Endoscopic radiofrequency ablation combined with endoscopic resection for early neoplasia in Barrett's esophagus longer than 10 cm

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Background: Radiofrequency ablation (RFA) is safe and effective for eradicating Barrett's esophagus (BE) and BE-associated early neoplasia. Most RFA studies have limited the baseline length of BE (<10 cm), and therefore little is known about RFA for longer BE.

Objective: To assess the safety and efficacy of RFA with or without prior endoscopic resection (ER) for BE ≥10 cm containing neoplasia.

Design: Prospective trial.

Setting: Two tertiary-care centers.

Patients: This study involved consecutive patients with BE ≥10 cm with early neoplasia.

Intervention: Focal ER for visible abnormalities, followed by a maximum of 2 circumferential and 3 focal RFA procedures every 2 to 3 months until complete remission.

Main Outcome Measurements: Complete remission, defined as endoscopic resolution of BE and no intestinal metaplasia (CR-IM) or neoplasia (CR-neoplasia) in biopsy specimens.

Results: Of the 26 patients included, 18 underwent ER for visible abnormalities before RFA. The ER specimens showed early cancer in 11, high-grade intraepithelial neoplasia (HGIN) in 6, and low-grade intraepithelial neoplasia (LGIN) in 1. The worst residual histology, before RFA and after any ER, was HGIN in 16 patients and LGIN in 10 patients. CR-neoplasia and CR-IM were achieved in 83% (95% confidence interval [CI], 63%-95%) and 79% (95% CI, 58%-93%), respectively. None of the patients had fatal or severe complications and 15% (95% CI, 4%-35%) had moderate complications. During a mean (± standard deviation) follow-up of 29 (± 9.1) months, no neoplasia recurred.

Limitations: Tertiary-care center, short follow-up.

Conclusion: ER for visible abnormalities, followed by RFA of residual BE is a safe and effective treatment for BE ≥10 cm containing neoplasia, with a low chance of recurrence of neoplasia or BE during follow-up. (Gastrointest Endosc 2011;73:682-90.)

Abbreviations: APC, argon plasma coagulation; BE, Barrett's esophagus; CI, confidence interval; CR-IM, complete removal of intestinal metaplasia; CR-neoplasia, complete removal of neoplasia; EC, early cancer; ER, endoscopic resection; HGIN, high-grade intraepithelial neoplasia; IM, intestinal metaplasia; IQR, interquartile range; LGIN, low-grade intraepithelial neoplasia; RFA, radiofrequency ablation.

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Barrett's esophagus (BE) is a premalignant condition characterized by the presence of a columnar-lined distal esophagus containing intestinal metaplasia (IM) on biopsy.[1] BE is caused by chronic gastroesophageal reflux and is found in 8% of patients undergoing endoscopy for reflux symptoms.[2] BE can undergo a multiple-step transition from low-grade intraepithelial neoplasia (LGIN) to high-grade intraepithelial neoplasia (HGIN) to invasive adenocarcinoma.[3] HGIN and mucosal cancer in BE have a low risk of lymph node metastases and can therefore be treated endoscopically by endoscopic resection (ER) techniques, endoscopic ablative techniques, or a combination thereof. ER techniques allow for histological evaluation of the resected specimen, which is the only reliable way to exclude patients with submucosal invading cancers from further endoscopic treatment.[4] After focal removal of endoscopically visible abnormalities, the remaining BE generally contains residual HGIN or LGIN, and recurrences occur in 19% to 30% of cases.[5-7] Therefore, ablation of the remaining BE has been advocated, and recent studies suggest that this reduces the chances of recurrent neoplasia elsewhere in the BE during follow-up.[7]

Radiofrequency ablation (RFA) is one of the most promising ablative techniques for BE. The technique uses a bipolar electrode that is available as a balloon-based device for primary circumferential ablation or as a cap-based device that can be mounted on the tip of the endoscope for focal ablation.

