Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 9/1/24**
(See policy history boxes for previous effective dates)

Title: Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus

Description/Background

Barrett Esophagus and Risk of Esophageal Carcinoma

The esophagus is normally lined by squamous epithelium. Barrett 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. Occurring in the distal esophagus, BE may be of any length; it 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 a 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 to 20 years).(1) 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%.(2) 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.(3,4) Both sampling bias and interobserver variability have been shown to be problematic. Therefore, analysis of progression to carcinoma in BE with intestinal metaplasia versus 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.(5)

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 versus inflammatory changes, and the resultant variability in pathology diagnosis may contribute to the variable rates of progression of LGD reported in the literature.(6) 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.(7) Curvers et al (2010) tested this hypothesis in 147 patients with BE who were given an initial diagnosis of LGD.(8) 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.(9) Of 511 patients with an initial diagnosis of LGD, 264 (52%) were excluded because the central expert panel reassigned the 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.(10) In this sample, 73% of subjects were down staged.

Management of Barrett Esophagus

The management of Barrett esophagus (BE) includes the treatment of GERD and surveillance endoscopy to detect progression to high grade dysplasia (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 study provided long-term results for EMR in 100 consecutive patients with early Barrett-associated adenocarcinoma (limited to the mucosa).(11) The 5-year overall survival (OS) was 98%, and after a mean of 36.7 months, metachronous lesions were observed in 11% of patients. In a review by Pech and Ell, the authors state 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%.(12)

Ablative Techniques

Available mucosal ablation techniques include several thermal (multipolar electrocoagulation [MPEC], argon plasma coagulation [APC], heater probe, neodymium-doped yttrium aluminum

garnet (Nd:YAG) laser, potassium titanyl phosphate (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 was shown to decrease, significantly, the risk of adenocarcinoma in BE.(13)

The CryoSpray Ablation™ System uses a low-pressure spray for spraying liquid nitrogen through an upper endoscope. Cryotherapy allows for the 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 (i.e., <1 second) delivery of a predetermined amount of RF energy to the catheter. The HALO90 or 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.

Radiofrequency ablation affects only the most superficial layer of the esophagus (i.e., the mucosa), leaving the underlying tissues unharmed. Measures of efficacy for the procedure are eradication of intestinal metaplasia and post-ablation 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 [e.g., 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%.(14) 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.(12)

Regulatory Status

In 2005, the HALO360 (now Barrx™ 360 RFA Balloon Catheter; Barrx Medical; acquired by Covidien in 2012 [now Medtronic]) 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.(15) The FDA-labeled indications are for use in coagulation of bleeding and non-bleeding sites in the gastrointestinal tract and include the treatment of BE. Other focal ablation devices from Barrx include the Barrx™ 60 RFA Focal Catheter, the Barrx™ Ultra Long RFA Focal Catheter, the Barrx™ Channel RFA Endoscopic Catheter.

FDA product code: GEI.

In 2007, the CryoSpray Ablation™ System (formerly the SprayGenix Cryo Ablation system; CSA Medical) was cleared for marketing by the 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."(16) The CryoBalloon Ablation System has also been cleared by the FDA through the 510(k) process for use as a cryosurgical tool in surgery for endoscopic applications, including ablation of BE with dysplasia.(17) The next-generation C2 CryoBalloon Ablation System was introduced in 2018.(18)

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 the 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."(19)

Medical Policy Statement

The safety and effectiveness of radiofrequency ablation for **high-** and **low-grade** dysplasia in Barrett esophagus have been established. It may be a useful therapeutic option when indicated.

Radiofrequency ablation for the treatment of Barrett esophagus is experimental/ investigational when the criteria are not met, including but not limited to Barrett esophagus in the absence of dysplasia. While this procedure may be safe, its effectiveness for this clinical indication has not been established.

Cryoablation for Barrett esophagus, with or without dysplasia, is experimental/ investigational. While this procedure may be safe, its effectiveness for this clinical indication has not been established.

Inclusionary and Exclusionary Guidelines

Inclusions:

- Radiofrequency ablation for Barrett esophagus with high-grade dysplasia may be used alone or in combination with endoscopic mucosal resection of nodular/visible lesions.
- Radiofrequency ablation for Barrett esophagus with low-grade dysplasia may be used when the initial diagnosis of LGD is confirmed by 2 pathologists with expertise in gastrointestinal (GI) histopathology.

Exclusions:

- Radiofrequency for Barrett esophagus in the absence of dysplasia.
- Cryoablation for Barrett esophagus, with or without dysplasia.

CPT/HCPCS Level II Codes *(Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) in this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.)*

Established codes:

43229 43270

Other codes (investigational, not medically necessary, etc.):

N/A

Note: Code(s) 43229 and 43270 may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

Rationale

Radiofrequency Ablation for Barrett Esophagus With High-Grade Dysplasia

Clinical Context and Therapy Purpose
Individuals diagnosed with BE with high grade dysplasia (HGD) or low-grade dysplasia (LGD), 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%.(20) Therefore, intervention with esophagectomy or RFA may be strongly indicated.

