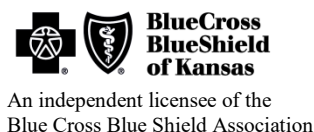


## Medical Policy



### Title: Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus

#### **Professional**

Original Effective Date: February 26, 2009  
 Revision Date(s): January 1, 2010;  
 August 3, 2010; December 21, 2010;  
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Populations	Interventions	Comparators	Outcomes
Individuals: • With Barrett esophagus with high-grade dysplasia	Interventions of interest are: • Endoscopic radiofrequency ablation	Comparators of interest are: • Esophagectomy • Endoscopic mucosal resection • Surveillance	Relevant outcomes include: • Overall survival • Change in disease status • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With Barrett esophagus with low-grade dysplasia	Interventions of interest are: • Endoscopic radiofrequency ablation	Comparators of interest are: • Surveillance	Relevant outcomes include: • Overall survival • Change in disease status • Morbid events • Treatment-related mortality • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>• With Barrett esophagus without dysplasia</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Endoscopic radiofrequency ablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Surveillance</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Overall survival</li> <li>• Change in disease status</li> <li>• Morbid events</li> <li>• Treatment-related mortality</li> <li>• Treatment-related morbidity</li> </ul>
Individuals: <ul style="list-style-type: none"> <li>• With Barrett esophagus with or without dysplasia</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Endoscopic cryoablation</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Esophagectomy</li> <li>• Endoscopic mucosal resection</li> <li>• Surveillance</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Overall survival</li> <li>• Change in disease status</li> <li>• Morbid events</li> <li>• Treatment-related mortality</li> <li>• Treatment-related morbidity</li> </ul>

**DESCRIPTION**

In Barrett's esophagus (BE), the normal squamous epithelium is replaced by specialized columnar-type epithelium, known as intestinal metaplasia. Intestinal metaplasia is a precursor to adenocarcinoma and may be treated with mucosal ablation techniques such as radiofrequency ablation (RFA) or cryoablation.

**Objective**

The objective of this evidence review is to evaluate the use of endoscopic radiofrequency ablation, with or without endomucosal resection if indicated, or endoscopic cryoablation improves the net health outcome for individuals who have Barrett esophagus without visible nodularity.

**Barrett’s Esophagus and the Risk of Esophageal Carcinoma**

The esophagus is normally lined by squamous epithelium. Barrett’s esophagus (BE) 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). Occurring in the distal esophagus, BE may be of any length, may be focal or circumferential, and can be seen on endoscopy as being a different color than the background squamous mucosa. Confirmation of BE requires biopsy of the columnar epithelium and microscopic identification of intestinal metaplasia.

Intestinal metaplasia is a precursor to esophageal adenocarcinoma, which is thought to result from a stepwise accumulation of genetic abnormalities in the specialized epithelium, resulting in the phenotypic expression of histologic features from low-grade dysplasia (LGD), to high-grade dysplasia (HGD), to carcinoma. Two large epidemiologic studies published in 2011 reported the risk of progression to cancer in patients with BE. One reported the rate of progression to cancer in more than 8000 patients with a mean duration of follow-up of 7 years (range, 1-20 years).<sup>1</sup> The de novo progression to cancer from BE at 1 year was 0.13%. The risk of progression was reported as 1.4% per year in patients with LGD and 0.17% per year in patients without dysplasia. This incidence translates into a risk of 10 to 11 times that of the general population. The other study identified more than 11,000 patients with BE and after a median follow-up of 5.2 years, it

reported that the annual risk of esophageal adenocarcinoma was 0.12%.<sup>2</sup> Detection of LGD 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 HGD were slightly higher.

The reported risk of progression to cancer in BE in older studies was much higher, with an annual incidence of risk of 0.4% to 0.5% per year, with risk estimated at 30 to 40 times that of the general population. Current surveillance recommendations have been based on these higher risk estimates.

There are challenges in diagnostically differentiating between nondysplastic BE and BE with LGD; they are important when considering treatment for LGD.<sup>3,4</sup> Both sampling bias and interobserver variability have been shown to be problematic. Therefore, analysis of progression to carcinoma in BE with intestinal metaplasia vs LGD is difficult. Initial diagnosis of BE can also be a challenge with respect to histologic grading because inflammation and LGD can share similar histologic characteristics.<sup>5</sup>

One approach to risk-stratify patients with an initial diagnosis of LGD has been to use multiple pathologists, including experts in gastrointestinal histopathology, to confirm the initial diagnosis of LGD. There is a high degree of interobserver variability among the pathology readings of LGD vs inflammatory changes, and the resultant variability in pathology diagnosis may contribute to the variable rates of progression of LGD reported in the literature.<sup>6</sup> Kerkhof et al (2007) reported that, in patients with an initial pathologic diagnosis of LGD, review by an expert pathologist would result in the initial diagnosis being downgraded to nondysplasia in up to 50% of cases.<sup>7</sup> Curvers et al (2010) tested this hypothesis in 147 patients with BE who were given an initial diagnosis of LGD.<sup>8</sup> All pathology slides were read by 2 expert gastrointestinal pathologists with extensive experience in BE; disagreements among experts in the readings were resolved by consensus. Once this process was completed, 85% of initial diagnoses of LGD were downgraded to nondysplasia, leaving 22 (15%) of 147 patients 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 0.5% for patients who had been downgraded to nondysplasia.

The strategy of having LGD confirmed by expert pathologists is supported by the results of a randomized controlled trial by Phoa et al (2014), which required confirmation of LGD by a central expert panel following initial diagnosis by a local pathologist.<sup>9</sup> 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. These findings were further confirmed in a retrospective cohort study by Duits et al (2015) who reported on 293 BE cases with LGD diagnosed over an 11-year period and submitted for expert panel review.<sup>10</sup> In this sample, 73% of subjects were downstaged.

## Management

The management of BE includes treatment of gastroesophageal reflux disease (GERD) and surveillance endoscopy to detect progression to HGD or adenocarcinoma. The finding of HGD or early-stage adenocarcinoma warrants mucosal ablation or resection (either endoscopic mucosal resection [EMR] or esophagectomy).

