Radiofrequency ablation for Barrett's esophagus and low-grade dysplasia in combination with an antireflux procedure: A new paradigm

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Objective: Radiofrequency ablation for Barrett's esophagus in combination with an antireflux procedure has not been widely documented. We report our initial experience with radiofrequency ablation in association with antireflux procedure for Barrett's metaplasia and low-grade dysplasia.

Methods: A total of 14 patients (10 male and 4 female patients) presented with Barrett's metaplasia (n = 11) or low-grade dysplasia (n = 3). Median age was 60 years (38–80 years). The severity of Barrett's esophagus was classified by length (in centimeters), appearance (circumferential/noncircumferential), and histology (1, normal; 2, Barrett's metaplasia; and 3, low-grade dysplasia). Radiofrequency ablation was performed with the HALO 360° or 90° systems (BARRX Medical, Sunnyvale, Calif).

Results: Median follow-up was 17 months. The mean number of ablative procedures undertaken was 2.6 (range, 1–6). There was no mortality, but there were 2 perioperative complications after the antireflux procedure (pneumonia, 1; atrial fibrillation, 1). One patient had mild dysphagia requiring a single dilation 2 months after ablation. The mean length of Barrett's esophagus decreased from 6.2 to 1.2 cm after treatment ($P = .001$). Barrett's grade decreased significantly ($P = .003$). Before therapy, circumferential Barrett's esophagus was present in 13 patients. At last endoscopy, only 1 patient had circumferential Barrett's esophagus present. The number of radiofrequency ablation treatments was significantly ($P < .05$) associated with success. All patients receiving 3 or more treatments had complete resolution of Barrett's metaplasia.

Conclusions: Radiofrequency ablation performed either before or after an antireflux procedure is safe. This approach is effective for reducing or eliminating metaplasia and dysplasia. Long-term studies will be necessary to determine whether this approach can provide durable control of both reflux and Barrett's esophagus. (J Thorac Cardiovasc Surg 2010;139:713-6)

Longstanding gastroesophageal reflux disease (GERD) has been documented as an important risk factor for esophageal adenocarcinoma.¹ Patients with GERD are at risk of presenting with esophageal mucosal abnormalities ranging from simple Barrett's metaplasia to low- or high-grade dysplasia, with adenocarcinoma culminating the disease spectrum.² The prevalence of Barrett's esophagus in a general adult population is estimated to be around 0.4% to 1.6%.³ In a high-risk population with chronic GERD, the incidence of Barrett's esophagus was estimated to be 5% to 15%.⁴

Barrett's metaplasia has an estimated risk of progression to cancer of 0.5% to 1.0% per patient-year of follow-up. Because of the risk for dysplasia and adenocarcinoma, endoscopic surveillance is recommended when Barrett's esophagus is present. The usual recommendation for surveillance endoscopy is every 3 years for metaplasia and yearly endoscopy for low-grade dysplasia.⁵

Radiofrequency ablation (RFA) of the esophageal mucosa has been gaining increasing popularity for treatment of esophageal dysplasia. RFA appears to be effective and well tolerated with minimal morbidity and, unlike some other mucosal ablation modalities, has been claimed to be associated with no buried glands after squamous re-epithelialization of the esophagus. For this reason, several centers are starting to use RFA for the treatment of nondysplastic Barrett's esophagus.^{6,7} The evidence supporting the routine use of fundoplication for Barrett's metaplasia and dysplasia is inconclusive, although some small series have demonstrated regression after fundoplication, particularly for patients with short-segment disease.^{8,9} In theory combining an antireflux procedure with mucosal ablation of Barrett's changes should provide superior control of Barrett's changes by eliminating or decreasing the high-risk metaplastic or

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Abbreviations and Acronyms

GERD = gastroesophageal reflux disease

RFA = radiofrequency ablation

dysplastic mucosa and decreasing further acid injury to the esophagus. We report our early experience with this combined approach. The primary goals are to demonstrate safety and feasibility and to report short-term outcomes.

MATERIALS AND METHODS

Patients with symptomatic GERD (on medical therapy) and evidence of Barrett's metaplasia or low-grade dysplasia were offered RFA and an anti-reflux procedure. Our current protocol is to initially perform RFA and then re-evaluate at 6 weeks. If further Barrett's esophagus is present, patients are retreated at least 1 more time and then undergo an antireflux operation 6 weeks later. After 3 months, repeat endoscopy is undertaken, as well as further RFA, if necessary. Some patients underwent fundoplication before RFA, and this included patients with symptomatic giant hiatal hernias and patients who had undergone fundoplication at other institutions. RFA was undertaken no sooner than 3 months after fundoplication. We do not offer fundoplication to patients whose symptoms are well controlled with medications. Fundoplication is only offered to symptomatic patients. This report does not include asymptomatic patients treated with RFA alone.

