Balloon-based, circumferential, endoscopic radiofrequency ablation of Barrett's esophagus: 1-year follow-up of 100 patients

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Objective: To assess the dose-response, safety, and efficacy of circumferential endoscopic ablation of Barrett's esophagus (BE) by using an endoscopic balloon–based ablation device (HALO^{360} System).

Design: This study was conducted in 2 serial phases (dosimetry phase and effectiveness phase) to evaluate a balloon-based ablation device that delivers a pre-set amount of energy density (J/cm^2) to BE tissue. The dosimetry phase evaluated the dose-response and the safety of delivering 6 to 12 J/cm^2. The effectiveness phase used 10 J/cm^2 (delivered twice [×2]) for all patients, followed by EGD with biopsies at 1, 3, 6, and 12 months. A second ablation procedure was performed if BE was present at 1 or 3 months. Patients received esomeprazole 40 mg twice a day for 1 month after ablation, and 40 mg every day thereafter. Postablation symptoms were quantified by using a 14-day symptom diary (scale, 0-100). A complete response (CR) was defined as all biopsy specimens negative for BE at 12 months.

Setting: Eight U.S. centers, between September 2003 and September 2005.

Patients: Patients were 18 to 75 years of age, with a diagnosis of BE (without dysplasia), with histopathology reconfirmation of the diagnosis within 6 months of enrollment.

Results: In the dosimetry phase, 32 patients (29 men; mean age, 56.8 years) were enrolled. Median symptom scores returned to a score of 0 of 100 by day 3. There were no dose-related serious adverse events, and the outcomes at 1 and 3 months permitted the selection of 10 J/cm^2 (×2) for the subsequent effectiveness phase of the study. In the effectiveness phase, 70 patients (52 men, 18 women; mean age, 55.7 years) were enrolled. Median symptom scores returned to a score of 0 of 100 by day 4. At 12 months (n = 69; mean, 1.5 sessions), a CR for BE was achieved in 70% of patients. There were no strictures and no buried glandular mucosa in either study phase (4306 biopsy fragments evaluated).

Conclusions: Circumferential ablation of nondysplastic BE by using this balloon-based ablation device can be performed with no subsequent strictures or buried glands and with complete elimination of BE in 70% of patients at 1-year follow-up. (Gastrointest Endosc 2007;65:185-95.)

Barrett's esophagus (BE) is defined as a transformation of the normal esophageal squamous epithelium to an abnormal intestinalized columnar epithelium.[1-3] The prevalence of BE in the adult population is 0.4% to 1.3%,[4,5] although recent reports from gastroenterology-selected populations suggest a higher prevalence.[6,7] The frequency of new cases of BE in 1 series rose from 2.9 to 8.9 cases per 1000 endoscopies over the last decade.[8]

Current management of BE includes treatment of GERD symptoms, prevention of erosive injury, and surveillance endoscopy to detect progression to high-grade dysplasia (HGD) and esophageal adenocarcinoma (EAC).[3,9,10] EAC has exhibited a rapid increase in incidence and carries a dismal 5-year survival rate of 14.9%.[11,12]

Nondysplastic BE can progress to HGD and EAC, according to a number of surveillance reports.[13-20] A review by Shaheen et al[13] concluded that the rate of progression

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to EAC is approximately 0.5% per patient per year. Sharma et al[14] confirmed that nondysplastic BE progresses to EAC and HGD at a rate of 0.5% and 0.9% per patient per year, respectively. Others reported rates of progression that bracket those of Sharma et al.[15-20]

Advances have been made in the development of resective and ablative techniques for BE, including multipolar electrocoagulation (MPEC), argon plasma coagulation (APC), laser ablation, cryotherapy, EMR, and photodynamic therapy (PDT).[21-36] A recent randomized trial of PDT versus surveillance for HGD found that PDT had a higher rate of HGD resolution than surveillance (77% vs 39%) and a reduced rate of EAC (13% vs 20%), although BE persisted in 48% of patients after PDT.[21] EMR was more recently used for staging dysplastic BE and for removing nodular disease.[26-28] Challenges that were reported for these techniques include safety, ease of use, persistent BE, subsquamous BE, a need for multiple treatment sessions, and cost.

The aim of this trial was to prospectively evaluate the dose-response, safety, and efficacy of a balloon-based ablation device for the elimination of nondysplastic BE. The device used in the study was designed, via its electrode array and high-power energy algorithm, to provide a uniform ablation effect of predictable depth to achieve safe and effective removal of BE.

Capsule Summary

What is already known on this topic

- Complete ablation of Barrett's esophagus can be achieved endoscopically but it may result in stricture formation and leave behind residual metaplastic mucosa.

What this study adds to our knowledge

- In an open prospective effectiveness study of 70 patients with Barrett's esophagus, circumferential endoscopic ablation using a balloon-based radiofrequency device eliminated the metaplasia completely in 70% and partially in 25% at 12 months.
- There were no strictures or buried metaplasia after ablation.

PATIENTS AND METHODS

Study summary

The Ablation of Intestinal Metaplasia Clinical Trial was conducted in 2 serial phases, a dosimetry phase and an effectiveness phase at 8 U.S. centers between September 2003 and September 2005. The protocol was reviewed and approved by the institutional review board for each institution. All enrolled subjects underwent the informed consent process and agreed to participate. The dosimetry phase (n = 32) included patients with 2 to 3 cm of nondysplastic BE and was designed to assess tolerability and safety outcomes (at 1 and 3 months) as the energy density of treatment was escalated. The effectiveness phase of the study (n = 70) included patients with 2 to 6 cm of nondysplastic BE and primarily assessed histologic outcomes (presence or absence of BE) by using a single energy density dose for all patients.

Study device

The ablation system (HALO^{360} System; BÂRRX Medical, Inc, Sunnyvale, Calif) consists of a high-power radiofrequency (RF) energy generator, sizing balloon catheters (sizes 22, 25, 28, 31, and 34 mm outer diameter [OD]), and ablation catheters (sizes 22, 25, 28, 31, and 34 mm OD). The system received 510(k) clearance by the Food and Drug Administration in 2001. The energy generator (1) provides automated, pressure-regulated, air inflation of the sizing balloon and ablation catheters; and (2) rapidly delivers a pre-set amount of RF energy density (J/cm^2) at 300 W to the ablation catheter electrode.

The sizing balloon catheters are used to measure the inner diameter (ID) of the targeted esophagus. At the distal end of the catheter, there is a noncompliant clear balloon and a guidewire lumen. The ablation catheters are used to deliver the ablative energy. As with the sizing balloon, the ablation catheter has a noncompliant clear balloon and a guidewire lumen. On the surface of the balloon is a 3-cm-long bipolar microelectrode consisting of 60 electrode rings. The electrode rings each completely encircle the balloon and alternate in polarity (plus/minus). Each band is approximately 250 μm wide and is spaced from neighboring bands by approximately 250 μm (Fig. 1).

Patients

Study patients were 18 to 75 years of age, with a diagnosis of BE (without dysplasia), with histopathology reconfirmation of the diagnosis within 6 months of enrollment. Allowable endoscopic BE length (measured from the proximal margin of BE to the top of gastric folds [TGF]) was 2 to 3 cm (dosimetry phase) and 2 to 6 cm (effectiveness phase). Patients were not eligible if they had the following: active esophageal stricture, esophagitis, or varices; prior ablation or resection within the esophagus; a history of esophageal malignancy; any prior radiation therapy to the esophagus; or implantable electrical devices.

Treatment parameters

In the dosimetry phase, patients were enrolled in a dose-escalated manner, with a planned 10 patients each being enrolled sequentially into the 6, 8, 10, and 12 J/cm^2 treatment groups. After ablation, patients were monitored for any ablation-related symptoms by using a 14-day symptom diary. All underwent EGD and biopsy at 1 and 3 months to monitor for acute dose-related adverse events (stricture, ulceration, perforation), with a ''stoppage

plan'' to halt dose-escalation to the next sequential dose if any such serious adverse events were noted.

