Salvage cryotherapy after failed radiofrequency ablation for Barrett's esophagus–related dysplasia is safe and effective

Neil Sengupta, MD,* Gyanprakash A. Ketwaroo, MD, MSc,* Daniel M. Bak, Vikram Kedar, BS, Ram Chuttani, MD, Tyler M. Berzin, MD, Mandeep S. Sawhney, MD, MS, Douglas K. Pleskow, MD

Boston, Massachusetts, USA

Background: Radiofrequency ablation (RFA) is an effective treatment for Barrett's esophagus (BE) dysplasia. For patients with dysplasia refractory to RFA, data are limited regarding efficacy of endoscopic therapy.

Objective: To assess the efficacy and safety of cryotherapy in patients with BE dysplasia who failed RFA.

Design: Single-center, retrospective, cohort study.

Setting: Tertiary-care center between 2006 and 2013.

Patients: Patients with BE and low-grade dysplasia (LGD), high-grade dysplasia (HGD), or intramucosal carcinoma (IMC) were referred for RFA every 2 to 3 months. Response was determined by complete eradication of dysplasia (CE-D).

Interventions: Patients without CE-D or those with recurrent dysplasia after initial eradication were offered cryotherapy.

Main Outcome Measurements: Eradication of dysplasia and/or cancer. Secondary outcome, eradication of intestinal metaplasia.

Results: A total of 121 patients underwent RFA for BE dysplasia (55% HGD, 26% LGD, 17% IMC, 2% indefinite dysplasia). After a median of 3 RFA sessions, 75% (n = 91) had CE-D. Patients without CE-D were more likely to have a longer BE length (7 cm vs 4 cm; $P = .004$) and a hiatal hernia (83% vs 55%; $P = .005$). Sixteen patients (14 with failed CE-D and 2 with recurrent dysplasia) were offered cryotherapy and had endoscopic follow-up. Seven (57%) had HGD before cryotherapy (6 with LGD, 2 with IMC, and 1 with indefinite dysplasia). After cryotherapy, 12 (75%) had CE-D, and 5 (31%) had eradication of intestinal metaplasia. Of patients with IMC, 100% had CE-D. Three patients developed strictures that responded to dilation.

Limitations: Single center, retrospective nature of study.

Conclusion: For patients with refractory dysplasia or recurrent dysplasia after RFA, salvage cryotherapy is a safe and effective endoscopic therapy. (Gastrointest Endosc 2015;82:443-8.)

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

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*Drs Sengupta and Ketwaroo contributed equally to this article.

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Current affiliations: Department of Medicine and Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts.

Reprint requests: Neil Sengupta, MD, Department of Medicine and Division of Gastroenterology, Harvard Medical School, 330 Brookline Avenue, Dana 501, Boston, MA 02215.

If you would like to chat with an author of this article, you may contact Dr Sengupta at nsengup1@bidmc.harvard.edu.

Barrett's esophagus (BE) is a known precursor to esophageal adenocarcinoma, the incidence of which has increased significantly over the last few decades.[1] When dysplasia is identified within BE, the risk of developing esophageal adenocarcinoma increases significantly. Endoscopic ablation therapy has become the preferred treatment for BE-associated high-grade dysplasia (HGD) and early esophageal adenocarcinoma.[2] Radiofrequency ablation (RFA) is highly durable and effective in eradicating dysplasia and intestinal metaplasia in patients with BE-associated dysplasia.[3-6] Low-pressure liquid nitrogen spray cryotherapy can be a safe and effective ablation modality for BE with HGD.[7-9] Cryotherapy can be an effective adjunctive tool to RFA for patients in whom the contact between the distal esophageal mucosa and the catheter is hampered.[10] Data regarding the safety and efficacy of cryotherapy in patients after failed eradication of BE-related dysplasia with RFA are limited.[11] Our aim was to report the results of ablation therapy in our cohort of patients with BE and to demonstrate the safety and efficacy of salvage cryotherapy for BE-related dysplasia refractory to RFA therapy.

