CLINICAL TRIAL OUTCOMES:
RADIOFREQUENCY ABLATION (RFA) FOR
BARRETT’S ESOPHAGUS
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1. INTRODUCTION

Barrett’s Esophagus

Barrett’s esophagus (BE) is defined as the replacement of a portion of the squamous epithelium of the distal esophagus by a specialized intestinal epithelium, also known as intestinal metaplasia (IM).\textsuperscript{1} This metaplastic change occurs primarily as a result of chronic injury due to the reflux of acidic gastric contents and bile seen in gastroesophageal reflux disease (GERD).\textsuperscript{1,2} Approximately 10% of patients with chronic GERD have BE, with estimates of the prevalence of BE among adults ranging from 1.6% to 5.6%.\textsuperscript{3-6}

On upper endoscopy, BE is initially suspected based on the detection of salmon-pink columnar epithelium proximal to the gastroesophageal junction. Biopsy samples are obtained for histological confirmation of the diagnosis, and to further characterize disease severity. BE encompasses a spectrum of neoplastic changes, and is categorized accordingly as non-dysplastic BE (NDBE), low-grade dysplasia (LGD), or high-grade dysplasia (HGD). Overall, the significance of BE lies in its role as the precursor lesion to esophageal adenocarcinoma (EAC), a cancer with a particularly poor 5-year survival rate of approximately 17%.\textsuperscript{7} The incidence of EAC has increased by more than 500% since the 1970s, outpacing that of melanoma, breast cancer, or prostate cancer.\textsuperscript{8}

Barrett’s Esophagus: Disease Progression to Esophageal Adenocarcinoma

The rate of progression to EAC for NDBE is 0.1 to 0.6% per patient year, which equates to a progression rate 33 to 200 times that of the general population.\textsuperscript{7,9,10} This effect is even more pronounced as disease severity increases. In LGD and HGD, annual progression rates of 1.7% and 6.6% confer 560 and 2,200 fold increased risks, respectively, of developing EAC per year, compared to the general population.\textsuperscript{7,9}

A recent meta-analysis and systematic review by Wani, et al. evaluated over 100 studies reporting on the natural history versus intervened (ablation) history of BE. The authors concluded that ablation significantly reduces the risk for cancer in patients with all grades of BE. The pooled natural history showed a relative risk reduction of 73%-91% in these patients, based on baseline disease grade.\textsuperscript{9} This translates to numbers needed to treat (NNT) of 45 NDBE, 13 LGD, and 4 HGD patients to prevent one case of EAC in each of these patient groups over the subsequent 5 years.

Historically, BE has been managed with endoscopic biopsy surveillance, with the intention to detect neoplastic progression, specifically EAC, at an early enough stage to prevent cancer-related death. Despite its widespread use, there are no prospective randomized trials that support the utility of this surveillance strategy. Because of the limitations of current diagnostic tools and techniques, one cannot predict which BE patients will progress to EAC or when they will do so. While neoplastic progression is believed to occur through a linear stepwise process in which NDBE advances to LGD to HGD and finally to EAC, one of the largest natural history studies to date reported that of the BE patients who progressed to HGD or EAC during the study, 53% had at least two initial consecutive endoscopies that showed only NDBE.\textsuperscript{11} Biopsy surveillance, as a management strategy, may miss these intermediary steps of neoplastic progression.\textsuperscript{11} Part of this shortcoming is due to biopsy sampling error, as the most advanced disease is often not associated with an identifiable endoscopic abnormality and, thus, may not be biopsied.\textsuperscript{12-14} Moreover, biopsy surveillance is beset by considerable inter-observer variability in histopathologic interpretation, with several studies demonstrating that inter-observer agreement, even among expert GI pathologists, is moderate.\textsuperscript{15-17}

In summary, Barrett’s esophagus is the recognized precursor lesion for EAC. The risk for EAC is higher depending on the severity of baseline dysplasia grade. Current surveillance strategies are not optimal for this disease state, as they are hindered by cost issues, inter-observer variability in histology interpretation, biopsy sampling error (under staging), and the fact that surveillance alone does not prevent disease progression. Radiofrequency ablation (RFA) is an endoscopic therapy that has been proven safe, effective, durable and cost-effective in the management of BE. Ablation using RFA may be considered medically necessary for all patients with dysplastic BE as well as those patients with non-dysplastic BE who are at high risk for neoplastic progression.
Clinical Evidence for Radiofrequency Ablation of Barrett’s Esophagus

The safety and efficacy of RFA has been studied in a wide spectrum of patients (NDBE, LGD, HGD, and early cancer) through a diverse set of study designs (randomized sham-controlled, prospective randomized, cohort, registry, and human and porcine dosimetry), and in a variety of settings (US and EU, tertiary academic centers, community referral centers). In these studies, RFA has shown an acceptable safety profile, high rates of complete histological eradication of IM and dysplasia, durability of effect, and significant reduction in cancer progression rates.

