

Medical Policy Manual

Topic: Endoscopic Radiofrequency Ablation or Cryoablation for Barrett's Esophagus **Date of Origin:** May 25, 2010

Section: Surgery

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION^[1]

Barrett's Esophagus and the Risk of Esophageal Carcinoma

The esophagus is normally lined by squamous epithelium. Barrett's esophagus is a condition in which the normal squamous epithelium is replaced by specialized columnar-type epithelium known as intestinal metaplasia, in response to irritation and injury caused by gastroesophageal reflux disease (GERD). Barrett's esophagus occurs in the distal esophagus, may be of any length, focal or circumferential, and can be visualized by the endoscopist as being a different color than the background squamous mucosa. Confirmation of Barrett's esophagus requires biopsy of the columnar epithelium and microscopic identification of intestinal metaplasia.

Intestinal metaplasia is a precursor to esophageal adenocarcinoma, and esophageal adenocarcinoma is thought to result from a stepwise accumulation of genetic abnormalities in the specialized epithelium, which results in the phenotypic expression of histologic features of low-grade dysplasia to high-grade dysplasia to carcinoma. Two large epidemiologic studies published in 2011 reported the risk of progression to cancer in patients with Barrett's esophagus. One study reported the rate of progression to cancer in more than 8,000 patients with a mean duration of follow-up of 7 years (range 1-20 years).^[2] The de novo progression to cancer from Barrett's esophagus at one year was 0.13%. The risk of progression was reported as 1.4% per year in patients with low grade dysplasia and 0.17% per year in patients without dysplasia. This incidence translates into a risk of 10-11 times that of the general

population. The other study identified over 11,000 patients with Barrett's esophagus and after a median follow-up of 5.2 years, reported that the annual risk of esophageal adenocarcinoma was 0.12%.^[3] Detection of low-grade dysplasia on index endoscopy was associated with an incidence rate for adenocarcinoma of 5.1 cases per 1000 person-years, and the incidence rate among patients without dysplasia was 1.0 case per 1000 person-years. Risk estimates for patients with high-grade dysplasia were slightly higher.

The reported risk of progression to cancer in Barrett's esophagus in older studies was much higher, with an annual incidence of risk of 0.4-0.5% per year, with risk estimated at 30-40 times the general population. It is upon these higher risk estimates that current surveillance recommendations have been based.

Management of Barrett's Esophagus

The current management of Barrett's esophagus includes treatment of GERD, and surveillance endoscopy to detect progression to low- or high-grade dysplasia or adenocarcinoma which may warrant mucosal ablation or resection (either endoscopic mucosal resection [EMR] or esophagectomy), or combined ablation and resection.

EMR, either focal or circumferential, provides a histologic specimen for examination and staging (unlike ablative techniques). A recent study^[4] provided long-term results for EMR in 100 consecutive patients with early Barrett's associated adenocarcinoma (limited to the mucosa). The 5-year overall survival (OS) was 98% and metachronous lesions were observed in 11% of patients after a mean of 36.7 months. In a recent review by Pech and colleagues, it is stated that circumferential EMR of the entire segment of Barrett's leads to a stricture rate of 50%, and recurrences occur at a rate of up to 11%.^[5]

Mucosal ablation techniques that are available consist of one of several thermal (multipolar electrocoagulation [MPEC], argon plasma coagulation [APC], heater probe, Nd:YAG laser, KTP-YAG laser, diode laser, argon laser, and cryoablation) or nonthermal (5-aminolevulinic acid [5-ALA] and photofrin photodynamic therapy [PDT]) techniques. However, the use of PDT for Barrett's esophagus with high-grade dysplasia has decreased dramatically recently, due to the fact that it is relatively expensive and associated with a high complication rate, including photosensitivity and esophageal stricture formation in up to 30% of patients treated with this method.^[5]

The CryoSpray Ablation™ System (formerly the SprayGenix™ Cryo Ablation System, CSA Medical, Inc.) uses a low-pressure spray for spraying liquid nitrogen through an upper endoscope. Cryotherapy allows for treatment of uneven surfaces, however, disadvantages include the uneven application inherent in spraying the cryogen.

