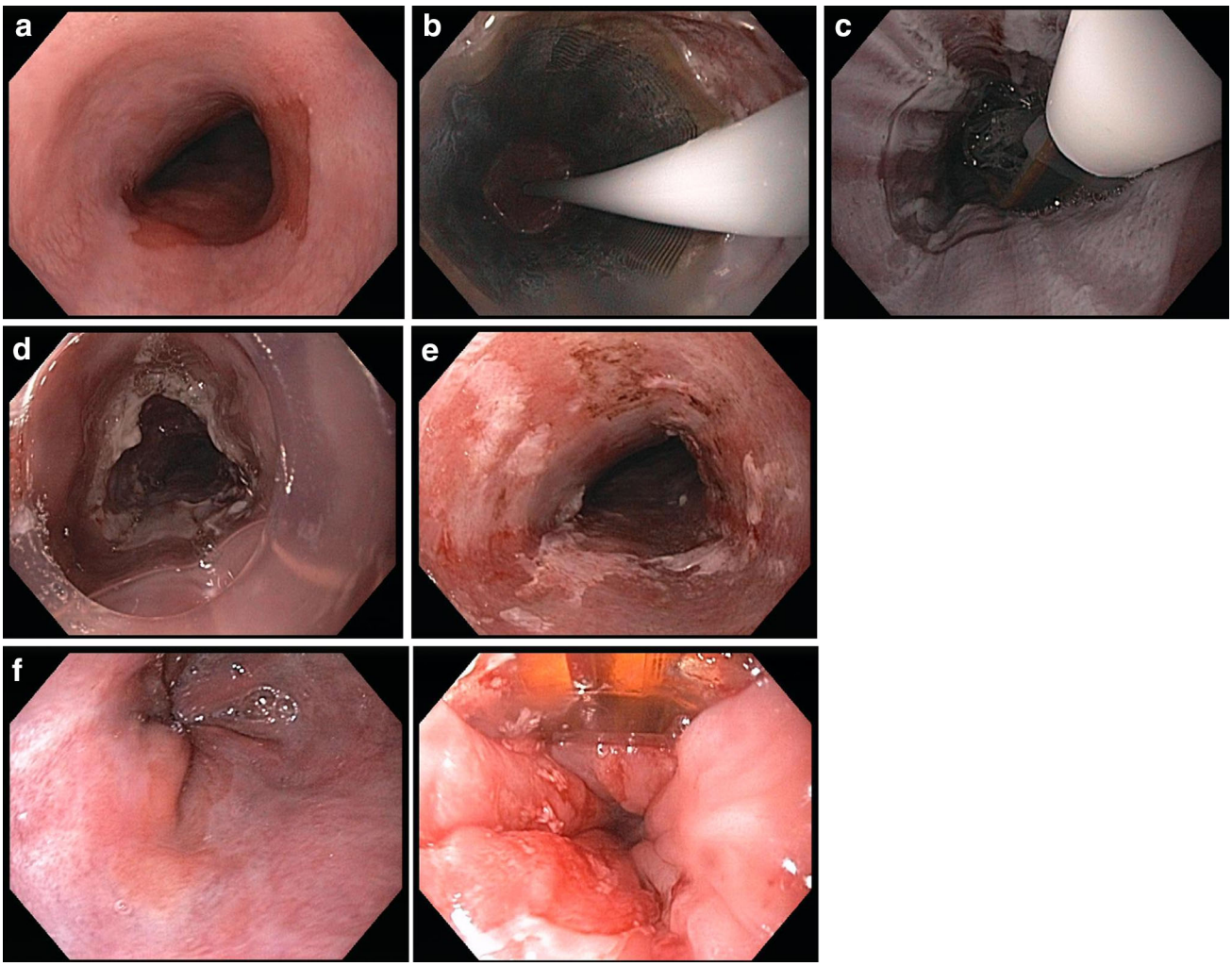


**Fig. 1** **a** Long segment circumferential Barrett's esophagus. **b** Endoscopic view of Barrett's esophagus treated with the HALO 360 balloon electrode. **c** Endoscopic appearance post-balloon treatment. **d** Treatment of a Barrett's island with the HALO 90 device