The 3-month EGD and histology data for this cohort, as well as symptom scores, were considered in the determination of the treatment parameters for the subsequent and separate effectiveness phase of the trial. All patients in the subsequent effectiveness phase were thus treated at 10 J/cm^2, with an immediate second application of energy (identified hereafter as ''10 J/cm^2 ($\times$2)''), based on the emerging work by Dunkin et al.[37]

Ablation procedure

All procedures were performed in the outpatient endoscopy unit by using conscious sedation, which consisted of midazolam plus either fentanyl or meperidine. One center used propofol as a single agent. An upper endoscopy was performed to determine the location of the most proximal extent of contiguous BE and the TGF to guide catheter placement. Before ablation, the esophagus was irrigated with 1% acetic acid mixed in plain water as a mucolytic.

A 22-mm sizing balloon catheter was passed over a guidewire and positioned within the tubular esophagus at the proximal margin of the BE. By using the energy generator inflation function, the balloon was inflated to 4 psi (0.28 atm) under direct endoscopic visualization. Upon full inflation, the endoscopist assessed the contact of the balloon against the esophageal wall. If there was incomplete contact, the sizing balloon catheter was exchanged over the guidewire for the next larger size. This process was repeated until complete circumferential contact was achieved and the balloon would not easily move with rotation or linear traction.

Based on this measurement, an appropriately sized ablation catheter was introduced over the guidewire and visually positioned so that the proximal edge of the electrode was 1 cm proximal to the proximal margin of BE (Fig. 2A). By using the energy generator inflation function, the electrode balloon was inflated and energy was delivered to the tissue in $<$1 second (Fig. 2B). The electrode was moved distally, repositioned visually, and the ablation steps were repeated until the region from 1 cm above the BE proximal margin to the TGFs was treated (Fig. 2C).

Postablation discharge instructions and antisecretory regimen

Subjects were provided with esomeprazole (Nexium; AstraZeneca LP, Wilmington, Del) 40 mg twice a day for 1 month after any ablation procedure, and 40 mg every day at all other times during the 12-month follow-up. Subjects were instructed to (1) use liquid acetaminophen in the event of developing discomfort after the procedure; (2) not use aspirin or nonsteroidal anti-inflammatory drugs for 7 days after the procedure; and (3) call the investigator in the event of significant chest pain, fever, abdominal discomfort, difficulty swallowing, vomiting, or nausea.

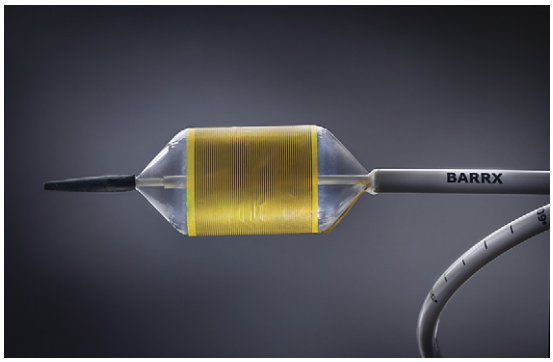

Figure 1. Ablation catheter (sizes 22, 25, 28, 31, 34 mm OD [34 mm shown]) used to deliver ablative energy to targeted portion of the esophagus. Note 60 electrode rings encircling the balloon, 250-micron width each with 250-micron intervening space. Total electrode length, 3 cm.

Postablation symptom monitoring

Before discharge from the recovery unit after any ablation procedure, patients completed a standardized ''exit survey,'' which queried for discomfort ''during'' and ''2 hours after'' the ablation procedure by using a 100-mm visual analog scale (VAS) (0-100). Once per day during the ensuing 14 days, patients entered responses into a standardized symptom diary, which queried for symptoms of chest pain, dysphagia, odynophagia, throat pain, and abdominal pain by using a 100-mm VAS (0-100). The amount of acetaminophen used was recorded daily.

Follow-up endoscopy with biopsy

Patient flow, including follow-up EGD with biopsy schedule, for the dosimetry and effectiveness phases of the trial is summarized in Figures 3 and 4. Biopsy specimens were obtained from 4 quadrants per level beginning just proximal to the TGF and moving proximally in 1- to 2-cm increments to encompass the entire baseline extent of BE. In addition to 4-quadrant biopsies, biopsy specimens were obtained from any area(s) in the esophagus that did not appear to be normal squamous epithelium. The investigator was not limited to the maximum number of biopsy fragments obtained at each EGD with biopsy. All biopsy fragments from 1 level or 1 focal area were submitted in 1 container and were labeled with the subject's confidential study identifier and the location of the biopsy.

Central pathology processing and interpretation

All tissue specimens were sent in a standardized kit to the core laboratory for the study, Gastrointestinal Pathology, LLC, Memphis, Tennessee. The formalin-fixed biopsy fragments from each container were embedded in paraffin, affixed to a glass slide, and stained with H&E. One

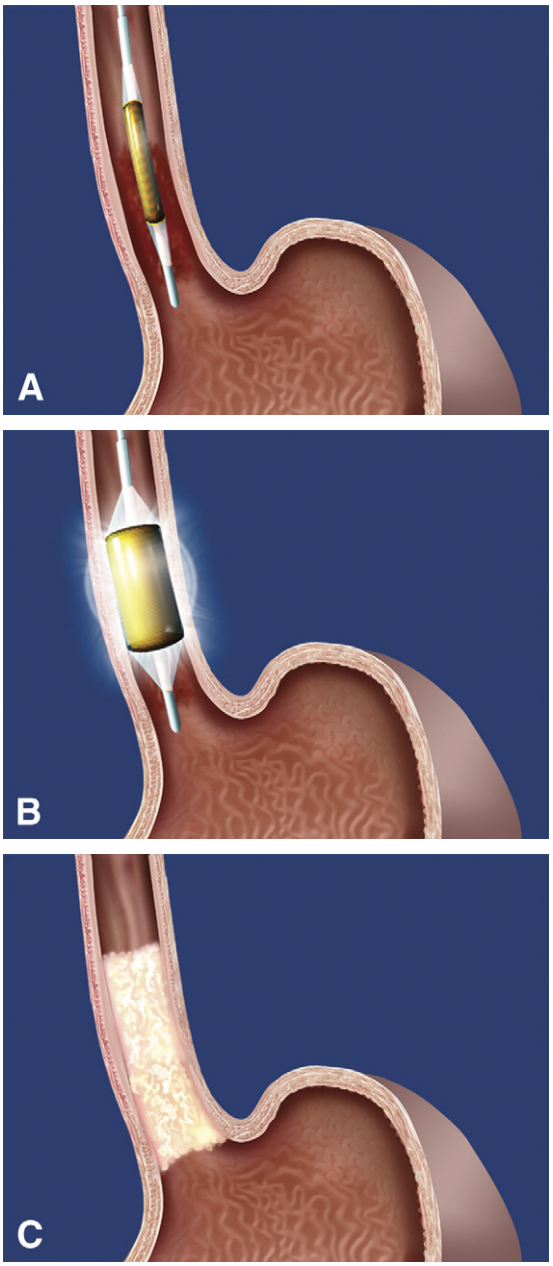

Figure 2. Procedure steps. **A,** Ablation catheter was introduced over the guidewire and positioned by using endoscopic visualization. **B,** Ablation catheter was inflated and energy was delivered to the tissue. **C,** After a second, more distal ablation, entire segment of BE was treated.

slide represented each level or focal biopsy. All slides were interpreted in a blinded manner by a board-certified pathologist specializing in GI pathology. Each fragment on each slide was evaluated for the presence or the absence of specialized columnar epithelium (ie, goblet cells of columnar epithelium). A tally of total fragments, fragments with BE, and fragments without BE was generated. These data were entered onto a standardized pathology case report form. A diagnosis of ''buried glandular mucosa'' was made for any fragment that met the a priori definition for the study of ''any specialized columnar epithelium covered by a layer of squamous epithelium with no communication with the surface.''

Patient safety and tolerability outcomes

Patient safety and tolerability were measured by using the described 14-day symptom diary. Daily scores were tallied for each patient. In addition, each study site coordinator and investigator was responsible for reporting all adverse events and serious adverse events to the study sponsor within 48 hours with a standardized adverse event form. The type, severity, frequency, and relation to the use of the study device of all adverse events were tracked during the study.

