Protocol

Endoscopic Radiofrequency Ablation or Cryoablation for Barrett's Esophagus

(20180)

Medical Benefit		**Effective Date**: 10/01/12	**Next Review Date**: 03/15
Preauthorization	No	**Review Dates**: 05/09, 03/10, 03/11, 03/12, 07/12, 03/13, 03/14	

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is not required.*** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Description

Barrett's esophagus is a condition in which 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 or cryoablation.

Background

Barrett's Esophagus and the Risk of Esophageal Carcinoma

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

Intestinal metaplasia is a precursor to esophageal adenocarcinoma, and esophageal adenocarcinoma is thought to result from a stepwise accumulation of genetic abnormalities in the specialized epithelium, which results in the phenotypic expression of histologic features of low-grade dysplasia (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 Barrett's esophagus. One study reported the rate of progression to cancer in more than 8,000 patients with a mean duration of follow-up of seven years (range 1-20 years). (1) The de novo progression to cancer from Barrett's esophagus at one year was 0.13%. The risk of progression was reported as 1.4% per year in patients with low-grade dysplasia and 0.17% per year in patients without dysplasia. This incidence translates into a risk of 10-11 times that of the general population. The other study identified over 11,000 patients with Barrett's esophagus and, after a median follow-up of 5.2 years, reported that the annual risk of esophageal adenocarcinoma was 0.12%. (2) Detection of low-grade dysplasia on index endoscopy was associated with an incidence rate for adenocarcinoma of 5.1 cases per 1,000 person-years, and the incidence rate among patients without dysplasia was 1.0 case per 1,000 person-years. Risk estimates for patients with high-grade dysplasia were slightly higher.

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

Management of Barrett's Esophagus

The current management of Barrett's esophagus includes treatment of GERD and surveillance endoscopy to detect progression to HGD or adenocarcinoma. The finding of LGD typically warrants only follow-up and surveillance biopsies, whereas 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). A study (3) provided long-term results for EMR in 100 consecutive patients with early Barrett's-associated adenocarcinoma (limited to the mucosa). The five-year overall survival (OS) was 98%, and metachronous lesions were observed in 11% of patients after a mean of 36.7 months. In a recent review by Pech and Ell, the authors state that circumferential EMR of the entire segment of Barrett's leads to a stricture rate of 50%, and recurrences occur at a rate of up to 11%. (4)

Mucosal ablation techniques that are available consist of one of several thermal (multipolar electrocoagulation [MPEC], argon plasma coagulation [APC], heater probe, Nd:YAG laser, KTP-YAG laser, diode laser, argon laser, and cryoablation) or nonthermal (5-aminolevulinic acid [5-ALA] and photofrin photodynamic therapy [PDT]) techniques. PDT has been the only therapy shown in a randomized Phase III trial to significantly decrease the risk of carcinoma in Barrett's esophagus. (5) Two hundred and eight patients with HGD were randomly assigned to PDT and omeprazole versus omeprazole alone. At 24 months' follow-up, 77% of patients treated with PDT had complete ablation of HGD versus 39% in the control group ($p < 0.0001$) and occurrence of adenocarcinoma within a follow-up time of 3.6 years was 13% in the PDT group versus 20% in the control group ($p < 0.006$) (PDT therapy for Barrett's esophagus is discussed in a separate Protocol.) However, the use of PDT for Barrett's esophagus with HGD has recently decreased dramatically, due to the fact that is relatively expensive and associated with a high complication rate, including photosensitivity and esophageal stricture formation in up to 30% of patients treated with this method. (4)

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

Treating HGD or mucosal cancer solely with ablative techniques risks undertreating the approximately 10% of patients who have undetected submucosal cancer, in whom esophagectomy would have been required. (4)

The HALO System from BÂRRX Medical, Inc. (Sunnyvale, CA – acquired by Covidien in 2012) uses radiofrequency (RF) energy and consists of two components: an energy generator and an ablation catheter. The generator provides rapid (i.e., less than one second) delivery of a predetermined amount of RF energy to the catheter. Both the HALO90 and HALO360 are inserted into the esophagus with an endoscope, using standard endoscopic techniques. The HALO90 catheter is plate-based and used for focal ablation of areas of Barrett's esophagus up to 3 cm. The HALO360 uses a balloon catheter that is sized to fit the individual esophagus and is inflated to allow for circumferential ablation.