The purpose of endoscopic RFA in individuals who have BE with HGD, with LGD, and without dysplasia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with BE with HGD, with LGD and without dysplasia.

Interventions
The therapy being considered is endoscopic RFA and endoscopic cryoablation.

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 (e.g., pain), and functional outcomes (including swallowing).

Beneficial outcomes include reductions progression to carcinoma and longer-term maintenance of eradication of dysplasia.

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

Morbidity from treatment would be assessed within 30 days after the procedure.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
Chadwick et al (2014) reported on a systematic review which compared RFA and complete endoscopic mucosal resection (EMR) for the treatment of Barrett esophagus (BE).(21) Twenty studies (22 articles) were reviewed including two RCTs, 10 cohort studies on EMR and eight cohort studies on RFA. The only study that compared RFA and EMR was an RCT by van Vilsteren et al (2011);(22) the other RCT was by Shaheen et al (2009, 2011; see below).(23,24) The studies were heterogeneous in design. A total of 1,087 (532 EMR, 555 RFA) patients with high-grade dysplasia (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 effects (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 individuals.

Randomized Controlled Trials
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.(25) At a median follow-up of 27 months, neoplasia and intestinal metaplasia had recurred in 4% and 8% of subjects, respectively.

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 containing HGD or early cancer.(22) Patients in the SRER group underwent a piecemeal EMR of 50% of BE followed by serial EMR. Patients in the EMR plus RFA group underwent focal ER for visible lesions followed by serial RFA. Follow-up endoscopy with biopsies (4-quadrant/2 cm BE) was performed at six and 12 months and then annually. The main outcome measures were: stenosis rate, complications, complete histologic response for neoplasia (CR-neoplasia); and complete histologic response for intestinal metaplasia (CR-IM). CR-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 in 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 median follow-up of 24 months, one SRER patient had recurrence of early cancer, requiring endoscopic resection.

This trial confirmed that both techniques achieve comparably high rates of CR-IM and CR-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 BE with dysplasia.(23) RFA was successful in eradicating HGD, with complete eradication at 12 months achieved in 81% of the ablation group versus 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 versus 2.4% in the RFA group ($p=0.04$). This represented a nearly 90% relative risk (RR) reduction for progression to cancer (RR=0.1; 95% CI, 0.01 to 1.0, $p=0.04$), and a number needed to treat of 6.0 to prevent one case of cancer over a 1-year period.

Longer term follow-up at two to three years reported that complete eradication of dysplasia was maintained in most participants with initial HGD.(24) 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 subjects, and all intestinal metaplasia was eradicated in 51 (91%) of 56 subjects. 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.

Section Summary: RFA for BE with HGD

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, the progression from HGD to cancer is reduced by approximately 90%, with rates of esophageal strictures of 6%.

RFA FOR BE WITH LOW-GRADE DYSPLASIA

Systemic Reviews

Wang et al (2022) performed a meta-analysis of 3 RCTs (N=282) comparing RFA with surveillance in patients with LGD.(26) Nearly 90% of the patients enrolled were male; other demographic information was not reported. The primary outcome was risk of progression to HGD or esophageal adenocarcinoma. Compared with endoscopic surveillance, RFA was associated with lower odds of progression to either HGD or esophageal adenocarcinoma (risk ratio [RR], 0.25; 95% CI, 0.07 to 0.93; p=.04).The findings had moderate heterogeneity ($I^2=55\%$), and the risk of bias was considered low. When analyzed separately, the risk of progression to HGD was significantly reduced with RFA (RR, 0.25; 95% CI, 0.07 to 0.71; p=.01; $I^2=15\%$); however, the results for progression to esophageal adenocarcinoma were not significant (RR, 0.56; 95% CI, 0.05 to 6.76; p=.65).

Klair et al (2021) performed a systematic review and meta-analysis of comparative studies of RFA versus endoscopic surveillance inpatients with BE with LGD.(27) The primary outcome was risk of progression to HGD or esophageal adenocarcinoma. The meta-analysis included 4 studies (N=543), including 2 retrospective studies and 2 RCTs. Compared with endoscopic surveillance, RFA was associated with lower odds of progression to either HGD or esophageal adenocarcinoma (odds ratio [OR], 0.17; 95% CI, 0.04 to 0.65).Individually, the progression to

HGD maintained significance compared with endoscopic surveillance (OR, 0.23; 95% CI, 0.08 to 0.61),while progression to adenocarcinoma was numerically lower (OR, 0.44; 95% CI, 0.17 to 1.16). However, the findings indicated moderate heterogeneity (I^2=0.63) and evidence of publication bias.