Effectiveness outcomes

The primary effectiveness outcome is based on histology obtained at follow-up EGD with biopsy. A complete response (CR) for a patient is defined as all biopsy fragments (100%) negative for BE for that patient for a specific endoscopy follow-up (excluding biopsy specimens obtained from the stomach or the gastric cardia). A partial response (PR) and a nonresponse (NR) are defined as 50% to 99% and 0% to less than 50%, respectively, of biopsy fragments negative for BE. A CR, PR, and NR percentage is reported for a patient group as the percentage of patients demonstrating each result.

Per-protocol and intention-to-treat analyses were applied to the 12-month histology outcomes for both the dosimetry and the effectiveness phases of the trial. In the ITT analysis, patients not available for follow-up at 12 months were considered treatment failures (NR, with all biopsy specimens positive for BE.)

Second ablation procedure opportunity

Patients in the dosimetry phase of the trial with any intestinal metaplasia (IM) on biopsy at 1 or 3 months underwent a second ablation procedure by using 10 J/cm^2 ($\times$2) and then continued follow-up to 12 months (Fig. 3). Patients in the effectiveness phase of the trial with any IM on biopsy at 1 or 3 months underwent a second ablation procedure at 4 months and then continued follow-up to 12 months (Fig. 4).

RESULTS

Dosimetry phase

Thirty-two patients were enrolled at 5 centers, with demographic information provided in Table 1. Ablation procedure details are summarized in Table 2. Exit survey symptom scores showed minimal acute symptoms (Table 2). Fourteen-day symptom diary scores (medians) were transiently and mildly elevated for some of the queried symptoms (chest pain and dysphagia), returning to 0 of 100 by day 4 (Fig. 5). Acetaminophen was used by 14 patients (44%) on day 1, declining to 2 patients (6%)

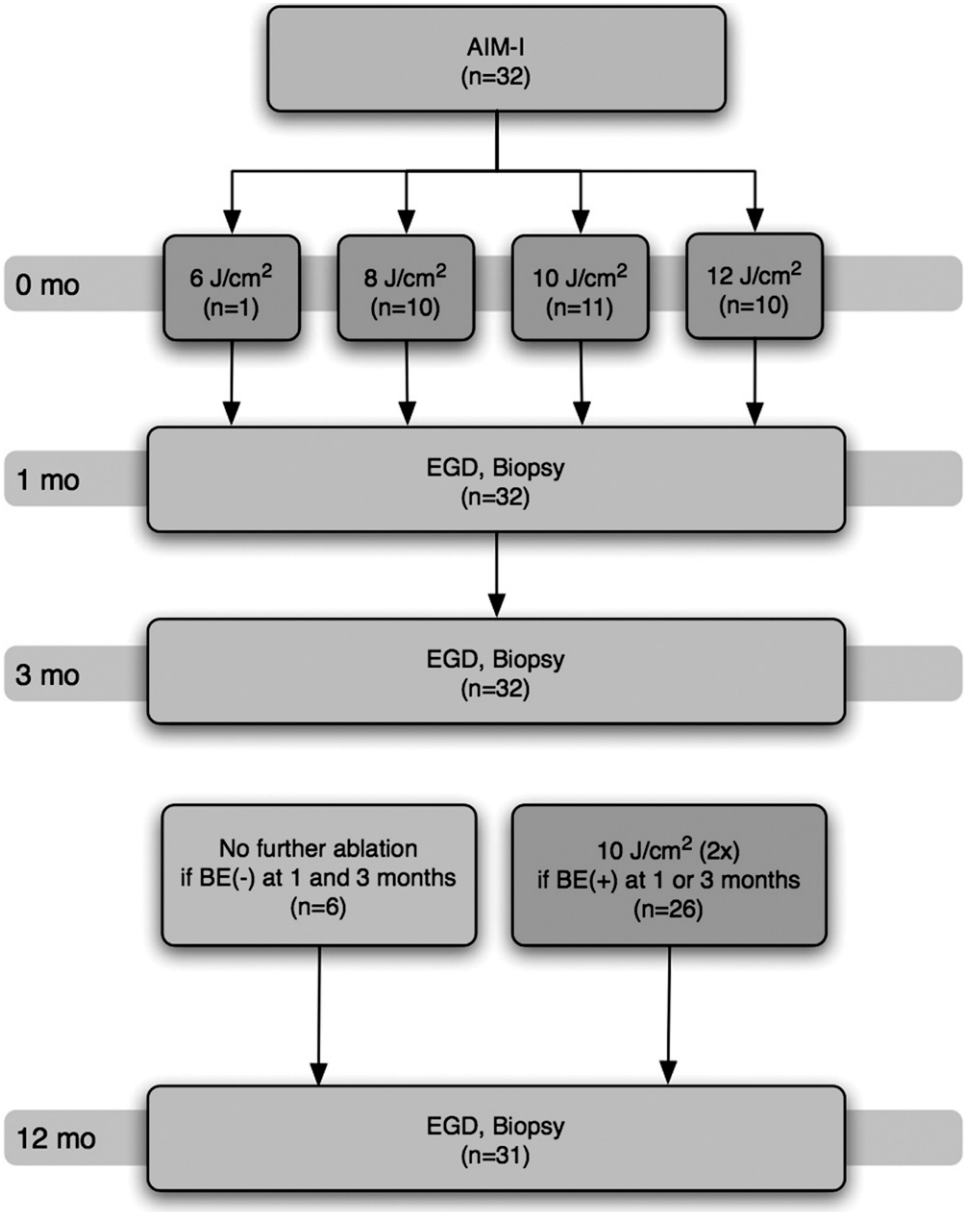

Figure 3. Patient flow, dosimetry trial phase. Patients were enrolled and underwent circumferential ablation of nondysplastic BE in a dose-escalated manner with 6, 8, 10, 12 J/cm^2 (×1). EGD and biopsy was performed at 1 and 3 months. Patients with persistent BE at 1 or 3 months had a second treatment session with 10 J/cm^2 (×2). EGD and biopsy were performed for all patients at 12 months.

by day 7. After the first ablation procedure, exit survey, and symptom diary scores were similar between energy density groups.

The first patient enrolled in the dosimetry phase was treated by using 6 J/cm^2, with no acutely visible treatment effect; therefore, the investigators terminated additional enrollment at the 6 J/cm^2 setting and commenced enrollment of the 8 J/cm^2 group. Thereafter, a visible effect was observed for 8 J/cm^2 and all subsequent doses.

There were 5 adverse events reported in 5 patients; all were transient and all resolved completely. These included a focal area of mucosal scarring noted at a 1-month EGD and resolved by a 3-month EGD (1), chest pain (3), and superficial linear mucosal injury (1). No acute dose-related adverse events occurred that met the study stoppage criteria; therefore, enrollment was completed for each of the groups (8, 10, and 12 J/cm^2).

At 1 and 3 months, histologic data were available for all 32 patients (100%). Histologic response rates (percentage of patients with CR) for the 10 and 12 J/cm^2 groups were similar in magnitude and superior to those of the 6 and 8 J/cm^2 groups (Table 3). These data were used, in part, to set the treatment parameters at 10 J/cm^2 (×2) for the effectiveness phase of the trial (see Patients and Methods section).