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

Regulatory Status

The HALO360 received U.S. Food and Drug Administration (FDA) 510(k) clearance for marketing in 2005 and the HALO90 in 2006. The FDA-labeled indications are for use in coagulation of bleeding and non-bleeding sites in the gastrointestinal tract, and include the treatment of Barrett's esophagus. (7) The CryoSpray Ablation™ System received FDA 510(k) marketing clearance in December 2007 for use as a "cryosurgical tool for destruction of unwanted tissue in the field of general surgery, specifically for endoscopic applications." (8)

Related Protocols

Confocal Laser Endomicroscopy

Oncologic Applications of Photodynamic Therapy, Including Barrett's Esophagus

Policy (Formerly Corporate Medical Guideline)

Radiofrequency ablation may be considered **medically necessary** for treatment of Barrett's esophagus with high-grade dysplasia (see Policy Guidelines).

Radiofrequency ablation may be considered **medically necessary** for treatment of Barrett's esophagus with low-grade dysplasia, when the initial diagnosis of low-grade dysplasia is confirmed by two physicians (see Policy Guidelines).

Radiofrequency ablation is considered **investigational** for treatment of Barrett's esophagus in the absence of dysplasia.

Cryoablation is considered **investigational** for Barrett's esophagus, with or without dysplasia.

Policy Guideline

Radiofrequency ablation for Barrett's esophagus with high-grade dysplasia may be used in combination with endoscopic mucosal resection of nodular/visible lesions. The diagnosis of high-grade dysplasia should be confirmed by two pathologists prior to radiofrequency ablation.

There is considerable interobserver variability in the diagnosis of low-grade dysplasia (LGD), and potential for overdiagnosis of LGD by non-expert pathologists. This is due primarily to the difficulty in distinguishing inflammatory changes from low-grade dysplasia. There is literature evidence that expert gastrointestinal (GI) pathologists will downgrade a substantial portion of biopsies that are initially read as low-grade dysplasia by non-experts. (9, 10) As a result, it is ideal that two experts in GI pathology agree on the diagnosis in order to confirm LGD; this may result in greater than 75% of initial diagnoses of low-grade dysplasia being downgraded to non-dysplasia. (9) A review by a single expert GI pathologist will also result in a large number of low-grade dysplasia being downgraded, although probably not as many downgrades as achieved by two expert pathologists. (10)

