Effective treatment of early Barrett’s neoplasia with stepwise circumferential and focal ablation using the HALO system

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HALO system for Barrett’s esophagus contains flat, high-grade dysplasia (HGD) or residual dysplasia after endoscopic resection for HGD or intramucosal cancer (IMC).

Methods: Visible abnormalities were removed with endoscopic resection prior to ablation. Persistence of dysplasia and absence of IMC were confirmed with biopsy after endoscopic resection. A balloon-based electrode was used for primary circumferential ablation and an endoscope-mounted electrode was used for secondary focal ablation.

Results: Twelve patients (nine men; median age 70 years) were treated (median Barrett’s length 7 cm). Visible abnormalities were removed by endoscopic resection in seven patients. The worst pathological grade of residual Barrett’s esophagus after resection and prior to ablation was low-grade dysplasia (LGD) (n = 1) and HGD (n = 11). Patients underwent a median of one circumferential and two focal ablation sessions.

Conclusions: Stepwise circumferential and focal ablation for Barrett’s esophagus with flat HGD or for Barrett’s with residual dysplasia after endoscopic resection for HGD/IMC is a safe and effective treatment modality. Its success rate and safety profile compare favorably with alternatives such as esophagectomy, widespread endoscopic resection or photodynamic therapy.

Introduction

Stepwise circumferential and focal ablation using the HALO ablation system is a relatively new endoscopic treatment for Barrett’s esophagus [1−4]. In circumferential ablation, radiofrequency energy is delivered via a specially designed balloon (HALO360), which contains multiple electrodes encircling its outer surface. For focal ablation of residual areas of Barrett’s esophagus, an articulated, cap-based electrode using the same technology is used (HALO90).

Study aims: The aim of the current study was to evaluate the efficacy and safety of stepwise circumferential and focal ablation using the HALO system for Barrett’s esophagus containing flat, high-grade dysplasia (HGD) or residual dysplasia after endoscopic resection for HGD or intramucosal cancer (IMC).

Complete remission of dysplasia was achieved in 12/12 patients (100%). Complete endoscopic and histological removal of Barrett’s esophagus was achieved in 12/12 patients (100%). There were no ablation-related stenoses, and no subsquamous Barrett’s esophagus was observed in 363 biopsies obtained from post-ablation neo-squamous mucosa. Protocolized cleaning of the ablation zone and electrode in between ablations resulted in superior regression of Barrett’s esophagus compared with previous studies. During a median follow-up of 14 months, no recurrence of dysplasia or Barrett’s esophagus was observed.

Recent studies suggest that stepwise circumferential and focal ablation is highly effective in removing Barrett’s mucosa and its associated dysplasia without the known drawbacks of other ablation techniques, such as residual dysplasia and intestinal metaplasia, esophageal stenosis, or residual subsquamous Barrett’s mucosa (“buried Barrett’s”) [1,2].

We have recently published the results of a study in which stepwise circumferential and focal ablation was used for treatment of 11 patients with Barrett’s esophagus presenting with either flat high-grade dysplasia (HGD) or residual dysplasia after prior endoscopic resection for HGD or intramucosal cancer (IMC) [2]. Ablation was found to be a highly effective. All patients achieved complete clearance of dysplasia as well as complete endoscopic and histological clearance of all intestinal metaplasia. All ablation sessions were performed as outpatient procedures, there were no severe complications, and post-ablation symptoms were generally mild and short-lasting [2].
In the study, the maximum allowable length of Barrett’s esophagus was 7 cm and a relatively high number of ablation procedures were required to achieve the impressive success rate: all patients underwent two circumferential ablations and up to three focal ablation sessions. This was partially due to the fact that the focal ablation technology only became available midway into the study period, which required us to treat small residual islands with circumferential ablation whereas focal ablation would have been a more logical choice. In addition, this was the first study in which the focal ablation device was used in clinical trials, and the optimal energy settings had to be adjusted during the study period [2].

The aim of the current study was therefore to use the knowledge developed in our first study to treat patients with Barrett’s esophagus with HGD or IMC under more optimal circumstances, now also allowing the inclusion of patients with a Barrett’s segment of > 7 cm.