Treating dysplasia or mucosal cancer solely with ablative techniques risks undertreating the approximately 10% of patients who have undetected submucosal cancer, in whom esophagectomy would have been required.^[5]

RFA may be performed alone or in combination with endoscopic mucosal resection of nodular/visible lesions. The HALO System from BÂRRX Medical, Inc. (Sunnyvale, Calif.) uses radiofrequency energy and consists of two components: an energy generator and an ablation catheter. The generator provides rapid (i.e., less than 1 second) delivery of a predetermined amount of radiofrequency energy to the catheter. Both the HALO90 and HALO360 are inserted into the esophagus with an endoscope, using standard endoscopic techniques. The HALO90 catheter is plate-based and used for focal ablation of

areas of Barrett’s esophagus up to 3 cm. The HALO360 uses a balloon catheter that is sized to fit the individual esophagus, and is inflated to allow for circumferential ablation.

The ablation with radiofrequency affects only the most superficial layer of the esophagus (the mucosa), leaving the underlying tissues unharmed. Efficacy measures of the procedure include eradication of intestinal metaplasia without leaving behind microscopic (or “buried”) foci and post-ablation regrowth of the normal squamous epithelium. Reports of the efficacy of the HALO system in ablating Barrett’s esophagus have been as high as 70% (comparable to alternative methods of ablation [e.g., APC and MPEC]), and even higher in some reports. The incidence of leaving behind “buried” foci of intestinal metaplasia has been reported to be 20%–44% with APC and 7% with MPEC; reports using the HALO system have been 0%.^[6,7] Another potential advantage to the HALO system is that because it is automated, it eliminates operator-dependent error that may be seen with APC and MPEC.

Regulatory Status

The HALO360 received U.S. Food and Drug Administration (FDA) 510(k) clearance for marketing in 2005 and the HALO90 in 2006. The FDA-labeled indications are for use in coagulation of bleeding and nonbleeding sites in the gastrointestinal tract, and include the treatment of Barrett’s esophagus.^[8] The CryoSpray Ablation™ System received FDA 510(k) marketing clearance in December 2007 for use as a “cryosurgical tool for destruction of unwanted tissue in the field of general surgery, specifically for endoscopic applications.”^[9]

MEDICAL POLICY CRITERIA

- I. Radiofrequency ablation (RFA) may be considered **medically necessary** for treatment of Barrett’s esophagus with dysplasia when either of the following criteria (I.A or I.B) are met:
 - A. High-grade dysplasia
 - B. Low-grade dysplasia (LGD) when *both* of the following criteria are met:
 - 1. The initial diagnosis of LGD must be confirmed by 2 pathologists
 - 2. Clinical documentation must include both pathology reports
- II. Ablation of Barrett’s esophagus that does not meet the above criteria is considered **investigational**, including but not limited to the following:
 - A. Radiofrequency ablation of Barrett’s esophagus in the absence of dysplasia
 - B. Radiofrequency ablation of Barrett’s esophagus with LGD that has not been confirmed by 2 pathologists
 - C. Cryoablation for Barrett’s esophagus, with or without dysplasia

SCIENTIFIC EVIDENCE

Radiofrequency Ablation (RFA)

Systematic Reviews

- The 2010 BlueCross BlueShield Technology Evaluation Center (TEC) Assessment^[10] on the use of radiofrequency ablation (RFA) plus surveillance versus surveillance alone in the treatment of nondysplastic and low-grade dysplastic Barrett's esophagus (BE) included 1 randomized trial^[11] and 4 single-arm studies.^[6,11-13] Studies were selected for inclusion if they were full-length, peer-reviewed articles in English, and studied Barrett's esophagus treated with RFA in a comparative study of any size, or a single-arm study of at least 40 patients. The conclusions of the Assessment were that among patients with nondysplastic or low-grade dysplastic Barrett's esophagus:
 - The available evidence is insufficient to show that RFA plus surveillance achieves a better net health outcome than surveillance alone.
 - The body of evidence on disease progression is too small and of too short duration to permit conclusions about the effects of RFA on this outcome.
 - There is considerable variation in the technique of performing RFA. It is unclear whether circumferential ablation should be used more than once, how many follow-up RFA treatments are needed, and to what degree endoscopic mucosal resection may contribute toward any effects RFA may have on disease progression.
- Almond and Barr conducted a systematic review of published studies related to all techniques currently used in the management of Barrett's esophagus.^[14] Conclusions for choice of ablation type were based upon two randomized trials^[11,15], and numerous nonrandomized trials. The authors reported that both RFA and photodynamic therapy (PDT) have consistently shown efficacy for high-grade dysplasia, but noted RFA to be widely preferred due to fewer side effects and ease of administration. Cryotherapy was included in the list of ablation types, but no other information or conclusions were provided.
- In a 2014 systematic review with meta-analysis of endoscopic therapy for low-grade dysplasia (LGD), Almond et al. reported heterogeneous studies, most of which had short follow-up.^[16] In addition, a high rate of over-diagnosis of LGD was also found. Progression of LGD to cancer was uncommon with or without ablation. The authors concluded that RFA was safe and effective for LGD in Barrett's esophagus, but did not eliminate the risk of progression to cancer.