delivers heat-energy to the esophageal mucosa. The depth of ablation is between 500 and 1,000 μm depending on the intrinsic properties of the esophagus and the energy setting used. Mucosal ablation is performed under endoscopic guidance followed by immediate debridement of the ablated area (Fig. 1). The ablation treatment is repeated in the same area, so that there is full treatment of the Barrett's segment all within one endoscopy session. Follow up EGD is performed in 2–3 months to assess tissue response. Multiple endoscopic treatments may be required to attain complete eradication of dysplasia and/or metaplasia, with the goal being total resolution of metaplasia. Treatments are usually performed every 2–3 months until therapeutic goals are met, then surveillance is continued.

Several studies have demonstrated the efficacy, safety and durability of RFA to treat dysplastic BE [16••, 16, 26–28]. In a randomized multicenter study, 127 patients with dysplastic BE were assigned to receive either radiofrequency ablation or sham procedure [16••]. 84 patients were randomized to the RFA treatment group, 42 patients had HGD and 42 had LGD. On average, patients received 3.5 treatments. Among patients with HGD, complete eradication of dysplasia (CE-D) occurred in 81 % of patients assigned to the ablation group as compared to 19 % of those assigned to the control group ($p < 0.001$). Among patients with LGD, eradication of dysplasia (CE-D) occurred in 90.5 % of patients in the treatment arm, as compared to 22.7 % of those assigned to the control group ($p < 0.001$). Overall, 77.4 % of patients in the RFA group had complete eradication of intestinal metaplasia (CE-IM) compared to 2.3 % of those in the control group ($p < 0.001$). Progression from HGD to cancer occurred in 4/21 patients in the control group and in only 1/42 patients in the RFA treated group ($p = 0.045$). Regarding

durability, at 2 years, among subjects with initial BE-HGD, there was CE-D in 93 % and CE-IM in 89 %. At 3 years, CE-D was reported in 98 % of patients and CE-IM in 91 %, but note should be made of a significant limitation in the study where only 56 patients completed the study. The annual rate of progression to EAC among those treated with RFA was 0.55 % per patient per year [26].

RFA is safe and well tolerated. The most common complications reported include: chest pain lasting less than 1 week, strictures requiring dilation (6–8 %), and gastrointestinal hemorrhage (1 %) [16••, 29].

Sub-squamous intestinal metaplasia (SSIM) or the presence of intestinal metaplasia beneath squamous epithelium (so called "pseudoregression" or "buried glands") has been reported following all ablative techniques, including photodynamic therapy (PDT), APC and multipolar electrocoagulation. The main concern with SSIM is that it cannot be detected by endoscopic visual examination. Studies examining the prevalence of SSIM following RFA treatment indicate that RFA might decrease the prevalence of SSIM. In the only randomized sham controlled trial of RFA for dysplastic BE, 25.2 % of subjects were reported to have SSIM prior to ablation. Among patients treated with RFA, the prevalence of SSIM decreased to 5.1 % after 12 months and 3.8 % after 24 months [16••, 16, 26]. Alternatively, SSIM was noted in 40 % of patients randomized to sham procedure at 12-month follow-up [16••]. In a prospective multicenter study of patients with non-dysplastic BE treated with RFA, biopsy specimens obtained from 50 patients at 5-year follow-up revealed no evidence of SSIM [28].

Following RFA treatment continued endoscopic surveillance is indicated to monitor for recurrence, which occurs with an incidence at 1-year ranging from 5 to 25 % [30, 31]. Currently, there are no consensus recommendations regarding surveillance interval in post-ablation patients. Some experts recommend surveillance endoscopy every 3 months for the 1st year, every 6 months for the 2nd year, and then annually [32].

## Cryotherapy

Cryotherapy is an ablative technique that causes tissue destruction by a non-contact application of liquid nitrogen or carbon dioxide gas (Fig. 2). Because the technique involves the use of an expansile gas, a decompression tube must be placed into the stomach to avoid iatrogenic perforation into the abdomen from over-distension [33, 34]. A spray catheter is advanced through the endoscope and cycles of rapid freezing and slow thawing are applied to a targeted area. Small areas can be treated (2–3 cm) while covering about one-third or one-half of the luminal circumference with each application. Multiple areas can be treated in one endoscopic session. On average, 3–4 endoscopies are needed to completely ablate a long segment of disease and the procedures can be performed about every 6–8 weeks.