RFA has been proven to be safe and effective for the removal of IM and neoplasia in BE in a wide range of clinical studies, including two randomized trials.[8-15] In addition, studies have shown that the regenerated neosquamous epithelium after RFA is free of the oncogenetic abnormalities as present in the BE before RFA and that subsquamous foci of IM (buried BE) are rare.[16] Furthermore, RFA preserves the diameter, compliance, and motility of the esophagus and is associated with a low rate of stenosis.[17]

From other endoscopic therapies, it is known that safety and efficacy may depend on the length of the BE segments treated: after radical mucosectomy and after photodynamic therapy, stenosis rates, for example, increase with the BE length treated.[18,19] In addition, the rate of complete removal of the whole BE segment is found to decrease with the length of the BE.[20] For these reasons, endoscopic therapy is thought to be more difficult in longer BE segments. Most studies on the use of ablation techniques for BE have therefore restricted the baseline BE length to less than 10 cm.

The aim of this study, therefore, was to assess the safety and efficacy of RFA with or without prior ER for BE of ≥10 cm containing early neoplasia.

Take-home Message

- Radiofrequency ablation preceded by endoscopic resection for visible abnormalities, when present, is also a safe and effective treatment for Barrett's esophagus longer than 10 cm in length containing neoplasia.

METHODS

Patient selection

Patients were consecutively included from January 2006 until November 2008. They were treated at two tertiary-care referral centers in The Netherlands: the Academic Medical Center in Amsterdam and the St. Antonius Hospital in Nieuwegein. Patients were eligible if they met all the following inclusion criteria: age ≥18 years; maximum BE length ≥10 cm; presence of LGIN, HGIN, or early cancer (EC) (defined as ≤ T1sm1 infiltration with good or moderate differentiation and no lymphatic/vascular invasive growth) confirmed by a study pathologist (F.T.K., M.V., C.S.) at two endoscopic procedures; no signs of metastasis on EUS (in case of HGIN and EC) or CT scan (in case of EC). Patients were excluded if they had any of the following exclusion criteria: previous treatment with photodynamic therapy or argon plasma coagulation (APC); prior ER larger than 3 cm in length or extending over more than 50% of the circumference; ER specimen showing cancer at the vertical (deep) resection margin, >T1sm1 invasion, poor tumor differentiation, or lymphatic/vascular invasive growth; persistent visible abnormalities after ER or invasive cancer in mapping biopsies (post-ER) before RFA.

The current study enrolled some patients who were included in other published or ongoing trials from our group as well as patients who were treated outside of these trials, mainly because of the length of their BE (Table 1). Patients who were not previously consented as part of prior internal review board–approved trials provided informed consent for participation in this study.

Endoscopic work-up before RFA

Patients underwent two high-resolution endoscopies of the BE with biopsies from all visible abnormalities (ie, any nodule, flat lesion, or mucosal irregularity, no matter how subtle) and random 4-quadrant biopsies every 2 cm. All lesions suspicious for EC were endoscopically resected, for removal and staging of these lesions before RFA. ER was performed with patients under conscious sedation as an outpatient procedure either with the ER-cap technique (after submucosal lifting) or the multi-band mucosectomy technique. Depending on the size, lesions were resected en bloc or in multiple pieces (piecemeal procedure). All resected specimens were retrieved, pinned down on paraffin with the mucosal side up, and fixed in formalin for histological evaluation. No attempts were made to reconstruct the piecemeal resections.

After ER, the residual BE was mapped twice to exclude residual lesions and residual cancer in the flat mucosa.

The RFA system and endoscopic procedure

The RFA system and endoscopic procedure have been described previously.[9-12] In short, RFA procedures were

TABLE 1. Patients of current study participating in other trials

Study	Design	Baseline pathology	BE inclusion length	No. of pts BE ≥10 cm included in this study
AMC-II[9]	Single-center, prospective study	HGIN/EC	2-10 cm	2
EURO-I[12]	Multicenter, prospective study	HGIN/EC	≤12 cm	8
EURO-II*	Multicenter, prospective study	HGIN/EC	≤12 cm	5
SURF*	Multicenter, randomized, controlled trial	LGIN	No restrictions	4
None	Prospective registration	HGIN/EC	No restrictions	7

BE, Barrett's esophagus; *HGIN,* high-grade intraepithelial neoplasia; *EC,* early cancer; *LGIN,* low-grade intraepithelial neoplasia.
*Ongoing trials.

performed as outpatient procedures with patients under conscious sedation with midazolam and fentanyl or pethidine. Patients were discharged after 2 to 4 hours of observation.