In their meta-analysis, Pandey et al (2018) evaluated both RCTs and observational studies to determine the efficacy of RFA in treating BE with LGD compared with surveillance.(28) The eight studies in the meta-analysis included 619 patients followed up for a median of 26 months. The overall pooled rate of complete eradication of intestinal metaplasia after RFA was 88.17% (95% CI, 88.13% to 88.20%; p <.001); the rate of complete eradication of dysplasia was 96.69% (95% CI, 96.67% to 96.71%; p <.001). Compared with surveillance, the rates of progression to high-grade dysplasia or cancer were significantly lower with RFA (odds ratio 0.07; 95% CI, 0.02 to 0.22). The pooled recurrence rate of intestinal metaplasia was 5.6% (95% CI, 5.57% to 5.63%; p <.001) and 9.66% (95% CI, 9.61% to 9.71%; p <.001) for dysplasia. Although the analysis was limited by its inclusion of observational cohort studies and the sample sizes of patients receiving RFA were all less than 100 patients, all studies supported the use of RFA for LGD BE. The authors concluded that RFA is safe and effective for eradicating intestinal metaplasia and dysplasia and reducing progression from LDG to HGD or cancer in the short term. Longer-term outcomes, however, warrant further research.

Section Summary: RFA for BE 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. Combined rates of progression to HGD or esophageal adenocarcinoma are lower in individuals with LGD treated with RFA compared with surveillance.

RFA FOR BE WITHOUT DYSPLASIA

Nonrandomized Trials

No RCTs were identified that evaluate 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 versus 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%.(1,2)

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.(29,30) The original study included 70 patients who underwent circumferential RFA and CR-IM; defined as complete eradication of nondysplastic BE.(29) CR-IM was seen in 70% of patients at one-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.(29) At 5-year follow-up, four-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.(30) 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 re-biopsy 2 months after RFA. No strictures were noted. The authors concluded that this first report of 5-year CR-IM outcomes lent support to the safety, efficacy, cost utility, 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

Systematic Reviews
Several meta-analyses have evaluated the efficacy of cryotherapy in patients with BE (Tables 1, 2, and 3). Tariq et al (2021) performed a meta-analysis of 14 retrospective and prospective observational studies (N=405) of patients with BE who were treated with cryotherapy.(31) The primary outcome of proportions of patients achieving complete eradication of dysplasia and complete eradication of intestinal metaplasia were 84.8% (95% CI, 72.2% to 94.4%) and 64.2% (95% CI, 52.9% to 74.8%), respectively. Both outcomes had a high degree of heterogeneity (I^2 of 88.3% and 77.9%, respectively). Subgroup analyses of only high-quality studies revealed rates of91.3% (95% CI, 83.0% to 97.4%; I^2=69.5%) and 71.6% (95% CI, 59.0% to 82.9%, I^2=80.9%), respectively.

In their meta-analysis, Westerveld et al (2020) evaluated 7 prospective and retrospective cohort studies that reported outcomes of balloon cryoablation across 272 patients with BE; 3 of the included studies were previously reported in abstract form only.(32) The pooled proportion for complete eradication of intestinal metaplasia was 85.8% (95% CI, 77.8% to 92.2%). Among 262 patients with BE with dysplasia, 238 reported complete eradication of dysplasia after cryoablation (pooled proportion, 93.8%; 95% CI, 85.5% to 98.7%). Both outcomes had a high degree of heterogeneity (I2 of 55% and 74.2%, respectively). However, when 2 low quality studies were excluded from the analysis results were consistent with the primary analysis. Adverse events were reported in 12.5% of patients, representing 34 adverse events. Half of the adverse events (n=16) were post-ablation stricture formation (5.8%).

Hamade et al (2019) evaluated the use of cryotherapy for BE in patients who were previously treatment naive.(33) Six uncontrolled trials were included in the systematic review, which included 232 patients overall. Complete eradication of intestinal metaplasia was achieved in 69.35% of cases (95% CI, 52.1% to 86.5%; I^2 = 89.3%). Complete eradication of dysplasia was achieved in 90.6% of cases (95% CI, 83.7% to 97.4%; I^2 = 75.7%). Progression to cancer occurred in 4% of cases (9/225). The pooled recurrence rate of intestinal metaplasia was 19.1 per 100 patient years. Post-procedure stricture formation rate was 4.9% and 3.9% of patients reported postprocedural pain.

Table 1. Comparison of Studies Included in Systematic Reviews & Meta-Analysis

Study	Tariq et al (2020)	Westerveld et al (2020)	Hamade et al (2019)
Canto et al (2019)		●	
Canto et al (2018)	●	●	●
Canto et al (2015)	●		●