RFA for dysplastic BE was assessed in a randomized sham-controlled trial (RCT) published in The New England Journal of Medicine by Shaheen, et al. The primary endpoints were complete response of IM (CR-IM) and dysplasia (CR-D) for dysplastic Barrett’s patients (LGD and HGD) randomized to RFA or Sham. In the LGD and HGD patient groups, CR-D occurred in 90.5% and 81.0% of the RFA patients (ITT), compared to 22.7% and 19.0% of the Sham patients, respectively. CR-IM occurred in 77.4% vs. 2.3% of the RFA and Sham patients, respectively (p<0.001 for all). Patients in the RFA group had less disease progression (3.6% vs. 16.3%, p=0.03), and fewer cancers (1.2% vs. 9.3%, p=0.045). The study conclusion was, “In patients with dysplastic Barrett’s esophagus, radiofrequency ablation was associated with a high rate of complete eradication of both dysplasia and intestinal metaplasia and a reduced risk for disease progression.”18 Two- and three-year data shows that ≥90% of these patients have complete eradication of IM and dysplasia.19

An additional prospective randomized trial compared RFA to stepwise radical endoscopic mucosal resection (SRER) in BE patients with HGD and early EAC. The study showed equivalent efficacy between RFA and SRER (96%-100% complete response rates), superiority of RFA over SRER for safety and tolerability, and decreased number of therapeutic sessions in the RFA group.20

In addition to these randomized trials, there are a large number of well-designed, prospective multi-center studies with rigorous a priori endpoints. These studies demonstrate positive efficacy outcomes and an exceptionally favorable safety profile for RFA of BE. Furthermore, several cost-utility papers have reported RFA to be a cost-effective management strategy for BE. The following results support the findings of the randomized trials and add additional important information:

- RFA resulted in complete eradication of disease in 98% of NDBE patients, with 2.5-years follow-up.21 At 5 years, 92% of patients maintained durable cure, and no patients demonstrated neoplastic progression.22
- Ablative therapy for all grades of BE is the dominant or preferred strategy in several cost-effectiveness reports.23-26
- A multi-center European study of EMR and RFA for HGD/early cancer had a complete response of 100% and 96% for neoplasia and IM, respectively.27
- Two community-based studies of RFA inclusive of dysplastic and non-dysplastic BE showed safety and efficacy outcomes similar to those of other studies conducted in investigational settings.28,29
- In patients with HGD and early (intra-mucosal) cancer, Pouw, et al. found that all patients had oncogenic abnormalities at baseline using FISH and IHC, whereas no patient demonstrated any oncogenic abnormalities after treatment with RFA.30
- RFA has repeatedly been shown to be safe. The highest published stricture rate in patients undergoing RFA alone is 7.6%, and 14% in those undergoing RFA after extensive ER.18,20 There have been no RFA-related deaths.

Comparison to Current Treatment or Management Alternatives

Established alternatives commonly utilized in the management of BE are surveillance endoscopy with biopsy (specifically for NDBE, LGD, and rarely for HGD) or esophagectomy (specifically for HGD). The mortality rate from esophagectomy ranges from 1% to 7% in centers of excellence with extensive experience in this procedure, and higher in hospitals where esophagectomy is less frequently performed.23 Due to the frequency and severity of complications associated with esophagectomy and the growing body of evidence supporting use of RFA for HGD, esophagectomy is now typically reserved for patients with invasive EAC. Compared to surveillance endoscopy (option for all Barrett’s patients), ablation has been shown to reduce the incidence of neoplastic progression for all stages of BE, whereas surveillance does not alter the natural history of disease.18,32,33 A less utilized therapy is SRER (complete removal of all BE tissue with resection), which is offered by few U.S. centers due to technical complexity and adverse event incidence (stricture rate in excess of 80%).20 In
the randomized trial described above, RFA and SRER both achieved high rates of complete eradication yet RFA had a superior safety profile compared to SRER. Another less utilized service is photodynamic therapy (specifically for HGD), which is now rarely used due to an unacceptable adverse event profile (36% stricture rate, 69% photosensitivity rate).^{34}

**RFA Results from Outside the Investigational Setting**

Over 110,000 RFA procedures for BE have been performed in the U.S. and Europe in the last 5 years, in both the academic and community practice settings. This adoption and utilization by a wide variety of gastroenterologists and endoscopic surgeons are indirect measures of the safety, efficacy, and utility of this intervention. Most academic and community institutions with divisions specializing in esophageal disease offer an ablative management strategy using RFA for Barrett’s esophagus.

In the Shaheen, et al. RCT, a number of the physicians were community practitioners. There were no differences in safety or efficacy outcomes between the academic institutions and community practices.\(^{18}\) A national U.S. registry comprises 134 centers and more than 5,500 patients enrolled over the last five years (approximately 40% of patients have dysplastic BE as their entry diagnosis, 50% ND BE, and the remainder early EAC or BE indeterminate for dysplasia). Community practices represent 80% of the investigative sites in this registry. There is no difference in the complete histological response rate according to site of service or practice type. Lyday, et al. published their community practice experience of 429 patients with BE of all grades treated with RFA.\(^{26}\) Of the total patients enrolled, 24% had dysplasia as their entry diagnosis. The investigators report that 100% of these patients achieved a complete response for dysplasia (CR-D) and 78% a complete response for IM (CR-IM), results comparable to those reported in the Shaheen, et al. RCT.\(^{18}\)