EMR, either focal or circumferential, provides a histologic specimen for examination and staging (unlike ablative techniques). One 2007 study provided long-term results for EMR in 100 consecutive patients with early Barrett-associated adenocarcinoma (limited to the mucosa).<sup>11</sup> The 5-year overall survival was 98% and, after a mean of 36.7 months, metachronous lesions were observed in 11% of patients. In a review by Pech and El (2009), the authors stated that circumferential EMR of the entire segment of BE leads to a stricture rate of 50%, and recurrences occur at a rate of up to 11%.<sup>12</sup>

## Ablative Techniques

Available mucosal ablation techniques that include several thermal (multipolar electrocoagulation [MPEC], argon plasma coagulation [APC], heater probe, Nd:YAG laser, KTP-YAG laser, diode laser, argon laser, cryoablation) or nonthermal (5-aminolevulinic acid, photodynamic therapy [PDT]) techniques. In a 2005 randomized phase 3 trial, PDT has been shown to decrease significantly the risk of adenocarcinoma in BE.<sup>13</sup>

The CryoSpray Ablation system uses a low-pressure spray for spraying liquid nitrogen through an upper endoscope. Cryotherapy allows for treatment of uneven surfaces; however, a disadvantage of the treatment is the uneven application inherent in spraying the cryogen.

The HALO system uses radiofrequency (RF) energy and consists of 2 components, an energy generator and an ablation catheter. The generator provides rapid (ie, <1 second) delivery of a predetermined amount of RF energy to the catheter. The HALO90 or the HALO360 is 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 BE up to 3 cm. The HALO360 uses a balloon catheter that is sized to fit the individual's esophagus and is inflated to allow for circumferential ablation.

Ablation with RF affects only the most superficial layer of the esophagus (ie, the mucosa), leaving the underlying tissues unharmed. Measures of efficacy for the procedure are eradication of intestinal metaplasia and postablation regrowth of the normal squamous epithelium. (Note: The eradication of intestinal metaplasia does not leave behind microscopic [or "buried"] foci). Reports of the efficacy of the HALO system in ablating BE have been as high as 70% (comparable with alternative methods of ablation [eg, APC, MPEC]), and even higher in some reports. The incidence of leaving behind buried foci of intestinal metaplasia has been reported to be between 20% and 44% with APC and 7% with MPEC; studies using the HALO system have reported 0%.<sup>14</sup> Another potential advantage to the HALO system is that because it is an automated process, it eliminates operator-dependent error that may be seen with APC or MPEC.

The risk of treating HGD or mucosal cancer solely with ablative techniques is undertreatment for approximately 10% of patients with undetected submucosal cancer, in whom esophagectomy would have been required.<sup>12</sup>

### **Regulatory Status**

In 2005, the HALO360 (now Barrx™ 360 RFA Balloon Catheter; Barrx Medical; acquired by Covidien in 2012) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process and, in 2006, the HALO90 (now Barrx™ 90 RFA Focal Catheter) received clearance. FDA-labeled indications are for use in coagulation of bleeding and nonbleeding sites in the gastrointestinal tract and include the treatment of BE.<sup>15</sup> FDA product code: GEI.

In 2007, the CryoSpray Ablation™ System (formerly the SprayGenix Cryo Ablation system; CSA Medical) was cleared for marketing by FDA through the 510(k) process for use as a “cryosurgical tool for destruction of unwanted tissue in the field of general surgery, specifically for endoscopic applications.”<sup>16</sup> FDA product code: GEH.

In 2002, the Polar Wand® device (Chek-Med Systems), a cryosurgical device that uses compressed carbon dioxide, was cleared for marketing by FDA through the 510(k) process. Indications for use are “ablation of unwanted tissue in the fields of dermatology, gynecology, general surgery, urology, and gastroenterology.”<sup>17</sup>

### **POLICY**

- A. Radiofrequency ablation may be considered **medically necessary** for the treatment of Barrett esophagus with high-grade dysplasia (see Policy Guidelines).
- B. Radiofrequency ablation may be considered **medically necessary** for the treatment of Barrett esophagus with low-grade dysplasia, when the initial diagnosis of low-grade dysplasia is confirmed by 2 physicians (see Policy Guidelines).
- C. Radiofrequency ablation is considered **experimental / investigational** for the treatment of Barrett esophagus when the above criteria are not met, including but not limited to Barrett esophagus in the absence of dysplasia.
- D. Cryoablation is considered **experimental/investigational** for the treatment of Barrett esophagus, with or without dysplasia.

### Policy Guidelines

1. Radiofrequency ablation (RFA) for Barrett esophagus with high-grade dysplasia (HGD) may be used in combination with endoscopic mucosal resection of nodular or visible lesions. The diagnosis of high-grade dysplasia should be confirmed by 2 pathologists before initiating radiofrequency ablation.
2. There is considerable interobserver variability in the diagnosis of low-grade dysplasia (LGD), and the potential exists for overdiagnosis of LGD by nonexpert pathologists (overdiagnosis is due primarily to the difficulty in distinguishing inflammatory changes from LGD). There is evidence in the literature that expert gastrointestinal (GI) pathologists will downgrade a substantial portion of biopsies that are initially read as LGD by nonexperts (Curvers et al [2010]; Kerkhof et al [2007]). As a result, it is ideal that 2 experts in GI pathology agree on the diagnosis in order to confirm LGD; this may result in greater than 75% of initial diagnoses of LGD being downgraded to nondysplasia (Curvers et al [2010]). A review by a single expert GI pathologist will also result in a large number of LGD diagnoses being downgraded, although probably not as many as achieved using 2 expert pathologists (Kerkhof et al, 2007).

### **RATIONALE**

This evidence review has been updated with searches of the MEDLINE database. The most recent literature update was performed through September 4, 2018.

This review was influenced in part by a TEC Assessment (2010) that assessed use of radiofrequency ablation (RFA) for treating nondysplastic Barrett esophagus (BE) or BE with low-grade dysplasia (LGD).<sup>6</sup>

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function<sup>¾</sup>including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

## **Radiofrequency Ablation for Barrett Esophagus With High-Grade Dysplasia Clinical Context and Therapy Purpose**

In patients diagnosed with Barrett esophagus (BE) with high-grade dysplasia (HGD), the risk of progression to cancer is relatively high, and esophageal adenocarcinoma is associated with high morbidity and a 5-year survival rate of up to 13%.<sup>18</sup> Therefore, intervention with esophagectomy or RFA may be strongly indicated.

The purpose of endoscopic RFA in patients who have BE with HGD is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in patients with BE with HGD?

The following PICOTS were used to select literature to inform this review.

### **Patients**

The relevant population of interest is patients with BE with HGD.

### **Interventions**

The therapy being considered is endoscopic RFA.

### **Comparators**

The following therapies and practices are currently being used to treat BE: esophagectomy, endoscopic mucosal resection, and surveillance.