There are no randomized controlled studies assessing the efficacy of cryotherapy in the treatment of dysplastic BE. In a multicenter retrospective study [34] of liquid nitrogen in patients with BE-HGD, 97 % of patients had complete eradication of HGD and 87 % had complete eradication of all dysplasia. 57 % of patients had CE-IM at a mean follow-up of 10.5 months. The most common adverse events reported included: strictures in 3 % which responded to endoscopic dilation, and chest pain in 2 %, managed on an outpatient basis. With regards to cryoablation for early cancer, a multicenter retrospective study of liquid nitrogen for esophageal cancer was published in 2010. Complete eradication of cT1a tumors occurred in 18/24 (75 %) patients. For cT1b (submucosal) tumors, complete eradication was seen in 4/6 patients (60 %) with a mean follow-up of 11.8 months [35]. Caveats must be made that these cancers were clinically staged with the inherent deficiencies of EUS staging, and because ablation was chosen over endoscopic resection, no tissue is provided to pathology for analysis.

There are no studies comparing cryotherapy to other ablative therapies and specific recommendations cannot be made regarding when to use cryotherapy over RFA. Among experts, cryotherapy has been used in patients who have failed RFA or to treat BE patients in the setting of strictures.

## Endoscopic Resection

Endoscopic mucosal resection (EMR) is currently indicated as part of the work up and potential treatment of areas of nodular BE and suspected early esophageal tumors [36•, 37, 38, 39•, 40•, 41, 42]. Short segments of flat HGD that can be completely resected endoscopically may also be amenable to EMR as a treatment option. Historically, the procedure gained acceptance as a treatment for polyps and early-staged cancers within the colon. It was later translated into a treatment for esophageal SCCA in Asian medical centers. Since then, groups in Germany, the Netherlands, and North America have shown that the utilization of this modality is a reasonable if not preferable option to surgery for the treatment of HGD and early esophageal and GEJ adenocarcinoma [39•, 40•, 41, 42]. For HGD, the main goal is to resect areas of esophagus that have visible lesions, whether that is a solitary nodule, an area of nodularity or a superficial ulcer. Quite frankly, areas of flat HGD are often adequately managed by endoscopic ablation therapies alone. As mentioned above, an exception to this would be an area containing HGD that could be totally resected by EMR (preferably without circumferential resections that will cause serious stricture issues).