**Cost Effectiveness**

Cost utility models have shown that RFA is the dominant or preferred strategy for managing BE. Inadomi, et al. performed a decision analysis comparing multiple strategies for managing all grades of BE. They employed a mathematical model assuming a 50 yr old population of BE patients, and compared management strategies of doing nothing, surveillance, esophagectomy, PDT, RFA, and other ablative methods. The model was biased against RFA, assuming low dysplasia and IM eradication rates. The authors concluded the following with regard to RFA:\(^{23}\)

- **HGD**: ablation is the dominant strategy, meaning it is less expensive, more cost-effective, and more clinically effective than all other strategies.
- **LGD**: ablation is the most cost-effective strategy if:
  - >28% of patients achieve CR-D
  - 0% patients need to achieve CR-IM
  - Endoscopic biopsy surveillance is continued in everyone
- **NDBE**: ablation is the most cost-effective strategy over surveillance if:
  - >40% or patients achieve CR-IM, and
  - Endoscopic biopsy surveillance is discontinued in patients who achieve CR-IM
- **NDBE**: ablation is next most cost-effective strategy over surveillance if:
  - >40% or patients achieve CR-IM, and endoscopic biopsy surveillance is continued in everyone

Das, et al. evaluated 3 competing strategies for a 50 yr old cohort with NDBE: natural history (i.e. doing nothing), surveillance per ACG guidelines, and RFA. The model was again biased against RFA. The authors determined that RFA is the most cost-effective strategy and results in the highest quality adjusted life years (QALYs) and lowest risk for cancer. Their conclusion was “… ablation for NDBE is more cost-effective than surveillance.”\(^{24}\)

**Conclusion**

The rationale for RFA treatment of BE is evidence-based and supported by the:

- high risk of neoplastic progression for all grades of BE,
- lack of predictable linear stepwise progression (i.e. NDBE to LGD to HGD to EAC),
- shortcomings associated with surveillance-alone in terms of biopsy sampling error and inter-observer variability in histology interpretation,
- superiority of RFA vs. surveillance-only (sham control) and RFA vs. SRER in randomized controlled trials, and
- cost-utility of RFA over surveillance-alone.
References

2. **BIBLIOGRAPHY OF PEER-REVIEWED PAPERS OF RFA FOR BE**


El-Serag HB, Graham DY. Routine polypectomy for colorectal polyps and ablation for Barrett’s esophagus are intellectually the same. Gastroenterology 2011;140:386-8.


The below citations refer to publications in peer-reviewed journals that pertain to the use of radiofrequency ablation for indications other than Barrett’s esophagus. They are listed for sake of completeness.


DEVICES

2.1. Regulatory Clearance

The HALO\textsuperscript{360} System first received 510(k) clearance from the FDA on December 18, 2001 (K013139). Improvements to the system have been described in subsequent 510(k) clearances (K051168 and K082202). The HALO\textsuperscript{360} system has CE mark for Europe, as well as clearance for use in Canada and Australia. The indication for use statements are:

**US:** The HALO\textsuperscript{360} System is indicated for use in the coagulation of bleeding and non-bleeding sites in the gastrointestinal tract including but not limited to, the esophagus. Indications include Esophageal Ulcers, Mallory-Weiss tears, Arteriovenous Malformations, Angiomata, Barrett’s Esophagus, Dieulafoy Lesions, and Angiodysplasia.

**EU, Canada:** The HALO\textsuperscript{360} System is indicated for use in the coagulation of bleeding and non-bleeding sites in the gastrointestinal tract including but not limited to Barrett’s Esophagus.

The HALO\textsuperscript{90} System first received 510(k) clearance from the FDA on April 21, 2006 (K060169). Improvements to the system have been described in subsequent 510(k) clearances, (K062723, K083737, and K062441). The HALO\textsuperscript{90} Ablation Catheter Instructions for Use document was amended on January 8, 2010 to include procedural steps for hemostatic applications (K093008). The HALO\textsuperscript{90} System has CE mark for Europe, as well as clearance for use in Canada and Australia. The indication for use statements are:

**US:** The HALO\textsuperscript{90} System is indicated for use in the coagulation of bleeding and non-bleeding sites in the gastrointestinal tract including, but not limited to, the esophagus. Indications include Esophageal Ulcers, Mallory-Weiss tears, Arteriovenous Malformations, Angiomata, Barrett’s Esophagus, Dieulafoy Lesions, and Angiodysplasia, Gastric Antral Vascular Ectasia (GAVE) and Radiation Proctitis (RP).

**EU and Canada:** The HALO\textsuperscript{90} System is indicated for use in the coagulation of bleeding and non-bleeding sites in the gastrointestinal tract including but not limited to Barrett’s Esophagus.

The HALO\textsuperscript{FLEX} Energy Generator first received 510(k) clearance from the FDA on November 10, 2009 (K092487). A memo was filed and accepted for hemostatic applications in the United States (K093008). The indication for use statement is:

**US:** The HALO\textsuperscript{FLEX} Energy Generator is indicated for use for the coagulation of soft tissue. The HALO\textsuperscript{FLEX} System is indicated for use in the coagulation of bleeding and non-bleeding sites in the gastrointestinal tract including, but not limited to, the esophagus. Indications include Esophageal Ulcers, Mallory-Weiss tears, Arteriovenous Malformations, Angiomata, Barrett’s Esophagus, Dieulafoy Lesions, and Angiodysplasia, Gastric Antral Vascular Ectasia (GAVE) and Radiation Proctitis (RP).