Circumferential RFA was performed with the balloon-based HALO^{360} system (Bârrx Medical Inc, Sunnyvale, Calif). The BE was ablated at 12J/cm^2 under endoscopic control. Two ablation passes of the BE were performed, with cleaning of the ablation after the first pass.

Focal RFA was performed with the cap-based HALO^{90} system (Bârrx) for treatment of residual BE after circumferential RFA. Areas were ablated twice by using the "double-double" 15J/cm^2 regimen (ie, 2 ablation passes consisting of 2 consecutive ablations with 15J/cm^2 each, with cleaning of the ablated area after the first pass), which is in accordance with our initial experience with the focal ablation device and all of our published and ongoing studies.[9-12] In all focal RFA sessions, the area of the neosquamocolumnar junction at the upper end of the gastric folds was ablated, irrespective of its endoscopic appearance.

After each RFA procedure, patients were treated for a period of 2 weeks with ranitidine 300 mg at bedtime and 5 mL sucralfate suspension (200 mg/mL) 4 times daily in addition to the maintenance medication of esomeprazole 40 mg twice daily.

Treatment protocol and follow-up

In case of prior ER, the first circumferential RFA of the whole BE segment was performed at least 6 weeks after ER. Subsequent RFA sessions were scheduled every 2 to 3 months until complete eradication of all visible BE was achieved. Patients underwent a maximum of 2 circumferential and 3 focal ablations. In case of residual BE after the maximum number of RFA sessions, an ER was performed as an "escape" procedure (Fig. 1). Once complete remission of all visible BE was achieved, and complete histological clearance of dysplasia and IM was documented (or 2-3 months after the escape procedure), patients were followed with high-resolution endoscopies with narrow-band imaging at 3, 6, and 12 months and annually thereafter. At these follow-up endoscopies, 4-quadrant biopsy specimens were obtained immediately distal (<5 mm) to the neosquamocolumnar

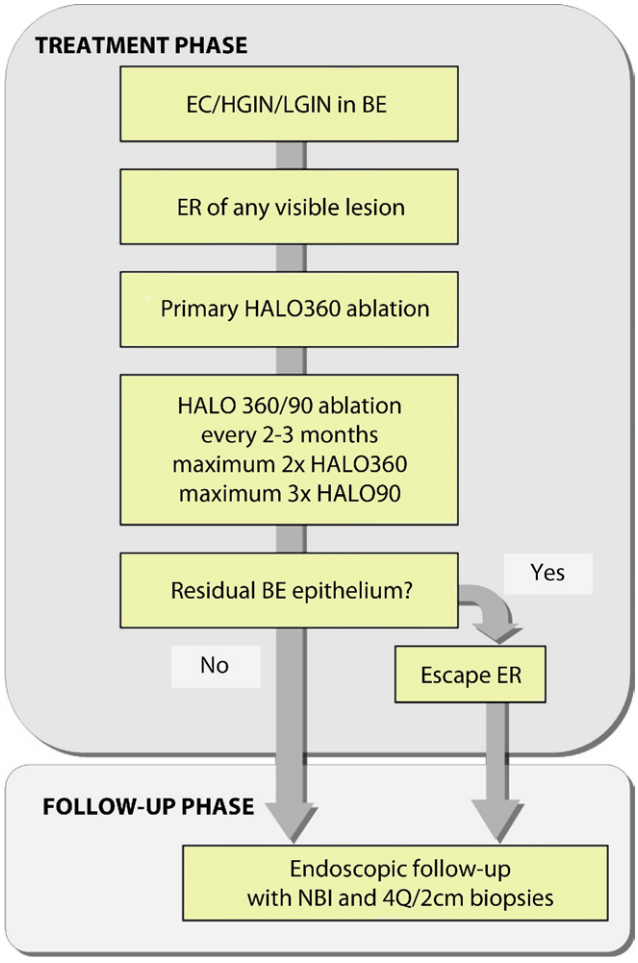

Figure 1. Flow-chart of treatment protocol. *EC,* early cancer; *HGIN,* high-grade intraepithelial neoplasia; *LGIN,* low-grade intraepithelial neoplasia; *BE,* Barrett's esophagus; *ER,* endoscopic resection; *HALO,* HALO^{360} system, HALO^{90} system, (Bârrx Medical Inc, Sunnyvale, Calif); *NBI,* narrow-band imaging; *Q,* quadrant.

junction and from the neosquamous epithelium at 2-cm intervals.