**Patients and methods**

**Patients selection**

Patients were eligible if they met all of the following inclusion criteria:

1. Barrett’s esophagus defined as a columnar-lined esophagus on endoscopy showing intestinal metaplasia upon biopsy; endoscopic Barrett’s length between 2 and 10 cm;
2. at baseline, HGD or IMC diagnosed at two separate endoscopies and assessed by an experienced gastrointestinal pathologist (PK);
3. any visible endoscopic abnormality on high-resolution endoscopy removed with endoscopic resection prior to ablation;
4. in cases of prior endoscopic resection, documented presence of residual low-grade dysplasia (LGD) or HGD in biopsies obtained after endoscopic resection;
5. age between 18 and 85 years;
6. written informed consent.

Patients were excluded in cases where one of the following exclusion criteria was present:

1. in cases of a prior endoscopic resection: vertical resection margin positive for cancer, submucosal invading cancer, poorly differentiated cancer, or presence of lymphatic/vascular invasion;
2. baseline esophageal stenosis with resistance to passage of a therapeutic endoscope (Olympus ITQ160 or IT140, Olympus Europe, Hamburg, Germany, outer diameter of 11.7 mm);
3. visible abnormalities after endoscopic resection, but prior to ablation;
4. invasive cancer in any biopsy obtained after endoscopic resection, but prior to ablation;
5. absence of residual dysplasia (i.e. LGD or HGD) after endoscopic resection, but prior to ablation.

**Endoscopic work-up and management prior to ablation**

All patients underwent at least two separate endoscopic procedures for mapping of the Barrett’s segment, performed with high-resolution endoscopes with narrow band imaging (NBI) capabilities (GIF-Q240Z, Lucera 260 system, Olympus, Tokyo, Japan or GIF-H180, Excera II-system and a high-definition monitor, Olympus Europe, Hamburg, Germany).

The length of the Barrett’s section was determined according to the Prague classification system [5]. The maximum proximal extent of the Barrett’s mucosa (i.e. including islands) was also documented, as isolated islands are not categorized in the Prague system. In addition, the location of the diaphragmatic pinch and the presence of a hiatal hernia were recorded. Visible lesions were classified according to the Japanese Classification of Early Gastric Carcinoma [6], and targeted biopsies were taken followed by random 4-quadrant biopsies at 2-cm intervals.

All patients underwent endoscopic ultrasonography (EUS) using electronic radial endoscopes (GF-UE160, Olympus GmbH, Hamburg, Germany) in conjunction with an Aloka SSD-5000 Procound processor (Aloka, Meerbusch, Germany). All patients with endoscopically visible abnormalities had their lesions removed by endoscopic resection for diagnostic purposes prior to ablation and to ensure that ablation was performed on an endoscopically flat mucosa.

Endoscopic resection was performed with the cap technique or with the multiband mucosectomy technique [7,8]. After endoscopic resection, all resection specimens were collected for histopathological analysis. High-resolution endoscopy was performed 6 weeks after endoscopic resection to exclude the presence of visible abnormalities prior to ablation, and to obtain biopsies to evaluate the presence of residual dysplasia in the remaining Barrett’s esophagus. Ablation was performed within 3 months after the last mapping endoscopy and at least 6 weeks after endoscopic resection.

**The HALO360 and HALO90 system (Fig. 1)**

Both ablation systems used in this trial (HALO Ablation Systems, BARRX Medical Inc., Sunnyvale, California, USA) have 510(k) clearance by the Food and Drug Administration in the USA and the CE Mark for Europe for the treatment of Barrett’s esophagus. Circumferential ablation is performed using the HALO360 system, consisting of an energy generator, ablation catheter, and sizing balloon (Fig. 1). The sizing balloon is used for measuring the inner diameter of the esophagus prior to ablation. The noncompliant balloon has a length of 4 cm and a central lumen for guide wire passage. Upon activation, the balloon is automatically inflated to 4 psi (0.28 atm) and the esophageal inner diameter is automatically calculated based on the baseline balloon volume/geometry and the inflated pressure-volume. The sizing balloon can measure esophageal diameters in the range of approximately 18–33.7 mm, and each measuring cycle takes approximately 6 seconds. The esophageal inner diameter is measured for every 1 cm of the Barrett’s segment and an appropriately sized HALO360 ablation catheter is selected based on these measurements.