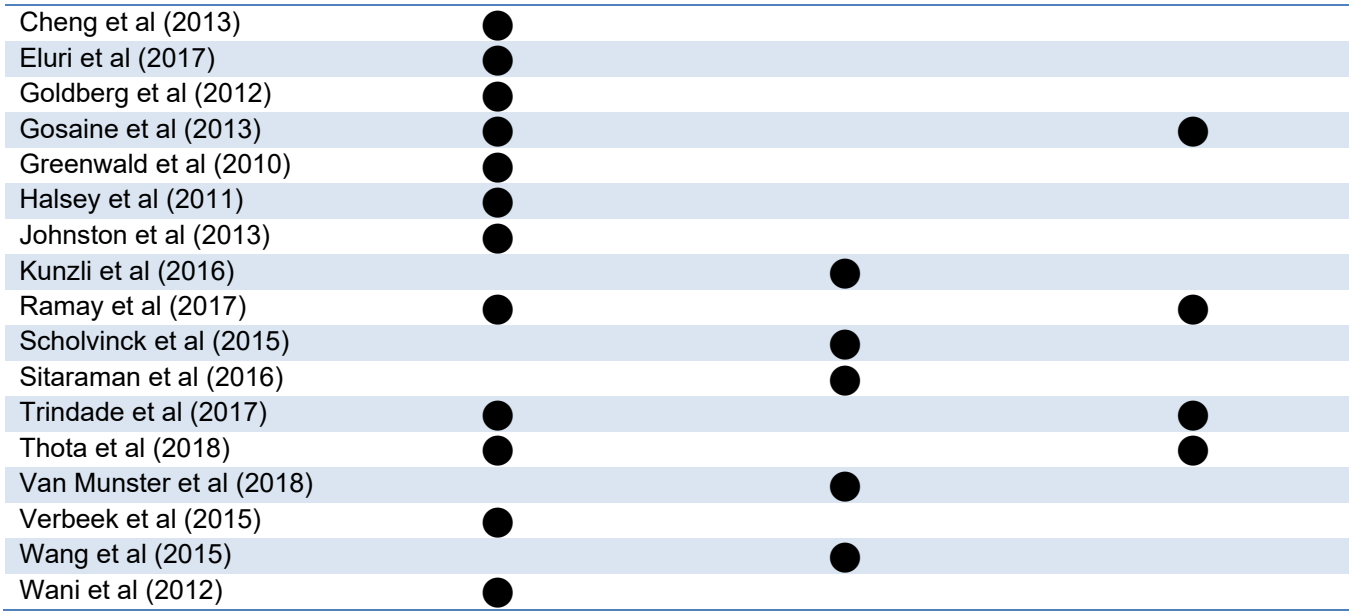

Table 2. Systematic Reviews & Meta-Analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Tariq et al (2020)	2006-2016	14	Patients with biopsy-confirmed dysplastic or neoplastic BE who underwent ≥1 session of cryotherapy	405 (20-81)	Retrospective, prospective observational	Range, 3-54 months
Westerveld et al (2020)	2015-2019	7	Patients with BE treated with cryoablation	272 (5-120)	Retrospective, prospective observational	NR
Hamade et al (2019)	NR	6	Treatment-naive patients with BE treated with cryotherapy	282 (22-81)	Retrospective observational	Range, 24 to 65 months

BE: Barrett's esophagus

Table 3. Systematic Reviews & Meta-Analysis Results

Study	Complete eradication of dysplasia	Complete eradication of intestinal metaplasia
Tariq et al (2020)		
Total N	405	393
Pooled effect (95% CI)	84.8% (72.2-94.4)	64.2% (52.9-74.8)
I^2 (%)	88.3	77.9
Westerveld et al (2020)		
Total N	262	272
Pooled effect (95% CI)	93.8% (85.5-98.7)	85.8% (77.8-92.2%)
I^2 (%)	74.2	55
Hamade et al (2019)		
Total N	282	282
Pooled effect (95% CI)	90.6 (83.7-97.4)	69.35 (52.1-86.5)
I^2 (%)	75.7	89.3

CI: confidence interval

Prospective and Retrospective Studies

Several small prospective and retrospective uncontrolled studies of cryoablation have been published (Tables 4 and 5). These studies are heterogenous in the proportion of patients with prior BE treatment, cryoablation techniques used and follow-up duration. Below is a summary of studies that were not included in the above-described systematic reviews and/or have notable characteristics (i.e., focus on subpopulations, have long-term follow-up).

A retrospective, single-center study by Sengupta et al (2015) evaluated cryoablation among 16 patients who failed RFA.(34) 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 2 who had 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.

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.(35) A total of 333 cryotherapy treatments (mean 3.4 per patient) were performed, each with the intent to eradicate all BE. Sixty patients completed all planned cryotherapy treatments and were assessed for efficacy by 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 three patients. The authors noted the limitations of the study: the study was nonrandomized and retrospective without a control group, lacked centralized pathology, used surrogate outcomes for decreased cancer risk, and 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.(36) 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. The authors noted the heterogeneous nature of the patient sample (high-risk, nonsurgical group of patients),which limited generalizability to patients in most BE ablation trials.

Two retrospective cohort studies compared RFA and cryotherapy in patients with BE undergoing endoscopic eradication therapy. Fasullo et al (2022) compared 100 RFA-treated patients with 62 cryotherapy-treated patients.(37) The majority of patients included in the study were white males, and cryotherapy was performed with liquid nitrogen spray. The rate of complete eradication of dysplasia was similar between groups (81% with RFA vs. 71% with cryotherapy; p=.14), and complete eradication of intestinal metaplasia was also similar between groups (64% with RFA and 66% with cryotherapy; p=.78). However, more sessions were required for complete eradication with cryotherapy, and treatment failure was also more common with cryotherapy (73.3% vs. 53.3%). Agarwal et al (2022) evaluated a cohort of 311 patients with BE undergoing endoscopic eradication therapy with either cryoballoon ablation (CBA) or RFA.(38) For the primary outcome of complete eradication of intestinal metaplasia, CBA versus RFA had similar outcomes (HR, 1.19; 95% CI, 0.82 to 1.73; p=.36). Patients treated with CBA had more strictures (10.4%) compared with RFA (4.4%; p=.04).

