



Liquid nitrogen spray cryotherapy for intramucosal carcinoma and extensive gastric intestinal metaplasia with dysplasia

Spencer Harris, MD, PhD,¹ Matt Fasullo, MD,² George Smallfield, MD, MSPH, MS,² Tilak Shah, MD, MHS²

Background and Aims: Gastric intestinal metaplasia with dysplasia (GIM-D) that is visible as a discrete limited lesion on endoscopy is readily treated using endoscopic mucosal resection or endoscopic submucosal dissection. However, there are few options for more extensive and invisible dysplasia. Ablating a wide swath of tissue with argon plasma coagulation or radiofrequency ablation can be challenging and carries risks, including postprocedure ulceration. Liquid nitrogen spray cryotherapy is an established treatment for dysplasia in Barrett's esophagus, but its use for GIM-D has not been previously reported.

Methods: Three patients with intramucosal adenocarcinoma and GIM-D underwent a total of 10 sessions of spray cryotherapy. In all cases, spray cryotherapy was performed after passing an orogastric decompression tube into the stomach for active suctioning. Ablations were performed in cycles of 20 to 40 seconds, with at least 45 seconds between cycles to allow for tissue thawing. Between 2 and 7 ablations were performed during each procedure. Before each procedure, Sydney protocol biopsy specimens were obtained. No patient reported any postprocedure adverse events.

Results: The first patient underwent 3 sessions of spray cryotherapy; there was no evidence of GIM-D after 1 session, no evidence of gastric intestinal metaplasia after 3 sessions, and no recurrence after 29 months. The second patient underwent 5 sessions of spray cryotherapy; after 1 session there was no adenocarcinoma, and at 14 months there was only GIM-D. The third patient underwent 2 spray cryotherapy sessions, and after 1 session there was gastric intestinal metaplasia but no GIM-D.

Conclusions: Very few treatment modalities exist for extensive GIM-D. We present 3 cases in which off-label spray cryotherapy was used to treat extensive high-grade dysplasia with good treatment effect and patient tolerance. This adds to the body of literature supporting spray cryotherapy as a safe, well-tolerated, and effective treatment for extensive GIM-D. (VideoGIE 2021;6:239-42.)

CASES

Patient 1 was a 73-year-old man with a 15-mm intramucosal adenocarcinoma in the fundus. The patient underwent resection using band ligation EMR (Table 1). Random biopsy specimens from the fundus demonstrated surrounding low-grade gastric intestinal metaplasia with dysplasia (GIM-D). The patient was discussed in a multidisciplinary conference with surgery and pathology. The consensus was that because deep margins were negative, lateral margins were without cancer, and the deepest level of invasion was muscularis mucosa, endoscopic resection was sufficient and surgery, chemotherapy, and radiation therapy were not necessary. Given the presence of GIM-D, careful examination with white-light imaging, narrow-band imaging, and mapping biopsy would be necessary to map areas of dysplasia, and ablation of dysplastic tissue endoscopically

could be considered. The patient subsequently underwent 3 sessions of spray cryotherapy throughout the fundus.

Patient 2 was a 72-year-old man who had prepyloric intramucosal adenocarcinoma, with a positive margin after endoscopic submucosal dissection (ESD). The clinical course was complicated by ulceration at the ESD resection site and extensive surrounding high-grade dysplasia in the antrum. The patient was not discussed at a multidisciplinary conference after discussion with the patient because patient preference was against more invasive surgical intervention. The patient underwent 5 sessions of liquid nitrogen spray cryotherapy to the ulcerated area of prior adenocarcinoma and surrounding antrum (Fig. 1).

Patient 3 was a 71-year-old man with GIM-D of the gastric antrum and incisura. The patient underwent attempted treatment with endoscopic mucosal resection; however, the

TABLE 1. Liquid nitrogen spray cryotherapy patient information

Patient	Demographic characteristics, sex, age (y)	Comorbidities	Location GIM-D	Highest grade of dysplasia/cancer
1	Male, 74	CAD, HLD, PBC, HTN, GERD, psoriasis, colonic adenocarcinoma	Fundus	Intramucosal adenocarcinoma
2	Male, 73	Obesity, diabetes, HTN, HLD, GERD, prior tobacco use	Antrum	Intramucosal adenocarcinoma
3	Male, 72	CAD, BPH, diabetes, HTN, HLD	Antrum	GIM-D

BPH, Benign prostatic hypertrophy; CAD, coronary artery disease; GERD, gastroesophageal reflux disease; GIM-D, gastric intestinal metaplasia with dysplasia; HLD, hyperlipidemia; HTN, hypertension; PBC, primary biliary cholangitis.