Histology

All ER specimens and biopsy specimens were routinely processed and stained with hematoxylin and eosin and assessed by three study pathologists (F.T.K., M.V., C.S.).[4] The ER specimens and biopsy specimens were evaluated for the presence of neoplasia and cancer according to the World Health Organization classification.[21] In the case of cancer in the ER specimens, tumor infiltration depth, tumor differentiation grade, the presence of lymphatic/vascular invasive growth, and radicality of the vertical resection margins were documented. Biopsy specimens of the neosquamous epithelium were also evaluated for the presence of subsquamous foci of IM.

Outcome parameters

Primary endpoints were (1) complete removal of neoplasia (CR-neoplasia), defined as the absence of LGIN, HGIN, and EC from all biopsy specimens obtained during the first follow-up endoscopy and (2) complete removal of intestinal metaplasia (CR-IM), defined as endoscopic resolution of all BE and no evidence of IM in any of the biopsy specimens obtained during the first follow-up endoscopy (including the biopsy specimens from the neosquamocolumnar junction and from the neosquamous mucosa).

Secondary endpoints were (1) recurrence of neoplasia during follow-up, (2) recurrence of BE during follow-up (either endoscopic or histological), and (3) the complication rate of ER and RFA.

Severity of the complications was graded as follows: mild (unplanned hospital admission, hospitalization ≤3 days, clinically significant bleeding with a hemoglobin drop of <3 g/dL and no need for transfusion); moderate (4-10 days' hospitalization, ≤4 units blood transfusion, need for repeat endoscopic intervention, radiologic intervention); severe (hospitalization >10 days, intensive care unit admission, need for surgery, >4 units blood transfusion. In the case of stenosis: >5 endoscopic dilatations, stent placement, or incision therapy); or fatal (death attributable to procedure <30 days or longer with continuous hospitalization).[22]

Statistics

Statistical analysis was performed with a statistical software package (Statistical Package for the Social Sciences 14.0.2; SPSS Inc, Chicago, Ill). Data with a normal distribution were described with the mean and standard deviation, whereas data with a skewed distribution were described by the median and interquartile ranges (IQR) or ranges. Confidence intervals (CI) of the proportions were calculated with Confidence Interval Analysis, version 1.0.[23]

TABLE 2. Patient characteristics (n = 26)

Characteristic	
Age, mean (± SD), y	66 (± 10.6)
Sex, no.	
Male	21
Female	5
BE length, mean (range) cm	
C	9 (6-19)
M	11 (10-20)
Overall worst histology, no.	
EC	11
HGIN	11
LGIN	4
ER before RFA, no.	
Yes	18
No	8
Histology flat mucosa before RFA, no.	
HGIN	16
LGIN	10

SD, Standard deviation; *BE,* Barrett's esophagus; *C,* circumferential extent; *M,* maximum extent; *EC,* early cancer; *HGIN,* high-grade intraepithelial neoplasia; *LGIN,* low-grade intraepithelial neoplasia; *ER,* endoscopic resection; *RFA,* radiofrequency ablation.

RESULTS

Patients

Between January 2006 and October 2008, 26 consecutive patients (21 men, mean [± SD] age 66 ± 10.6 years) were included in this study. Patient characteristics are described in Table 2. Median BE length was C9M11 cm (IQR C8-10, M10-12). None of the patients showed signs of active reflux disease, yet 13 patients (50%) were found to have reflux stenosis at the proximal end of the BE segment. These stenoses were generally asymptomatic and allowed passage of the therapeutic endoscopes. In 3 patients, however, endoscopic bougienage of the reflux stenosis was required before treatment to facilitate the introduction of an ER cap and RFA catheters.