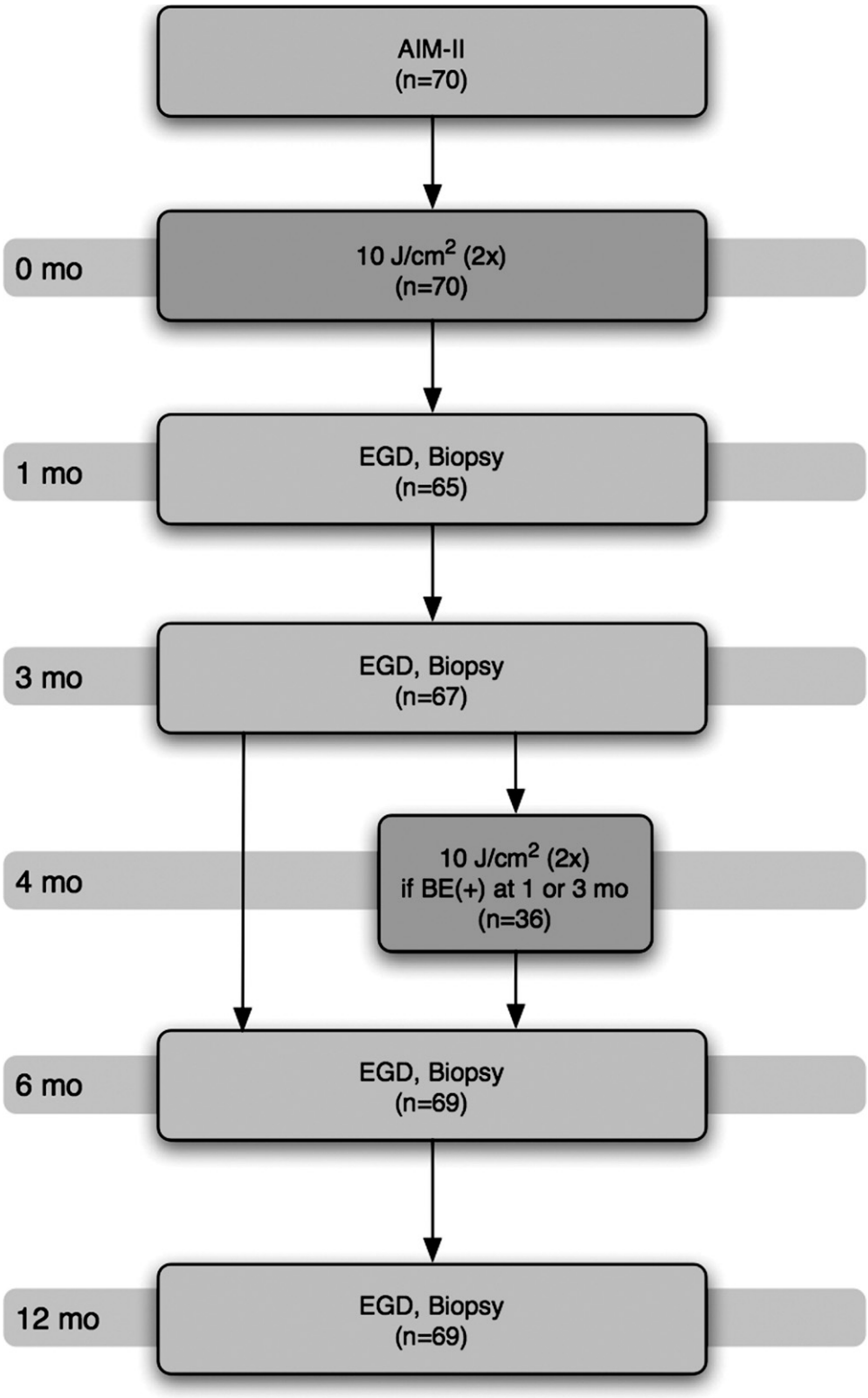

Figure 4. Patient flow, effectiveness trial phase. Patients were enrolled and underwent circumferential ablation of nondysplastic BE with 10 J/cm^2 (×2). EGD and biopsy were performed at 1, 3, 6, and 12 months. If positive for BE at 1 or 3 months, patients underwent a second ablation at 4 months.

Ablation procedure details for those patients (n = 26) who underwent a second procedure 10 J/cm^2 (×2) in the dosimetry phase are summarized in Table 2. Specific to this second procedure, there were 7 adverse events reported in 6 patients, all were transient, and all resolved completely. These included fever (3), focal area of mucosal scarring resolved by 12-month EGD (1), abdominal pain/constipation (1), sedation-related nausea (1), and sedation-related hypotension (1). One of the 3 fever events occurred 42 days after treatment and was deemed unrelated to the procedure.

At 12 months, 31 of 32 patients (97%) were available for follow-up. One patient elected not to undergo endoscopic follow-up and reported no adverse effects. A CR for BE was achieved in 19 patients (61%) (Table 4). Residual BE, when present, was in the form of small islands or short tongues. There were no strictures, and there were no buried glands in 1299 biopsy specimens.

Effectiveness phase

Seventy patients were enrolled at 8 centers, with demographic information provided in Table 1. Ablation-procedure details are summarized in Table 2. Exit survey symptom scores showed minimal symptoms (Table 2). Treatment diary symptom scores (medians) were transiently elevated for some of the queried symptoms, returning to 0 of 100 by day 3 or 4. Acetaminophen was used by 36 patients (55%) on day 1, declining to 6 patients (9%) by day 7. There was no difference between first and second ablations for the exit survey or symptom diary scores. There were 24 adverse events reported in 16 patients (encompassing 106 total treatment sessions). All were transient, and all resolved completely. These included fever (2); chest/throat pain (9); superficial linear mucosal injury (1); mild bleeding during ablation, stopped spontaneously (1); mucosal scarring at 1-month EGD, resolved by 3-month EGD (1); sedation-related transient airway obstruction (1); sedation-related hypotension (1); and transient nausea (8).

At 12 months, 69 of 70 patients (99%) were available for follow-up. All patients (n = 70) had at least 1 treatment session, whereas 36 patients had a second treatment (mean, 1.5 sessions per patient). One patient chose not to participate in the study beyond 3 months and reported no adverse effects. A CR for BE was achieved in 48 patients (70%) (Table 4). There were no strictures and no buried glands in 3007 biopsy fragments. Endoscopic images at baseline, immediately post-ablation, and at 12-months follow-up for one patient enrolled in the effectiveness phase of the study are shown in Figure 6.

TABLE 1. Patient demographics

	Dosimetry phase	Effectiveness phase
No. patients	32	70
Sex (M/F)	29/3	52/18
Age, mean, SD, y	56.8 ± 11.2	55.7 ± 11.2
Age range, y	35-75	26-79
Body weight, mean, SD, kg	91.5 ± 15.9	80.6 ± 16.6
Ethnicity, no. (%)		
White race	32 (100)	47 (67)
African descent		2 (3)
Hispanic/Latino		21 (30)
History of GERD	32 (100)	70 (100)
BE length, mean, SD, cm	2.3 ± 0.7	3.2 ± 1.4
BE length, range, cm	1-4	2-6
Hiatal hernia, Y/N	28/4	60/10
Hiatal hernia length, when present, mean, SD, cm	3.4 ± 2.3	2.6 ± 1.2
Baseline PPI use, Y/N	32/0	70/0

SD, Standard deviation.

DISCUSSION

This trial was conducted in 2 serial phases at 8 U.S. institutions to prospectively evaluate tolerability, dose-response, and effectiveness associated with a balloon-based circumferential ablation system for nondysplastic BE. The 2 trial phases are presented together to provide the reader with insight into the stepwise process of (1) the initial assessment of dosimetry, (2) the selection of dose and technique for the effectiveness phase, (3) the analysis of effectiveness phase outcomes, and (4) the improvement of techniques and devices for future trials.

Before this trial, Ganz et al,[38] reported complete ablation of porcine esophageal epithelium, without submucosal injury or stricture when using 8 to 12 J/cm^2. Ganz et al[38] also created circumferential ablations in human esophagus (10-12 J/cm^2) before esophagectomy, again with no submucosal injury. Dunkin et al[37] reported complete ablation of human esophageal epithelium, without submucosal injury when using 10 J/cm^2 (×2) and 12 J/cm^2 (×1 or ×2). Based on these data, the dosimetry phase of this trial evaluated 6, 8, 10, and 12 J/cm^2 in a serial manner (n = 32). Because there was no visible treatment effect in the first patient treated at 6 J/cm^2, this dose group was discontinued and enrollment commenced at the next higher dose (8 J/cm^2).

