

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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The Use of Cryotherapy for Treatment of Barrett Esophagus



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G&H What are the most important risk factors for Barrett esophagus?

JD Heartburn and regurgitation are the key risk factors when assessing patients for Barrett esophagus from a symptomatic approach. Other features of the typical patient with Barrett esophagus include being male, having a high waist-to-hip ratio, and, possibly, having a family member with Barrett esophagus.

G&H Do all patients with Barrett esophagus have gastroesophageal reflux disease and vice versa?

JD All patients with Barrett esophagus have gastroesophageal reflux disease (GERD), but not all patients with GERD or even erosive esophagitis have Barrett esophagus. It is unclear why some patients with GERD are predisposed to Barrett esophagus and others are not. Based on limited familial studies, it is likely that this condition occurs on a genetic basis. Barrett esophagus seems to be a natural or adaptive response to acid and bile exposure in some patients.

G&H Does early treatment of GERD prevent the development of Barrett esophagus?

JD I am unaware of any data that show that early treatment of GERD prevents Barrett esophagus. Proton pump inhibitor treatment has been shown to heal LA class C or D erosive esophagitis with Barrett esophagus found in 1 out of 10 patients on follow-up endoscopy. With that in mind,

if clinicians were going to intervene early to prevent Barrett esophagus in patients with GERD, they would have to start treatment before the development of erosions and reflux damage, which we know can occur very early in life because Barrett esophagus has been reported in pediatric populations with GERD. Most experts believe that once Barrett esophagus is well established, regression with medical therapy alone is highly unlikely. There are cases of ultra-short segments of Barrett esophagus regressing over time with biopsy surveillance. This is probably because the biopsies themselves tend to affect the Barrett mucosa with neosquamous epithelium healing in an acid-suppressed environment.

G&H What are the current treatment options for Barrett esophagus?

JD The current treatment options for Barrett esophagus include continued surveillance, endoscopic resection or ablation, and surgery (esophagectomy). Within endoscopic resection, there are 2 treatment options: mucosal resection or endoscopic submucosal dissection for removal of lesions en bloc. Endoscopic resection is frequently performed in conjunction with radiofrequency ablation and cryotherapy with liquid nitrogen or carbon dioxide. For limited surface areas, argon plasma coagulation and bipolar probes are a less expensive alternative, although they may have higher recurrence rates. The choice of treatment for Barrett esophagus is based entirely on the stage of the Barrett pathology and key features of the patient's esophagus. All of these techniques are complementary.

G&H How is cryotherapy performed?

JD In patients with Barrett esophagus, cryotherapy is most commonly performed with liquid nitrogen, which is delivered to the mucosal surface at -176°C to freeze the tissue, fracturing cell membranes and denaturing proteins. The treatment effect is minimal at first, with the development of a cherry red appearance and slight ooze of blood in the tissue compared with the tissue's normal salmon pink appearance. Within days, the tissue sloughs off and potentially heals with neosquamous epithelium in an acid-suppressed state. Patients undergo a follow-up examination in 2 to 3 months, at which time retreatment is performed for any residual areas of Barrett esophagus. Usually, 1 to 5 treatment sessions are needed, depending on the length of the Barrett esophagus and the response to treatment. I know of several patients who have undergone 10 or more treatments over a long period of time for persistent long-segment Barrett esophagus.

As mentioned above, cryotherapy is frequently used in combination with other therapies. Patients with nodular high-grade dysplasia are usually treated with endoscopic resection followed by ablation therapy of the remaining flat areas of Barrett esophagus. Failure to remove the nodular areas with endoscopic resection limits the effectiveness of other ablation modalities that require flat target lesions. Cryotherapy is uniquely suited for ablation of residual areas that remain irregular due to nodular tissue or scarring from prior resections. Cryotherapy also is useful for residual dysplasia and neoplasia after definitive chemoradiotherapy.

G&H How effective is cryotherapy for the treatment of Barrett esophagus?

JD The effectiveness of cryotherapy appears to be approximately 80% for eradication of high-grade dysplasia, 75% for eradication of all dysplasia, and 50% for eradication of all intestinal metaplasia. However, long-term data are lacking, and much of what is currently known comes from multicenter registry studies with both retrospective and prospective data.

G&H Does the grade of dysplasia or the length of Barrett esophagus have an impact on the effectiveness of cryotherapy?

JD Both the length and degree of dysplasia or neoplasia appear to have an influence on the effectiveness of cryotherapy. Other challenging factors include the presence of large hiatal hernias, which result in ongoing acid and bile exposure to the esophageal lumen. These patients often have a dilated esophageal lumen and very poor motility with little clearance of refluxed gastric juice.