METHODS

Patients

This is a retrospective analysis of consecutive patients who underwent RFA for BE-related dysplasia at a tertiary-care, academic medical center. We identified patients with BE-related indefinite dysplasia, low-grade dysplasia (LGD), HGD, or intramucosal carcinoma who underwent RFA between 2006 and 2013. Prior EMR was allowed as long as residual dysplasia was present. Biopsy specimens from all patients were reviewed by an expert GI pathologist before initiation of treatment. Baseline demographics, length of BE mucosa, and presence of a hiatal hernia were recorded. The local institutional review board approved creation of the research database.

RFA therapy

RFA was performed by 3 endoscopists (R.C., M.S.S., D.K.P.), all of whom had at least 5 years of experience with ablation and had received formal, structured training with RFA through Barrx Medical, Inc. (Covidien, Sunnyvale, Calif). All RFA procedures were performed at a single endoscopy site. Advanced endoscopy fellows assisted in RFA under the direct supervision of the attending endoscopist. Treatment protocol at our center was as described by Shaheen et al.[3] In all cases, the esophageal mucosa was washed with a solution of 1% n-acetylcysteine, and subsequently a sizing balloon was used to select the appropriate catheter size. An initial treatment was performed with the circumferential HALO^{360} device (Barrx), with settings of 12 J/cm^2 and 300 W. Follow-up treatments of residual BE were performed with a HALO^{90} device according to the extent of disease and endoscopist preference. Ablation sessions occurred every 2 to 3 months, with intent for complete eradication of BE mucosa. Follow-up endoscopy occurred 3 months after the last therapeutic endoscopy, with biopsies performed per the modified Seattle protocol: 4-quadrant biopsies performed at every 1-cm interval of the original extent of the non-dysplastic BE mucosa and every 1 cm for BE mucosa with dysplasia. Patients received twice-daily doses of proton pump inhibitors as maintenance therapy.

Patients who had progression of dysplasia while on treatment, those who did not have complete eradication of dysplasia after $\geq$3 RFA sessions, or those deemed treatment failures by the treating gastroenterologist were categorized as having failure of eradication of dysplasia. Recurrence of dysplasia was defined as histologic evidence of dysplasia seen during the surveillance period after initial eradication of dysplasia. Patients with failed eradication of dysplasia or those who experienced recurrent dysplasia were offered salvage cryotherapy. Patients with persistent intestinal metaplasia after RFA who were offered cryotherapy were excluded from the analysis. Patients who were agreeable to treatment were treated with liquid nitrogen spray cryotherapy (CryoSpray Ablation System; CSA Medical, Inc, Lexington, Mass) at our center.

Cryotherapy protocol

Cryotherapy was performed by the same endoscopist (D.K.P.), who had at least 3 years of experience with the technology and had received formal, structured training. After routine endoscopy with identification of the BE segment, a dual-lumen decompression tube was introduced over a guidewire into the gastric antrum, followed by proper placement of the dual black bands of the dual-lumen decompression tube at the GE junction. The dual-lumen decompression tube was then connected to suction, the guidewire removed, and the endoscope reintroduced by using an extension cap in a side-to-side manner with the dual-lumen decompression tube. The CryoSpray catheter was inserted into the channel of the endoscope via the introducer and/or biopsy channel and placed proximal to the distal tip of the cap. This was determined by direct visualization of the catheter tip through the endoscope. A one-half circumferential, 2-cm long section of visible BE was treated with cryoablation for 20 seconds for 2 cycles. Low-pressure liquid nitrogen ($<$5 psi) at -196°C, with energy delivery of 25 W was sprayed onto the target tissue. Spray was applied until a deep frost was achieved, and therapy was continued for an additional 20 seconds. This cycle was repeated after the treated section had completely thawed. This process was repeated until all of the visible BE mucosa had been treated. During application of the liquid nitrogen, suction via the dual-lumen decompression tube was activated during the CryoSpray procedure, with a nurse monitoring the abdomen for any signs of gastric distension.