Histology results after 1 treatment session with 8, 10, or 12 J/cm^2 revealed that 8 J/cm^2 had minimal effect (CR, 0%), whereas 10 and 12 J/cm^2 demonstrated an approximately equal effect (CR, 30% and 36%, respectively). Adverse events were mild and transient, and were not dose concentrated. There were no strictures or buried

TABLE 2. Ablation procedure details

	Dosimetry phase*		Effectiveness phase*	
	First ablation	Second ablation	First ablation	Second ablation
No.	32	26	70	36
Procedure time, min	24 (20-35)	30 (23-35)	28 (24-33)	27 (23-37)
Midazolam, mg†	8 (6-10)	8 (6-10)	8 (7-10)	8 (5-9)
Fentanyl, μg†	175 (150-200)	150 (100-150)	200 (162.5-200)	200 (125-250)
Meperidine, mg†	100 (87-112)	100 (100-125)	100 (75-125)	100 (75-150)
Propofol, mg†	440 (385-610)	500 (445-625)	650 (525-830)	732 (606-885)
Exit survey results‡				
Discomfort during procedure	3 (1-6)	0 (0-1)	3 (0-7)	1 (0-4)
Discomfort 2 h after procedure	3 (1-9)	3 (1-8)	15 (4-23)	2 (0-11)

*Values presented are medians (interquartile range).
†For conscious sedation, all but 1 site used midazolam plus either fentanyl or meperidine. One site used propofol as single agent for conscious sedation.
‡Exit survey questions were scored with VAS (0-100).

glandular mucosa. Therefore, 10 J/cm^2 was used for the subsequent effectiveness phase of the trial, with a second immediate application of energy (×2) based on the emerging work from Dunkin et al.[37]

In the effectiveness phase, 70 patients were treated at 10 J/cm^2 (×2). At 12 months, 70% of patients demonstrated a CR for BE, whereas 25% had achieved a PR. There were no strictures or evidence of buried glandular mucosa. Posttreatment symptoms were assessed by a standardized exit survey and the 14-day diary. Exit survey results (Table 2) showed minimal discomfort during and 2 hours after the procedure, although a limitation is the possible influence of conscious sedation on patient responses. The diary results indicate that posttreatment symptoms were typically mild and transient. A limitation is that the diary was designed for this trial and thus was not previously validated. Nonetheless, we believe that collecting daily symptom data after treatment by using a standardized methodology is valuable. This allows reporting of symptom data in a standardized, quantifiable manner.

The present trial permitted a maximum of 2 treatment sessions, unlike some previous ablation trials, which allowed a more liberal number of sessions. This may account for why the median number of treatments was only 1.5 for the effectiveness phase of this trial.

Conventional wisdom would suggest that a circumferential injury to the lining of the esophagus results in a high rate of stricture formation. Although this may be the case for PDT and EMR, there were no strictures observed in this trial. This may be a result of controlling the depth of the ablation effect. Depth control is partly related to a tightly spaced bipolar array, which limits the depth of the electrical field generated during ablation. Energy density and power are controlled by the system, eliminating operator variability. The high power of treatment (300 W) permits rapid heating, thus preventing long ''on'' times and deep thermal conduction. As a result, controlling depth protects the submucosa and likely preserves the ability of the esophagus to reestablish a normal squamous epithelium and avoid stricture formation.[37,38]

Subsquamous glandular mucosa (also called ''buried glands'') has been reported as a common consequence of ablative therapy when using other thermal modalities. In this trial, ''buried glandular mucosa'' was defined a priori as ''specialized columnar epithelium covered by a layer of squamous epithelium with no communication with the surface.'' Dulai et al[33] recently used a similar definition that compared APC and MPEC for BE ablation. In the present trial, there were a total of 4306 esophageal mucosal biopsy fragments obtained from patients during the 12 months after ablation. All fragments were assessed in a blinded manner by the central pathology service. No fragment met the definition of buried glandular mucosa. By using a slightly different, perhaps more inclusive, definition deemed ''squamous overgrowth,'' Bronner et al[39] reported that glandular mucosa was found in patients who were ablated and nonablated alike. Patients, after PDT, had squamous overgrowth in 1.2% of biopsy fragments, an occurrence rate that was actually less than that from the proton pump inhibitor–only surveillance control arm of the study (2.2% per biopsy fragment).[39] Buried glandular mucosa will remain a topic of debate related to BE ablation until the final goal of ablative therapy is achieved. We believe this final goal to be the safe, assured, and complete eradication of all Barrett's mucosa in any treated patient. If there is no Barrett's mucosa remaining after ablation, to state the obvious, there can be no buried Barrett's mucosa.

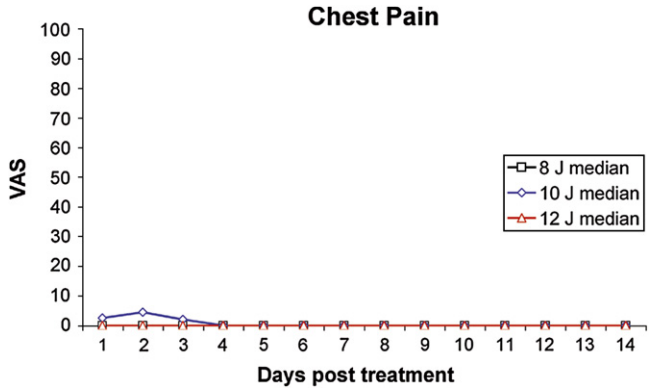

Figure 5. Symptom diary results (14 day) for dosimetry trial phase after primary treatment; responses for chest pain. Scores represent median values for each postablation day and for each energy density group (8, 10, 12 J/cm^2). Symptom scores for dysphagia, odynophagia, throat pain, and abdominal pain were minimal and are not shown for brevity.

TABLE 3. Three-month histology results: dosimetry phase

	Dosimetry phase			
Energy density, J/cm^2	6	8	10	12
No. patients enrolled	1	10	10	11
No. patients with data at 3 mo	1	10	10	11
CR, no. (%)	0 (0)	0 (0)	3 (30)	4 (36)
PR, no. (%)	1 (100)	8 (80)	5 (50)	5 (45)
NR, no. (%)	0 (0)	2 (20)	2 (20)	2 (18)

TABLE 4. Twelve-month histology results

	Dosimetry phase		Effectiveness phase	
No. patients enrolled	32		70	
No. patients with data at 12 mo	31		69	
Analysis, no. (%)	PP	ITT	PP	ITT
CR	19 (61)	19 (59)	48 (70)	48 (69)
PR	8 (26)	8 (25)	17 (25)	17 (24)
NR	4 (13)	5 (16)	4 (6)	5 (7)

ITT, Intention to treat analysis; *PP,* per protocol analysis.

We experienced some technical challenges in this trial, each a probable contributor to the persistence of BE at 1 year in 30% of patients in the effectiveness phase. The most important challenges and their resolution for subsequent studies are described hereafter.

Selecting an ablation balloon size (OD) that precisely fit the targeted esophagus was challenging. If the ablation balloon was too small, areas of BE could be left untreated. If too large, the stretch on the esophageal wall could result in balloon migration and a failure to treat some areas of BE. The resolution for future trials is an automated sizing technology in which a 34-mm OD balloon is inflated by using a pressure-volume algorithm that precisely measures the ID of the esophagus, allowing selection of a more optimally sized ablation balloon.

Acetic acid (1%) was used to remove mucous and to allow better tissue contact of the electrode. In subsequent studies, 1% N-acetylcysteine was used instead, because BE mucosa swells after exposure to acetic acid and a thicker mucosa could compromise effectiveness.

We did not clean the electrode or the ablation zone after the first pass (×1) in the effectiveness phase. Coagulum, mucous, and sloughed epithelium on the electrode and ablation zone significantly impede delivery of energy. We believe this to be a primary cause for persistent focal BE in some patients. In subsequent trials, the electrode and ablation zone are cleaned after the first pass. Early results show that this results in higher rates of complete eradication of BE.

Another challenge was related to the fit of a cylindrical ablation device at the flared portion of the gastroesophageal junction (GEJ), which may have caused focal areas of BE to be untreated. Applying gentle traction on the balloon while in the GEJ achieved a more uniform ablation.

Residual BE was present in 36 of 70 patients after 1 treatment, most commonly as islands or tongues. The protocol allowed for a second treatment with the balloon electrode, which required ablation of much of the normal neosquamous epithelium as well. Some persistent BE was in the GEJ and, thus, was more difficult to target. To enable focal treatment of residual BE, a focal ablation device (endoscope mounted) was designed and implemented in subsequent clinical trials.