Table 4. Summary of Key Nonrandomized Studies

Study	Study Type	Country	Dates	Participants	Treatment	Follow-Up
Agarwal et al (2022)	Retrospective, observational	US	2014-2020	Patients who underwent RFA or cryotherapy for dysplastic BE	Cryoablation or RFA	Median, 1.5 years in RFA group and 2 years in the cryoablation group
Fasullo et al (2022)	Retrospective, observational	US	2009-2020	Patients who underwent RFA or cryotherapy for BE with LGD, HGD, or intramucosal adenocarcinoma	Cryoablation or RFA	>12 months
Sengupta et al (2015)	Retrospective, observational	US	2006-2013	Patients who underwent RFA for BE with LGD, HGD, or intramucosal carcinoma	Cryoablation	Median, 2.5 months
Shaheen et al (2010)	Retrospective, observational	US	2007-2009	Patients who had BE with HGD	Cryoablation	Mean, 10.5 months
Dumot et al (2009)	Prospective, observational	US	2005-2008	Patients who had BE with HGD or intramucosal carcinoma	Cryoablation	Median, 12 months

BE: Barrett's esophagus; HGD: high-grade dysplasia; LGD: low-grade dysplasia; RFA: radiofrequency ablation.

Table 5. Summary of Key Nonrandomized Study Results

Study	Complete eradication of dysplasia	Complete eradication of intestinal metaplasia	Downgrading of pathology stage	Elimination of cancer or downgrading of HGD
Agarwal et al (2022)	N=311; n=226 RFA and 85 cryoablation			
Cryotherapy, %	85.7	69.8	NR	NR
RFA, %	78.3	57.3	NR	NR
Fasullo et al (2022)	N=162; n=100 RFA and 62 cryoablation			
Cryotherapy, n %	44 (71)	41 (66.1)	NR	NR
RFA, n %	81 (81)	64 (64)	NR	NR
Sengupta et al (2015)[41],	N=121			
Cryotherapy, n (%)	91 (75)	NR	NR	NR
Shaheen et al (2010)[42],	N=60	N=60		
Cryotherapy, n (%)	58 (97)	34 (57)	NR	NR
Dumot et al (2009)[43],			N=30	N=30
Cryotherapy, n (%)	NR	NR	27 (90)	Pts with HGD: 20 (68) Pts with intramucosal carcinoma: 24 (80)

HGD: high-grade dysplasia; NR: not reported. RFA: radiofrequency ablation

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. In observational studies comparing RFA with cryoablation for patients with BE, similar outcomes have been noted; however, RCTs are lacking. These data are not sufficient to determine the comparative efficacy of cryoablation and RFA.

Summary of Evidence
For individuals who have BE with high-grade dysplasia (HGD) who receive endoscopic RFA, the evidence includes a randomized controlled trial (RCT) comparing radical endoscopic resection with focal endoscopic resection followed by RFA, one RCT comparing RFA with surveillance alone, and a number of observational studies, some of which compared RFA with other endoscopic treatment modalities. The 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 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 an improvement in the net health outcome.

For individuals who have BE with low-grade dysplasia (LGD) who receive endoscopic RFA, the evidence includes at least 3 RCTs comparing RFA with surveillance alone, a number of observational studies, and systematic reviews of these studies. The relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related morbidity and mortality. For patients with confirmed LGD, evidence suggests that RFA reduces progression to HGD and adenocarcinoma. The evidence is sufficient to determine that the technology results in an 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. The 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 that the technology results in an improvement in the net health outcome.

For individuals who have BE with or without dysplasia who receive endoscopic cryoablation, the evidence includes noncomparative studies reporting outcomes after cryoablation. The 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. Recent observational studies comparing RFA with cryoablation show similar outcomes. However, there are no RCTs comparing cryoablation with surgical care or RFA. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

CLINICAL INPUT RECEIVED THROUGH 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 six academic medical centers and from one subspecialty medical society while this policy was under review in 2012. Input related to the treatment of LGD, was mixed, with two reviewers stating that 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 subpopulations of patients with LGD who have a 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 three academic medical centers and one 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 9 considering it medically necessary and 4 considering it investigational.

PRACTICE GUIDELINES AND POSITION STATEMENTS

American College of Gastroenterology

The American College of Gastroenterology (ACG; 2022) issued guidelines on the diagnosis and management of Barrett esophagus (BE), which made statements about ablation techniques.(39) The ACG recommends ablation of remaining BE tissue when endoscopic eradication therapy is chosen for patients with LGD, HGD, or intramucosal carcinoma. Both RFA and cryoablation are discussed in the ACG guideline without a specific recommendation; however, the guideline notes the lack of RCTs for cryoablation methods and the more established evidence for RFA. The ACG does recommend cryotherapy as an alternative in patients unresponsive to RFA.