### **Outcome**

The general outcomes of interest are symptoms (eg, pain), functional outcomes (including swallowing), and cancer-specific survival.

Beneficial outcomes include reductions in esophageal dysplasia and mortality.

Harmful outcomes include damage to the esophagus resulting in difficulty swallowing.

### **Timing**

Morbidity from treatment would be assessed within 30 days after the procedure. Overall survival and disease-specific survival would be measured at 3 to 5 years.

### **Setting**

Endoscopic RFA is administered in an outpatient care setting by gastroenterologists.

### **Systematic Reviews**

Chadwick et al (2014) reported on a systematic review that compared RFA with complete endoscopic mucosal resection (EMR) for treatment of BE.<sup>19</sup> Twenty studies (22 articles) were reviewed, including 2 RCTs, 10 cohort studies on EMR, and 8 cohort studies on RFA. The only study that compared RFA with EMR was an RCT by van Vilsteren et al (2011)<sup>20</sup>; the other RCT was by Shaheen et al (2009, 2011; see below).<sup>21,22</sup> The studies were heterogeneous in design. A total of 1087 (532 EMR, 555 RFA) patients with HGD or intramucosal carcinoma were included in the studies reviewed. The median number of resections or RFA sessions required for the eradication of BE was two. Complete EMR and RFA eradicated BE dysplasia in 95% and 92% of

patients, respectively. Eradication was maintained in 95% of EMR patients at a median follow-up of 23 months and in 94% of RFA patients at a median follow-up of 21 months. Fewer RFA patients experienced short-term adverse events (2.5%) than those who received complete EMR (12%). Esophageal strictures requiring additional treatment occurred in 4% of RFA patients and 38% of complete endoscopic resection patients.

### **Randomized Controlled Trials**

Van Vilsteren et al (2011) reported on the results of a multicenter randomized trial that compared the safety of stepwise radical endoscopic resection (SRER) with focal EMR followed by RFA for complete eradication of BE 5 cm or less with HGD or early cancer.<sup>20</sup> Patients in the SRER group underwent piecemeal EMR of 50% of BE followed by serial EMR. Patients in the EMR plus RFA group underwent focal EMR for visible lesions followed by serial RFA. Follow-up endoscopy with biopsies (4-quadrant/2 cm BE) was performed at 6 and 12 months and then annually. The main outcome measures were: stenosis rate; complications; complete histologic response for neoplasia; and complete histologic response for intestinal metaplasia (CR-IM). Complete histologic response for neoplasia was achieved in 25 (100%) of 25 SRER patients and in 21 (96%) of 22 patients receiving EMR plus RFA. CR-IM was achieved in 23 (92%) SRER patients and 21 (96%) patients receiving EMR plus RFA. The stenosis rate was significantly higher with SRER (88%) than with EMR plus RFA (14%;  $p < 0.001$ ), resulting in more therapeutic sessions in SRER (6 vs 3;  $p < 0.001$ ) due to dilations. After a median follow-up of 24 months, 1 SRER patient had a recurrence of early cancer, requiring endoscopic resection. This trial confirmed that both techniques achieved comparably high rates of CR-IM and complete histologic response for neoplasia but found that SRER was associated with more complications and therapeutic sessions.

The randomized multicenter, sham-controlled trial by Shaheen et al (2009) compared RFA with surveillance alone in patients with BE and dysplasia.<sup>21</sup> RFA was successful in eradicating HGD, with complete eradication at 12 months achieved in 81% of the ablation group vs 19% in the control group ( $p < 0.001$ ). This trial also confirmed a high risk of progression to cancer in patients with HGD and established that this progression was significantly reduced in patients treated with RFA. Among 63 patients with HGD in the trial, 19% in the control group progressed to cancer vs 2.4% in the RFA group ( $p = 0.04$ ). This represented a nearly 90% relative risk reduction for progression to cancer (relative risk, 0.1; 95% confidence interval [CI], 0.01 to 1.0,  $p = 0.04$ ), and a number needed to treat of 6.0 to prevent 1 case of cancer over a 1-year period.

Longer term follow-up at 2 to 3 years reported that complete eradication of dysplasia was maintained in most participants with initial HGD.<sup>22</sup> For 54 patients with HGD available for follow-up, all dysplasia was eradicated in 50 (93%) of 54, and all intestinal metaplasia was eradicated in 48 (89%) of 54. After 3 years, dysplasia was eradicated in 55 (98%) of 56 of subjects, and all intestinal metaplasia was eradicated in 51 (91%) of 56. More than 75% of patients with HGD remained free of intestinal metaplasia with a follow-up of longer than 3 years, with no additional therapy.

RFA may be used alongside focal endoscopic resection. In the intention-to-treat analysis of a prospective interventional study by Phoa et al (2016) that included 132 subjects with BE and HGD or early cancer treated with endoscopic resection followed by RFA, complete eradication of neoplasia and complete eradication of intestinal metaplasia occurred in 92% and 87% of subjects, respectively.<sup>23</sup> At a median follow-up of 27 months, neoplasia and intestinal metaplasia had recurred in 4% and 8% of subjects, respectively.



## **Section Summary: Radiofrequency Ablation for Barrett Esophagus With High-Grade Dysplasia**

For patients who have BE with HGD, there is a relatively high risk of progression to cancer, and interventions to prevent progression are warranted. RFA results in high rates of complete eradication of dysplasia that is durable for at least 2 years. One RCT demonstrated that, following RFA, progression from HGD to cancer is reduced by approximately 90%, with rates of esophageal strictures of 6%.

### **RFA for BE WITH Low-Grade Dysplasia**

#### **Clinical Context and Therapy Purpose**

The purpose of endoscopic RFA in patients who have BE with low-grade dysplasia (LGD) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in patients with BE with LGD?

The following PICOTS were used to select literature to inform this review.

#### **Patients**

The relevant population of interest is patients with BE with LGD.

#### **Interventions**

The therapy being considered is endoscopic RFA.

#### **Comparators**

The following practice is currently being used to treat BE with LGD: surveillance.

#### **Outcome**

The general outcomes of interest are symptoms (eg, pain), functional outcomes (including swallowing), and cancer-specific survival.

Beneficial outcomes include reductions in esophageal dysplasia and mortality.

Harmful outcomes include damage to the esophagus resulting in difficulty swallowing.

#### **Timing**

Morbidity would be assessed within 30 days after the procedure. Conversion to HGD would be measured at 2 to 5 years.

#### **Setting**

Endoscopic RFA is administered in an outpatient care setting by gastroenterologists.