The effectiveness phase of the present study was extended to a 2.5-year follow-up. This trial incorporated an opportunity for persistent BE to be treated with a focal ablation device, as described above, with the goal of achieving a CR in 100% of patients by the 2.5-year follow-up.

Within the spectrum of BE disease, the rationale for ablating HGD is perhaps the most obvious. The rate of progression from HGD to EAC is high, to the point where HGD is often an indication for esophagectomy.[1,10] The rationale for ablating nondysplastic BE or low-grade dysplasia (LGD) may be less overtly obvious but no less worthy of study. These latter entities are often mislabeled as benign, although their rates of progression to HGD and EAC are well documented.[13-20] Shaheen et al[13] concluded the rate of progression from nondysplastic BE to EAC was 0.5% per patient per year. Sharma et al[14] confirmed that

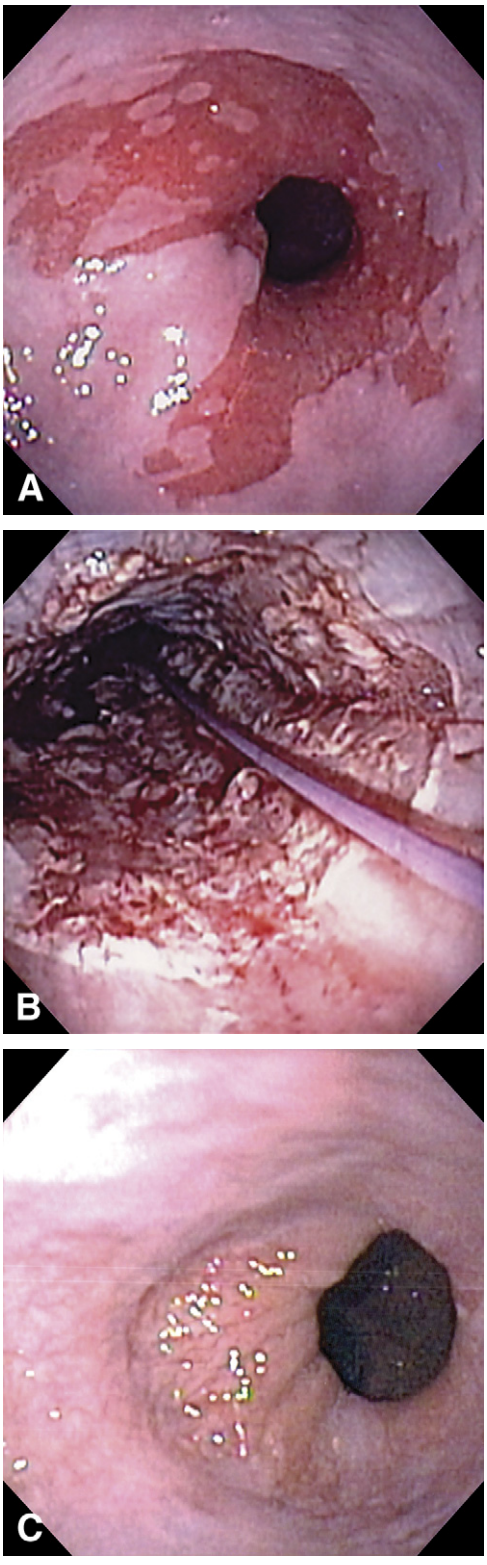

Figure 6. A, Patient in effectiveness trial phase, baseline 4 cm of nondysplastic BE. **B,** Acute endoscopic appearance of ablation zone after treatment 10 J/cm^2 (×2). **C,** 12-month endoscopic follow-up, showing complete endoscopic resolution of BE. Biopsy specimens confirmed no histologic evidence of BE at 12 months, indicating patient was CR for study primary effectiveness end point.

nondysplastic BE progresses to EAC and HGD at a rate of 0.5% and 0.9% per patient per year, respectively. This represents a 1.4% per patient per year development of a condition that is an indication for esophagectomy at many U.S. centers.

When assuming achievement of 100% eradication of BE in a treated patient, without significant adverse events, such an intervention could have multiple potential benefits, including a lengthening of the surveillance interval by down-staging or eliminating BE, a reduction in the rate of progression to higher grades of dysplasia or carcinoma, a lessening of patient anxiety associated with this disease state, reestablishment of availability and/or affordability of life insurance and health insurance, and a reduction in health care costs associated with life-long surveillance and disease progression. We believe it is important to continue to evaluate ablative modalities for the entire spectrum of BE disease, not just HGD. The present study represents an excellent first step, and several well-designed studies are currently underway that will address each of these potential benefits for nondysplastic BE, LGD, and HGD.

CONCLUSIONS

This trial demonstrated that complete elimination of nondysplastic BE can be safely achieved in 70% of patients when using a first-generation balloon-based ablation device, with the possibility of higher efficacy rates in light of new procedural and device developments being evaluated in ongoing trials.

DISCLOSURE

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Editor's commentary:

Following the tradition of ''pro'' and ''con'' editorials in the pages of *GIE*, I asked 2 authorities in the area of Barrett's esophagus to comment on the article in this issue by Sharma et al, describing efficacy and safety of radiofrequency ablation for Barrett's esophagus. Against their own biases, I asked Dr Weston to take the ''con'' position, trying to oppose the new technology, while I asked Dr. Bergman to present to our readers the ''pro'' perspective, defending it. What interested readers will quickly appreciate is the power of dialogue, brought forward—intentionally—to debate a challenging and highly controversial issue: how to best manage Barrett's esophagus in 2007. Reading through these invited opinion pieces, defense and offense become blurred amidst enthusiasm and optimism, caution and reserve, and ''pro/con'' become ''pro?/con?'' Lots of food for thought, so enjoy....

George Triadafilopoulos, MD
Editor-in-Chief, GIE

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EDITORIAL: Con?

Automated circumferential Barrett's ablation by using radiofrequency energy: a welcome step in the right direction

Numerous thermal (multipolar electrocoagulation [MPEC], argon plasma coagulation [APC], heater probe, Nd:YAG laser, KTP-YAG laser, diode laser, argon laser, cyroablation) and nonthermal (5-aminolevulinic acid [5-ALA] and photoprin photodynamic therapy [PDT]) techniques have been studied in conjunction with either medical or surgical gastroesophageal reflux control to eliminate Barrett's mucosa (nondysplastic, dysplastic, and frankly cancerous) for over 15 years. Paramount to any endoscopic Barrett's ablative technique is patient safety as well as efficacy. Additional features include simplicity of application and cost.

In this issue of *GIE*, Sharma et al[1] report on the results of a newly developed and still evolving ablative method, the HALO^{360} system from BÂRRX Medical, Inc (Sunnyvale, Calif). This ablation system utilizes a radiofrequency generator in conjunction with a balloon ablation catheter that is correctly sized for the tubular esophagus harboring the Barrett's metaplasia. The radiofrequency generator provides rapid (under 1 second) delivery of a predetermined amount of radiofrequency energy (in J/cm^2) to a 3-cm long bipolar microelectrode ablation catheter containing 60 encircling electrode rings spaced 250 μm apart. The generator is also responsible for the automated, pressure-regulated inflation of both a ''sizing balloon'' as well as the actual bipolar ablation balloon catheter. Because the HALO^{360} radiofrequency ablation device is an automated system, the nuisances of operator variability and inconsistencies are eliminated. The automation of this Barrett's ablative therapy should lead to enhanced safety and efficacy.

Safety is paramount in Barrett's ablative interventions, especially if one is treating nondysplastic or even low-grade dysplastic Barrett's mucosa. The low incidence of adverse events reported by Sharma et al[1] in the 10 J/cm^2 (×2) effectiveness phase arm in 70 patients is very noteworthy.

> The efficacy of Barrett's ablation involves not only the endoscopic confirmation of complete regrowth of squamous epithelium throughout the tubular esophagus starting at the gastroesophageal junction, but also histologic confirmation of complete absence of underlying ''buried'' or microscopic specialized intestinal metaplasia.