Eighteen patients underwent ER of visible abnormalities before RFA. The ER cap technique was used in 5 patients and multi-band mucosectomy in 13 patients. The ER specimens showed early cancer in 11 patients (intramucosal [n = 10], sm1 [n = 1], all with good or moderate differentiation and no lymphatic/vascular invasive growth), HGIN in 6 patients, and LGIN in 1 patient. Before RFA, and after ER if applicable, all patients had flat mucosa

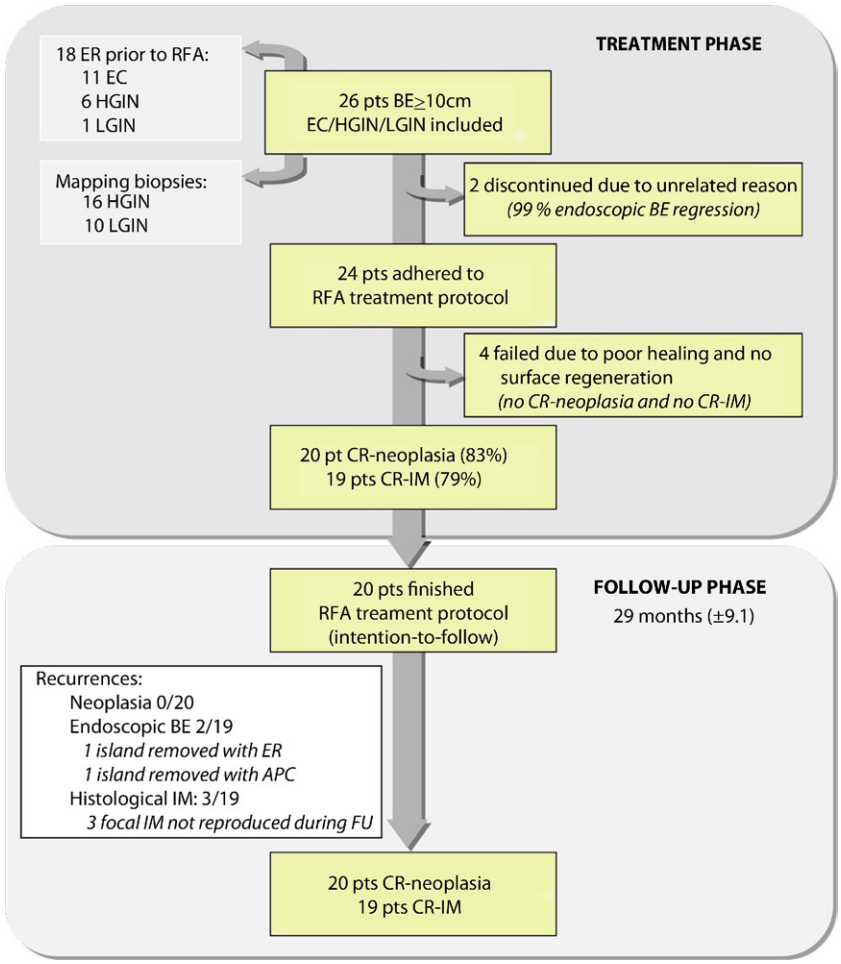

Figure 2. Enrollment and outcomes. *ER,* endoscopic resection; *RFA,* radiofrequency ablation; *EC,* early cancer; *HGIN,* high-grade intraepithelial neoplasia; *LGIN,* low-grade intraepithelial neoplasia; *pts,* patients; *BE,* Barrett's esophagus; *CR-neoplasia,* complete removal of neoplasia; *CR-IM,* complete removal of endoscopically visible BE and histological intestinal metaplasia; *APC,* argon plasma coagulation; *IM,* intestinal metaplasia; *FU,* follow-up.

without visible abnormalities, with random mapping biopsies showing HGIN in 16 and LGIN in 10 patients.

Primary outcomes: eradication of early cancer, neoplasia, and intestinal metaplasia

In 2 patients (8%), the treatment protocol was discontinued because of unrelated comorbidity (psychiatric disorder and lung cancer). In both, at the last endoscopy before discontinuation, endoscopic regression of BE was 99% without histological information available. These patients were excluded from analysis of the primary endpoints.

CR-neoplasia was achieved in 20 of 24 patients: 83% (95% CI, 63%-95%). CR-IM was achieved in 19 of 24 patients: 79% (95% CI, 58%-93%) (Figs. 2 and 3). In 4 patients (15% [95% CI, 4%-35%]), the RFA treatment was discontinued after 1 to 3 sessions because of poor healing and no or almost no regeneration of neosquamous mucosa (Fig. 4). These patients were therefore considered as failures for the primary endpoints of the study (CR-neoplasia and CR-IM).