### **Systematic Reviews**

Almond et al (2014) reported on the results of a meta-analysis of studies using endoscopic therapy to treat BE with LGD.<sup>24</sup> The analysis included 37 studies, nine of which evaluated RFA alone, including the RCT by Shaheen et al (2009). Most studies were small, with the Shaheen RCT representing the largest study (52 with LGD treated with RFA). For patients treated with RFA, the pooled incidence of cancer or progression to HGD was 10.77 per 1000 patient-years (95% CI, 2.22 to 31.48 per 1000 patient-years). For RFA-treated patients, pooled rates of

complete eradication of intestinal metaplasia and complete eradication of dysplasia were 87.2% (95% CI, 76.2% to 93.5%) and 90.6% (95% CI, 81.0% to 95.6%), respectively.

### **Randomized Controlled Trials**

Since the systematic review by Almond et al (2014) and the TEC Assessment (2010), an RCT comparing RFA with surveillance in patients with LGD was published by Phoa et al (2014).<sup>9</sup> This trial randomized 140 patients with BE and confirmed LGD; 4 patients were excluded after randomization for not meeting study inclusion criteria at further review, leaving 136 patients in the modified intention-to-treat analysis. "Confirmed" LGD was defined as a diagnosis of LGD by the local pathologist with confirmation by a centralized expert panel of pathologists convened for the trial. The primary outcome measure was the occurrence of either HGD or adenocarcinoma up to 3 years after randomization. Secondary outcomes were the complete eradication of dysplasia, the absence of intestinal metaplasia, and adverse events.

The trial was terminated early after an interim analysis determined the superiority of RFA. At termination, all patients had reached the 24-month follow-up time point, and the median follow-up was 36 months. The occurrence of adenocarcinoma was significantly lower in the RFA group (1.5%) than in the surveillance group (8.8%;  $p < 0.03$ ), and the occurrence of HGD was also significantly lower for the RFA group (1.5%) than for the surveillance group (26.5%;  $p < 0.001$ ). For patients treated with RFA, complete eradication of dysplasia during follow-up was 98.4% and the absence of metaplasia was 90.0%. There were 3 serious adverse events in 2 patients who received RFA (1 case each of abdominal pain requiring hospitalization, bleeding, fever/chills following dilation for stricture), and 12 other adverse events (8 strictures requiring dilation, 3 mucosal lacerations, 1 retrosternal pain).

In the Shaheen RCT, 64 patients with LGD were reported in a subgroup analysis.<sup>21</sup> At 12-month follow-up, dysplasia was completely eradicated in 90.5% of those in the RFA group compared with 22.7% of those in the control group ( $p < 0.001$ ). No patients in the LGD group progressed to cancer over the initial 12 months. Progression to HGD was noted in 2 (5%) of 42 patients in the RFA group compared with 3 (14%) of 22 in the control group. The difference in rates of progression to HGD was not statistically significant (relative risk, 0.3; 95% CI, 0.1 to 1.9;  $p = 0.33$ ). After 2 years, 52 subjects were available who had initial LGD treated with RFA. Progression from LGD to HGD or cancer occurred in 1 patient, for an estimated rate of 2.0% per patient-year. In patients with initial LGD, all dysplasia was eradicated in 51 (98%) of 52, and all intestinal metaplasia was eradicated in 51 (98%) of 52.

### **Section Summary: RFA for With Low-Grade Dysplasia**

The risk of progression from LGD to cancer is not well-defined, with highly variable rates reported in the published literature. Evidence from randomized and nonrandomized studies has established that RFA can achieve complete eradication of dysplasia in patients with LGD that is durable for at least 2 years. One RCT of 136 subjects reported a lower rate of progression to HGD or adenocarcinoma for patients who had confirmed LGD treated with RFA. This trial supported the strategy of selecting a population at a higher risk of progression by subjecting the initial pathologic diagnosis of LGD to review by an expert in GI pathology. The expert review has reduced the number of patients diagnosed with LGD by 50% to 75%, presumably by reducing the number of patients with inflammatory changes who are miscategorized as having LGD.

## **RFA for BE Without Dysplasia**

### **Clinical Context and Therapy Purpose**

The purpose of endoscopic RFA in patients who have BE without dysplasia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of RFA improve the net health outcome in patients with BE without dysplasia?

The following PICOTS were used to select literature to inform this review.

### **Patients**

The relevant population of interest is patients with BE without dysplasia.

### **Interventions**

The therapy being considered is endoscopic RFA.

### **Comparators**

The following practice is currently being used to treat BE without dysplasia: surveillance.

### **Outcome**

The general outcomes of interest are symptoms (eg, pain), functional outcomes (including swallowing), and cancer-specific survival.

Beneficial outcomes include reductions in mortality.

Harmful outcomes include damage to the esophagus resulting in difficulty swallowing.

### **Timing**

Morbidity would be assessed within 30 days after the procedure. Conversion to dysplasia would be measured at 2 to 5 years.

### **Setting**

Endoscopic RFA is administered in an outpatient care setting by gastroenterologists.

### **Nonrandomized Trials**

No RCTs were identified that evaluated RFA treatment of BE without dysplasia. The evidence on this issue consists of single-arm trials that have reported outcomes of RFA. There is no high-quality evidence on the comparative efficacy of RFA vs surveillance alone. Progression to cancer in cases of nondysplastic BE is lower than that for LGD or HGD, with rates in the literature ranging from 0.05% to 0.5%.<sup>1,2,</sup>

Fleischer et al (2008, 2010) reported on the 5-year follow-up of a single-arm study of patients with nondysplastic BE treated with RFA.<sup>25,26,</sup> The original study included 70 patients who underwent circumferential RFA and CR-IM, defined as complete eradication of nondysplastic BE.<sup>25,</sup> CR-IM was seen in 70% of patients at 1-year follow-up; patients with persistent BE underwent focal RFA. At the 2.5-year follow-up, CR-IM was found in 60 (98%) of 61 patients.<sup>25,</sup> At 5-year follow-up, 4-quadrant biopsies were obtained from every 1 cm of the original extent of BE, and the authors reported the proportion of patients demonstrating CR-IM.<sup>26,</sup> If nondysplastic BE was identified at the 5-year follow-up, focal RFA was performed 1

month later, and biopsies were repeated 2 months afterward to assess histologic response. Primary outcomes were the proportion of patients demonstrating CR-IM at 5-year biopsy or after a single session of focal RFA. For the 5-year follow-up, there were 60 eligible patients, 50 (83%) of whom participated. Forty-six (92%) of 50 patients showed CR-IM at the 5-year biopsy visit. The 4 patients found to have BE at 5 years underwent a single session of RFA 1 month after biopsy; all 4 patients had CR-IM at subsequent rebiopsy 2 months after RFA. No strictures were noted. The authors concluded that this first report of 5-year CR-IM outcomes supported the safety, efficacy, and reduction in neoplastic progression in treating nondysplastic BE with RFA.