American Gastroenterological Association

In 2020, the American Gastroenterological Association published a best practice clinical update on the role of endoscopic therapy in patients with BE with dysplasia and/or early cancer.(40) This best practice document was not based on a formal systematic review; thus, no ratings for strength of recommendation and quality of evidence were provided.

For BE with LGD, best practice advice included the following:

- "The reading of LGD in BE should be confirmed by an experienced gastrointestinal pathologist."
- "In BE patients with confirmed LGD, a repeat examination within 3–6 months with HD-WLE [high-definition white-light endoscopy] and preferably optical chromoendoscopy should be performed to rule out the presence of a visible lesion, which should prompt endoscopic resection (see section on HGD)."
- "Both BET [Barrett's endoscopic therapy] and continued surveillance are reasonable options for the management of BE patients with confirmed and persistent LGD."

For BE with HGD, best practice advice included the following:

- "The reading of HGD in BE should be confirmed by an experienced gastrointestinal pathologist."

- "The diagnosis of flat HGD should prompt a repeat HD-WLE (6–8 weeks) to evaluate for the presence of a visible lesion; these visible lesions should be removed by EMR [endoscopic mucosal resection]."
- "BET is the preferred treatment, over esophagectomy, for BE patients with HGD."

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.(41) These guidelines made the following recommendations on endoscopic eradication therapy, consisting of endoscopic mucosal resection of visible lesions and ablative techniques that include radiofrequency ablation and cryotherapy (see Table 6).

Table 6. Guidelines on Use of Endoscopy for Barrett Esophagus and Intramucosal Cancer

Recommendation	SOR	QOE[a]
In BE patients with LDG and HGD being considered for EET, we suggest confirmation of diagnosis by at least one expert GI pathologist or panel of pathologists compared with review by a single pathologist.	Conditional	Low
In BE patients with LDG, 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
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
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; LOE: level of evidence; QOE: quality of evidence; SOR: strength of recommendation.
[a] Quality assessed using GRADE system.

National Comprehensive Cancer Network

National Comprehensive Cancer Network guidelines Esophageal and Esophagogastric Cancers make recommendations about BE and early-stage esophageal adenocarcinomas.(42). For primary treatment; "The goal of endoscopic therapy, [by 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 LVI) and pre-neoplastic tissue (Barrett esophagus).

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently ongoing and unpublished trials that might influence this review are listed in Table 7.

Table 7. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02514525	Multi-center Clinical Study to Evaluate the C2 CryoBalloon Focal Ablation System for the Treatment of Patients with Previously Untreated Dysplastic Barrett's Epithelium	150	June 2023
Unpublished			
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 (Last update posted 2022)
NCT02558504	Clinical and Medico-economic Evaluation of Radiofrequency Ablation Versus Oesophagectomy in the Treatment of High-Grade Dysplasia in Barrett's Oesophagus	87	Jan 2021 (Last update posted Apr 2022)

NCT: national clinical trial

Government Regulations

Medicare has no national or local coverage determination for radiofrequency ablation or cryotherapy for Barrett esophagus.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Confocal Laser Endomicroscopy
- Magnetic Esophageal Sphincter Augmentation to Treat Gastroesophageal Reflux Disease (GERD)
- Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease (GERD) (Transoral Incisionless Fundoplication)

References

1. Bhat S, Coleman HG, Yousef F et al. Risk of malignant progression in Barrett esophagus patients: results from a large population-based study. J Natl Cancer Inst 2011; 103(13):1049-57. PMID 21680910
2. Hvid-Jensen F, Pedersen L, Drewes AM et al. Incidence of adenocarcinoma among patients with Barrett esophagus. N Engl J Med 2011; 365(15):1375-83. PMID 21995385
3. Downs-Kelly E, Mendelin JE, Bennett AE et al. Poor interobserver agreement in the distinction of high-grade dysplasia and adenocarcinoma in pretreatment Barrett esophagus biopsies. American Journal of Gastroenterology 2008; 103(9):2333-40; quiz 2341. PMID 18671819
4. Yerian L. Histology of metaplasia and dysplasia in Barrett esophagus. Surgical Oncology Clinics of North America 2009; 18(3):411-422. PMID 19500733