Patients achieved CR-neoplasia and CR-IM after a median of one (IQR 1-2) circumferential and two (IQR 1-3) focal ablations. Three patients underwent an escape ER for persisting BE islands after the maximum number of RFA treatments. Another two patients were treated with APC after RFA: in one patient for a small, persisting BE island (1×2 mm), which in the opinion of the endoscopist did not justify ER; in the other patient, APC was performed for small (<5 mm), remaining BE islands after two circumferential RFA sessions, because the focal RFA catheter could not pass the reflux stenosis despite dilatation.

Two patients underwent a diagnostic ER during the treatment protocol of slightly elevated BE islands in order to avoid having RFA performed on possibly invading cancers (thus not to supplement the efficacy of RFA). Histology of both ER specimens showed only LGIN.

Secondary outcome: complications after ER and RFA

No fatal or severe complications occurred. Four patients (15% [95% CI, 4%-35%]) developed complications after ER

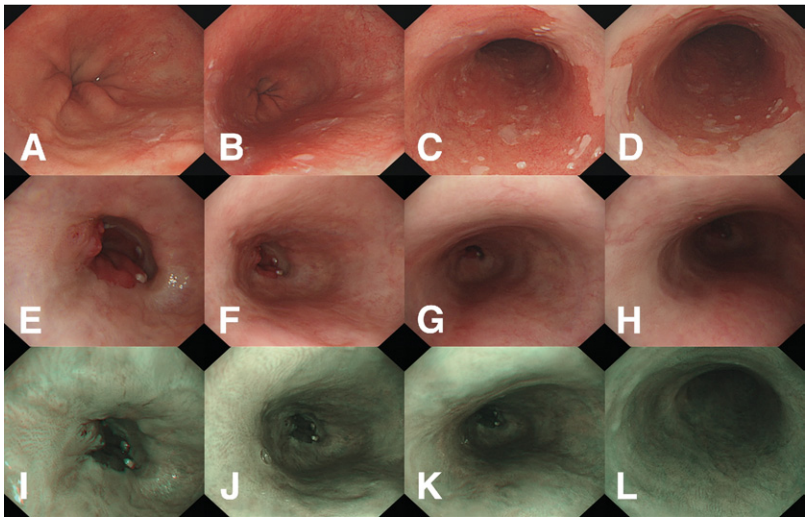

Figure 3. Barrett's esophagus (BE) with C7M10 length treated with endoscopic resection for mucosal cancer and radiofrequency ablation for the remaining BE segment, resulting in complete eradication of neoplasia and intestinal metaplasia. **A, B, C,** and **D,** BE before any treatment. **E, F, G,** and **H,** Complete removal of the whole BE segment after endoscopic resection and 3 ablation sessions. **I, J, K,** and **L,** Corresponding images with narrow-band imaging. *C,* circumferential extent (cm); *M,* maximum extent (cm).