Randomized Controlled Trials (RCTs)

- In 2014, Phoa et al. published the results of an RCT in which 140 patients with BE and LGD confirmed by local pathologist and expert panel of pathologists.^[17] The study was scheduled for 3-year follow-up but was terminated early due to interim analysis at 2 years that determined the superiority of RFA over surveillance. Specifically, the occurrence of adenocarcinoma was significantly lower in the RFA group ($p < 0.001$). Complete eradication of dysplasia was 98.4% and the absence of metaplasia was 90.0%. Three serious adverse events occurred in 2 patients, 1 abdominal pain requiring hospitalization, 1 bleeding episode, and 1 episode of fever/chills following dilation for stricture). There were a total of 12 other adverse events (8 strictures requiring dilation, 3 mucosal lacerations, and 1 retrosternal pain).
- A randomized, multicenter, sham-controlled trial assigned 127 patients with dysplastic Barrett's esophagus in a 2:1 ratio to receive RFA or a sham procedure.^[11] The groups were randomized according to the grade of dysplasia (low-grade [$n=64$] or high-grade [$n=63$]) and length of the Barrett's esophagus (<4 cm or 4-8 cm). Primary outcomes were the proportion of patients with

low-grade or high-grade dysplasia who had complete eradication of dysplasia at 12 months and the proportion of all patients who had complete eradication of intestinal metaplasia at 12 months. Secondary outcomes included the proportion of patients who had progression of dysplasia, including low to high-grade dysplasia or to cancer, and the progression of high-grade dysplasia to cancer. Among patients in the RFA group, the entire segment of Barrett's esophagus was ablated. Patients in the RFA group could receive up to 4 ablation sessions, performed at baseline, and at 2, 4, and 9 months. In patients with low-grade dysplasia, the dysplasia was completely eradicated in 90.5% of those in the RFA group, compared with 22.7% of those in the control group ($p<0.001$). In patients with high-grade dysplasia, complete eradication occurred in 81% of the ablation group versus 19% in the control group ($p<0.001$). Overall, complete eradication of intestinal metaplasia was 77.4% in the ablation group compared with 2.3% of the control group ($p<0.001$). Patients who did not receive RFA were more likely to have disease progression (16.3%) than those that received RFA (3.6%; $p=0.03$). Among patients with high-grade dysplasia, 19% of those in the control group progressed to cancer, versus 2.4% progression to cancer in the RFA group ($p=0.04$). Three serious adverse events occurred in the RFA group, including one episode of upper gastrointestinal hemorrhage, which was treated endoscopically, one overnight hospitalization for new-onset chest pain 8 days after RFA, and one night of hospitalization for an episode of chest discomfort and nausea immediately after RFA. No adverse events were observed in the control group. No esophageal perforations or procedure-related deaths occurred. Among patients in the RFA group, esophageal stricture developed in 5 patients (6%), all of whom successfully underwent dilated endoscopy.

In the follow-up trial, Shaheen and colleagues reported on eradication of dysplasia or intestinal metaplasia, durability of response, disease progression, and adverse events at 2 and 3 years.^[18] After crossover, which was allowed after 1 year for those initially randomized to the sham group, 119 participants received RFA. Subjects were followed for a mean time of 3.05 years. The study was extended to 5 years for patients with eradication of intestinal metaplasia at 2 years. After 2 years, 101 of 106 patients had complete eradication of all dysplasia (95%) and 99 of 106 had eradication of intestinal metaplasia (93%). After 2 years, among subjects with initial low-grade dysplasia, all dysplasia was eradicated in 51 of 52 (98%) and intestinal metaplasia was eradicated in 51 of 52 (98%). For subjects with initial high-grade dysplasia, all dysplasia was eradicated in 50 of 54 (93%) and intestinal metaplasia was eradicated in 48 of 54 (89%). After 3 years, dysplasia was eradicated in 55 of 56 of subjects (98%) and intestinal metaplasia was eradicated in 51 of 56 (91%). More than 75% of high-grade and low-grade patients remained free of intestinal metaplasia with a follow-up of longer than 3 years, with no additional therapy. Serious adverse events occurred in 4 of 119 subjects (3.4%). No perforations or procedure-related deaths occurred. The rate of esophageal stricture was 7.6%. The rate of esophageal adenocarcinoma was 1 per 181 patient-years (0.55%/patient-years); there was no cancer-related morbidity or mortality. The annual rate of any neoplastic progression was 1 per 73 patient-years (1.37%/patient-years). The authors concluded that, for patients with dysplastic Barrett's esophagus, RFA is durable and associated with a low rate of disease progression for up to 3 years.