5. Wang KK, Sampliner RE. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett esophagus. The American Journal of Gastroenterology. Mar 2008; 103(3):788-797. PMID 18341497
6. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Radiofrequency ablation of nondysplastic or low-grade dysplastic Barrett's esophagus. TEC Assessments. 2010;Volume 25:Tab 5.
7. 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. Jun 2007; 50(7): 920-7. PMID 17543082
8. Curvers WL, ten Kate FJ, Krishnadath KK, et al. Low-grade dysplasia in Barrett's esophagus: overdiagnosed and underestimated. Am J Gastroenterol. Jul 2010; 105(7): 1523-30. PMID 20461069
9. 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. Mar 26 2014;311(12):1209-1217. PMID 24668102
10. Duits LC, Phoa KN, Curvers WL, et al. Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel. Gut. May 2015;64(5):700-706. PMID 25034523
11. Ell C, May A, Pech O et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett cancer). *Gastrointestinal endoscopy*. Jan 2007; 65(1):3-10. PMID 17185072
12. Pech O, Ell C. Endoscopic therapy of Barrett esophagus. *Curr Opin Gastroenterol* 2009; 25(5):405-411. PMID 19474724
13. Overholt BF, Lightdale CJ, Wang KK, et al. Photodynamic therapy with porfimer sodium for ablation of high-grade dysplasia in Barrett's esophagus: international, partially blinded, randomized phase III trial. *Gastrointest Endosc*. Oct 2005;62(4):488-498. PMID 16185958
14. 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*. Jul 2008;68(1):35-40. PMID 18355819
15. Food and Drug Administration. 510(k) Summary: BARRX Channel RFA Endoscopic Catheter. No. K130623. 2013; https://www.accessdata.fda.gov/cdrh_docs/pdf13/K130623.pdf. Accessed September 12, 2022.
16. Food and Drug Administration. 510(k) Safety Summary: CryoSpray Ablation System. No. K072651. 2007; https://www.accessdata.fda.gov/cdrh_docs/pdf7/K072651.pdf. Accessed September 9, 2022.
17. Food and Drug Administration. 510(k) Summary: C2 Cryoballoon Ablation System. No. K163684. 2018; https://www.accessdata.fda.gov/cdrh_docs/pdf16/K163684.pdf. Accessed September 9, 2022.
18. Pentax Medical. Pentax Medical Introduces Next-Generation C2 Cryoballoon Ablation System for Treatment of Barrett's Esophagus. 2018. https://www.pentaxmedical.com/pentax/en/99/1/pentax-medical-introduces-next-generation-c2-cryoballoon-ablation-system-for-treatment-of-barretts-esophagus. Accessed September 13, 2022.
19. U.S. Food and Drug Administration. 510(k) Premarket Notification to Check-Med Systems, Inc. 2002; https://www.accessdata.fda.gov/cdrh_docs/pdf2/k021387.pdf. Accessed September 14, 2023
20. Eloubeidi MA, Wallace MB, Hoffman BJ et al. Predictors of survival for esophageal cancer patients with and without celiac axis lymphadenopathy: impact of staging

endosonography. *Annals of Thoracic Surgery*. Jul2001; 72(1):212-219; discussion 219-220. PMID 11465182
21. Chadwick G, Groene O, Markar SR, et al. Systematic review comparing radiofrequency ablation and complete endoscopic resection in treating dysplastic Barrett's esophagus: a critical assessment of histologic outcomes and adverse events. *Gastrointestinal Endoscopy*. May;79(5):718-713. PMID 24462170
22. van Vilsteren FG, Pouw RE, Seewald S et al. Stepwise radical endoscopic resection versus radiofrequency ablation for Barrett oesophagus with high-grade dysplasia or early cancer: a multicentre randomized trial. *Gut.* Jun 2011;60(6):765-773. PMID 21209124
23. Shaheen NJ, Sharma P, Overholt BF et al. Radiofrequency ablation in Barrett esophagus with dysplasia. *N Engl J Med*. May 28 2009;360(22):2277-2288. PMID 19474425
24. Shaheen NJ, Overholt BF, Sampliner RE et al. Durability of radiofrequency ablation in Barrett esophagus with dysplasia. *Gastroenterology*. Aug 2011;141(2):460-468. PMID 21679712
25. Phoa KN, Pouw RE, Bisschops R, et al. Multimodality endoscopic eradication for neoplastic Barrett oesophagus: results of an European multicentre study (EURO-II). *Gut*. Mar 2 2015. PMID 25731874
26. Wang Y, Ma B, Yang S, et al. Efficacy and Safety of Radiofrequency Ablation vs. Endoscopic Surveillance for Barrett's Esophagus With Low-Grade Dysplasia: Meta-Analysis of Randomized Controlled Trials. Front Oncol. 2022; 12: 801940. PMID 35296005
27. Klair JS, Zafar Y, Nagra N, et al. Outcomes of Radiofrequency Ablation versus Endoscopic Surveillance for Barrett's Esophagus with Low-Grade Dysplasia: A Systematic Review and Meta-Analysis. Dig Dis. 2021; 39(6):561-568. PMID 33503615
28. Pandey G, Mulla M, Lewis WG et al. Systematic review and meta-analysis of the effectiveness of radiofrequency ablation in low grade dysplastic Barrett's esophagus. Endoscopy, 2018 Apr 25;50(10). PMID 29689573.
29. Fleischer DE, Overholt BF, Sharma VK et al. Endoscopic ablation of Barrett esophagus: a multicenter study with 2.5-year follow-up. *Gastrointest Endosc*. Nov 2008;68(5):867-876. PMID 18561930
30. Fleischer DE, Overholt BF, Sharma VK et al. Endoscopic radiofrequency ablation for Barrett esophagus: 5-year outcomes from a prospective multicenter trial. *Endoscopy* Oct 2010; 42(10):781-789. PMID 20857372
31. Tariq R, Enslin S, Hayat M, et al. Efficacy of Cryotherapy as a Primary Endoscopic Ablation Modality for Dysplastic Barrett's Esophagus and Early Esophageal Neoplasia: A Systematic Review and Meta-Analysis. Cancer Control. Jan-Dec 2020; 27(1): 1073274820976668. PMID 33297725
32. Westerveld DR, Nguyen K, Banerjee D, et al. Safety and effectiveness of balloon cryoablation for treatment of Barrett's associated neoplasia: systematic review and meta-analysis. Endosc Int Open. Feb 2020; 8(2): E172-E178. PMID 32010750
33. Hamade N, Desai M, Thoguluva Chandrasekar V, et al. Efficacy of cryotherapy as first line therapy in patients with Barrett's neoplasia: a systematic review and pooled analysis. Dis Esophagus. Dec 30 2019; 32(11). PMID 31076753
34. Sengupta N, Ketwaroo GA, Bak DM, et al. Salvage cryotherapy after failed radiofrequency ablation for Barrett's esophagus-related dysplasia is safe and effective. *Gastrointestinal Endoscopy.* Sep 2015;82(3):443-448. PMID 25887715
35. Shaheen NJ, Greenwald BD, Peery AF et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett esophagus with high-grade dysplasia. *Gastrointestinal endoscopy.* Apr 2010;71(4):680-685. PMID 20363409