The ablation catheter consists of a noncompliant balloon with a 3-cm long bipolar electrode on its outer surface (Fig. 1). The electrode contains 60 250-μm-wide electrode rings, which completely encircle the balloon, each ring being 250 μm apart from its neighboring rings. The ablation catheter is available in five outer diameter sizes (22, 25, 28, 31, and 34 mm), and is introduced over a guide wire. Ablation settings were 12 J/cm² and 40 W/cm².

Focal ablation is performed using the HALO90 system, consisting of an energy generator and a cap-based device that is mounted on the distal tip of an endoscope (compatible with endoscope outer diameter in the range of 8.6–12.8 mm). The device (Fig. 1) has a 20 × 15-mm articulated platform on its upper surface with an electrode array identical to that of HALO360.
focal device is mounted with the electrode surface positioned at the 12 o'clock position in the video image, and is used for ablation of tongues and islands with a maximum length of 2 cm and less than 50% of the circumference. Ablation settings were 12–15 J/cm² and 40 W/cm².

Endoscopic procedures and medication

Endoscopic treatments were performed under conscious sedation with midazolam and/or fentanyl. Patients were clinically observed for 3–4 hours after the ablation procedures and then discharged. Patients were prescribed esomeprazole 40 mg bid as a maintenance dosage and ranitidine 300 mg at bedtime plus 5 mL sucralfate suspension (200 mg/mL) qid for a period of 2 weeks after each treatment endoscopy.

Circumferential ablation technique

In the first ablation session the whole circumference of the Barrett’s segment was treated using the HALO³⁶⁰ device (Fig. 2). The Barrett’s segment was first flushed with 10–20 mL of acetylcysteine (1%) for mucolysis followed by flushing with 40–60 mL of tap water. Subsequently, a 0.035-inch guide wire (Amplatz extra stiff, Cook Endoscopy, Limerick, Ireland) was introduced into the duodenum and the endoscope was removed. The sizing balloon was then introduced over the guide wire and positioned 3–5 cm above the proximal margin of the Barrett’s esophagus. The inner diameter of the esophagus was then measured at 1-cm linear increments along the Barrett’s length. Based on this sizing procedure an ablation catheter with the appropriate diameter was chosen and introduced over the guide wire. Alongside the ablation catheter the endoscope was then introduced and, under visual control, the Barrett’s esophagus was ablated, starting 1 cm above the most proximal extent of the Barrett’s segment (including islands) and continuing into the hiatal hernia (Fig. 2). Each ablation resulted in a 3-cm mucosal segment being treated, and a small overlap (i.e., < 1 cm) between ablation zones was accepted. After the entire Barrett’s segment was treated, the endoscope was removed followed by removal of the ablation balloon. While the balloon electrode was cleaned manually outside the patient to remove adherent tissue, the endoscope was reintroduced to remove all ablated and sloughing tissue from the ablation zone by a combination of suctioning and vigorous flushing with tap water (Fig. 2). The stomach was then emptied and deflated, the endoscope was removed followed by reintroduction of the ablation catheter and the endoscope to repeat the whole ablation procedure so that all areas received two applications of energy (Fig. 2).

Focal ablation technique system (Fig. 3)

At subsequent ablation sessions, the Barrett’s segment was first evaluated for the presence of strictures and the presence of residual Barrett’s mucosa using white light and NBI endoscopy. The Barrett’s segment was flushed with acetylcysteine (1%) followed by flushing with tap water. The endoscope was subsequently withdrawn and the proximal esophagus was thoroughly inspected to exclude the presence of a Zenker’s diverticulum that might impair subsequent introduction of the focal ablation catheter.