**EU and Canada:** The HALO\textsuperscript{FLEX} System is indicated for use in the coagulation of bleeding and non-bleeding sites in the gastrointestinal tract including but not limited to Barrett’s Esophagus.

2.2. HALO\textsuperscript{360} System

The HALO\textsuperscript{360} System includes an energy generator, sizing balloons, and ablation catheters. The energy generator is used to inflate the sizing balloons in order to measure the inner diameter of the esophagus. The generator also delivers RF energy to the ablation catheters to achieve the ablative effect. All catheters are single use, disposable medical devices.
2.3. HALO\textsuperscript{90} System

Focal ablation of residual Barrett’s tissue may be conducted with the HALO\textsuperscript{360} System or the HALO\textsuperscript{90} System. The HALO\textsuperscript{90} System includes an energy generator and the HALO\textsuperscript{90} Ablation Catheter. The HALO\textsuperscript{90} Ablation Catheter is similar to the HALO\textsuperscript{360+} Ablation Catheter, having the same electrode design and delivering the same energy density and power density to the tissue. In comparison to the HALO\textsuperscript{360+} Ablation Catheter, the HALO\textsuperscript{90} Ablation Catheter has a smaller surface area, allowing more focal selective ablation of residual Barrett’s tissue, and, attaches to the endoscope, rather than to a balloon catheter.

2.4. HALO\textsuperscript{FLEX} Energy Generator

The HALO\textsuperscript{FLEX} Energy Generator provides the flexibility to choose from the HALO\textsuperscript{360+} or HALO\textsuperscript{90} Ablation Catheter. The generator provides a platform for future clinical and product innovation.
3. **Abstracts from Peer-Reviewed Papers of RFA for BE**

3.1. **Radiofrequency ablation in Barrett’s esophagus with dysplasia**


**Background:** Barrett’s esophagus, a condition of intestinal metaplasia of the esophagus, is associated with an increased risk of esophageal adenocarcinoma. The condition may progress through stages of dysplasia before cancer. We assessed whether an endoscopic intervention, radiofrequency ablation, could eradicate dysplastic Barrett’s esophagus and decrease the rate of neoplastic progression.

**Methods:** In a multicenter, sham-controlled trial, we randomly assigned 127 patients with dysplastic Barrett’s esophagus in a 2:1 ratio to receive either radiofrequency ablation (ablation group) or a sham procedure (control group). Randomization was stratified according to the grade of dysplasia (low-grade or high-grade) and the length of Barrett’s esophagus (<4 cm or 4 to 8 cm). Primary outcomes at 12 months included the complete eradication of dysplasia and intestinal metaplasia. Secondary outcomes included progression to more severe dysplasia or cancer and adverse events.

**Results:** In the intention-to-treat analyses, among patients with low-grade dysplasia, complete eradication of dysplasia occurred in 90.5% of those in the ablation group, as compared with 22.7% of those in the control group (P<0.001). Among patients with high grade dysplasia, complete eradication occurred in 81.0% of those in the ablation group, as compared with 19.0% of those in the control group (P<0.001). Overall, 77.4% of patients in the ablation group had complete eradication of intestinal metaplasia, as compared with 23.0% of those in the control group (P<0.001). Patients in the ablation group had less disease progression (3.6% vs. 16.3%, P = 0.03) and fewer cancers (1.2% vs. 9.3%, P = 0.045). Patients reported having more chest pain after the ablation procedure than after the sham procedure. In the ablation group, one patient had upper gastrointestinal hemorrhage, and five (6.0%) patients had esophageal stricture.

**Conclusions:** In patients with dysplastic Barrett’s esophagus, radiofrequency ablation was associated with a high rate of complete eradication of both dysplasia and intestinal metaplasia and a reduced risk of disease progression. (ClinicalTrials.gov number, NCT00282672.)
3.2. Durability of radiofrequency ablation in Barrett’s esophagus with dysplasia


Gastroenterology 2011:141; 460-8

**Background & aims:** Radiofrequency ablation (RFA) can eradicate dysplasia and intestinal metaplasia in patients with dysplastic Barrett’s esophagus (BE), and reduce rates of esophageal adenocarcinoma. We assessed long-term rates of eradication, durability of neosquamous epithelium, disease progression, and safety of RFA in patients with dysplastic BE.

**Methods:** We performed a randomized trial of 127 subjects with dysplastic BE; after cross-over subjects were included 119 received RFA. Subjects were followed for a mean time of 3.05 years; the study was extended to 5 years for patients with eradication of intestinal metaplasia at 2 years. Outcomes included eradication of dysplasia or intestinal metaplasia after 2 and 3 years, durability of response, disease progression, and adverse events.

