MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

Medical Policy

# Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus

## Table of Contents



## Policy Number: 218

BCBSA Reference Number: 2.01.80
NCD/LCD: NA

## Related Policies

- Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus, #454
- Confocal Laser Endomicroscopy, #618

## Policy

### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

Radiofrequency ablation may be considered **MEDICALLY NECESSARY** for treatment of Barrett esophagus with high-grade dysplasia.

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 two pathologists prior to the ablation procedure.

Radiofrequency ablation is considered **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.

Cryoablation is considered **INVESTIGATIONAL** for Barrett esophagus, with or without dysplasia.

## Prior Authorization Information

**Inpatient**

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

**Outpatient**

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

| | Outpatient |
|---|---|
| **Commercial Managed Care (HMO and POS)** | Prior authorization is **not required**. |
| **Commercial PPO and Indemnity** | Prior authorization is **not required**. |
| **Medicare HMO Blue℠** | Prior authorization is **not required**. |
| **Medicare PPO Blue℠** | Prior authorization is **not required**. |

## CPT Codes / HCPCS Codes / ICD Codes

*Inclusion or exclusion of a code 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 as it applies to an individual member.*

*Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.*

*The following codes are included below for informational purposes only; this is not an all-inclusive list.*

**The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:**

### CPT Codes

| CPT codes: | Code Description |
|---|---|
| 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) |

### ICD-10 Diagnosis Codes

| ICD-10-CM Diagnosis codes: | Code Description |
|---|---|
| D13.0 | Benign neoplasm 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 |

## Description

**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 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).[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 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.[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 vs 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 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 downstaged.

**Management**

The management of BE includes treatment of gastroesophageal reflux disease 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).[11] 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 Ell (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%.[12]

**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) techniques. In a randomized phase 3 trial reported by Overholt et al (2005), photodynamic therapy was shown to decrease significantly the risk of adenocarcinoma in BE.[13] (Photodynamic therapy for BE is discussed in policy #454.)

The CryoSpray Ablation system uses a low-pressure spray for applying 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 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 radiofrequency 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. 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 (ie, the mucosa), leaving the underlying tissues unharmed. Measures of efficacy for the procedure are the eradication of intestinal metaplasia and postablation regrowth of the normal squamous epithelium. (Note: The eradication of intestinal metaplasia does not leave behind microscopic 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 microscopic 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 it is an automated process that eliminates operator-dependent error, which 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]

## Summary

In Barrett 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.

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, 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 low-grade dysplasia (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.

Clinical input was obtained in 2012, and it generally supported the use of RFA for BE with LGD. Input indicated that it is possible to define a population with a higher risk of progression by having the initial diagnosis of LGD reconfirmed by an expert in gastrointestinal pathology.

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.

## Policy History

| Date | Action |
|---|---|
| 1/2019 | BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged. |
| 1/2018 | New references added from BCBSA National medical policy. |
| 12/2016 | New references added from BCBSA National medical policy. |
| 1/2016 | New references added from BCBSA National medical policy. |
| 6/2015 | BCBSA National medical policy review.<br>Investigational indications clarified. Added coding language. Effective 6/1/2015. |
| 7/2014 | New references added from BCBSA National medical policy. |
| 5/2014 | Updated Coding section with ICD10 procedure and diagnosis codes. Effective 10/2015. |
| 1/2014 | Updated to add new CPT code 43229 and remove deleted code 43228 |
| 9/2012 | Added coverage for RFA for treatment of Barrett's esophagus with low-grade dysplasia. Effective 9/1/2012. |
| 11/2011-4/2012 | Medical policy ICD 10 remediation: Formatting, editing and coding updates.<br>No changes to policy statements. |
| 10/2011 | Reviewed - Medical Policy Group – GI, Nutrition and Organ Transplantation.<br>No changes to policy statements. |
| 3/2011 | Reviewed - Medical Policy Group – Allergy/Asthma/Immunology and ENT/Otolaryngology.<br>No changes to policy statements. |
| 8/1/2010 | Medical Policy #218 effective 8/1/2010 describing covered and non-covered indications. |

## Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

## References


1. Bhat S, Coleman HG, Yousef F, et al. Risk of malignant progression in Barrett's esophagus patients: results from a large population-based study. *J Natl Cancer Inst.* Jul 6 2011;103(13):1049-1057. PMID 21680910
2. Hvid-Jensen F, Pedersen L, Drewes AM, et al. Incidence of adenocarcinoma among patients with Barrett's esophagus. *N Engl J Med.* Oct 13 2011;365(15):1375-1383. 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's esophagus biopsies. *Am J Gastroenterol.* Sep 2008;103(9):2333-2340; quiz 2341. PMID 18671819
4. Yerian L. Histology of metaplasia and dysplasia in Barrett's esophagus. *Surg Oncol Clin N Am.* Jul 2009;18(3):411-422. PMID 19500733
5. Wang KK, Sampliner RE. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. *Am J Gastroenterol.* 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):920-927. 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):1523-1530. 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's cancer). *Gastrointest Endosc.* Jan 2007;65(1):3-10. PMID 17185072
12. Pech O, Ell C. Endoscopic therapy of Barrett's esophagus. *Curr Opin Gastroenterol.* Sep 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 Models HALO360 and HALO360+ Coagulation Catheters. No. K080557. 2008; https://www.accessdata.fda.gov/cdrh_docs/pdf8/K080557.pdf. Accessed October 29, 2018.
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 October 29, 2018.
17. 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 Oct 23, 2018.
18. 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. *Ann Thoracic Surg.* Jul 2001;72(1):212-219; discussion 219-220. PMID 11465182
19. 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. *Gastrointest Endosc.* May 2014;79(5):718-731 e713. PMID 24462170
20. van Vilsteren FG, Pouw RE, Seewald S, et al. Stepwise radical endoscopic resection versus radiofrequency ablation for Barrett's oesophagus with high-grade dysplasia or early cancer: a multicentre randomised trial. *Gut.* Jun 2011;60(6):765-773. PMID 21209124
21. Shaheen NJ, Sharma P, Overholt BF, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. *N Engl J Med.* May 28 2009;360(22):2277-2288. PMID 19474425
22. Shaheen NJ, Overholt BF, Sampliner RE, et al. Durability of radiofrequency ablation in Barrett's esophagus with dysplasia. *Gastroenterology.* Aug 2011;141(2):460-468. PMID 21679712
23. Phoa KN, Pouw RE, Bisschops R, et al. Multimodality endoscopic eradication for neoplastic Barrett oesophagus: results of a European multicentre study (EURO-II). *Gut.* Apr 2016;65(4):555-562. PMID 25731874

24. Almond LM, Hodson J, Barr H. Meta-analysis of endoscopic therapy for low-grade dysplasia in Barrett's oesophagus. *Br J Surg.* Sep 2014;101(10):1187-1195. PMID 24965075
25. Fleischer DE, Overholt BF, Sharma VK, et al. Endoscopic ablation of Barrett's esophagus: a multicenter study with 2.5-year follow-up. *Gastrointest Endosc.* Nov 2008;68(5):867-876. PMID 18561930
26. Fleischer DE, Overholt BF, Sharma VK, et al. Endoscopic radiofrequency ablation for Barrett's esophagus: 5-year outcomes from a prospective multicenter trial. *Endoscopy.* Oct 2010;42(10):781-789. PMID 20857372
27. Canto MI, Shin EJ, Khashab MA, et al. Safety and efficacy of carbon dioxide cryotherapy for treatment of neoplastic Barrett's esophagus. *Endoscopy.* Jul 2015;47(7):582-591. PMID 25826275
28. Sengupta N, Ketwaroo GA, Bak DM, et al. Salvage cryotherapy after failed radiofrequency ablation for Barrett's esophagus-related dysplasia is safe and effective. *Gastrointest Endosc.* Sep 2015;82(3):443-448. PMID 25887715
29. Greenwald BD, Dumot JA, Horwhat JD, et al. Safety, tolerability, and efficacy of endoscopic low-pressure liquid nitrogen spray cryotherapy in the esophagus. *Dis Esophagus.* Jan 2010;23(1):13-19. PMID 19515183
30. Shaheen NJ, Greenwald BD, Peery AF, et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's esophagus with high-grade dysplasia. *Gastrointest Endosc.* Apr 2010;71(4):680-685. PMID 20363409
31. Dumot JA, Vargo JJ, 2nd, Falk GW, et al. An open-label, prospective trial of cryospray ablation for Barrett's esophagus high-grade dysplasia and early esophageal cancer in high-risk patients. *Gastrointest Endosc.* Oct 2009;70(4):635-644. PMID 19559428
32. 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
33. Standards of Practice Committee, Wani S, Qumseya B, et al. Endoscopic eradication therapy for patients with Barrett's esophagus-associated dysplasia and intramucosal cancer. *Gastrointest Endosc.* Apr 2018;87(4):907-931 e909. PMID 29397943
34. Sharma P, Katzka DA, Gupta N, et al. Quality Indicators for the Management of Barrett's Esophagus, Dysplasia, and Esophageal Adenocarcinoma: International Consensus Recommendations from the American Gastroenterological Association Symposium. *Gastroenterology.* Nov 2015;149(6):1599-1606. PMID 26296479
35. Stefanidis D, Hope WW, Kohn GP, et al. Guidelines for surgical treatment of gastroesophageal reflux disease. *Surgical Endoscopy.* Nov 2010;24(11):2647-2669. PMID 20725747
36. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Junction Cancers. Version 2.2018. https://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf. Accessed October 29, 2018.