

Protocol

Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus

(20180)

Medical Benefit		Effective Date: 01/01/16	Next Review Date: 09/17
Preauthorization	No	Review Dates: 05/09, 03/10, 03/11, 03/12, 07/12, 03/13, 03/14, 09/14, 09/15, 09/16	

Preauthorization is not required.

The following Protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. 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.

Populations	Interventions	Comparators	Outcomes
Individuals: • With Barrett esophagus with high-grade dysplasia	Interventions of interest are: • Endoscopic radiofrequency ablation	Comparators of interest are: • Esophagectomy • Mucosal resection • Observation • Photodynamic therapy	Relevant outcomes include: • Overall survival • Change in disease status • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With Barrett esophagus with low-grade dysplasia	Interventions of interest are: • Endoscopic radiofrequency ablation	Comparators of interest are: • Observation • Photodynamic therapy	Relevant outcomes include: • Overall survival • Change in disease status • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With Barrett esophagus without dysplasia	Interventions of interest are: • Endoscopic radiofrequency ablation	Comparators of interest are: • Observation	Relevant outcomes include: • Overall survival • Change in disease status • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With Barrett esophagus (with or without dysplasia)	Interventions of interest are: • Endoscopic cryoablation	Comparators of interest are: • Esophagectomy • Mucosal resection • Endoscopic radiofrequency ablation • Observation • Photodynamic therapy	Relevant outcomes include: • Overall survival • Change in disease status • Morbid events • Treatment-related mortality • Treatment-related morbidity

Description

Barrett esophagus (BE) 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 (RFA) or cryoablation.

Summary of Evidence

The evidence for the use of endoscopic RFA for the treatment of patients who have BE with high-grade dysplasia (HGD) includes one 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. Relevant outcomes are overall survival, change in disease status, morbid events, and treatment-related morbidity and mortality. The evidence available indicates that RFA of HGD in BE has been shown to be at least as effective in eradicating HGD as other ablative techniques, with a lower progression rate to cancer, and may be considered as an alternative to esophagectomy. Evidence from at least one RCT demonstrates higher rates of eradication than surveillance alone. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for the use of endoscopic RFA for the treatment of patients who have BE with low-grade dysplasia (LGD) includes at least two 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 confirmed to have LGD, evidence from one RCT suggests 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 treatment decisions for LGD. 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 qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for the use of RFA for the treatment of patients who have BE without dysplasia include 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 suggest 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.

The evidence for the use of cryoablation in patients who have BE (with or without dysplasia) 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 generally demonstrate high rates of eradication of dysplasia. However, the available evidence does not allow comparisons with surgical care or RFA. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy

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 when the above criteria are not met, including but not limited to Barrett's esophagus in the absence of dysplasia.

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

Policy Guidelines

Radiofrequency ablation for BE with HGD may be used in combination with endoscopic mucosal resection of nodular/visible lesions. The diagnosis of HGD should be confirmed by two pathologists prior to radiofrequency ablation (RFA).

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.^{28,27} 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 LGD being downgraded to non-dysplasia.²⁸ A review by a single expert GI pathologist will also result in a large number of LGD being downgraded, although probably not as many downgrades as achieved by two expert pathologists.²⁷

Background

Barrett's Esophagus and the Risk of Esophageal Carcinoma

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

Intestinal metaplasia is a precursor to esophageal adenocarcinoma, which is thought to result from a stepwise accumulation of genetic abnormalities in the specialized epithelium, resulting in the phenotypic expression of histologic features from LGD, to HGD, to carcinoma. Two large epidemiologic studies published in 2011 reported the risk of progression to cancer in patients with BE. One study reported the rate of progression to cancer in more than 8000 patients with a mean duration of follow-up of seven years (range, 1-20 years).¹ The de novo progression to cancer from BE at one 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, 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.

Management of BE

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

EMR, either focal or circumferential, provides a histologic specimen for examination and staging (unlike ablative techniques). One study provided long-term results for EMR in 100 consecutive patients with early Barrett-associated adenocarcinoma (limited to the mucosa).³ The five-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 Eli, 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%.⁴

Ablation 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, and cryoablation) or nonthermal (5-ALA and Photofrin photodynamic therapy [PDT]) techniques. In a randomized phase 3 trial, PDT has been shown to significantly decrease the risk of adenocarcinoma in BE.⁵ (PDT therapy for BE is discussed in a Protocol; refer to the Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus Protocol.)

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

The HALO system from Barrx™ Medical (Sunnyvale, CA; acquired by Covidien in 2012, and now known as the Barrx line of products) 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. 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 three cm. The HALO360 uses a balloon catheter that is sized to fit the individual's esophagus and is inflated to allow for circumferential ablation.

Ablation with RF affects only the most superficial layer of the esophagus (i.e., the mucosa), leaving the underlying tissues unharmed. Measures of efficacy for the procedure are eradication of intestinal metaplasia, without leaving behind microscopic (or "buried") foci, and postablation regrowth of the normal squamous epithelium. 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%.⁶ 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.⁴

Regulatory Status

In 2005, the HALO360 (now Barrx™ 360 RFA Balloon Catheter) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process and, in 2006, the HALO90 (now Barrx™ 90 RFA Focal Catheter) received clearance. FDA-labeled indications are for use in coagulation of bleeding and nonbleeding sites in the gastrointestinal tract, and include the treatment of BE.⁷ FDA product code: GEI.

In December 2007, the CryoSpray Ablation™ System was cleared for marketing by FDA through the 510(k) process for use as a "cryosurgical tool for destruction of unwanted tissue in the field of general surgery, specifically for endoscopic applications."⁸ FDA product code: GEH.

In July 2002, the Polar Wand® device (Chek Med Systems, Willington, CT), a cryosurgical device that uses compressed carbon dioxide, was cleared for marketing by FDA through the 510(k) process. Indications for use are,

“ablation of unwanted tissue in the fields of dermatology, gynecology, general surgery, urology, and gastroenterology.”

Related Protocols

Confocal Laser Endomicroscopy

Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus

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.

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