The focal ablation catheter was then mounted on the tip of the endoscope and introduced into the distal esophagus. Targeted areas were positioned at the 12 o’clock position in the videendoscopic image, the endoscope deflected upwards so as to bring the ablation surface into firm contact with the tissue, and ablation delivered successively two times to each area in an automated manner (Fig. 3). In cases where the squamocolumnar junction (SCJ) had an irregular appearance, suggesting possible residual Barrett’s mucosa, the SCJ was treated circumferentially using the same technique. After all targeted areas had been treated, the ablated tissue was cleaned of adherent coagulum using the leading edge of the device. The device and the endoscope were subsequently removed to clean the electrode surface and then reintroduced to treat all areas a second time (again with two successive ablations to each area).

Study protocol system (Fig. 4)

After the endoscopic work-up (with or without endoscopic resection for removal of visible lesions), the primary circumferential ablation was performed within 3 months after the last mapping endoscopy and at least 6 weeks after any endoscopic resection. Subsequent ablation sessions were scheduled at 2-month intervals, using high-resolution endoscopy with NBI. Islands with a maximum length of 2 cm and less than 50% of the circumference were treated with focal ablation using the “double-double 12 J/cm² regimen” described above. For larger areas of residual Barrett’s mucosa, circumferential ablation was repeated. After a maximum of two circumferential ablation sessions and two focal ablation sessions using the double-double 12 J/cm² regimen, mapping of the original Barrett’s segment was repeated (Fig. 4). After this was completed, all patients underwent a high-resolution endoscopy with NBI to evaluate the presence of...
residual Barrett’s mucosa and to estimate the percentage surface regression. Targeted biopsies were taken of any residual Barrett’s mucosa present and random biopsies (4Q Bx/1cm) were taken from neo-squamous epithelium throughout the full extent of the original Barrett’s esophagus and from the area immediately distal to the neo-SCJ. No additional ablation was performed at this time point.

Patients who demonstrated residual intestinal metaplasia at this stage were eligible for an additional focal ablation using the aforementioned double-double regimen, but now performed at an energy density setting of 15 J/cm². This was again followed by a high-resolution endoscopy with NBI at 2 months. If there was residual Barrett’s mucosa at that point, it was removed with endoscopic resection using the multiband mucosectomy technique as an escape treatment.

Final outcome was assessed 2 months after the last treatment by high-resolution endoscopy with NBI and biopsies from any visible islands or tongues of columnar-appearing mucosa, neo-squamous mucosa, and immediately distal to the neo-SCJ.

Subsequent follow-up endoscopies were scheduled at 6 and 12 months and yearly after the last treatment session with EUS for those patients who were treated for an invasive cancer initially.

**Histopathological review**

All biopsies and endoscopic resection specimens were routinely processed and stained with hematoxylin and eosin. They were evaluated by a junior pathologist supervised by a senior gastrointestinal pathologist. For the purpose of this study, all specimens were further reviewed by an experienced pathologist (FtK) and scored on standardized case report forms. Endoscopic resection specimens were evaluated for the presence of intestinal metaplasia, LGD, HGD, and invasive cancer. In cases of invasive cancer, tumor differentiation, penetration depth, and lymphatic/vascular invasion were assessed. In addition, the vertical and lateral margins of the resection specimens were evaluated for the presence of dysplasia or cancer. Biopsy specimens were evaluated for the presence of intestinal metaplasia, LGD, HGD or IMC as well as for the presence of residual glands underneath neo-squamous epithelium (buried Barrett’s), irrespective of whether such glands communicated with the epithelial surface.

**Outcome measures**

The primary endpoint of the study was the complete histological clearance of dysplasia and cancer after treatment. In addition, the following secondary endpoints were assessed: the rate of...
complete endoscopic and histological eradication of intestinal metaplasia (including biopsies obtained from neo-squamous mucosa and distal to the neo-SCJ), the rate of acute and late complications of ablation, and the number of treatment sessions required.

Ethical considerations and statistics
The study was approved by the Medical Ethics Committee of our institute, and informed consent was obtained from all participants.

Data were analyzed using the SPSS statistical software package (SPSS Inc., Chicago, USA). For descriptive statistics, the mean (±SD) was used in cases of a normal distribution of variables, and the median (25%–75%) was used for variables with a skewed distribution. Where appropriate, the Mann-Whitney test and Fisher exact test were used.