**Results:** After 2 years, 101 of 106 patients had complete eradication of all dysplasia (95%) and 99 of 106 had eradication of intestinal metaplasia (93%). After 2 years, among subjects with initial low-grade dysplasia, all dysplasia was eradicated in 51 of 52 (98%) and intestinal metaplasia was eradicated in 51 of 52 (98%); among subjects with initial high-grade dysplasia, all dysplasia was eradicated in 50 of 54 (93%) and intestinal metaplasia was eradicated in 48 of 54 (89%). After 3 years, dysplasia was eradicated in 55 of 56 of subjects (98%) and intestinal metaplasia was eradicated in 51 of 56 (91%). Kaplan-Meier analysis showed that dysplasia remained eradicated in _85% of patients and intestinal metaplasia in _75%, without maintenance RFA. Serious adverse events occurred in 4 of 119 subjects (3.4%); the rate of stricture was 7.6%. The rate of esophageal adenocarcinoma was 1 of 181 patient-years (0.55%/patient-years); there was no cancer-related morbidity or mortality. The annual rate of any neoplastic progression was 1 of 73 patient-years (1.37%/ patient-years).

**Conclusions:** In subjects with dysplastic BE, RFA therapy has an acceptable safety profile, is durable, and is associated with a low rate of disease progression, for up to 3 years.
3.3. **Endoscopic radiofrequency ablation for Barrett’s esophagus: 5-year outcomes from a prospective multicenter trial**


*Endoscopy* 2010;42:781-9

**Background & study aims:** The AIM-II Trial included patients with nondysplastic Barrett’s esophagus (NDBE) treated with radiofrequency ablation (RFA). Complete eradication of NDBE (complete response-intestinal metaplasia [CRIM]) was achieved in 98.4% of patients at 2.5 years. We report the proportion of patients demonstrating CR-IM at 5-year follow-up.

**Patients & methods:** Prospective, multicenter US trial (NCT00489268). After endoscopic RFA of NDBE up to 6 cm, patients with CR-IM at 2.5 years were eligible for longer-term follow-up. At 5 years, we obtained four-quadrant biopsies from every 1 cm of the original extent of Barrett’s esophagus. All specimens were reviewed by one expert gastrointestinal pathologist, followed by focal RFA and repeat biopsy if NDBE was identified. Primary outcomes were (i) proportion of patients demonstrating CR-IM at 5-year biopsy, and (ii) proportion of patients demonstrating CR-IM at 5-year biopsy or after the single-session focal RFA.

**Results:** Of 60 eligible patients, 50 consented to participate. Of 1473 esophageal specimens obtained at 5 years 85% contained lamina propria or deeper tissue (per patient, mean 30 [13], standard deviation [SD] 13). CR-IM was demonstrated in 92% (46 / 50) of patients, while 8% (4 / 50) had focal NDBE; focal RFA converted all these to CR-IM. There were no buried glands, dysplasia, strictures, or serious adverse events. Kaplan-Meier CR-IM survival analysis showed probability of maintaining CR-IM for at least 4 years after first durable CR-IM was 0.91 (95% confidence interval [CI] 0.77–0.97) and mean duration of CR-IM was 4.22 years (standard error [SE] 0.12).

**Conclusions:** In patients with NDBE treated with RFA, CR-IM was demonstrated in the majority of patients (92%) at 5-year follow-up, biopsy depth was adequate to detect recurrence, and all failures (4/4, 100%) were converted to CR-IM with single session focal RFA.
3.4. Stepwise radical endoscopic resection versus radiofrequency ablation for Barrett’s oesophagus with high-grade dysplasia or early cancer: A multicentre randomized trial

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Gut 2011;60:765-73

Objective: After focal endoscopic resection (ER) of high-grade dysplasia (HGD) or early cancer (EC) in Barrett’s oesophagus (BO), eradication of all remaining BO reduces the recurrence risk. The aim of this study was to compare the safety of stepwise radical ER (SRER) versus focal ER followed by radiofrequency ablation (RFA) for complete eradication of BO containing HGD/EC.

Methods: A multicentre randomised clinical trial was carried out in three tertiary centres. Patients with BO ≤5 cm containing HGD/EC were randomised to SRER or ER/RFA. Patients in the SRER group underwent piecemeal ER of 50% of BO followed by serial ER. Patients in the ER/RFA group underwent focal ER for visible lesions followed by serial RFA. Follow-up endoscopy with biopsies (four-quadrant/2 cm BO) was performed at 6 and 12 months and then annually. The main outcome measures were: stenosis rate; complications; complete histological response for neoplasia (CR-neoplasia); and complete histological response for intestinal metaplasia (CR-IM).

Results: CR-neoplasia was achieved in 25/25 (100%) SRER and in 21/22 (96%) ER/RFA patients. CR-IM was achieved in 23 (92%) SRER and 21 (96%) ER/RFA patients. The stenosis rate was significantly higher in SRER (88%) versus ER/RFA (14%; p<0.001), resulting in more therapeutic sessions in SRER (6 vs 3; p<0.001) due to dilations. After median 24 months follow-up, one SRER patient had recurrence of EC, requiring ER.