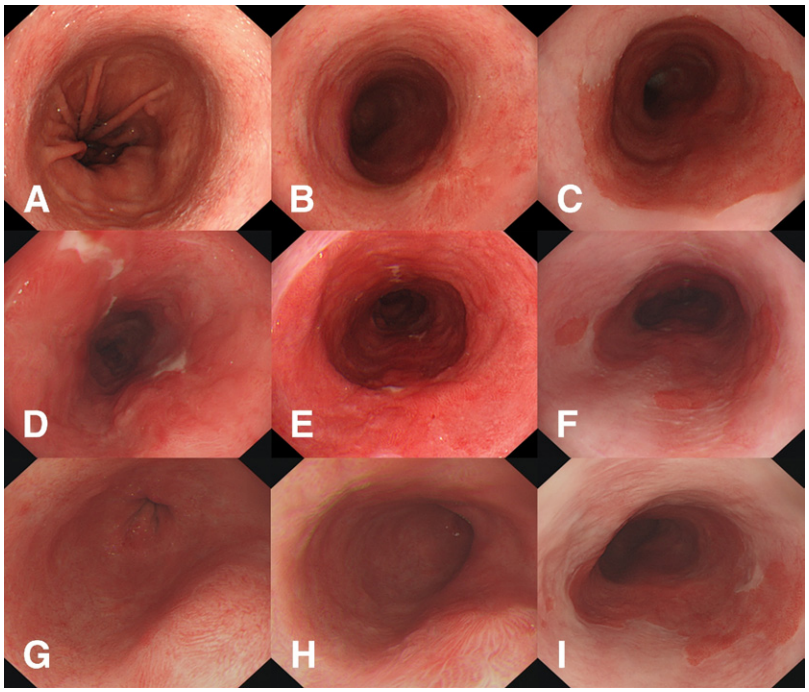

Figure 4. Barrett's esophagus (BE) with C10M11 length, treated with endoscopic resection for a mucosal cancer and radiofrequency ablation for the remaining BE segment. Radiofrequency ablation failed to remove the BE segment. **A, B,** and **C,** BE after endoscopic resection and before ablation. **D, E,** and **F,** Three months after the first ablation the esophagus had not completely healed, with only limited regression into neosquamous mucosa. A second circumferential ablation was performed at a later stage. **G, H,** and **I,** Again, no significant visible response was seen after the second ablation. As a consequence, ablations were stopped. *C,* circumferential extent (cm); *M,* maximum extent (cm).

or RFA, which were graded as moderate. One patient developed delayed bleeding 6 days after ER. This patient received blood transfusion and was treated successfully with endoscopic hemostatic therapy (adrenaline injection, bipolar probe coagulation, and clip placement). Two patients had unplanned admissions: one patient was admitted for observation after a superficial laceration that showed no transmural leakage on the swallowing contrast examination. However, this 80-year-old patient became delirious and, as a result, the admission was prolonged; another patient was admitted 3 days after the RFA procedure because of pain, nausea, and vomiting that resolved

with conservative treatment. Because both admissions were for >4 days, these complications were graded as moderate. The fourth patient with a moderate complication had a relative stenosis after ER and developed symptoms of dysphagia after RFA, which resolved after two dilatations.

In 7 patients (27% [95% CI, 12%-48%]), a superficial laceration was observed during the circumferential ablation procedure. Six of these superficial lacerations remained asymptomatic, did not require intervention, and were therefore not considered to be complications. However, one patient was admitted for observation (see previously), because this was the first laceration we observed during our RFA experience. This patient, again, did not experience symptoms attributable to the laceration. Lacerations were located either at the level of the reflux stenosis (n = 4) or at the level of the ER scar (n = 3). In 4 of the 7 patients, the laceration was noted after the first circumferential ablation pass, and the second pass was either therefore not performed (n = 1) or was modified by the use of a balloon with a smaller diameter (n = 1) or by skipping the zone containing the laceration during the second RFA pass (n = 2). All patients were able to continue the RFA according to the protocol 2 to 3 months later.

Secondary outcome: follow-up

Patients who achieved CR-neoplasia and CR-IM were followed-up for a mean (± SD) duration of 29 ± 9.1 months (21 ± 11.7 months since last treatment session). None of the 20 patients developed neoplasia during follow-up, thus 100% (95% CI, 82%-100%) continued to have CR-neoplasia status.

Two patients had small islands of BE during follow-up. One patient had a 3-mm island 6 months after treatment, located at the upper part of the initial BE segment immediately distal to a reflux stenosis that was likely to be overlooked initially. After removal of this island with ER, this patient continued to have CR-IM status. Another patient had a 1-mm island 18 months after treatment, located near the Z-line, and the island was treated with APC.

Focal IM below the neosquamocolumnar junction was found in 3 patients in single biopsy specimens obtained during follow-up. This finding was not reproduced in 33 follow-up biopsy specimens obtained at the neosquamocolumnar junction in 6 procedures. Of the 1272 biopsy specimens taken from neosquamous epithelium, only 1 biopsy specimen (2 cm proximal to the neosquamocolumnar junction) showed focal subsquamous IM without neoplasia.

DISCUSSION

In this study, 83% of the patients with BE ≥10 cm containing early neoplasia were effectively treated with RFA preceded by ER for visible abnormalities, when present. The treatment not only resulted in complete removal of all neoplasia but also complete endoscopic and histological removal of the whole BE segments. There were no severe complications, and, remarkably, these results were achieved by using an apparently similar number of treatments as are used for BE <10 cm.[8-13,15]