### **Section Summary: RFA for BE Without Dysplasia**

Nondysplastic BE has a relatively low rate of progression to cancer. Although available research has indicated that nondysplastic metaplasia can be eradicated by RFA, the risk-benefit ratio and the net effect on health outcomes is uncertain.

### **Cryoablation of BE**

#### **Clinical Context and Therapy Purpose**

The purpose of endoscopic cryoablation in patients who have BE is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of cryoablation improve the net health outcome in patients with BE?

The following PICOTS were used to select literature to inform this review.

#### **Patients**

The relevant population of interest is patients with BE with or without dysplasia.

#### **Interventions**

The therapy being considered is endoscopic cryoablation.

#### **Comparators**

The following therapies and practices are currently being used to treat BE: esophagectomy, endoscopic mucosal resection, and surveillance.

#### **Outcomes**

The general outcomes of interest are symptoms (eg, pain), functional outcomes (including swallowing), and cancer-specific survival.

Beneficial outcomes include reductions in mortality.

Harmful outcomes include damage to the esophagus resulting in difficulty swallowing.

#### **Timing**

Morbidity would be assessed within 30 days after the procedure. Overall survival and disease-specific survival would be measured at 3 to 5 years.

#### **Setting**

Endoscopic cryoablation is administered in an outpatient care setting by gastroenterologists.

### **Prospective and Retrospective Studies**

Published efficacy data for cryoablation in BE are limited. Canto et al (2015) reported on a retrospective, single-center study that evaluated a carbon dioxide cryosurgery device for treatment of patients with neoplasia or HGD who were treatment-naïve or who had persistent or recurrent neoplasia after initial treatment.<sup>27</sup> The authors analyzed 68 patients who were offered treatment with cryoablation for either initial therapy (n=21) or after previous therapy with any ablative technique (n=47). At 1 year, the complete response for dysplasia was 89% (57/64) overall, and 95% (19/20) and 86% (38/44) in treatment-naïve and previously treated patients, respectively. Over a median follow-up of 4.2 years, the differences in complete response for HGD at 3 years or study end did not differ statistically between treatment-naïve (100%) and previously treated (84%) patients (p=0.08).

A retrospective, single-center study by Sengupta et al (2015) evaluated cryoablation among 16 patients who failed RFA.<sup>28</sup> The cohort of 16 patients was derived from an original cohort of 121 patients who underwent RFA for BE with LGD, HGD, or intramucosal carcinoma. After a median of 3 treatments with RFA, 91 subjects had complete eradication of dysplasia. Of 21 patients offered cryotherapy, 16 underwent cryotherapy and had adequate follow-up. Fourteen of those who did not have complete eradication and two who had a recurrence of dysplasia underwent salvage cryotherapy. Over a median follow-up of 2.5 months, and with a median of 3 cryotherapy treatments, 12 (75%) patients had complete eradication of dysplasia after cryotherapy, and 14 (88%) had some improvement in pathology after cryotherapy.

Greenwald et al (2010) reported on the safety, tolerability, and efficacy of low-pressure liquid nitrogen spray cryotherapy in 77 patients from multiple institutions who underwent a total of 377 procedures for BE with HGD (58.4%), intramucosal carcinoma (16.9%), invasive carcinoma (13%), BE without dysplasia (9.1%), and severe squamous dysplasia (2.6%).<sup>29</sup> The main outcome measure was the incidence of serious adverse events and adverse events from treatments. The most common were chest pain (18%), dysphagia (13%), odynophagia (12.1%), and sore throat (9.6%). Esophageal stricture occurred in 3 patients, all of whom were successfully treated with dilation, and gastric perforation in 1 patient. No adverse events were reported by 28.6% of patients. Complete response for HGD, any dysplasia, intestinal metaplasia, and cancer were assessed in patients completing therapy during the study period and having at least 1 follow-up endoscopy with biopsy for assessment of histologic regression of the underlying lesion (n=23). For patients with HGD (n=17), complete response of the HGD, any dysplasia, and intestinal metaplasia were 94%, 88%, and 53%, respectively. For patients with intramucosal carcinoma (n=4), complete response was 100% for cancer, HGD, and any dysplasia, and 75% for intestinal metaplasia. For patients with invasive cancer (n=3), complete response was 100% for cancer, HGD, and any dysplasia, and 67% for intestinal metaplasia.

Shaheen et al (2010) reported on a multicenter, retrospective cohort study that assessed the safety and efficacy of spray cryotherapy in 98 consecutive patients who had BE with HGD.<sup>30</sup> A total of 333 cryotherapy treatments (mean 3.4 per patient) were performed, all with the intent to eradicate all BE. Sixty patients completed all planned cryotherapy treatments and were assessed for efficacy at follow-up endoscopy sessions with 4-quadrant biopsies performed every 1 to 2 cm. Fifty-eight (97%) patients had complete eradication of HGD, 52 (87%) had complete eradication of all dysplasia with persistent nondysplastic intestinal metaplasia, and 34 (57%) had complete eradication of all intestinal metaplasia. There were no esophageal perforations, and esophageal stricture occurred in 3 patients. The authors noted several study limitations: it was

nonrandomized and retrospective without a control group, it lacked centralized pathology, it used surrogate outcomes for decreased cancer risk, and it had a short follow-up (10.5 months).

An open-label, single-center, prospective, nonrandomized cohort study by Dumot et al (2009) assessed the safety of cryoablation as a treatment option for BE with HGD or intramucosal carcinoma.<sup>31</sup> Thirty patients who were either deemed high-risk surgical candidates or who refused esophagectomy underwent cryoablation. Twenty-seven (90%) patients had their pathology stage downgraded after treatment. After a median follow-up of 12 months, elimination of cancer or downgrading of HGD was 68% for HGD and 80% for intramucosal carcinoma.

### **Section Summary: Cryoablation of BE**

No controlled trials have evaluated cryoablation for the treatment of BE. The evidence from uncontrolled studies has reported high rates of success in eradicating dysplasia, with low rates of complications. These data are not sufficient to determine the comparative efficacy of cryoablation and RFA.