Conclusions: In patients with BO ≤5 cm containing HGD/EC, SRER and ER/RFA achieved comparably high rates of CR-IM and CR-neoplasia. However, SRER was associated with a higher number of complications and therapeutic sessions. For these patients, a combined endoscopic approach of focal ER followed by RFA may thus be preferred over SRER.
3.5. Radiofrequency ablation for dysplasia in Barrett’s esophagus restores β-catenin activation within esophageal progenitor cells

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_Dig Dis Sci_ 2012;57:294-302

**Background & aims:** Endoscopic therapies for Barrett’s esophagus (BE) associated dysplasia, particularly radiofrequency ablation (RFA), are popular alternatives to surgery. The effect of such therapies on dysplastic stem/progenitor cells (SPC) is unknown. Recent studies suggest that AKT phosphorylation of β-Catenin occurs in SPCs and may be a marker of activated SPCs. We evaluate the effect of RFA in restoring AKT-mediated β-Catenin signaling in regenerative epithelium.

**Methods:** Biopsies were taken from squamous, non-dysplastic BE, dysplastic BE and esophageal adenocarcinoma (EAC). Also, post-RFA, biopsies of endoscopically normal appearing neosquamous epithelium were taken at 3, 6, and 12 months after successful RFA. Immunohistochemistry and Western blot analysis was performed for Pβ-Catenin^{552} (Akt-mediated phosphorylation of β-Catenin), Ki-67 and p53.

**Results:** There was no difference in Pβ-Catenin^{552} in squamous, GERD, small bowel and non-dysplastic BE. There was a fivefold increase in Pβ-Catenin^{552} in dysplasia and EAC compared to non-dysplastic BE (P < 0.05). Also, there was a persistent threefold increase in Pβ-Catenin^{552} in neosquamous epithelium 3 months after RFA compared to native squamous epithelium (P < 0.05) that correlated with increased Ki-67. Six months after RFA, Pβ-Catenin^{552} and Ki-67 are similar to native squamous epithelium.

**Conclusions:** Enhanced AKT-mediated β-Catenin activation is seen in BE-associated carcinogenesis. Three months after RFA, squamous epithelial growth from SPC populations exhibited increased levels of Pβ-Catenin^{552}. This epithelial response becomes quiescent at 6 months after RFA. These data suggest that elevated Pβ-Catenin^{552} after RFA denotes a repair response in the neosquamous epithelium 3 months post-RFA.
3.6. Safety of prior endoscopic mucosal resection in patients receiving radiofrequency ablation of Barrett’s esophagus

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Clin Gastroenterol Hepatol 2012;10:150-4

Background and aims: Radiofrequency ablation (RFA) is safe and effective treatment for flat dysplasia associated with Barrett’s esophagus (BE). However, there is limited data on the safety of RFA in patients who had prior endoscopic mucosal resection (EMR), which might increase the risk of complications. We compared complications and histologic outcomes between patients who had EMR before RFA and those who received only RFA.

Methods: We performed a retrospective analysis of data collected from patients treated for BE, associated with dysplasia or intramucosal cancer, at the Mayo Clinic in Rochester, MN, from 1998 to 2009. Patients were divided into groups that had RFA following EMR (Group 1, n=44) or only RFA (Group 2, n=46). We compared the incidence of complications (strictures, bleeding, and esophageal perforation) and histologic features (complete resolution of dysplasia [CR-D] and complete resolution of intestinal metaplasia [CR-IM]) between groups. Logistic regression analysis was performed to assess predictors of stricture formation.

Results: Stricture rates were 14% in group 1 and 9% in group 2 (odds ratio [OR], 1.53; 95% confidence interval [CI], 0.26–9.74). The rates of CR-IM were 43% in group 1 and 74% in group 2 (OR, 0.33; 95% CI 0.14–0.78). The rates of CR-D were 76% in group 1 and 71% in group 2 (OR, 1.28; CI, 0.39–4.17). The adjusted OR for CR-IM in Group 1 (adjusting for age, segment length, and grade of dysplasia) was 0.50 (95% CI, 0.15–1.66).

Conclusions: Stricture rates among patients who receive only RFA are comparable to those of patients who had prior EMR. EMR appears safe to perform prior to RFA.
3.7. **Radiofrequency ablation of Barrett’s esophagus: Outcomes of 429 patients from a multicenter community practice registry**

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*Endoscopy* 2010;42:272-8

**Background & study aims:** The use of radiofrequency ablation (RFA) for complete eradication of Barrett’s esophagus has shown promise in trials conducted at predominantly tertiary academic centers; however less is known regarding outcomes in the community. We evaluated the safety and efficacy of RFA for Barrett’s esophagus delivered in a community practice setting.

**Patients & methods:** This was a multicenter registry conducted in community-based gastroenterology practices. Patients had confirmed intestinal metaplasia with or without dysplasia on biopsy of a Barrett’s esophagus. Intervention was step-wise RFA with follow-up esophageal biopsies. Endpoints were histology-based; complete response was defined as all biopsies at most recent endoscopy negative for intestinal metaplasia (CR-IM) or dysplasia (CR-D). Three cohorts were reported: 1) safety cohort, all patients; 2) efficacy cohort A, patients with at least one biopsy session after initial treatment; 3) efficacy cohort B, patients with at least one biopsy session ≥1 year after initial treatment.

**Results:** The safety cohort included 429 patients (71% men, median age 59 years, median Barrett’s segment 3.0 cm). There were no serious adverse events (bleeding, perforation, death), and a stricture occurred after 1.1% of cases (2.1% of patients). In efficacy cohort A (n = 338), CR-IM and CR-D were achieved in 72% and 89% of patients, respectively (median follow-up 9 months). In efficacy cohort B (n = 137), CR-IM and CR-D were achieved in 77% and 100% of patients, respectively (median follow-up 20 months).