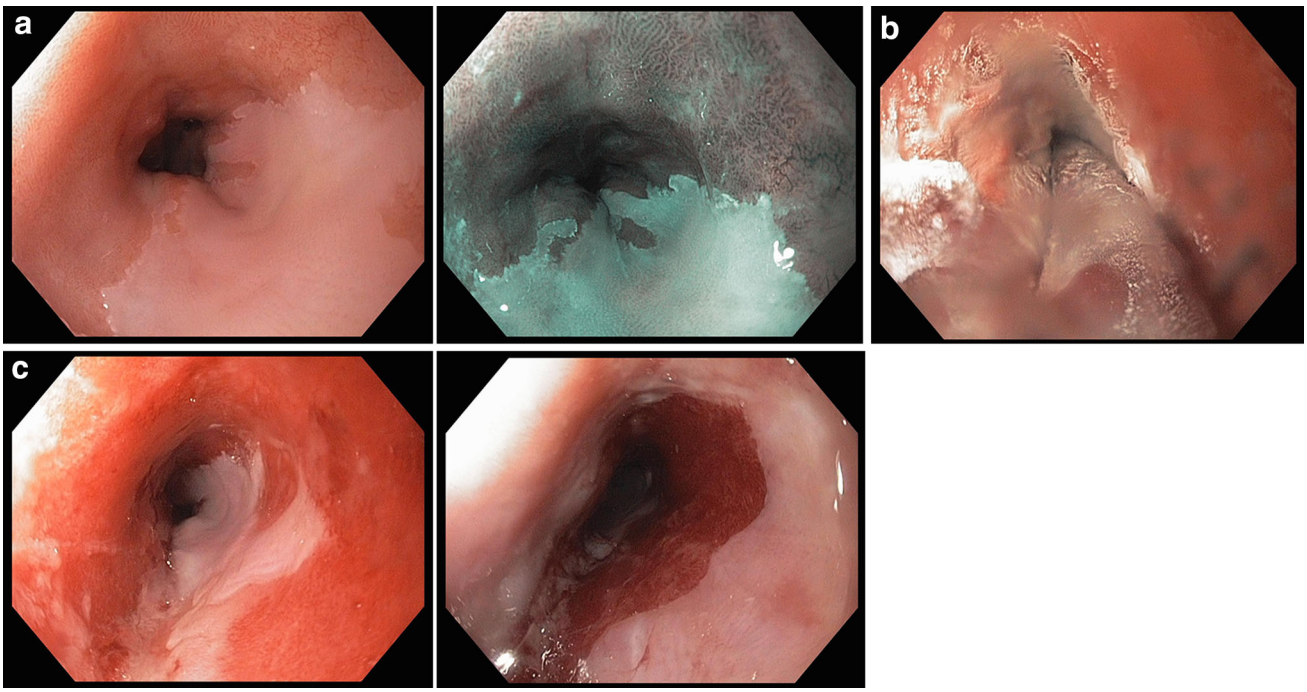


**Fig. 2** **a** Endoscopic appearance of a Barrett's island, **b** cryoablation treatment, **c** healing after cryotherapy