- van Vilsteren and colleagues reported on the results of a multicenter, randomized trial which compared the safety of stepwise radical endoscopic resection (SRER) versus focal ER followed by RFA for complete eradication of Barrett's esophagus ≤ 5 cm containing high-grade dysplasia/early cancer.^[19] Patients in the SRER group underwent piecemeal ER of 50% of Barrett's esophagus followed by serial ER. Patients in the ER/RFA group underwent focal ER for visible lesions followed by serial RFA. Follow-up endoscopy with biopsies (four-quadrant/2

cm Barrett's esophagus) was performed at 6 and 12 months and then annually. Main outcome measures were: stenosis rate, complications, complete histological response for neoplasia (CR-neoplasia); and complete histological response for intestinal metaplasia (CR-IM). CR-neoplasia was achieved in 25/25 (100%) SRER and in 21/22 (96%) ER/RFA patients. CR-IM was achieved in 23 (92%) SRER and 21 (96%) ER/RFA patients. The stenosis rate was significantly higher in SRER (88%) versus ER/RFA (14%; $p < 0.001$), resulting in more therapeutic sessions in SRER (6 vs 3; $p < 0.001$) due to dilations. After median follow-up of 24 months, one SRER patient had recurrence of early cancer, requiring endoscopic resection. The authors concluded that both techniques used in the study achieved comparably high rates of CR-IM and CR-neoplasia, but, that SRER was associated with a higher number of complications and therapeutic sessions.

Non-randomized Studies

To date, the remainder of the studies of RFA for Barrett's esophagus has been conducted to investigate the safety and efficacy of this technique, and consisted mainly of small numbers of patients with relatively short follow-up:

- Ganz and colleagues reported registry data from 142 patients with Barrett's esophagus who underwent circumferential ablation for high-grade dysplasia.^[7] The patients were from 16 academic and community centers, treated between 2004 and 2007, and ranged in age from 59–75 years (median age, 66 years). Median length of Barrett's esophagus segment was 6 cm (range, 3–8 cm). No adverse events were reported. Ninety-two of the patients had at least one follow-up biopsy (median follow-up: 12 months; range: 8–15 months). Outcome measures were defined as histologic complete response (CR), defined as all biopsy specimens negative for high-grade dysplasia, any dysplasia, or intestinal metaplasia. CR was achieved for high-grade dysplasia in 90.2%, any dysplasia in 80.4%, and intestinal metaplasia in 54.3%.
- In a follow-up of the Sharma et al. trial^[6], summarized in the 2010 TEC Assessment, Fleischer and colleagues reported the 5-year outcomes of the original study.^[20] At 5 years, four-quadrant biopsies were obtained from every 1 cm of the original extent of Barrett's esophagus, and the authors reported the proportion of patients demonstrating complete-response-intestinal metaplasia (CR-IM), defined as complete eradication of nondysplastic Barrett's esophagus. If nondysplastic Barrett's esophagus was identified at the 5-year follow-up, focal RFA was performed 1 month later and re-biopsy 2 months after to assess histologic response. Primary outcomes were the proportion of patients demonstrating CR-IM at 5-year biopsy or after single session focal RFA. For the 5-year follow-up, there were 60 eligible patients, 50 (83%) of whom were willing to participate. Forty-six of fifty patients (92%) showed CR-IM at the 5-year biopsy visit. The four patients found to have Barrett's esophagus at 5 years underwent a single session of RFA 1 month after biopsy, and all were found to have CR-IM at subsequent re-biopsy 2 months after RFA. No strictures were noted. The authors concluded that this first report of 5-year CR-IM outcomes lends support to the safety, efficacy, cost-utility, and reduction in neoplastic progression in treating nondysplastic Barrett's esophagus with RFA.
- Roorda and colleagues reported their experience using radiofrequency ablation in 13 patients with Barrett's esophagus (3 with high-grade dysplasia, 4 with low-grade dysplasia, and 6 with nondysplastic intestinal metaplasia).^[21] Mean baseline Barrett's esophagus length was 6 cm (range: 2–12 cm). Complete eradication of Barrett's esophagus was achieved in 6 of 13 patients (46%). Complete elimination of dysplasia was achieved in 5 of 7 (71%) patients.