Results

Patients system (Table 1)
Eligible patients were recruited between September 2005 and January 2006, during which period endoscopic work-up and endoscopic resection (if required) were carried out. All patients were then treated with their first ablation session in February 2006. Twelve patients (nine men; median age 70 years [range, 53–76 years]) were included. The median length of the Barrett’s segment was 7 cm (range, 6.5–8 cm). Seven patients (58%) underwent endoscopic resection for focal removal of visible abnormalities prior to ablation. There were six piecemeal procedures with a median of 2 resections (IQR 2–3). There were no immediate resection-related complications. The resection specimens showed IMC (n = 2) and HGD (n = 5). The worst pathological grade after endoscopic resection and prior to ablation was LGD (n = 1) and HGD (n = 11).

Clearance of dysplasia and intestinal metaplasia system (Fig. 5)
Complete histological eradication of dysplasia was finally achieved in all patients (100%: Fig. 6). In eleven patients (92%) this endpoint was reached after one circumferential ablation and two focal ablation sessions. One patient underwent two circumferential ablations and two focal ablation sessions but still had residual HGD in the distal part of the esophagus (Fig. 7). Subsequent focal ablation at 2 × 2.15 J/cm² did not result in complete removal of Barrett’s esophagus and he was finally treated with three endoscopic resection sessions until complete removal of all Barrett’s esophagus and dysplasia was achieved (Fig. 7). The resection specimens of the first two escape resection procedures contained HGD and IMC; the resection specimens of the third resection contained only gastric-type mucosa.

Complete endoscopic and histological eradication of intestinal metaplasia (including biopsies obtained from neo-squamous mucosa and distal to the neo-SCJ) was achieved in all patients.
Barrett’s esophagus with HGD/IMC (n = 12)
Endoscopic resection of visible lesions (n = 7)
IMC (n = 2); HGD (n = 5)
Histology prior to ablation
HGD (n = 11); LGD (n = 1)

3 ablations (n = 11), 4 ablations (n = 1)
Clearance of dysplasia 11/12
HGD 1/12
Clearance of intestinal metaplasia 8/12
Surface regression 99.9 %

Additional HALO® (n = 4), escape endoscopic resection (n = 1)
Clearance of dysplasia 12/12
Clearance of intestinal metaplasia 12/12
Intestinal metaplasia of cardia 0/12
Surface regression 100 %

Follow up since start therapy (months) 14
Follow up since last treatment (months) 9.5
Number follow up endoscopies 2
Number follow up biopsies 30

Clearance of dysplasia 12/12
Clearance of intestinal metaplasia 12/12
Intestinal metaplasia of cardia 0/12
Surface regression 100 %

In 8 patients (67%) this endpoint was reached after one circumferential ablation and two focal ablation sessions. Three other patients had small residual Barrett’s islands or an irregular Z-line left; the median percentage surface regression being 100% (IQR 99–100). These three patients were effectively treated with an additional focal ablation at 2 × 2 15 J/cm². Finally, one patient had 85% surface area regression after two circumferential ablations and two focal ablation sessions but still had a significant amount of Barrett’s esophagus left that was found to contain HGD upon biopsy. As mentioned above he was treated with an additional focal ablation at 2 × 2 15 J/cm² but finally required endoscopic resection for complete removal of all Barrett’s esophagus and dysplasia.

Patients were followed up for a median period of 14 months (IQR 13–15) after the first ablation session and 9.5 months (IQR 8–10) after the last treatment session. All patients underwent the 6-month follow-up assessment whereas three patients underwent the 12-month follow-up assessment. After a median number of 2 follow-up endoscopies, none of the patients showed recurrence of dysplasia or endoscopic signs of recurrent Barrett’s mucosa. A total of 363 biopsies were obtained from normal-appearing neo-squamous mucosa (median number per patient 30 [IQR 22–39]). In none of these biopsies was intestinal metaplasia encountered, neither at the surface epithelium nor buried below the neo-squamous mucosa (buried Barrett’s).

Number of treatment sessions and complications
Eleven patients underwent a single circumferential ablation; one patient was treated twice with circumferential ablation. Eight patients had two focal ablations and four patients had three focal ablations. Only one patient underwent endoscopic resection as escape treatment (three sessions).