36. Dumot JA, Vargo JJ, 2nd, Falk GW et al. An open-label, prospective trial of cryospray ablation for Barrett esophagus high-grade dysplasia and early esophageal cancer in high-risk patients. Gastrointestinal Endoscopy. Oct 2009;70(4):635-644. PMID 19559428
37. Fasullo M, Shah T, Patel M, et al. Outcomes of Radiofrequency Ablation Compared to Liquid Nitrogen Spray Cryotherapy for the Eradication of Dysplasia in Barrett's Esophagus. Dig Dis Sci. Jun 2022; 67(6):2320-2326. PMID 33954846
38. Agarwal S, Alshelleh M, Scott J, et al. Comparative outcomes of radiofrequency ablation and cryoballoon ablation in dysplastic Barrett's esophagus: a propensity score-matched cohort study. Gastrointest Endosc. Mar 2022; 95(3): 422-431.e2. PMID 34624303
39. Shaheen NJ, Falk GW, Iyer PG, et al. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. Am J Gastroenterol. Jan 2016;111(1):30-50; quiz 51. PMID 26526079
40. Sharma P, Shaheen NJ, Katzka D, et al. AGA Clinical Practice Update on Endoscopic Treatment of Barrett's Esophagus With Dysplasia and/or Early Cancer: Expert Review. Gastroenterology. Feb 2020;158(3): 760-769. PMID 31730766National Comprehensive Cancer Network (NCCN).
41. Wani S, Qumseya B, Sultan S, et al. Endoscopic eradication therapy for patients with Barrett's esophagus-associated dysplasia and intramucosal cancer. Gastrointest Endosc. Apr 2018; 87(4): 907-931.e9. PMID 29397943
42. NCCN Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Junction Cancers. Version 1.2024. https://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf. Accessed March 24, 2023.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 3/26/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
9/1/11	6/21/11	6/21/11	Joint policy established
11/1/12	8/21/12	8/21/12	Routine maintenance; added low-grade dysplasia as an inclusion; references updated; Description and Rationale sections revised
3/1/15	12/12/14	12/29/14	Routine maintenance; added code 43229, removed 43499.
3/1/16	12/10/15	12/10/15	Routine maintenance; added "when the above criteria are not met" to the policy statement to clarify that radiofrequency ablation for Barrett esophagus is considered experimental/investigational for all cases in which the coverage criteria do not apply. References and rationale updated.
3/1/17	12/13/16	12/13/16	Routine maintenance
3/1/18	12/12/17	12/12/17	Routine maintenance
3/1/19	12/11/18		Routine maintenance
9/1/19	6/18/19		Routine maintenance
9/1/20	6/16/20		Physicians changed to pathologists under inclusions: Radiofrequency ablation for Barrett esophagus with low-grade dysplasia may be used when the initial diagnosis of LGD is confirmed by two pathologists with expertise in gastrointestinal (GI) histopathology. Backed by AGA 2015 position statement
9/1/21	6/15/21		Routine maintenance
9/1/22	6/21/22		Routine maintenance
9/1/23	6/13/23		Routine maintenance (slp) Vendor Managed: N/A
9/1/24	6/11/24		Routine maintenance (slp) Vendor Managed: N/A

Next Review Date: 2nd Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: ENDOSCOPIC RADIOFREQUENCY ABLATION OR CRYOABLATION FOR BARRETT ESOPHAGUS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered, policy criteria apply
BCNA (Medicare Advantage)	Refer to the Medicare information under the Government Regulations section of this policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.