- Hernandez and colleagues reported on a pilot series in 10 patients with Barrett's esophagus, followed up for at least 12 months.^[22] Seven patients had Barrett's esophagus without dysplasia, 2 with low-grade dysplasia, and 1 with high-grade dysplasia. Complete eradication of Barrett's esophagus was achieved in 7 patients and partial eradication in 3.

Cryoablation

Published efficacy and safety studies for cryoablation in Barrett's esophagus are limited to small (range 11-98 participants), nonrandomized, short-term (≤ 12 months) case series and retrospective reviews of patients with high-grade dysplasia.^[23-26] These studies reported promising results for the downgrading of high-grade dysplasia and eradicating intestinal metaplasia. However, this evidence is insufficient to permit conclusions about the benefits and risks of cryoablation compared with current standard care for this condition due to the methodological limitations of these case series and retrospective studies, including but not limited to the following:

- Lack of randomized comparison with standard medical or surgical treatment, or radiofrequency ablation;
- Small sample sizes which limit the ability to rule out the role of chance as an explanation of study findings;
- Lack of long-term health outcomes data to determine the durability of any beneficial effects, the rate of recurrence or progression to cancer, or the long-term rate of adverse events.

Confirmation of Low-Grade Dysplasia

There are challenges in diagnostic differentiation between nondysplastic BE and BE with LGD that are important in the consideration of treatment for LGD.^(24,25) Both sampling bias and interobserver variability have been shown to be problematic. There is a high degree of intraobserver variability in pathologists' reading of LGD versus inflammatory changes.^[27] Therefore, initial diagnosis of BE can be a challenge with respect to histologic grading because inflammation and LGD can share similar histologic characteristics.

Expert review has been reported to reduce the number of patients diagnosed with LGD by 50% to 75%, presumably by reducing the number of patients with inflammatory changes who are mislabeled as having LGD. Thus, one approach to risk-stratify patients with an initial diagnosis of low-grade dysplasia has been to use multiple pathologists, including experts in gastrointestinal (GI) histopathology, to confirm the initial diagnosis of LGD.

- Kerkhof et al. reported that in patients with an initial pathologic diagnosis of LGD, review by an expert pathologist will result in downgrading the initial diagnosis to nondysplasia in up to 50% of cases.^[28]
- The strategy of having LGD confirmed by expert pathologists is supported by the results of the RCT by Phoa et al, which required confirmation of LGD by a central expert panel following initial diagnosis by a local pathologist.^[17] Of 511 patients with an initial diagnosis of LGD, 264 (52%) were excluded because the central expert panel reassigned classification of LGD, most often from LGD to indefinite or nondysplasia.
- Curvers et al. tested this hypothesis in 147 patients with BE who were given an initial diagnosis of LGD.^[29] All pathology slides were then read by 2 expert GI pathologists with extensive experience in BE, with disagreements among experts resolved by consensus. After review by expert pathologists, 85% of initial diagnoses of LGD were downgraded to nondysplasia, leaving a total of

only 22 of 147 patients (15%) with a confirmed diagnosis of LGD. All patients were followed for a mean of 5.1 years for progression to HGD or cancer. For patients with confirmed LGD, the rate of progression was 13.4%, compared with a rate of 0.5% for patients who had been downgraded to nondysplasia.

Clinical Practice Guidelines

American College of Gastroenterology^[30]

According to guidelines from the American College of Gastroenterology, "...high-grade dysplasia is associated with a 30% risk of cancer development. Treatment needs to be individualized with options of careful intensive surveillance, endoscopic ablation therapy, and surgical resection being presented to the patient based on their appropriateness for these options and the expertise available to provide them. At the current time, it appears as if surveillance with intensive biopsies, endoscopic ablative techniques (most likely a combination of techniques), or esophagectomy may produce similar outcomes in retrospective cohort studies from expert centers. The selection of which of these therapies must be individualized and will depend on the expertise available in the patient's community, the patient's preferences, and the gastroenterologist's own experience (Grade B recommendation)".

Society of Thoracic Surgeons^[31]

The Society of Thoracic Surgeons practice guidelines state that for the management of Barrett's esophagus, RFA may be considered to treat patients with Barrett's metaplasia, and that it may be effective for ablation of high-grade dysplasia, but that further trials are needed before this can be recommended in preference to currently available ablative therapies.