The study was undertaken in 2 institutions, and institutional review board approval was present in both centers. This was a retrospective analysis of data collected from prospective registries in both centers. We recorded and compared the following endoscopic findings before and after therapy: (1) the length of Barrett's esophagus, (2) the appearance of the Barrett's esophagus (circumferential/noncircumferential), and (3) the severity of the histologic findings. To enable comparison of these endoscopic findings, we graded the appearance of the Barrett's esophagus as follows: 1, no Barrett's; 2, single island; 3, noncircumferential or multiple islands; and 4, circumferential. Histologic findings are graded in the registry as follows: 1, normal mucosa; 2, Barrett's metaplasia; 3, low-grade dysplasia; 4, high-grade dysplasia; and 5, cancer. However, in the current report there are no patients with high-grade dysplasia or cancer. Surveillance endoscopy included 4 quadrant biopsies performed every 2 cm along the length of the previously noted Barrett's changes. All data were entered into an SPSS file (version 14.0 for Windows; SPSS, Inc, Chicago, Ill), and analysis included paired *t* test analysis of pretreatment and posttreatment endoscopic findings.

An upper endoscopy was performed to determine the location of the most proximal extent of contiguous Barrett's esophagus and the top of the gastric folds to guide catheter placement. Before ablation, the esophagus was irrigated with acetylcysteine solution 20% (200 mg/mL) mixed in plain water as a mucolytic to provide a direct contact surface between the lesion and the RFA device. After lesion mapping, a metal guide wire was introduced through the endoscope for the subsequent introduction of a sizing balloon and then insertion of a HALO 360 device. For short-segment noncircumferential Barrett's esophagus or for islands of Barrett's esophagus, the HALO 90 device was used. The detailed technique for the RFA has been previously described.¹⁰ All procedures were performed after achievement of general anesthesia.

RESULTS

From May 2006 to August 2008, 14 patients were treated with this protocol. The median age was 62 years (range, 38–80 years). This included 10 male and 4 female patients.

Eleven patients had metaplasia only, and 3 had low-grade dysplasia. The median follow-up was 17 months (range, 3–33 months). The median number of RFA treatments was 2 (range, 1–6).

The mean length of Barrett's esophagus decreased significantly ($P = .001$), from 6.4 cm (range, 1–12 cm) to 1.2 cm (range, 0–5 cm). This corresponded to a median decrease of 93% compared with the original length of Barrett's esophagus.

Before therapy, 13 of 14 patients had circumferential Barrett's esophagus (mean grade, 3.8). After therapy, only 1 patient had circumferential Barrett's esophagus (mean grade, 1.7), representing a significant ($P = .001$) improvement in the endoscopic appearance of the Barrett's esophagus. The one patient with persistent circumferential Barrett's esophagus originally presented with a 10-cm segment of Barrett's esophagus and a giant hiatal hernia. After laparoscopic repair of his hiatal hernia, 2 RFA treatments have been performed, with reduction in the length of Barrett's esophagus to 5 cm.

Histologic severity also improved significantly ($P = .003$), with the mean grade improving from 2.2 to 1.5. Before therapy, 3 patients had low-grade dysplasia, and 11 had metaplasia. After therapy, there were 7 (50.0%) patients with persistent Barrett's metaplasia only and 7 (50.0%) patients with complete resolution of the Barrett's metaplasia. The number of treatments was significantly associated with successful improvement in the length ($P = .017$), appearance ($P = .037$), and histologic severity ($P = .001$). All patients with 3 or more RFA treatments had complete resolution of metaplasia and dysplasia.

Eleven patients underwent laparoscopic fundoplication, and 3 patients underwent endoscopic fundoplication with the NDO plicator ($n = 2$; NDO Surgical, Mansfield, Mass) or the Esophyx system ($n = 1$; EndoGastric Solutions, Redmond, Wash). Mucosal ablation both before and after the antireflux operation was undertaken in 4 patients.

There were no deaths, but there were 2 perioperative complications after an antireflux procedure. One patient had atrial fibrillation, which resolved in the hospital, and the second patient had pneumonia after repair of a giant hiatal hernia. Additionally, one other patient had mild dysphagia requiring dilation 2 months after mucosal ablation and previous fundoplication. The single esophageal dilation resulted in complete resolution of his symptoms.