### **Summary of Evidence**

For individuals who have BE with HGD who receive endoscopic RFA, the evidence includes an RCT comparing radical endoscopic resection with focal endoscopic resection followed by RFA, an RCT comparing RFA with surveillance alone, and a number of observational studies, some of which compared RFA with other endoscopic treatment modalities. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related morbidity and mortality. The available evidence has shown that using RFA to treat BE with HGD is at least as effective in eradicating HGD as other ablative techniques, with a lower progression rate to cancer, and may be considered an alternative to esophagectomy. Evidence from at least 1 RCT has demonstrated higher rates of eradication than surveillance alone. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have BE with LGD who receive endoscopic RFA, the evidence includes at least 2 RCTs comparing RFA with surveillance alone, a number of observational studies, and systematic reviews of these studies. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related morbidity and mortality. For patients with confirmed LGD, evidence from an RCT has suggested that RFA reduces progression to HGD and adenocarcinoma. Challenges exist in differentiating between nondysplastic BE and BE with LGD; making the correct diagnosis has important implications for LGD treatment decisions. One of the available RCTs required that LGD be confirmed by an expert panel, which supports the use of having a gastrointestinal pathologist confirm LGD before treatment of BE with LGD can begin. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have BE without dysplasia who receive endoscopic RFA, the evidence includes single-arm studies reporting outcomes after RFA. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related morbidity and mortality. The available studies have suggested that nondysplastic metaplasia can be eradicated by RFA. However, the risk-benefit ratio and the net effect of RFA on health outcomes are unknown. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have BE with or without dysplasia who receive endoscopic cryoablation, the evidence includes noncomparative studies reporting outcomes after cryoablation. Relevant outcomes include overall survival, change in disease status, morbid events, and treatment-related morbidity and mortality. These studies have generally demonstrated high rates of eradication of dysplasia. However, the available evidence does not compare cryoablation with surgical care or RFA. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Clinical Input From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

**2012 Input**

In response to requests, input was received from reviewers at 6 academic medical centers and from 1 subspecialty medical society while this policy was under review in 2012. Input related to the treatment of low-grade dysplasia (LGD) was mixed, with 2 reviewers stating that radiofrequency ablation (RFA) for LGD should be investigational, three indicating that it should be medically necessary, and two indicating that it was a split decision. There was a general consensus among reviewers that there are subsets of patients with LGD who have higher risk and should, therefore, be treated. Reviewers mentioned that factors useful in defining higher risk populations for whom treatment is warranted are the confirmation of LGD diagnosis by multiple pathologists and/or the application of clinical high-risk factors such as lesion length.

**2009 Input**

In response to requests, input was received from 3 academic medical centers and 1 subspecialty medical society (with 12 reviewers) while this policy was under review in 2009. All reviewers agreed that RFA (cryoablation was not included in the request) should be considered medically necessary for the treatment of Barrett esophagus with high-grade dysplasia. Reviewers were split for the use of RFA for LGD, with nine considered it medically necessary and four considering it investigational.

**Practice Guidelines and Position Statements**

**American College of Gastroenterology**

The American College of Gastroenterology (2016) issued guidelines on the diagnosis and management of Barrett esophagus (BE), which made statements about endoscopic therapies in general, as outlined in Table 1.<sup>32</sup>

**Table 1. Guidelines on the Diagnosis and Management of BE**

Recommendation	SOR	LOE
Patients with nodularity in the BE segment should undergo endoscopic mucosal resection of the nodular lesion(s) as the initial diagnostic and therapeutic maneuver.... Histologic assessment of the EMR specimen should guide further therapy. In subjects with EMR specimens demonstrating HGD, or IMC, endoscopic ablative therapy of the remaining BE should be performed.	Strong	High
In patients with EMR specimens demonstrating neoplasia at a deep margin, residual neoplasia should be assumed, and surgical, systemic, or additional endoscopic therapies should be considered	Strong	Low

<b>Recommendation</b>	<b>SOR</b>	<b>LOE</b>
Endoscopic ablative therapies should not be routinely applied to patients with nondysplastic BE because of their low risk of progression to EAC. Endoscopic eradication therapy is the procedure of choice for patients with confirmed LGD, and confirmed HGD, as noted above	Strong	Very low
In patients with T1a EAC, endoscopic therapy is the preferred therapeutic approach, being both effective and well tolerated	Strong	Moderate
In patients with T1b EAC, consultation with multidisciplinary surgical oncology team should occur before embarking on endoscopic therapy. In such patients, endoscopic therapy may be an alternative strategy to esophagectomy, especially in those with superficial (sm1) disease with a well-differentiated neoplasm lacking lymphovascular invasion, as well as those who are poor surgical candidates	Strong	Low
Routine staging of patients with nodular BE with EUS or other imaging modalities before EMR has no demonstrated benefit. Given the possibility of over- and understaging, findings of these modalities should not preclude the performance of EMR to stage-early neoplasia	Strong	Moderate
In patients with known T1b disease, EUS may have a role in assessing and sampling regional lymph nodes, given the increased prevalence of lymph node involvement in these patients compared with less advanced disease	Strong	Moderate
In patients with dysplastic BE who are to undergo endoscopic ablative therapy for nonnodular disease, radiofrequency ablation is currently the preferred endoscopic ablative therapy	Strong	Moderate

BE: Barrett esophagus; EAC: esophageal adenocarcinoma; EMR: endoscopic mucosal resection; EUS: endoscopic ultrasound; HGD: high grade dysplasia; IMC: intramucosal carcinoma; LGD: low-grade dysplasia; LOE: level of evidence; SOR: strength of recommendation.

### American Society for Gastrointestinal Endoscopy

The American Society for Gastrointestinal Endoscopy (2018) issued guidelines on the role of endoscopy in BE-associated dysplasia and intramucosal cancer.<sup>33</sup> These guidelines made the following recommendations on endoscopic eradication therapy, consisting of endoscopic mucosal resection of visible lesions and ablative techniques that include RFA and cryotherapy (see Table 2).