American Gastroenterological Association (AGA)^[32]

The 2011 AGA evidence-based Medical Position Statement (MPS) on the management of Barrett's esophagus acknowledges that developing recommendations was challenging due to limited data on this topic. Per the guideline:

- "Published rates of progression from LGD to HGD or esophageal adenocarcinoma range from 0.5% to 13.4% per patient per year, depending on the rigor of pathologic confirmation of dysplasia." The quality of evidence on the rate of progression is described as low and the MPS acknowledges that it remains controversial. In addition, the guideline states that "because dysplasia progresses to cancer in a manner that lacks definitive markers of progression, there are no well-defined cutoff points that separate low-grade from high-grade dysplasia at this time."
- Although the guideline does recommend RFA for high-grade dysplasia, RFA for low-grade dysplasia and nondysplastic Barrett's esophagus is not included in the recommendation section. Instead, both are addressed in the discussion section along with some concerns specific to the grade of dysplasia:
 - "RFA, with or without EMR [endoscopic mucosal resection], should be a therapeutic option for select individuals with nondysplastic Barrett's esophagus who are judged to be at increased risk for progression to high-grade dysplasia or cancer." However, per the MPS, the specific criteria to define these at-risk individuals are not well defined at this time.
 - "Endoscopic eradication therapy with RFA should also be a therapeutic option for treatment of patients with confirmed low-grade dysplasia in Barrett's esophagus."

However, the guideline notes that the risk of progression to cancer in low-grade dysplasia can vary greatly among individuals. “RFA therapy for patients with low-grade dysplasia leads to reversion to normal-appearing squamous epithelium in >90% of cases. Quality of evidence: High”

- “The statement regarding ‘confirmed’ low-grade or high-grade dysplasia refers to patients in whom the diagnosis is confirmed by at least 2 pathologists, preferably one of whom is an expert in esophageal histopathology. We recommend that the diagnosis of dysplasia be confirmed in this manner before initiating endoscopic eradication therapy for any stage of dysplasia.”

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)^[33]

The 2010 SAGES guideline for surgical treatment of gastroesophageal reflux disease (GERD) is based on both a review of the evidence and expert opinion. Per the guideline, RFA has been shown to achieve high rates of complete histological eradication of IM (no neoplasia), IND (indefinite for neoplasia), and LGIN (low-grade neoplasia) with an acceptable adverse event profile. Although the level of evidence concerning RFA for this recommendation is graded as I (evidence from properly conducted randomized controlled trials), only one of the nine references provided is a randomized controlled trial (Shaheen 2009). The guideline does not include a critical appraisal of the evidence provided in support of this recommendation.

National Comprehensive Cancer Network Guidelines (NCCN)^[34]

The 2013 NCCN clinical practice guidelines for treatment of esophageal cancer state the following:

- Ablative therapy (type not specified) of residual flat Barrett’s esophagus associated with Tis (carcinoma in situ; also called high-grade dysplasia) or T1a (intramucosal invasion) disease should be performed following mucosal resection.
- Ablation of postoperative residual or recurrent high-grade and low-grade dysplasia using RFA or cryoablation should be considered.
- Ablation of non-dysplastic Barrett’s esophagus is not recommended.

Summary

Radiofrequency ablation (RFA) of high-grade dysplasia in Barrett’s esophagus has been shown to be at least as effective in eradicating high-grade dysplasia as other ablative techniques with a lower progression rate to cancer, and may be considered as an alternative to esophagectomy. Therefore, RFA of high-grade dysplasia may be considered medically necessary.

For patients with Barrett’s esophagus with low-grade dysplasia or no dysplasia (nondysplastic), the benefit of radiofrequency ablation (RFA) is uncertain, as the rate of progression to cancer is variable in the literature. This variable natural progression makes it difficult to determine whether changes in progression rates following RFA are due to the RFA or the natural history of the disease. More data are required that compare the use of RFA with standard treatments for the eradication of low-grade dysplasia and nondysplastic Barrett’s esophagus; therefore, RFA for the treatment of these indications is considered investigational. Longer follow-up is needed to show that eradication will persist, and that the benefits will outweigh potential complications in these patients who show a lower rate of progression to adenocarcinoma than those with high-grade dysplasia.

Data for the efficacy of cryoablation of Barrett's esophagus with or without dysplasia are limited. The current evidence consists of nonrandomized trials with no control group for comparison, small numbers of patients, and short-term follow-up that do not permit conclusions about long-term effectiveness, rates of recurrence or progression to cancer, or the rate of adverse events compared with standard treatments. Therefore, cryoablation is considered investigational for the treatment of Barrett's esophagus with or without dysplasia.