**Conclusion:** In this multicenter registry conducted at four community-based practices, the observed safety and efficacy outcomes associated with RFA for Barrett’s esophagus are comparable to those previously reported in multicenter trials from predominantly tertiary academic centers.
3.8. Efficacy of radiofrequency ablation combined with endoscopic resection for Barrett’s esophagus with early neoplasia


*Clin Gastroenterol Hepatol* 2010;8:23-9

**Background & aims:** Radiofrequency ablation (RFA) is safe and effective for eradicating intestinal metaplasia and neoplasia in patients with Barrett’s esophagus. We sought to assess the safety and efficacy of RFA in conjunction with baseline endoscopic resection for high-grade intraepithelial neoplasia (HGIN) and early cancer.

**Methods:** This multicenter, prospective cohort study included 24 patients (mean age, 65 y; median Barrett’s esophagus, 8 cm), with Barrett’s esophagus of 12 cm or less containing HGIN or early cancer, from 3 European tertiary-care medical centers. Visible lesions were resected endoscopically, followed by serial RFA. Focal escape endoscopic resection was used if Barrett tissue persisted despite RFA. Complete response, defined as all biopsies negative for intestinal metaplasia and neoplasia, was assessed during endoscopy with 4-quadrant biopsies every 1 cm of the original Barrett’s segment 2 months after the last treatment.

**Results:** Twenty-three patients underwent pre-RFA endoscopic resection for visible lesions; 16 patients had early cancer and 7 patients had HGIN. The worst residual histology pre-RFA (after any endoscopic resection) was as follows: HGIN (10), low-grade intraepithelial neoplasia (11), and intestinal metaplasia (3). Eradication of neoplasia and intestinal metaplasia was achieved in 95% and 88% of patients, and after additional escape endoscopic resection in 2 patients in 100% and 96%, respectively. Complications after RFA included melena (n = 1) and dysphagia (n = 1). After additional follow-up evaluation (median, 22 mo; interquartile range, 17.2 - 23.8 mo) no neoplasia recurred.

**Conclusions:** This European multicenter study showed that early neoplasia in Barrett’s esophagus can be treated effectively and safely with RFA, in combination with prior endoscopic resection of visible lesions.
3.9. Endoscopic management of early esophageal neoplasia: An emerging standard

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*J Gastrointest Surg* 2011;15:1728-35

**Introduction:** Endoscopic mucosal resection (EMR) and ablation technologies have markedly changed the treatment of early esophageal neoplasia. We analyzed treatment and outcomes of patients undergoing multimodal endoscopic treatment of early esophageal neoplasia at our institution.

**Methods:** Records of patients undergoing endoscopic treatment for esophageal low-grade intraepithelial neoplasia (LGIN, n=11), high-grade intraepithelial neoplasia (HGIN, n=24), or T1N0M0 neoplasia (n=10), presenting between 2007 and 2009, were reviewed. Outcomes included eradication of neoplasia/intestinal metaplasia, development of metachronous neoplasia, and progression to surgical resection.

**Results:** There were 45 patients, 96% male, with a mean age 67 years. The degree of neoplasia prior to intervention was intramucosal (8) or submucosal (2) carcinoma in 10, HGIN in 24, and LGIN in 11. Patients underwent a total of 166 procedures (median 3/patient, range 1–9). These included 120 radiofrequency ablation sessions, 38 EMRs, and 8 cryoablations. Mean follow-up was 21.3 months. Neoplasia and intestinal metaplasia were eradicated in 87.2% and 56.4% of patients, respectively, while 15.4% developed metachronous neoplasia. Three patients underwent esophagectomy. No patient developed unresectable disease or died.

**Conclusion:** Endoscopic treatment of early esophageal neoplasia is safe and effective in the short term. A minority of treated patients developed recurrent neoplasia, which is usually amenable to further endoscopic therapy. Complications are relatively minor and uncommon. Endoscopic therapy as the initial treatment for early esophageal neoplasia is an emerging standard of care.
3.10. Increased risk for persistent intestinal metaplasia in patients with Barrett’s esophagus and uncontrolled reflux exposure before radiofrequency ablation

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Gastroenterology 2012 May 8. [Epub ahead of print]

Background & Aims: Radiofrequency ablation (RFA) is a safe alternative to esophagectomy for patients with dysplastic Barrett’s esophagus (BE). Although some studies have indicated that RFA is effective at eradicating dysplasia, most have found that RFA is not as effective in eradicating intestinal metaplasia. We investigated whether uncontrolled reflux is associated with persistent intestinal metaplasia after RFA.

Methods: Thirty-seven patients with BE underwent RFA, high resolution manometry, and 24 hour impedance-pH testing; they received proton pump inhibitors twice daily. Patients returned every 2 months for repeat treatment or standard surveillance. Patients were classified as complete responders (CRs) if all intestinal metaplasia was eradicated in fewer than 3 ablation sessions. We analyzed clinical parameters to identify factors associated with a CR or incomplete response (ICR).