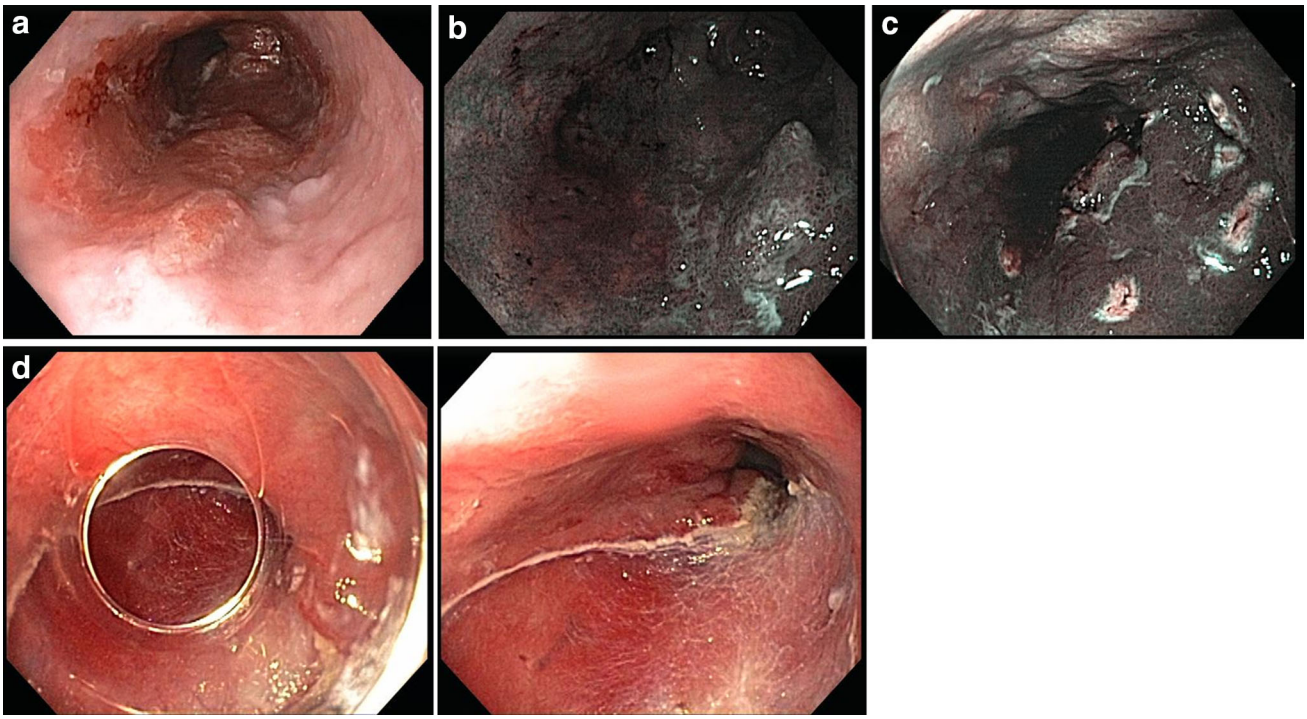


**Fig. 3** **a** Endoscopic appearance of an early adenocarcinoma at the gastroesophageal junction. **b** Appearance under narrow-band imaging (Olympus). **c** Cautery marks the margins of resection, **d** post-resection appearance

Lesions amenable to EMR must be superficial (Tis-T1) and small enough to be completely resected endoscopically. Patients with the lowest risk for regional or systemic disease will have lesions that are less than two cm in maximal dimension. Mucosal adenocarcinomas are associated with very low rates of lymph node metastases

(<3 %) and can be managed with endoscopic therapies; whereas tumors invading the submucosa have a substantial risk of lymph node metastases (in excess of 20 %) and should be referred for esophagectomy [39•].

The critical steps in the procedure involve (Fig. 3a–d):

(1) Identification of the lesion

Endoscopists must be experienced at detecting normal from abnormal. The endoscopy equipment is critical to the outcome of therapy. High definition equipment is mandatory.

(2) Outline the area of resection

The area to be removed must be marked prior to introducing the cap. We are frequently surprised at how an obvious lesion becomes difficult to see once a scope with a cap partially obstructs our view in the esophagus. The endoscopist may also choose to place marks (cautery, ink or clips) on the tissue to be resected to orient the tissue margins for the clinician and pathologist.

(3) Perform the resection

Multiple methods of EMR or endoscopic submucosal dissection (ESD) are currently utilized. EMR with a cap and snare technique with or without a rubber band followed by a cauterized snare to resect down to the submucosal level are quite facile. Smaller lesions and selected lesions that are up to 2 cm can be removed entirely en bloc with suction cap techniques. Larger lesions are resected with an EMR-cap by a "piecemeal" approach where the lesion is removed by multiple applications of the cap and snare to include overlapping areas ultimately resulting in a complete resection [40•]. On the other hand, ESD is more likely to achieve an en bloc resection for larger or deeper lesions but it is technically more difficult and results in more frequent complication such as perforation or bleeding. For this reason it is performed only in selected centers where specialized training has been performed.

(4) Post-resection management

The procedure is often performed with the help of sedation; anesthesia support is welcomed but not critical. Patients are discharged home the same day unless there are co-morbidities or complications that mandate otherwise. We typically allow liquids the first day, and liberalize the diet when symptoms allow. Patients and family need to be educated on expected outcomes and potential signs of complications. Expected short-term outcomes will include chest discomfort and odynophagia for a few days after resection so we provide a prescription compound that includes an ionic binder to help heal the iatrogenic ulcer and a local anesthetic to alleviate symptoms. Mild to moderate dysphagia can also be a frequent complaint associated with healing but most often subsides after 6–8 weeks.

Complications specific to EMR include perforation, an event that is seen in less than 1 % of cases using most cap techniques. This is in contrast to reports of perforation in upwards of 40 % for aggressive ESD procedures. However, almost all perforations, including those associated with ESD can be handled non-operatively. Bleeding risk is 2–3 % for EMR. Stricture may occur and this depends on previous pathology in the individual patient and the amount of circumference removed at the time of resection. Removing over 50 % circumference significantly increases the risk of stricture. Complete circumferential resections can be performed, but we typically like to stage procedures that will require circumferential resections into several episodes.

(5) Interpretation of pathology

Lesions that are treated successfully with EMR are most often limited to the mucosa. Submucosal invasion increases the risk of lymph node invasion and/or cancer related events of recurrence or death. Lymphovascular invasion (LVI) is the most important prognostic determinant of outcome for resected early stage cancer [39•]. Typical risk of nodal involvement increases from 2 to 3 % for a T1a lesion without LVI to 60 %+ for T1b lesions with LVI [39•, 41]. Size of tumor and differentiation have been shown to be independent prognostic variables in some studies, where lesions less than 2 cm and well to moderately differentiated are less likely to harbor concurrent adenopathy [39•, 42].