At 10 J/cm^2 (×2), minor post HALO^{360} ablation symptoms of odynophagia, throat pain, abdominal pain, chest pain, and dysphagia were minimal and fully resolved within 2 to 4 days. Such side effects are commonly noted in 13% to 56% of patients for several days up to several weeks after APC,[2-5] and to a much lesser extent with MPEC.[2,4,6] However, more important are the serious adverse events such as acute upper GI bleeding (from ablation induced esophageal

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ulceration), stricture formation (neccessitating dilation), perforation, and death. No serious adverse events (0%) were noted in Sharma et al's[1] multicenter experience with the HALO^{360} system. This is in stark contrast to the unacceptable serious adverse events that can be seen in 10% to 15% of patients who undergo moderate to high-voltage APC Barrett's ablation, which include esophageal perforation (up to 7%)[3,7-9] resulting in several fatalities, stricture formation (4%-8%),[2,3,5,8] and acute upper GI bleeding (3%).[3] Indeed, the continued study of APC for Barrett's mucosal ablation appears to be very difficult to justify given the results of the HALO^{360} system. Serious adverse events after MPEC Barrett's ablation are much lower compared to those after APC and have been limited to stricture formation with an incidence of less than 2%,[6] and no perforations or bleeding.[2,4]

The efficacy of Barrett's ablation includes not only endoscopic confirmation of complete regrowth of squamous epithelium throughout the tubular esophagus starting at the gastroesophageal junction but also histological confirmation of squamous regrowth without any foci whatsoever of underlying ''buried'' or microscopic specialized intestinal metaplastic epithelium. Again, the HALO^{360} BÂRRX device has achieved a 70% success rate at endoscopically eliminating Barrett's,[1] similar to the overall range reported for both MPEC and APC. However, unlike the unacceptably high incidence of buried Barrett's mucosa noted in 20% to 44% of patients treated with APC[4,10,11] and 7% with MPEC,[6] the HALO system appears to have none. This is a huge and critical step for the success of any ablative Barrett's device. It is likely that the success of the HALO^{360} device is, in part, directly related to the fact that the system is automated, eliminating the operator-dependent error seen with MPEC and APC paint-brushing of mucosa, which can produce uneven, nonuniform destruction of the metaplastic mucosa layer. In addition, the circumferential targeting of the esophageal mucosa with a set energy level for less than 1 second by an automated machine and the immediate repetition (10 J/cm^2 $\times$2), based upon the work of Dunkin et al[12] and now the AIM II clinical trial,[1] also likely plays a valuable role in the efficacy of ablation. The success of the HALO^{360} system can also be attributed to the valuable observations and technique modifications undertaken by Drs Panjehpour and Overholt during the evolution of esophageal PDT. For Barrett's high-grade dysplasia and esophageal cancer, these investigators promoted the use of a ''centering'' balloon device in conjunction with appropriately sized laser diffuser fiber in order to evenly distribute the red light to the esophageal surface for PDT.[13] Similarly, in order to deliver uniform radiofrequency energy to Barrett's mucosa (ie, the HALO^{360} device), ''sizing catheters'' were used to select the appropriate size (diameter) of the actual balloon catheter ablation device.

Sharma et al[1] selected medical therapy with a proton pump inhibitor in conjunction with the HALO^{360} system to ablate Barrett's mucosa. Although this combined approach was effective at eliminating Barrett's mucosa entirely in 70% of patients during only a relatively short period of follow-up (1 year), the use of laparoscopic antireflux surgery must not be overlooked as a method to control pathologic reflux in patients with Barrett's in conjunction with endoscopic ablation. Laparoscopic surgery alone has provided regression of Barrett's,[14-16] especially in those with shorter preoperative segments ($<$3 cm) of Barrett's. Salo et al[17] first reported the success of destroying Barrett's mucosa with the Nd:YAG laser after fundoplication. Others have followed suit by combining Nissen fundoplication followed by either APC,[18-21] heater probe,[22] or KTP-YAG laser.[23] The success of Barrett's ablation in concert with surgical intervention for control of GERD may be related to the fact that a properly performed wrap eliminates not only gastric acid reflux into the esophagus but also reflux of duodenal juice (containing both bile and pancreatic secretions), currently measured clinically with the Bilitek probe. Medical treatment with a proton pump inhibitor may improve acid reflux in patients with Barrett's esophagus, but they do so unreliably, even with twice-daily dosing,[24-26] and they are even less effective at controlling bile reflux.[25,26] Duodenogastroesophagaeal reflux appears to be an important factor in the development of intestinal metaplasia within the columnar epithelium found in the distal esophagus[27] and has been implicated as a factor in Barrett's carcinogenesis.

Attention will also need to be directed toward determining what is different about those patients who were completely ablated by the Halo^{360} system and those who had partial or no ablation effect. The importance lies in the fact that clinical features such as a medium to large-sized hiatal hernia ($\geq$4 cm?) or the length of Barrett's esophagus ($\geq$6 cm?) will likely predict increased difficulty in completely eliminating Barrett's metaplasia. Hence, one may instead find it much better to correct the anatomic defect first, and then proceed to ablation. Factors predicting lack of long-term resolution of Barrett's after ablation have already been identified, including length of Barrett's pre-ablation and normalization of acid reflux.[10] In addition, the importance of continued surveillance of not only the esophagus but also the cardia must not be forgotten for patients undergoing ablation. Dysplasia[28] and adenocarcinomas of the cardia[29] have been noted during long-term follow-up after a complete Barrett's esophageal ablation.

The use of mucosal ablation by any technique to treat nondysplastic Barrett's and Barrett's with low-grade dysplasia should be undertaken only under bona fide research study and should be used only after careful risk stratification of Barrett's mucosa. It should not be undertaken simply because a tumor ablation billing code exists (Barrett's esophagus is not a tumor). Sharma et al[1] have proved that the Halo^{360} system works. However, rather than embarking on ablating nondysplastic Barrett's mucosa in a theoretical effort to reduce the likelihood of Barrett's progressing to cancer, risk stratification (Table 1) can and should be undertaken for patients with nondysplastic

TABLE 1. Potential future studies of Barrett's ablation using the HALO^{360} device

Barrett's high-grade dysplasia
Study 1: Effectiveness study: To determine energy level needed for maximal effect (J/cm^2)
Study 2: Comparison study: Compare the HALO^{360} device to photoprin PDT (both in conjunction with twice daily proton pump inhibitor therapy)
Nondysplastic or low-grade dysplastic (by consensus agreement) Barrett's mucosa with any of the following features:
Loss of heterozygosity of 17p (p53)
DNA flow cytometry positive for aneuploidy
DNA flow cytometry positive for elevated G2/4N fraction
Length $\geq$ 6 cm
Study 1: Safety, effectiveness, and cost: HALO^{360} versus MPEC study
Study 2: Reducing the Incidence of high-grade dysplasia and cancer: Observation alone versus HALO^{360} or MPEC ablative intervention
Study 3: HALO^{360} or MPEC ablation at same time as scheduled surveillance Barrett's esophagus follow-up exams versus Barrett's esophagus surveillance alone
Study 4: Reducing the incidence of high-grade dysplasia and cancer: Medical treatment alone versus laparoscopic fundoplication alone versus laparoscopic fundoplication plus ablation (HALO versus MPEC or other)

Barrett's mucosa, utilizing simple endoscopic features such as the length of Barrett's mucosa,[30,31] size of hiatal hernia,[30,31] or with more elegant risk stratification techniques such as aneuploidy and/or elevated G2/4N fractions detected with DNA flow cytometry[32,33] or the presence of the molecular biomarker of loss of heterozygosity (LOH) of 17q.[34]

Now that the proof of the principle that radiofrequency can destroy uncomplicated Barrett's mucosa has been established, the more important task is to prospectively study—in a research setting—the Halo^{360} system in an already well-known higher risk group, namely Barrett's mucosa with high-grade dysplasia (Table 1). Undoubtedly, the radiofrequency energy (J/cm^2) used will need to be higher than that used for nondysplastic Barrett's mucosa. It is hoped that the incidence of stricture formation with deeper injury to the esophageal wall will not lead to an incidence of stricture formation such as that seen in photophrin PDT. In addition, another future direction—given the safety and efficacy of the BÂRRX device—of the approach toward routinely scheduled Barrett's endoscopic surveillance examinations would be to initially perform surveillance biopsy sampling followed immediately (at the same time) by a single Barrett's mucosal ablation treatment. In this manner, additional endoscopies simply to ablate Barrett's mucosa are not undertaken, but, rather, ablation sessions are scheduled at already-defined Barrett's surveillance intervals. The goal of such an approach would be that, after 1 or several surveillance examinations, very little if any Barrett's mucosa will remain, and sampling would be simply of the neosquamous regrowth. The outlook of Barrett's interventional studies using safe and efficacious ablative equipment is looking brighter and brighter. Hopefully the proper prospective, long-term trials can and will be undertaken to justify this approach.