All ablation sessions were performed as outpatient procedures. There were no severe complications. One patient initially underwent endoscopic resection with resection of two specimens (Fig. 8), with relative narrowing of the esophagus noted at the 6-week follow-up (without dysphagia). At the time of primary circumferential ablation 6 weeks later, we noted an 8-mm nodule. We ablated and then performed a focal endoscopic resection with the multiband mucosectomy technique in the same session, with the specimen showing HGD. Due, perhaps, to the previous narrowing and simultaneous endoscopic resection and ablation, the patient developed dysphagia that resolved after one Savary dilatation procedure.

No other complications occurred during the treatment protocol or follow-up period.

Discussion

HGD or IMC in Barrett’s esophagus can be effectively treated with a combined approach of endoscopic resection followed by stepwise circumferential and focal ablation [2]. Endoscopic resection removes thicker, visible lesions and enables proper patient selection based on the histological assessment of the resection specimen: patients showing submucosal invasion are referred for surgery and those with mucosal neoplasia are amendable for endoscopic management [8–11]. As endoscopic resection generally only results in removal of focal lesions, recurrent lesions may develop elsewhere in the Barrett’s segment during follow-up [10–13]. Endoscopic resection is therefore often combined with ablative techniques for removal of residual dysplasia as well as removing the entire remaining nondysplastic Barrett’s mucosa. Ablation techniques, such as photodynamic therapy (PDT) and argon plasma coagulation (APC) are, however, asso-
associated with significant drawbacks [14–20]. PDT and APC often do not result in complete removal of the whole Barrett’s segment and/or require multiple treatment sessions [14–18]. In addition, PDT and APC may cause residual areas of intestinal metaplasia to become hidden underneath the neo-squamous mucosa that regenerates after treatment (i.e. buried Barrett’s), and anecdotal reports have suggested that these foci can progress to cancer [21–23]. Furthermore, areas of Barrett’s mucosa remaining after PDT or APC have been found to contain the same genetic abnormalities as those present prior to treatment, suggesting persistent malignant potential [24,25]. Finally, significant complications may occur after APC and PDT, of which esophageal stenosis is the most frequently reported [15,26].

Recent studies suggest that stepwise circumferential and focal ablation using the HALO ablation system is a highly effective ablation technique that, due to its design and metered dosing, is not associated with the aforementioned drawbacks [1,2]. We have recently published the first study on the use of this ablation technique for treatment of 11 Barrett’s patients with either flat HGD or with residual dysplasia after prior endoscopic resection for HGD or IMC [2]. In that trial, all patients had complete clearance of dysplasia and complete endoscopic and histological removal of all Barrett’s mucosa. These impressive results were reproduced in the current study: all 12 patients had complete eradication of dysplasia and complete endoscopic and histological clearance of intestinal metaplasia. All treatment sessions were performed as outpatient procedures, and there were no severe complications or hospital admissions.

Patients in the current study had a longer Barrett’s segment than the ones included in our first study (median Barrett’s length 7 cm [IQR 6.5–8] vs. 5 cm [IQR 4–7], P = 0.07). Despite the larger surface area to be treated, patients required fewer ablation sessions than in the previous study (mean 3.4 sessions vs. 4.2 sessions; P = 0.02). The apparently higher efficacy in the current study has three plausible explanations. First, the current study incorporated the use of the focal ablation system from the beginning of the study, whereas it was incorporated only halfway into the previous study [2]. Second, our present study avoided the learning curve and dose-escalation issues that were worked out in the first study. Nevertheless, four of our patients still required a step up of focal ablation to double-double 15 J/cm². As this was not associated with any significant complications or side effects, we suggest that this double-double 15 J/cm² setting is used for subsequent ablation studies. Third, in the current study we included in the protocol the technical step of removing the adherent coagulum of the ablation zone and cleaning of the electrode between the two ablation passes of the circumferential ablation procedure. In our first study, this was done by just superficially...