Our data are in accordance with the reported rates of complete remission of neoplasia and IM by Shaheen et al,[13] even though longer BE segments were treated in our study. However, in contrast to the study of Shaheen et al, our treatment protocol permitted two instead of one circumferential ablation as well as an escape treatment with ER after the maximum number of RFA treatments in the case of residual endoscopic BE. Thus, our study shows similar complete remission rates of neoplasia and IM but with a more extensive treatment protocol. Compared with previous RFA studies from our own group in which we used the same protocol, the remission rates for BE ≥10 cm were lower and did not reach the 95% to 100% complete remission of neoplasia and IM.[9-12,15] This difference in remission rate was a result of our decision in 4 patients to discontinue treatment because of poor healing and no visible regression in the surface area of BE despite medication compliance and increased esomeprazole dosage (80 mg twice daily). We hypothesize that this reflects the severity of the underlying reflux disease in this selected group of BE patients. Nevertheless, in the remaining patients, complete remission of neoplasia and IM was achieved with a median of 3 RFA treatments, which is similar to the 3 to 4 RFA treatments that have been reported for shorter BE segments.[9-13,15]

During treatment of our patients, we encountered several technical challenges that have not been reported in patients with shorter BE. First, half of the patients were found to have a relative reflux stenosis at the upper end of the BE. In some patients, prior dilatation of this stenosis was required to allow introduction of ER-caps and RFA catheters. In addition, reflux stenoses may have led to a conservative selection of the ablation balloon-catheter diameter. In theory, a conservative balloon choice may result in less contact between the electrode and the mucosa in the wider distal part of the esophagus, therefore resulting in suboptimal treatment. Further difficulties encountered during RFA treatment of BE ≥10 cm were nontransmural lacerations that were seen in 27% of patients after circumferential ablation, occurring at the reflux stenosis or previous ER site (ie, the narrowest part of the esophagus). These lacerations were, however, asymptomatic and did not require intervention. When a laceration was noticed after the first pass, further RFA was modified or stopped during that session to prevent deeper laceration and further ablation of the deeper layers. Nevertheless, lacerations did not impede subsequent treatment 2 to 3 months later.

Only one patient (4%), who underwent previous ER, developed symptoms of dysphagia after RFA, which

resolved after two dilatations. Dysphagia was rare after RFA, unlike after other endoscopic treatment modalities, such as radical ER and photodynamic therapy, which, despite the fact that they are generally applied in shorter BE, are associated with stenosis in more than 25% of patients.[15,18,19]

During follow-up, 3 patients were found to have focal IM below the neosquamocolumnar junction. IM was, however, found only in a single biopsy specimen during one follow-up endoscopy, and it was not reproduced during subsequent follow-up endoscopies. It might be that IM in this region is a physiological finding, because others have reported that approximately 25% of the normal population shows IM in biopsies of the cardia.[24,25] On the other hand, we cannot completely exclude that IM below the neosquamocolumnar junction after RFA is a remnant of persisting IM not found previously because of sampling error or even being the start of more widespread new-onset IM. Further follow-up is needed to elucidate the relevance of IM in the neosquamocolumnar junction.

This study has some limitations that need to be addressed. First, it was performed in tertiary-care referral centers. Endoscopies were performed by experienced endoscopists in the field of BE imaging, and therapy and pathology were reviewed in consensus by expert GI pathologists. Second, the patients in this study were a highly selected group not frequently seen in common practice. The results may therefore not be generalized to centers with different set-ups. Finally, the follow-up time is relatively short. Longer follow-up is needed to show whether the complete remission will be sustained in this selected group of patients with probably more severe reflux disease. Nevertheless, previous studies in this field have reported neoplasia recurrence rates of approximately 19% to 30% during a median follow-up of 1.5 to 5 years, with most of the recurrences developing within the first 15 months after treatment.[5-7]

In our opinion, the treatment of patients with BE ≥10 cm should be performed in centers with experience in imaging and therapy of BE. It is not only essential to recognize all subtle abnormalities that may harbor cancer in such a long BE, but the treatment itself also is technically more demanding because of the reflux stenoses and the ER scars. In addition, the number of patients with no or poor regeneration of neosquamous epithelium after RFA is relatively high. Further research is necessary to predict which patients will not respond adequately to RFA as well as which mechanisms underlie this lack of response.

In conclusion, RFA of BE segments ≥10 cm seems to be more challenging: ablations were stopped in 15% of patients because of poor healing and no regression, which probably reflects the severity of the reflux disease in this selected group of patients. Nevertheless, the vast majority of this complex group of patients with BE reached complete removal of neoplasia and complete reversal of the BE segment without severe complications and with a similar number of treatment sessions as reported for patients with shorter BE segments.

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