(6) Follow up

It has been our practice to perform endoscopy every 2–3 months while in the process of ablating residual metaplasia/dysplasia, followed by increasing intervals between procedures depending on individual findings. The need for cross-sectional imaging is debated in small T1a lesions given the low risk of regional or distant metastasis, and it is not at all indicated for patients with dysplasia only. Patients at higher risk for regional and distant disease such as those with deeper, or larger lesions, or those patients with LVI who have opted for endoscopic treatment alone based on risk for esophageal resection should undergo imaging every 4–6 months and consider EUS to screen for regional disease.

## Combining Endoscopic Resection with Mucosal Ablation

After EMR the remaining BE segment should be eradicated even in the absence of dysplasia. If the remaining BE segment is left untreated, the risk of metachronous lesions has been reported to be as high as 30 % [43, 44]. A number

of studies have evaluated the efficacy and safety of combining EMR with radiofrequency ablation to eradicate residual intestinal metaplasia. Pouw et al. reported their experience with 23 patients who underwent EMR for visible lesions; 16 patients had early cancer and 7 patients had BE-HGD. RFA was performed at least 6 weeks after the EMR. Complete eradication (CE)-neoplasia was achieved in 100 % of patients (median follow-up 22 months) and CE-IM in 88 % of patients [43].

In a another retrospective study of 65 patients treated with EMR and RFA for nodular disease, and 104 patients treated with RFA alone for flat BE, there were no significant differences in eradication of dysplasia and intramucosal carcinoma between the two groups. Furthermore, the complication rates were similar, including strictures that occurred in 4.6 % of patients in the EMR-before-RFA group and in 7.7 % of patients in the RFA only group [44]. This underscores the premise that endoscopic resection can be reserved for dysplasia-associated lesions that are visible while RFA alone may suffice for flat pathology.

Combined EMR with RFA may be the preferred approach over stepwise radical endoscopic resection for the treatment of BE-HGD associated with early cancer. In a multicenter study from The Netherlands, patients with a BE segment $\leq$5 cm containing HGD/early cancer were randomized to stepwise radical endoscopic resection (SSER) or endoscopic resection followed by RFA. Both groups achieved excellent (>90 %) comparable rates of CE-neoplasia and CE-IM; however, those in the SSER group developed a significantly higher number of strictures requiring endoscopic dilation (88 % in the SSER group compared to 14 % in the EMR-RFA group, $p < 0.001$) [45].

But how does endoscopic treatment compare to esophagectomy? One specialized center retrospectively compared endoscopic therapy performed in 40 patients (22 with HGD and 18 with IMC) to esophagectomy in 61 patients (13 with HGD and 48 with IMC). Endoscopic therapy consisted of 102 endoscopic resections and 79 ablations. There was no difference in survival between the two groups (94 % at 3 years), but compared to esophagectomy, endoscopic therapy was associated with significantly lower morbidity (39 vs. 0 %, $p < 0.0001$) [46].

In summary, EMR followed by RFA is an effective treatment modality for early cancer arising in the setting of Barrett's esophagus. However, these techniques are best performed at high-volume referral centers by experienced endoscopists. The outcomes may not apply to general practices.

## Conclusions

Endoscopic therapies have been shown to be effective and safe in the treatment of patients with BE-HGD and early esophageal cancer while preserving the esophagus. Patients with mucosal adenocarcinoma arising from BE can be effectively treated with a combination of endoscopic resection followed by ablation. Close surveillance of these patients is recommended after endoscopic therapy because of the risk of recurrence. Given the complexities in the evaluation and management of these patients, it is best to manage them by a multidisciplinary team in a tertiary referral center with expertise in esophageal diseases.

### Compliance with Ethics Guidelines

**Conflict of Interest** Wayne L. Hofstetter consultant for Ethicon. Marta L. Davila nothing to disclose.

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Papers of particular interest, published recently, have been highlighted as:
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