DISCLOSURE

The author has nothing to disclose regarding the BÂRRX device or any Barrett's ablative device.

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Radiofrequency energy ablation of Barrett's esophagus: the best is yet to come!

In this issue of *GIE*, Sharma et al[1] report on the use of a new, promising ablation technique for treatment of Barrett's esophagus: balloon-based radiofrequency energy ablation (RFA). This ablation system uses an over-the-wire ablation balloon with a 3-cm long bipolar electrode on its outer surface and an energy generator for a high-power and rapid (<1 second) delivery of a preset amount of radiofrequency energy density to the electrode. The study was conducted in 2 serial phases, a dosimetry phase and an effectiveness phase, at 8 U.S. centers between September 2003 and September 2005. The dosimetry phase was performed to assess tolerability and safety of different energy settings and included 32 patients with nondysplastic Barrett's esophagus with a length of 2 to 3 cm. The data of the dosimetry study were then used to set the treatment parameters at 10 J/cm^2 (delivered twice) for the effectiveness phase of the study, in which an additional 70 patients with a 2- to 6-cm Barrett's esophagus were treated. Follow-up endoscopies were performed at 1, 3, 6, and 12 months, with a second ablation performed if Barrett's esophagus was present at 1 or 3 months. A complete response, defined as all biopsies negative for Barrett's esophagus at 12 months, was achieved in 70% of patients. The majority of the remaining patients had only small residual islands or tongues of Barrett's epithelium. Ablations were performed as outpatient procedures with no serious complications. Postablation symptoms were generally mild and easily controlled with standard dosages of first-line analgetics, and resolved within 4 days. Despite the circumferential extend of the ablation, none of the patients were diagnosed with postablation esophageal stenosis or had dysphagia. Earlier studies in the porcine esophagus and in humans before a planned esophagectomy have shown that RFA at 8 to 12 J/ cm^2 results in complete epithelial ablation without submucosal injury or stricture formation.[2] This is a remarkable advantage compared with other ablation techniques, such as argon plasma coagulation (APC), photodynamic therapy (PDT), or endoscopic mucosal resection (EMR).[3-5] An even more remarkable finding was the absence of areas of columnar epithelium buried underneath the neosquamous mucosa (eg, ''buried Barrett's''). Other ablation techniques in Barrett's esophagus have invariably shown the occurrence of buried Barrett's, and some fear that these areas may progress to cancer without being detected endoscopically because of their ''hidden'' nature.[4,6-8] In the present study, more than 4000 biopsy specimens were assessed blindly by a central pathology service, and no specimen met the definition of buried Barrett's esophagus. The authors may be criticized for their definition of ''buried Barrett's esophagus.'' They defined this as any special columnar epithelium covered by a layer of squamous epithelium *with no communication to surface epithelium*. The fact that, upon histologic evaluation, areas of subsquamous Barrett's mucosa apparently can be found to communicate with the surface does not imply that the endoscopist can actually detect these areas. To this end, changing the term ''buried Barrett's'' into ''hidden Barrett's esophagus'' may be more appropriate. The question therefore arises of whether the absence of ''buried Barrett's'' in the present study simply reflects the definition used by the authors or hidden areas of specialized intestinal metaplasia were indeed absent. The authors also excluded biopsy specimens obtained from the gastric cardia to assess the complete response rate of the study. After RFA it may, however, be difficult to assess whether the neo-squamo-columnar junction is really at the top of the gastric folds or whether a small rim of columnar-lined esophagus is still present. If biopsy specimens obtained from this area would show specialized intestinal metaplasia, this might imply an incomplete removal of the pre-existing Barrett's segment. On the other hand, it may be difficult to distinguish residual Barrett's epithelium

A larger group of patients needs to be treated with radiofrequency ablation in order to really prove the safety of the technique; longer follow-up is required to show that complete eradication actually persists. Furthermore, evidence that a reduction in surface area or removal of Barrett's epithelium reduces or eliminates the risk of cancer needs to be provided.

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from pre-existing intestinal metaplasia of the cardia, the clinical relevance of which is debated.

Apart from these minor points of criticism, the absence of esophageal stenosis in more than 100 treated patients and the apparent absence of buried Barrett's metaplasia in more than 4000 biopsies suggest that this ablation technique is the first to find the right trade-off between effectiveness on one hand (causing complete removal and no ''hidden Barrett's esophagus'') and, on the other, the avoidance of damage to the deeper layers, causing complications such as stricture formation. Do these results then justify the use of RFA for the ablation of nondysplastic Barrett's esophagus?

Clearly it is too early to embrace RFA as the ultimate solution for this indication. Many requirements still remain: a larger group of patients needs to be treated to really prove the safety of the technique, longer follow-up is required to show that complete eradication actually persists, and evidence for the hypothesis that a reduction in surface area or removal of Barrett's epithelium reduces or eliminates the risk of cancer needs to be provided. In a recent editorial on the use of ablation techniques for treatment of nondysplastic Barrett's esophagus, we argued that new ablation techniques should be performed through a ''top-down approach'': first show efficacy and safety in dysplastic patients before applying techniques to patients who have less to gain and more to lose.[9]

What would then be the arguments to accept and defend the protagonist's standpoint in this editorial? This has to do with the negative impact that Barrett's esophagus has both socioeconomically, as from a quality-of-life perspective, and some unique promising features of RFA as its treatment.

The current American College of Gastroenterology guidelines for Barrett's esophagus surveillance advise a surveillance interval of 2 to 3 years after 2 consecutive endoscopies showing no dysplasia.[10] This places a heavy burden on healthcare costs, and the estimated annual costs of a population-wide surveillance program in the United States are estimated at $290 million.[11] Several studies have suggested that Barrett's esophagus surveillance according to current guidelines may not be cost-effective and that the surveillance interval needs to be lengthened.[12] Furthermore, Barrett's esophagus patients worry more about their condition than appears necessary, overestimating their risk to develop cancer, which reduces their quality of life.[13] In addition, insurance premiums of patients with Barrett's esophagus have been doubled in the United States.[14] Surely a technique that deals with the condition effectively and safely and eliminates the need for continuing surveillance would have a positive impact on the quality of life of Barrett's patients and health-care costs. From a theoretical standpoint, RFA holds the promise to meet many of the criteria of an ideal ablation technique.[9] The current study suggests that the balloon-based RFA is easy and safe and that esophageal strictures and ''buried Barrett's'' are rare, if not absent. Ongoing studies into the presence of oncogenetic abnormalities of the neosquamous epithelium after RFA and the preservation of the functional integrity of the esophagus have yielded promising results. The effectiveness of RFA in the present study—''only'' 70% of patients had complete removal of intestinal metaplasia—may not meet the standard of an ideal ablation technique, but there are good reasons to believe that there is room for improvement here. First, the standard operating procedures for the ablation technique have been changed considerably in the last 18 months, making the procedure easier and more effective. Second, the minimal amount of residual Barrett's in those patients with incomplete removal of intestinal metaplasia suggests that an additional treatment, for instance by a focal ablation device mounted onto the endoscope, will likely increase its success rate.

It is too early to determine the exact position of RFA in the field of ablative techniques for Barrett's esophagus. The data presented in the current feasibility study, however, hold the promise for a dominant role by RFA. Keep your eye out for more studies on this technique: the best is yet to come!

DISCLOSURE

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