REFERENCES

1. BlueCross BlueShield Association Medical Policy Reference Manual "Endoscopic Radiofrequency Ablation or Cryoablation for Barrett's Esophagus." Policy No. 2.01.80
2. Bhat, S, Coleman, HG, Yousef, F, et al. Risk of malignant progression in Barrett's esophagus patients: results from a large population-based study. *J Natl Cancer Inst*. 2011 Jul 6;103(13):1049-57. PMID: 21680910
3. Hvid-Jensen, F, Pedersen, L, Drewes, AM, Sorensen, HT, Funch-Jensen, P. Incidence of adenocarcinoma among patients with Barrett's esophagus. *N Engl J Med*. 2011 Oct 13;365(15):1375-83. PMID: 21995385
4. Ell, C, May, A, Pech, O, et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett's cancer). *Gastrointest Endosc*. 2007 Jan;65(1):3-10. PMID: 17185072
5. Pech, O, Ell, C. Endoscopic therapy of Barrett's esophagus. *Curr Opin Gastroenterol*. 2009 Sep;25(5):405-11. PMID: 19474724
6. Sharma, VK, Wang, KK, Overholt, BF, et al. Balloon-based, circumferential, endoscopic radiofrequency ablation of Barrett's esophagus: 1-year follow-up of 100 patients. *Gastrointest Endosc*. 2007 Feb;65(2):185-95. PMID: 17258973
7. Ganz, RA, Overholt, BF, Sharma, VK, et al. Circumferential ablation of Barrett's esophagus that contains high-grade dysplasia: a U.S. Multicenter Registry. *Gastrointest Endosc*. 2008 Jul;68(1):35-40. PMID: 18355819
8. U.S. Food and Drug Administration. 510(k) Premarket Notification Database. BARRX MODELS HALO360 AND HALO360+ COAGULATION CAT. No. K080557. April 2, 2008. [cited 11/2008]; Available from: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=27156>
9. U.S. Food and Drug Administration. 510(k) Premarket Notification Database. CryoSpray Ablation System. No. K072651. December 7, 2007. [cited 12/2009]; Available from: http://www.accessdata.fda.gov/cdrh_docs/pdf7/K072651.pdf
10. Outbreaks of 2009 pandemic influenza A (H1N1) among long-term-care facility residents - three states, 2009. *MMWR Morb Mortal Wkly Rep*. 2010 Jan 29;59(3):74-7. PMID: 20110935
11. Shaheen, NJ, Sharma, P, Overholt, BF, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. *N Engl J Med*. 2009 May 28;360(22):2277-88. PMID: 19474425
12. Fleischer, DE, Overholt, BF, Sharma, VK, et al. Endoscopic ablation of Barrett's esophagus: a multicenter study with 2.5-year follow-up. *Gastrointest Endosc*. 2008 Nov;68(5):867-76. PMID: 18561930
13. Pouw, RE, Gondrie, JJ, Sondermeijer, CM, et al. Eradication of Barrett esophagus with early neoplasia by radiofrequency ablation, with or without endoscopic resection. *J Gastrointest Surg*. 2008 Oct;12(10):1627-36; discussion 36-7. PMID: 18704598
14. Max Almond, L, Barr, H. Management controversies in Barrett's oesophagus. *J Gastroenterol*. 2013 Jun 5. PMID: 23736794