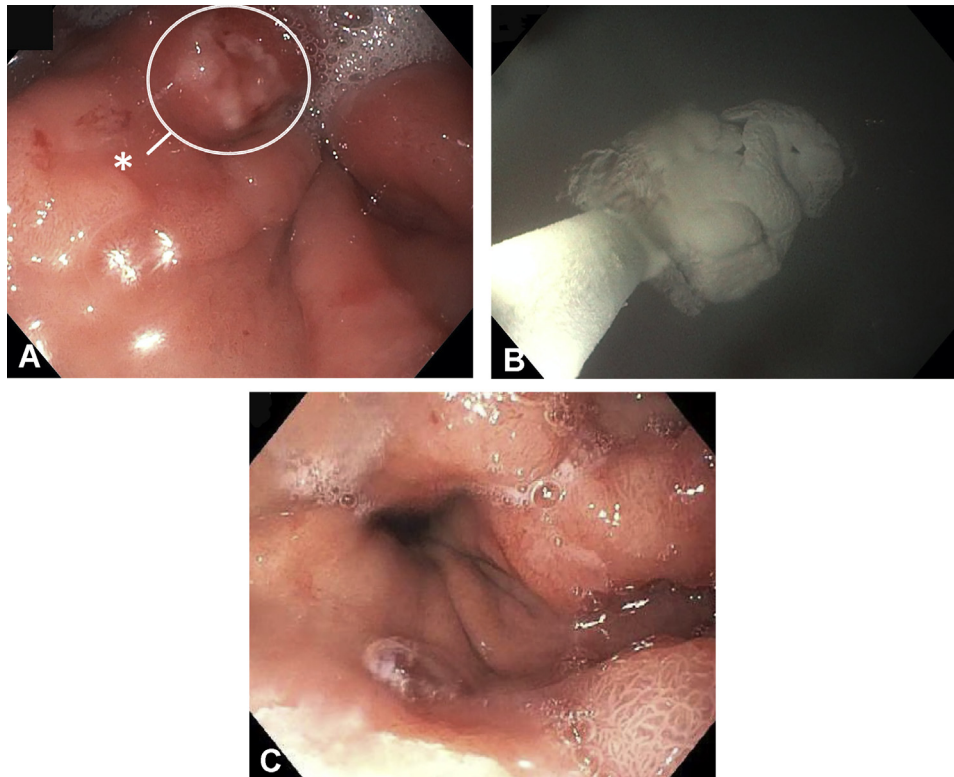


Figure 1. **A**, Gastric intestinal metaplasia with high-grade dysplasia throughout the antrum and ulceration at the prior resection site of intramucosal adenocarcinoma (*asterisk*). **B**, Liquid nitrogen spray cryotherapy, which allows for ablation of a wide swath of the antrum. **C**, Image from postcryotherapy surveillance endoscopy showing improvement on visual inspection and pathology showing no further dysplasia.

patient continued to have nodular-appearing mucosa. Pathology showed persistent GIM-D (Fig. 2). In a discussion with the patient, the preference was to perform surveillance endoscopy with cryoablation and monitoring with regular biopsies instead of gastrectomy. The patient underwent 2 sessions of spray cryotherapy over the course of 3 months.

PROCEDURE

The steps for successful spray cryotherapy are outlined as follows (Fig. 3). First, visual endoscopic surveillance is performed using white-light endoscopy and narrow-band imaging to identify any areas of nodularity or mucosal

irregularity. We then obtain targeted biopsy specimens of any nodular or irregular areas, as well as mapping Sydney protocol biopsy specimens. A Savary guidewire (Cook Medical, Bloomington, Ind, USA) then is advanced into the stomach.

An orogastric tube is then advanced over the guidewire and is confirmed to be in position in the stomach to allow for active suctioning during ablation. This step is important because it prevents excessive distension that could occur with the accumulation of inert nitrogen gas. We then direct the endoscope toward the area to be ablated and subsequently advance the ablation catheter through the working channel of the endoscope. The catheter is aimed toward the area of interest, and spray cryotherapy is initiated.

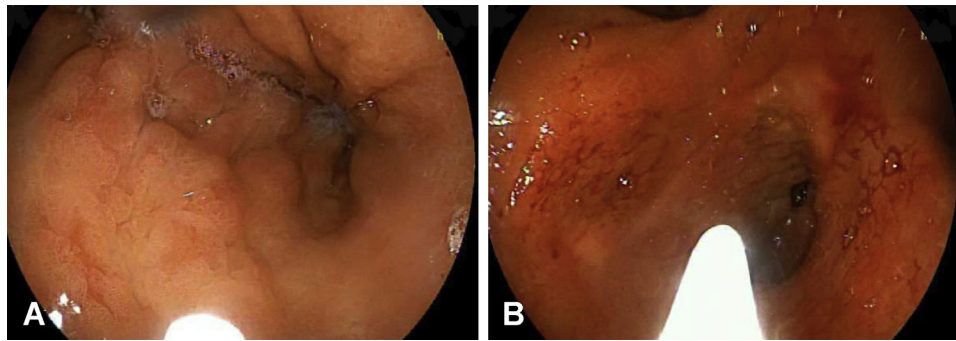


Figure 2. **A**, Endoscopy image from patient with nodularity of mucosa on white-light visual inspection and diffuse gastric intestinal metaplasia with dysplasia throughout the antrum on biopsy. **B**, Post-liquid nitrogen spray cryotherapy treatment with interval improvement in nodularity and resolution of dysplasia on biopsy.