G&H Who is the ideal candidate for cryotherapy?

JD The ideal candidate for cryotherapy would be any patient with Barrett esophagus who has confirmed high-grade dysplasia and is motivated to undergo endoscopic ablation. Another way to answer this question is to ask, are there situations in which cryotherapy is more effective than other endoscopic therapies? The answer is yes, in patients with high-grade dysplasia or intramucosal cancer with a nodular surface in an area in which it is difficult to perform endoscopic resection due to scarring from acid reflux or prior therapy. These patients are not candidates for radiofrequency ablation because the depth of penetration is too superficial to penetrate nodular areas. Also, uneven surfaces are difficult to treat with contact-type ablation methods but ideal for cryotherapy spray ablation. Along those lines, I have seen a limited number of patients with early squamous cell cancer in the upper esophagus that has dramatically responded to cryotherapy when other resection or ablation methods would have presented significant challenges.

G&H Are there any other advantages of cryotherapy over other therapies for Barrett esophagus?

JD Besides the advantages discussed above that are inherent with a no-touch spray delivery system, cryotherapy is very comfortable for patients, as it is associated with a low incidence of severe pain or discomfort. A very low stricture rate also appears to be associated with this treatment method. In addition, cryotherapy appears to be safe in patients on antithrombotic therapy and is my treatment of choice in high-risk patients who cannot stop their anticoagulants.

G&H What are the disadvantages of cryotherapy over other therapies for Barrett esophagus?

JD Disadvantages of cryotherapy include the technical challenges associated with delivery of liquid nitrogen compared with focal or balloon-based radiofrequency ablation methods. Gaseous distention must be managed with a decompression tube that is placed in the stomach before the procedure. In addition, visibility can be a challenge because the freezing of the tissue causes the endoscope lens to frost.

G&H Is this treatment method associated with any significant complications or concerns?

JD Complications of cryotherapy are similar to those of other ablation techniques. A new decompression tube

has dramatically reduced the risk of perforation. Discomfort and stricture formation are the most common adverse effects of cryotherapy.

G&H Is cryotherapy associated with a significant learning curve?

JD It probably takes 5 to 10 treatment sessions for a physician to become comfortable performing this technique, provided that he or she has the skill set to perform mucosal resection and other ablation techniques. It is commonly thought that liquid nitrogen cryotherapy is difficult to perform, but with proper training and patient sedation, this technique can be easy.

G&H What are the recommended surveillance intervals for patients treated with cryotherapy?

JD The surveillance intervals associated with this technique are no different from those associated with other forms of endoscopic therapy and are not standardized. Expert consensus suggests that patients should undergo a follow-up examination at least every 6 months during the first year after the treatment goal has been achieved and then yearly thereafter. My colleagues and I usually obtain consent from patients to undergo retreatment (including mucosal resection if indicated) of any residual or recurrent Barrett esophagus in every surveillance examination. If an area of nodular Barrett esophagus mucosa recurs, that site would normally be removed with mucosal resection in a follow-up examination to provide pathologic evaluation and treatment in the same session. If patients have disease that cannot be resected, mucosal biopsies are usually obtained with repeat cryotherapy.

G&H How widespread is the use of this treatment option thus far?

JD Approximately 63 centers in the United States offer cryotherapy. This technology is spreading among therapeutic gastroenterologists and expanding into the pulmonary field with treatments in the airway during bronchoscopy.

G&H How does cryotherapy compare with other treatments for Barrett esophagus in terms of cost-effectiveness?

JD The cost-effectiveness of cryotherapy has not been compared with that of other ablation methods, but I believe it would be similar, particularly because the cost is similar to that of focal radiofrequency devices.

G&H Do you foresee cryotherapy becoming a first-line treatment option in all patients with Barrett esophagus?

JD Yes, I foresee cryotherapy becoming a first-line treatment option for patients with Barrett esophagus as longer follow-up data become available. Cryoablation outside the esophagus is well established in the fields of dermatology and gynecology. In addition, a new generation of the cryotherapy delivery system is now available, making application of the technology easier for physicians.

G&H What ongoing or upcoming studies in this area are you anticipating?

JD The DOSE study is currently underway under the direction of Nicholas Shaheen, MD, of the University of North Carolina to determine the optimal dose for patients with low- and high-grade dysplasia. Results are expected within the next 2 years.

Dr Dumot has received research funding from CSA Medical for ClinicalTrials.gov identifier: NCT01845454.

Suggested Reading

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