15. Overholt, BF, Wang, KK, Burdick, JS, et al. Five-year efficacy and safety of photodynamic therapy with Photofrin in Barrett's high-grade dysplasia. *Gastrointest Endosc.* 2007;66:460-8. PMID: 17643436
16. Almond, LM, Hodson, J, Barr, H. Meta-analysis of endoscopic therapy for low-grade dysplasia in Barrett's oesophagus. *Br J Surg.* 2014 Jun 25. PMID: 24965075
17. Phoa, KN, van Vilsteren, FG, Weusten, BL, et al. Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial. *JAMA.* 2014;311:1209-17. PMID: 24668102
18. Shaheen, NJ, Overholt, BF, Sampliner, RE, et al. Durability of radiofrequency ablation in Barrett's esophagus with dysplasia. *Gastroenterology.* 2011 Aug;141(2):460-8. PMID: 21679712
19. van Vilsteren, FG, Pouw, RE, Seewald, S, et al. Stepwise radical endoscopic resection versus radiofrequency ablation for Barrett's oesophagus with high-grade dysplasia or early cancer: a multicentre randomised trial. *Gut.* 2011 Jun;60(6):765-73. PMID: 21209124
20. Fleischer, DE, Overholt, BF, Sharma, VK, et al. Endoscopic radiofrequency ablation for Barrett's esophagus: 5-year outcomes from a prospective multicenter trial. *Endoscopy.* 2010 Oct;42(10):781-9. PMID: 20857372
21. Roorda, AK, Marcus, SN, Triadafilopoulos, G. Early experience with radiofrequency energy ablation therapy for Barrett's esophagus with and without dysplasia. *Dis Esophagus.* 2007;20(6):516-22. PMID: 17958728
22. Hernandez, JC, Reicher, S, Chung, D, et al. Pilot series of radiofrequency ablation of Barrett's esophagus with or without neoplasia. *Endoscopy.* 2008 May;40(5):388-92. PMID: 18459075
23. Johnston, MH, Eastone, JA, Horwhat, JD, Cartledge, J, Mathews, JS, Foggy, JR. Cryoablation of Barrett's esophagus: a pilot study. *Gastrointest Endosc.* 2005 Dec;62(6):842-8. PMID: 16301023
24. Dumot, JA, Vargo, JJ, 2nd, Falk, GW, Frey, L, Lopez, R, Rice, TW. An open-label, prospective trial of cryospray ablation for Barrett's esophagus high-grade dysplasia and early esophageal cancer in high-risk patients. *Gastrointest Endosc.* 2009 Oct;70(4):635-44. PMID: 19559428
25. Greenwald, BD, Dumot, JA, Horwhat, JD, Lightdale, CJ, Abrams, JA. Safety, tolerability, and efficacy of endoscopic low-pressure liquid nitrogen spray cryotherapy in the esophagus. *Dis Esophagus.* 2010 Jan;23(1):13-9. PMID: 19515183
26. Shaheen, NJ, Greenwald, BD, Peery, AF, et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's esophagus with high-grade dysplasia. *Gastrointest Endosc.* 2010 Apr;71(4):680-5. PMID: 20363409
27. TEC Assessment 2010. "Radiofrequency Ablation of Nondysplastic or Low-Grade Dysplastic Barrett's Esophagus." BlueCross BlueShield Association Technology Evaluation Center, Vol. 25, Tab 5.
28. Kerkhof, M, van Dekken, H, Steyerberg, EW, et al. Grading of dysplasia in Barrett's oesophagus: substantial interobserver variation between general and gastrointestinal pathologists. *Histopathology.* 2007 Jun;50(7):920-7. PMID: 17543082
29. Curvers, WL, ten Kate, FJ, Krishnadath, KK, et al. Low-grade dysplasia in Barrett's esophagus: overdiagnosed and underestimated. *Am J Gastroenterol.* 2010 Jul;105(7):1523-30. PMID: 20461069
30. Wang, KK, Sampliner, RE. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. *Am J Gastroenterol.* 2008 Mar;103(3):788-97. PMID: 18341497
31. Fernando, HC, Murthy, SC, Hofstetter, W, et al. The Society of Thoracic Surgeons practice guideline series: guidelines for the management of Barrett's esophagus with high-grade dysplasia. *Ann Thorac Surg.* 2009 Jun;87(6):1993-2002. PMID: 19463651

32. Spechler, SJ, Sharma, P, Souza, RF, Inadomi, JM, Shaheen, NJ. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. *Gastroenterology*. 2011 Mar;140(3):1084-91. PMID: 21376940
33. Stefanidis D, Hope WW, Kohn GP, Reardon PR, Richardson WS, Fanelli RD; Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Guidelines Committee. Guidelines for Surgical Treatment of Gastroesophageal Reflux Disease (GERD). 2010. *Surg Endosc*. 2010 Nov;24(11):2647-69. PMID: 20725747. [cited 09/27/2013]; Available from: <http://www.sages.org/publication/id/22/>
34. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Esophageal and Esophagogastric Junction Cancers. v.1.2014. [cited 08/07/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf

CROSS REFERENCES

[Radiofrequency Ablation of Tumors \(RFA\)](#), Surgery, Policy No. 92

[Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease \(GERD\)](#), Surgery, Policy No. 110

[Cryosurgical Ablation of Miscellaneous Solid Organ and Breast Tumors](#), Surgery, Policy No. 132

CODES	NUMBER	DESCRIPTION
CPT	There are no specific CPT codes for endoscopic radiofrequency ablation or cryoablation for Barrett's esophagus.	
	43228	Esophagoscopy, rigid or flexible; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique Deleted 1/1/2014
	43229	Esophagoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
	43258	Upper gastrointestinal endoscopy including esophagus, stomach and either the duodenum and/or jejunum as appropriate; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique Deleted 1/1/2014
	43270	Esophagogastroduodenoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
	43499	Unlisted procedure, esophagus
HCPCS	None	