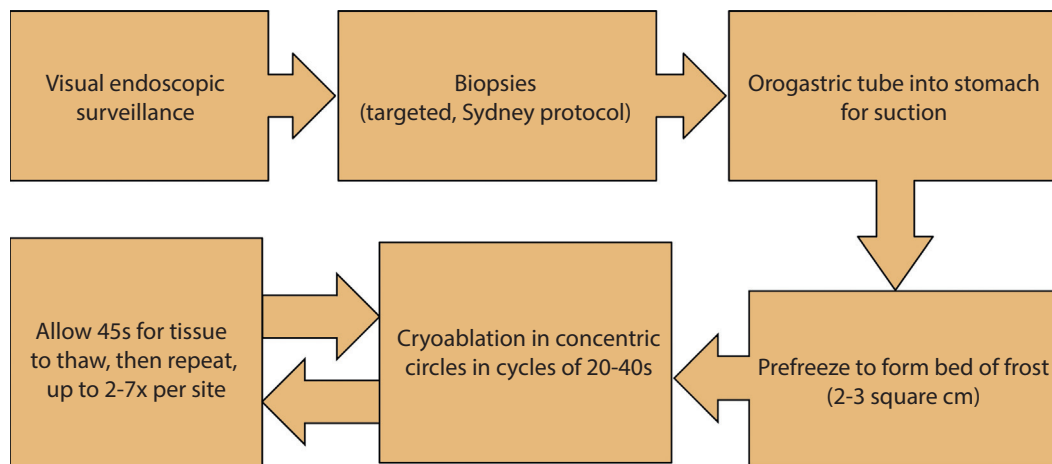


Figure 3. Schematic of protocol for spray cryotherapy treatment for gastric intestinal metaplasia with dysplasia.

TABLE 2. Liquid nitrogen spray cryotherapy treatment results

Patient	Pathology results before cryotherapy	Pathology results after initial treatment	Most recent pathology results	No. of spray cryotherapy sessions	Duration of follow-up, mo	Side effects
1	GIM-D	Intestinal metaplasia	Intestinal metaplasia	3	29	None noted
2	Intramucosal adenocarcinoma	GIM-D	GIM-D	6	24	None noted
3	GIM-D	Intestinal metaplasia	Intestinal metaplasia	2	3	None noted

GIM-D, Gastric intestinal metaplasia with dysplasia.

Our practice is to prefreeze an area of approximately 2 to 3 cm² until a bed of frost forms. We then perform spray cryotherapy of this area for an additional 20 to 40 seconds. We allow 45 seconds between ablation cycles to allow for tissue to thaw; this is important because these freeze-thaw cycles cause intracellular disruption and ischemia, which leads to the ablative effect on dysplastic tissue.

Our practice is to perform between 2 and 7 ablations during each procedure. Spray cryotherapy may be challenging in the proximal stomach. In our experience, we have been able to successfully perform spray cryotherapy

in the cardia by advancing the catheter through the endoscope and then retroflexing and ablating. Between cycles, we may need to completely defrost the endoscope to get back into position for a repeat ablation.

OUTCOME

In patient 1, after 1 session of spray cryotherapy, there was no evidence of GIM-D on Sydney protocol biopsy results. After 3 sessions of spray cryotherapy,

there was no evidence of gastric intestinal metaplasia. The patient continued to be followed, receiving surveillance upper endoscopies with biopsy, which have shown no recurrence after 29 months of follow-up (Table 2).

In patient 2, after 1 session, no adenocarcinoma was noted on surveillance biopsy. At 24 months, there was still nodular-appearing mucosa on visual inspection and GIM-D on biopsy of the antrum, but no adenocarcinoma. The patient continues to undergo quarterly endoscopy and spray cryotherapy treatment.

In patient 3, after 1 session, there was gastric intestinal metaplasia but no GIM-D on surveillance biopsy. The patient continues to undergo twice-yearly surveillance EGD with spray cryotherapy treatment.

CONCLUSIONS

There are very few effective treatment modalities for extensive GIM-D because it is difficult to visualize endoscopically.¹⁻⁵ We present 3 cases in which spray cryotherapy was used to treat extensive high-grade dysplasia with good treatment effect and patient tolerance. Our data support the idea that spray cryotherapy is a safe and effective treatment modality for extensive GIM-D (Video 1, available online at www.VideoGIE.org).

DISCLOSURE

Dr Smallfield received research funding from Steris Medical, Pentax, and Lucid Diagnostics. Dr Shab received research funding from AbbVie and an ASGE Endoscopic Research Grant and is on the research advisory board

for Steris Medical. All other authors disclosed no financial relationship.

Abbreviations: ESD, endoscopic submucosal dissection; GIM-D, gastric intestinal metaplasia with dysplasia.

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Department of Internal Medicine, Virginia Commonwealth University Health System, Richmond, Virginia (1), Department of Internal Medicine, Division of Gastroenterology, Hepatology, and Nutrition, Virginia Commonwealth University Health System, Richmond, Virginia (2).

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