**Table 2. Guidelines on Use of Endoscopy for BE and IMC**

<b>Recommendation</b>	<b>SOR</b>	<b>QOE<sup>a</sup></b>
In BE patients with LGD and HGD being considered for EET, we suggest confirmation of diagnosis by at least 1 expert GI pathologist or panel of pathologists compared with review by a single pathologist.	Conditional	Low
In BE patients with LGD, we suggest EET compared with surveillance; however, patients who place a high value on avoiding adverse events related to EET may choose surveillance as the preferred option.	Conditional	Moderate
In BE patients with confirmed HGD, we recommend EET compared with surveillance	Strong	Moderate
In BE patients with HGD/IMC, we recommend against surgery compared with EET	Strong	Very low quality
In BE patients referred for EET, we recommend endoscopic resection of all visible lesions compared with no endoscopic resection of visible lesions.	Strong	Moderate
In BE patients with visible lesions who undergo endoscopic resection, we suggest ablation of the remaining Barrett’s segment compared with no ablation.	Conditional	Low
In BE patients with dysplasia and IMC referred for EET, we recommend against routine complete endoscopic resection of entire Barrett’s segment compared with endoscopic resection of visible lesion followed by ablation of remaining Barrett’s segment.	Strong	Very low



Recommendation	SOR	QOE <sup>a</sup>
In BE patients with dysplasia and IMC who have achieved CE-IM after EET, we suggest surveillance endoscopy versus no surveillance.	Conditional	Very low

BE: Barrett esophagus; CE-IM: complete eradication of intestinal metaplasia; EET: endoscopic eradication therapy; HGD: high-grade dysplasia; LGD: low-grade dysplasia; IMC: intramucosal cancer; QOE: quality of evidence; SOR: strength of recommendation.

<sup>a</sup> Quality assessed using GRADE system.

### American Gastroenterological Association

The American Gastroenterological Association (2015) published consensus recommendations on the management of BE, dysplasia, and esophageal adenocarcinoma (see Table 3).<sup>34</sup>

**Table 3. Recommendations on Management of BE, Dysplasia, and Esophageal Adenocarcinoma**

Recommendation	Agreement	Strongly Agree	Agree	Neither	Disagree	Strongly Disagree
Statements with ≥80% consensus agreement but generally low-quality evidence relevant to RFA for BE						
In patients with BE undergoing endoscopic therapy, endoscopic resection of more than two-thirds of the circumference is not generally recommended due to the risk of stricture.	83	13	70	17		
RFA is an acceptable treatment option for BE patients with flat mucosa containing HGD without any visible lesions confirmed by high-resolution, high-definition endoscopy.	87	35	52	13		
Statements with consensus agreement <80% relevant to RFA for BE						
In patients with BE, all cases of possible dysplasia (indefinite, low grade, high grade) should be reviewed by at least 2 additional pathologists with specific expertise in Barrett’s pathology.	60.8			8.7	26.1	4.3

Values are percent.

BE: Barrett esophagus; HGD: high-grade dysplasia; RFA: radiofrequency ablation.

### Society of American Gastrointestinal and Endoscopic Surgeons

The Society of American Gastrointestinal and Endoscopic Surgeons (2010) published guidelines on the surgical treatment of gastroesophageal reflux disease, which included recommendations for the treatment of BE (see Table 4).<sup>35</sup>

**Table 4. Guidelines on Surgical Treatment of Gastroesophageal Reflux Disease**

Recommendation	GOR
HGIN and IMC can be effectively treated with endoscopic therapy including PDT, EMR, and RFA, alone or in combination.	B
Antireflux surgery may be performed in a patient with non-neoplastic IM, IND, or LGIN, with or without endoscopic therapy to eradicate the Barrett’s tissue. Specifically, RFA has been shown to be safe, clinically effective, and cost-effective in these disease states and may be performed in eligible patients before, during, or after antireflux surgery.	B

EMR: endoscopic mucosal resection; GOR: grade of recommendation; HGIN: high-grade dysplasia; IM: intestinal metaplasia; IMC: intramucosal carcinoma; IND: indeterminate dysplasia; LGIN: low-grade dysplasia; PDT: photodynamic therapy; RFA: radiofrequency ablation.

### **National Comprehensive Cancer Network**

National Comprehensive Cancer Network guidelines (v.2.2018) for esophageal cancer make the following recommendations about BE and early-stage esophageal adenocarcinomas<sup>36</sup>:

#### **Primary Treatment**

“The goal of endoscopic therapy, endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), and/or ablation, is the complete removal or eradication of early-stage disease (pTis, pT1a, and selected superficial pT1b without lymphovascular invasion (LVI)) and pre-neoplastic tissue (Barrett’s esophagus).

Early state disease Tis, also known as HGD, needs to be fully characterized, including evaluating presence of nodularity, lateral spread, and ruling out multifocal disease, as well as ruling out lymph node metastases by EUS [endoscopic ultrasound] in select high risk cases. This is important to permit decisions on endoscopic therapy with ablative methods such as radiofrequency ablation (RFA), cryoablation, photodynamic therapy (PDT) and/or ER [endoscopic resection].... Larger flat lesions (>2 cm) can be treated effectively by ER, but this is associated with greater risk of complications. Such lesions can be effectively treated by ablation alone, but there are very limited data on treating squamous cell HGD [high-grade dysplasia] by ablation alone.

Lesions that are found to be pathologically limited to the lamina propria or muscularis mucosae (pT1a), or the superficial submucosa (pT1b), in the absence of evidence of lymph node metastases, LVI, or poor differentiation grade can be treated with full ER..... Ablative therapy of residual Barrett’s esophagus should be performed following ER. Complete eradication of Barrett’s esophagus can also be performed with more aggressive application of EMR (wide field EMR) or ESD at the initial intervention, if necessary to completely resect an area of superficial tumor or mucosal nodularity less than or equal to 2 cm in maximal dimension.”

“Ablative therapy of residual Barrett’s esophagus should be performed following ER. Complete eradication of Barrett’s esophagus can also be performed with more aggressive application of EMR (wide field EMR) or ESD at the initial intervention, if necessary to completely resect an area of superficial tumor or mucosal nodularity less than or equal to 2 cm in maximal dimension.”

### **U.S. Preventive Services Task Force Recommendations**

Not applicable.

### **Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 5.

**Table 5. Summary of Key Trials**

NCT No.	Trial Name	Planned Enrollment	Completion Date
<b>Ongoing</b>			
NCT02558504	Clinical and Medico-economic Evaluation of Radiofrequency Ablation Versus Oesophagectomy in the Treatment of High Grade Dysplasia in Barrett's Oesophagus	250	Nov 2018
NCT01961778	Prospective Randomized Trial Comparing Radiofrequency Ablation (Barrx™) and Cryotherapy (truFreeze™) for the Treatment of Barrett's Esophagus With High-Grade Dysplasia and/or Early Adenocarcinoma	50	Feb 2020

NCT: national clinical trial.

**CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**CPT/HCPCS**

- 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)
- 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

- There is no CPT code specific to radiofrequency or cryoablation of tissue in the esophagus. These procedures would likely be coded using one of the following CPT codes: 43229, 43270.