DISCUSSION

Endoscopic mucosal ablation of the esophagus has been increasingly reported since 1992 with the work of Brandt and Kauvar¹¹ and Berenson and colleagues,¹² who demonstrated esophageal re-epithelialization after therapeutic injury to the metaplastic epithelium.

Currently, mucosal ablation is regarded as an option for selected patients with high-grade dysplasia and even for early adenocarcinoma.¹³ Photodynamic therapy, the most widely reported ablative modality, has been proved to be

effective for dysplasia.¹⁴ However, the complication rate and side effects characterized by strictures and photosensitivity make the use of photodynamic therapy practically prohibitive for simple Barrett's metaplasia, a relatively benign condition compared with high-grade dysplasia.

Several studies have reported on a variety of ablation methods and have demonstrated difficulty in achieving complete eradication of Barrett's metaplasia.¹⁵⁻¹⁷ Although many questions still remain without answers, eradication of Barrett's esophagus has moved from a concept to reality in recent years. In a study with 100 patients, circumferential ablation of nondysplastic Barrett's esophagus with a balloon-based RFA device was performed with no subsequent strictures and with complete elimination of Barrett's esophagus in 70% of patients at 1 year's follow-up, proving this to be a safe and effective method for ablation of Barrett's metaplasia.⁷ A subsequent smaller study of only 11 patients but with longer follow-up (2.5 years) demonstrated complete eradication of Barrett's metaplasia in 98% of patients using the same protocol for RFA. A complete remission of dysplasia and complete endoscopic and histologic removal of Barrett's esophagus was 100% achieved. There were no adverse events or strictures in this series.¹⁸

The role of RFA for dysplastic Barrett's metaplasia is becoming more established. In a recent multi-institutional randomized study,¹⁹ 127 patients were assigned to receive either RFA (ablation group) or a sham procedure (control group). Among patients with low-grade dysplasia, complete eradication occurred in 90.5% of those in the ablation group compared with 22.7% of those in the control group ($P < .001$). Similar results were observed among patients with high-grade dysplasia (81% eradication vs 19% in the control group, $P < .001$). Overall, complete eradication of Barrett's esophagus occurred at a rate of 77.4% compared with 2.3% of those in the control group. A lower incidence of cancer and less disease progression were also positive effects of ablation compared with the sham procedure.

Our preliminary data demonstrates a 50% complete remission rate of Barrett's esophagus, which is lower than that reported in the above studies. This might be explained in part by a lower number of treatments in our series (median, 2) compared with that seen in a recent randomized study in which a mean of 3.5 treatments were used.¹⁹ In our series any patient who received 3 or more ablation therapies achieved 100% control of metaplasia or dysplasia. All patients are still under surveillance, and further treatments will be performed for refractory Barrett's esophagus. Another factor is that we have not excluded any patients based on the length of Barrett's esophagus, whereas previous studies have excluded patients with longer segments of Barrett's esophagus.

Antireflux surgery is usually performed to control reflux symptoms; however, it might also prevent progression and possibly result in regression of dysplastic and metaplastic

changes in the esophagus. This is, however, difficult to prove, and the evidence supporting this is inconclusive. A retrospective study of 49 patients who underwent fundoplication for GERD complicated with Barrett's esophagus demonstrated 18% of patients with mucosal normalization at a median follow-up of 18 months; however, progression to adenocarcinoma in situ was also observed in 1 patient in this series.²⁰

In another study with 97 patients with Barrett's esophagus undergoing fundoplication; 79% of patients were asymptomatic after surgical intervention. Low-grade dysplasia regressed to nondysplastic metaplasia in 44% of (7/16) patients, and metaplasia regressed to normal squamous mucosa in 14% (9/63) of patients. Of note, 6% of patients progressed to low-grade dysplasia, but no patient had high-grade dysplasia or cancer in 410 patient-years of follow-up in this series.²¹

This report describes a new clinical pathway for Barrett's esophagus, offering patients a combination of 2 treatment modalities: RFA of abnormal esophageal mucosa and an antireflux procedure to minimize continuing acid injury to the esophagus. This approach theoretically should allow optimal healing and minimize progression to cancer. Although we have demonstrated that this combined approach can be undertaken safely, the small number of patients and short follow-up cannot address the question of long-term success. Patients will still need continued surveillance until further data are available. The increasing incidence of esophageal adenocarcinoma over the last few decades²² and the relative mortality associated with this indicate the need for a different approach for the prevention of cancer.

Our preliminary results with this new paradigm approach demonstrate its safety and possible effectiveness to treat Barrett's esophagus in patients with symptomatic GERD. Further evaluation with larger controlled trials will be necessary to better define the success and durability of this approach for preventing progression to esophageal cancer.

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