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced

procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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 2011; 103(13):1049-57.
2. Hvid-Jensen F, Pedersen L, Drewes AM et al. Incidence of adenocarcinoma among patients with Barrett's esophagus. N Engl J Med 2011; 365(15):1375-83.
3. Ell C, May A, Pech O et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett's cancer). Gastrointest Endosc 2007; 65(1):3-10.
4. Pech O, Ell C. Endoscopic therapy of Barrett's esophagus. Curr Opin Gastroenterol 2009; 25(5):405-11.
5. 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 2005; 62(4):488-98.
6. Ganz RA, Overholt BF, Sharma VK et al. Circumferential ablation of Barrett's esophagus that contains high-grade dysplasia: a U.S. Multicenter Registry. Gastrointest Endosc 2008; 68(1):35-40.
7. U.S. Food and Drug Administration. BARRX MODELS HALO360 AND HALO360+ COAGULATION CAT. No. K080557. 510(k) Premarket Notification Database. 2008. Available online at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn_template.cfm?id=k080557. Last accessed March 2013.
8. U.S. Food and Drug Administration. CryoSpray Ablation System. No. K072651. 510(k) Premarket Notification Database 2007. Available online at: http://www.accessdata.fda.gov/cdrh_docs/pdf7/K072651.pdf. Last accessed March 2013.
9. Curvers WL, ten Kate FJ, Krishnadath KK et al. Low-grade dysplasia in Barrett's esophagus: overdiagnosed and underestimated. Am J Gastroenterol 2010; 105(7):1523-30.
10. Kerkhof M, van Dekken H, Steyerberg EW et al. Grading of dysplasia in Barrett's oesophagus: substantial interobserver variation between general and gastrointestinal pathologists. Histopathology 2007; 50(7):920-7.
11. Hernandez JC, Reicher S, Chung D et al. Pilot series of radiofrequency ablation of Barrett's esophagus with or without neoplasia. Endoscopy 2008; 40(5):388-92.
12. Pouw RE, Gondrie JJ, Sondermeijer CM et al. Eradication of Barrett esophagus with early neoplasia by radiofrequency ablation, with or without endoscopic resection. J Gastrointest Surg 2008; 12(10):1627-36; discussion 36-7.
13. Roorda AK, Marcus SN, Triadafilopoulos G. Early experience with radiofrequency energy ablation therapy for Barrett's esophagus with and without dysplasia. Dis Esophagus 2007; 20(6):516-22.
14. Sharma VK, Wang KK, Overholt BF et al. Balloon-based, circumferential, endoscopic radiofrequency ablation of Barrett's esophagus: 1-year follow-up of 100 patients. Gastrointest Endosc 2007; 65(2):185-95.

15. Semlitsch T, Jeitler K, Schoefl R et al. A systematic review of the evidence for radiofrequency ablation for Barrett's esophagus. Surg Endosc 2010; 24(12):2935-43.
16. van Vilsteren FG, Pouw RE, Seewald S et al. Stepwise radical endoscopic resection versus radiofrequency ablation for Barrett's oesophagus with high-grade dysplasia or early cancer: a multicentre randomised trial. Gut 2011; 60(6):765-73.
17. Shaheen NJ, Sharma P, Overholt BF et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med 2009; 360(22):2277-88.
18. Shaheen NJ, Overholt BF, Sampliner RE et al. Durability of radiofrequency ablation in Barrett's esophagus with dysplasia. Gastroenterology 2011; 141(2):460-8.
19. 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 Thorac Surg 2001; 72(1):212-9; discussion 19-20.
20. 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.
21. 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 2008; 103(9):2333-40; quiz 41.
22. Yerian L. Histology of metaplasia and dysplasia in Barrett's esophagus. Surg Oncol Clin N Am 2009; 18(3):411-22.
23. Wang KK, Sampliner RE. Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. Am J Gastroenterol 2008; 103(3):788-97.
24. Fleischer DE, Overholt BF, Sharma VK et al. Endoscopic radiofrequency ablation for Barrett's esophagus: 5-year outcomes from a prospective multicenter trial. Endoscopy 2010; 42(10):781-9.
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 2008; 68(5):867-76.
26. Johnston MH, Eastone JA, Horwhat JD et al. Cryoablation of Barrett's esophagus: a pilot study. Gastrointest Endosc 2005; 62(6):842-8.
27. 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 2009; 70(4):635-44.
28. 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 2010; 23(1):13-9.
29. Shaheen NJ, Greenwald BD, Peery AF et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's esophagus with high-grade dysplasia. Gastrointest Endosc 2010; 71(4):680-5.
30. Spechler SJ, Sharma P, Souza RF et al. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology 2011; 140(3):1084-91.
31. Stefanidis D, Hope WW, Kohn GP et al. Guidelines for surgical treatment of gastroesophageal reflux disease. Surg Endosc 2010; 24(11):2647-69.

32. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Esophageal cancer (v.1.2013). Available online at: http://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf. Last accessed March 2013.