**DIAGNOSIS**

ICD-10 Diagnosis (Effective October 1, 2015)

- D00.1 Carcinoma in situ of esophagus
- K22.710 Barrett's esophagus with low grade dysplasia
- K22.711 Barrett's esophagus with high grade dysplasia
- K22.719 Barrett's esophagus with dysplasia, unspecified

<b>REVISIONS</b>	
08-03-2010	Description Section updated. In Policy Section: <ul style="list-style-type: none"> <li>▪ Liberalized policy to current policy language from:                             <ul style="list-style-type: none"> <li>A. Radiofrequency ablation may be considered medically necessary for treatment of Barrett's esophagus with high-grade dysplasia. (see policy guidelines)</li> <li>B. Radiofrequency ablation is considered experimental / investigational for treatment of Barrett's esophagus with low-grade dysplasia or Barrett's esophagus in the absence of dysplasia.</li> </ul> </li> </ul>

<b>REVISIONS</b>	
	<p>C. Cryoablation is considered experimental / investigational for Barrett's esophagus, with or without dysplasia.</p> <p>Rationale Section updated.</p> <p>In Coding Section:</p> <ul style="list-style-type: none"> <li>▪ Added CPT Code: 43499</li> </ul> <p>References Section updated.</p>
12-21-2010	<p>Rationale section updated.</p> <p>Reference section updated.</p>
03-28-2012	<p>Description section updated.</p> <p>In the Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item 3, B, removed "cryotherapy" and inserted "cryoablation"</li> </ul> <p>Rationale section updated.</p> <p>In the Coding section:</p> <ul style="list-style-type: none"> <li>▪ Removed duplicate nomenclature listed with CPT code 43117</li> <li>▪ Removed CPT code 43324, deleted code, effective 01.01.2011</li> <li>▪ Added "injection" to HCPCS code J9600</li> </ul> <p>Reference section updated.</p>
02-15-2013	<p>In the Policy Title, inserted "Ablative" to read "Barrett's Esophagus Ablative Treatments"</p> <p>Description section updated.</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item A, inserted "ablative" to read "The following ablative interventions are considered medically necessary..."</li> <li>▪ In Item A #1, removed "Esophagectomy"</li> <li>▪ In Item A #2, removed "Fundoplication"</li> <li>▪ In Item A #3, removed "Endoscopic mucosal resection"</li> <li>▪ In Item B, replaced "and photodynamic therapy is considered experimental / investigational for low grade dysplasia or nondysplastic Barrett's esophagus" with "medically necessary for low-grade dysplasia, when the initial diagnosis of low-grade dysplasia is confirmed by two physicians" to read "Radiofrequency ablation is considered medically necessary for low-grade dysplasia, when the initial diagnosis of low-grade dysplasia is confirmed by two physicians."</li> <li>▪ Added Policy Guidelines section.</li> </ul> <p>Rationale section updated.</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Removed CPT codes: 43100, 43101, 43116, 43117, 43118, 43121, 43122, 43123, 43124, 43280</li> </ul> <p>Reference section updated.</p>
07-12-2013	<p>Description section updated.</p> <p>Rationale section updated.</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Added ICD-10 Diagnoses (<i>Effective October 1, 2014</i>)</li> </ul> <p>Reference section updated.</p>
12-31-2013	<p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Removed CPT codes: 43228, 43258 (<i>Deleted codes, effective December 31, 2013</i>)</li> <li>▪ Added CPT codes: 43229, 43233, 43253, 43254, 43266, 43270 (<i>New codes, effective January 1, 2014</i>)</li> <li>▪ Added ICD-10 Diagnosis codes (<i>Effective October 1, 2014</i>)</li> </ul>
01-01-2015	<p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Revised CPT Codes: 43216, 43226, 43229, 43233, 43253, 43254, 43266, 43270 (<i>Effective January 1, 2015</i>)</li> </ul>
04-25-2016	<p>Published 03-24-2016. Effective 04-25-2016.</p>

<b>REVISIONS</b>	
	Title changed from "Barrett's Esophagus Ablative Treatments" to "Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus"
	Description section updated.
	In Policy section: <ul style="list-style-type: none"> <li>▪ Policy revised to remove references to all therapies except radiofrequency ablation and cryoablation.</li> <li>▪ In Item A removed "The following ablative interventions are" and "when medical therapy (e.g., proton pump inhibitors, H-2 receptor, antagonists, or prokinetic agents) have failed: Photodynamic therapy" and added"(see Policy Guidelines)" to read, "Radiofrequency ablation may be considered medically necessary for treatment of Barrett esophagus with high-grade dysplasia (see Policy Guidelines)."</li> <li>▪ In Item B added "treatment of Barrett esophagus with" and "(see Policy Guidelines)" to read "Radiofrequency ablation may be considered medically necessary for treatment of Barrett esophagus with low-grade dysplasia, when the initial diagnosis of low-grade dysplasia is confirmed by 2 physicians (see Policy Guidelines)."</li> <li>▪ In Item C added "when the above criteria are not met, including but not limited to Barrett esophagus" to read "Radiofrequency ablation is considered experimental / investigational for treatment of Barrett esophagus when the above criteria are not met, including but not limited to Barrett esophagus in the absence of dysplasia."</li> <li>▪ In Item D removed "The following ablative interventions are", "because their effectiveness for these indications has not been established:" and "Argon plasma coagulation, Laser therapy, Multi-polar electro-coagulation, Ultrasonic therapy" to read "Cryoablation is considered experimental / investigational for treatment of Barrett esophagus, with or without dysplasia."</li> </ul>
	Rationale section updated
	In Coding section: <ul style="list-style-type: none"> <li>▪ Removed CPT Codes: 96570, 96571</li> <li>▪ Removed HCPCS Code: J9600</li> </ul>
	References updated
02-01-2017	Description section updated
	In Policy section: <ul style="list-style-type: none"> <li>▪ Policy Guidelines updated to add / remove policy related abbreviations and definitions.</li> </ul>
	Rationale section updated
	References updated
01-05-2018	Description section updated
	In Policy section: <ul style="list-style-type: none"> <li>▪ Policy Guidelines updated</li> </ul>
	Rationale section updated
	In Coding section: <ul style="list-style-type: none"> <li>▪ Removed CPT Codes: 43216, 43226, 43233, 43235, 43253, 43254, 43257, 43266, 43325 (These codes are not appropriate for this policy topic.)</li> </ul>
	References updated
02-18-2019	Description section updated
	Rationale section updated
	References updated

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