**Fig. 6** Endoscopic appearance of a C7M8 Barrett’s esophagus with high-grade dysplasia. a, b Appearance of the Barrett’s esophagus prior to ablation. c, d After complete endoscopic removal of all Barrett’s esophagus. e, f Corresponding view with narrow band imaging.
cleaning the ablation zone with the ablation balloon being passed into the stomach. In the current study the ablation balloon was removed from the esophagus and extensive water rinses and suctioning were used to clean the ablated segment before applying the second ablation (Fig. 2). When we compared the amount of surface regression after just one primary circumferential ablation session between the two studies, the current study had a superior outcome (median percentage surface regression 99% vs. 90%; P = 0.04). In our opinion, cleaning the electrode and ablation zone after the first pass provides a more assured eradication allowing for more optimal focal ablation of any residual Barrett’s esophagus at follow-up sessions.

The current study also differs from the first study in a higher rate of piecemeal resections in patients who underwent an endoscopic resection prior to ablation (6/7 vs. 0/6; P < 0.05). This implies that patients with larger visible lesions and thus a more widespread resection were included in the present study. One patient suffered from a symptomatic stenosis after a piecemeal resection procedure was followed by a session in which a small lesion located opposite the original resection site was resected immediately after circumferential ablation (Fig. 8). Although we can not exclude the possibility that the ablation contributed to the esophageal narrowing, we speculate that the stenosis mainly resulted from damage incurred by the subsequent resections at this site. This premise is strengthened by the results of trials of ablation as single therapy for nondysplastic Barrett’s esophagus or LGD, in which no strictures have been reported in over 100 patients treated [1].

In this study, we required that all endoscopically visible abnormalities had to be removed by endoscopic resection prior to ablation. This allowed for optimal staging of patients and ensured that only flat mucosa was ablated, preventing possible undertreatment of patients with deeper invading lesions. The results of the current study again suggest that stepwise circumferential and focal ablation can be applied safely after a prior endoscopic resection. The extent of the prior endoscopic resection in the cur-

Fig. 7 C7M8 Barrett’s esophagus with high-grade dysplasia (HGD) and intramucosal cancer (IMC) treated with endoscopic resection of visible abnormalities followed by stepwise circumferential and focal ablation using the HALO ablation system. a–c Prior to treatment: C7M8 Barrett’s esophagus with subtle mucosal abnormalities (b) that were resected endoscopically, showing IMC and HGD. d–f Effect after two circumferential and three focal ablation sessions: surface area regression is 85% but a nearly circumferential segment of Barrett’s esophagus remains distally with biopsies showing HGD. g–i Result after stepwise endoscopic resection of residual Barrett’s mucosa with the multiband mucosectomy technique: complete endoscopic and histological removal of dysplasia and Barrett’s esophagus.
rent study, however, did not encompass more than 50% of the circumference or measure more than 2 cm in length. Performing an endoscopic resection is inevitably associated with esophageal scarring. Depending on the extent of the resection this may either lead to just a small visible scar, a relative narrowing of the esophageal lumen, or a clearly visible stenosis causing dysphagia. From a theoretical standpoint, a significant stenosis after endoscopic resection may impair the efficacy and safety of subsequent ablation procedures. More studies have to be conducted to evaluate the combined use of endoscopic resection and this ablation technique to continue to optimize this endoscopic treatment strategy.

The current study also shows that Barrett’s mucosa that persists after multiple ablation sessions can be easily treated by using endoscopic resection as an escape treatment. In one of our patients, five ablation sessions resulted in 85% surface regression of a C7M8 Barrett’s with persistent HGD. This was easily resected without any submucosal lifting using the multiband mucosectomy technique (Fig. 7). This again illustrates the lack of significant submucosal scarring after stepwise circumferential and focal ablation therapy with the HALO system, which is an important advantage over other ablation techniques that generally do not allow subsequent use of endoscopic resection as an escape treatment.

Another unique feature of this ablation technique is the lack of subsquamous intestinal metaplasia after treatment, a finding commonly associated with other ablation therapies. In the current study we obtained a total number of 363 biopsies from neo-squamous epithelium after ablation without detecting any areas of buried Barrett’s. These results are in accordance with both our previous study on the use of this technique for Barrett’s neoplasia [2] the AIM study, in which stepwise circumferential and focal ablation was used for ablation of nondysplastic Bar-
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