Results: Among the 37 patients, 22 had a CR and 15 had an ICR. Mann-Whitney U tests revealed that length of BE, size of hiatal hernia, and frequency of reflux, but not acid reflux, differed between CRs and ICRs. CRs had fewer weakly acidic than ICRs (29.5 vs 52; \( P < .05 \)) and total reflux events (33.5 vs 60; \( P < .05 \)), and a trend towards fewer weakly alkaline events (1.0 vs 5.0; \( P = .06 \)). No other clinical or manometric features differed between groups.

Conclusion: Uncontrolled, predominantly weakly acidic reflux despite twice daily proton pump inhibitor therapy before RFA increases the incidence of persistent intestinal metaplasia after ablation in patients with BE. Length of BE and size of a hiatal hernia were also associated with persistent intestinal metaplasia after RFA.
3.11. Effect of hiatal hernia size and columnar segment length on the success of radiofrequency ablation for Barrett’s esophagus: A single-center, phase II clinical trial


**Objective:** Hiatal hernia is common in patients with Barrett’s esophagus. We sought to evaluate the effect of hiatal hernia size and initial columnar segment length on the success of radiofrequency ablation of Barrett’s esophagus.

**Methods:** A phase II clinical trial was conducted aimed at evaluating the success of radiofrequency ablation in eradicating Barrett’s esophagus. Success was defined as complete replacement of the columnar lining with squamous mucosa and lack of intestinal metaplasia using light microscopy. Hiatal hernia size and columnar segment length were measured endoscopically.

**Results:** Sixty-seven patients were accrued to the protocol. In the 55 patients who completed radiofrequency ablation (43 successes, 12 failures), the mean hiatal hernia size was 3.3 cm (range, 0–10 cm), and the mean columnar segment length was 5.4 cm (range, 1–18 cm). The median length of the columnar segment was 3 cm in the successful cases and 8.5 cm in the failed cases (P = .002). Although the median hiatal hernia size was identical in the successful and failed cases (3 cm, P = .38), the median hiatal hernia size was 7 cm (P = .001) in the 6 patients who experienced nonhealing after the initial ablation. Patients who were successfully ablated but had larger hiatal hernias and longer columnar segment lengths required significantly more radiofrequency ablation sessions than those with smaller hernias and shorter segments (P = .003 and P = .007, respectively).

**Conclusion:** Patients with larger hiatal hernias and longer columnar segments are more likely to experience failure or nonhealing after radiofrequency ablation. These patients also require more radiofrequency ablation treatments to achieve successful eradication of Barrett’s esophagus.
3.12. Radiofrequency ablation associated to mucosal resection in the oesophagus: Experience in a single centre

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*Clin Res Hepatol Gastroenterol* 2012 Feb 21. [Epub ahead of print]

**Objective:** Endoscopic resection (EMR) and radiofrequency ablation (RFA) form part of the treatment of Barrett’s oesophagus (BO), dysplasia, superficial adenocarcinoma (OAC) associated with BO.

**Patients and methods:** Between June 2008 and April 2011, 34 patients underwent treatment with RFA (HALO system®), in a tertiary centre. For the study, patients were divided into two groups. Group 1 (16 patients of average 60 years old; 14 men, two women) received EMR and RFA. Group 2 (18 patients averaging 59 years age; 14 men, four women) received RFA without EMR in the year preceding the RFA.

**Results:** In group 1, high grade dysplasia (HGD) was eradicated in 12 cases (92%), low grade dysplasia (LGD) in three cases (100%). Complete response occurred in nine cases (56%), partial response in 100% of cases. Mean follow up was 15 months. In group 2, HGD was eradicated in one patient (100%), LGD in three patients (64%). A complete response was achieved in eight patients, partial response in four cases (77%). Mean follow up was 10 months. The complication rate for groups 1 and 2 was of 18% and 10% respectively. No complication prevented completion of treatment or continued monitoring. Recurrence was evaluated to 5% in both groups.

**Conclusion:** RFA associated with EMR is feasible, offering probably better results and a very important advantage: a more complete histology before followup. Our results show effective treatment of BO and associated dysplasia with a low rate of complication. Nevertheless, when new techniques of BO ablation are used, the need to obtain histology before treatment should not be forgotten.
3.13. The role of radiofrequency ablation in the management of Barrett’s esophagus

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Despite the presence of Barrett’s esophagus (BE) in 1% to 2% of the US population, its association with progression to esophageal adenocarcinoma, and a 500% increase in the incidence of esophageal adenocarcinoma (EAC) since the 1970s, the optimal management strategy for BE has not been clearly defined. When BE does progress, it seems to do so through a series of morphologic changes, from low-grade dysplasia (LGD), to high-grade dysplasia (HGD), and on to cancer. Given the 5-year survival rate of 13% for esophageal adenocarcinoma, 3 treatment strategies have been used for patients with BE and HGD: esophagectomy, intensive endoscopic surveillance, and mucosal eradication. Although usually curative, esophagectomy is associated with 3% to 5% mortality, 40% to 50% morbidity, and permanent loss of esophageal function. Meanwhile, intensive endoscopic surveillance is time and resource intensive, and still has a risk of disease progression to EAC as high as 19% at 1 year and 50% at 3 years. Given the shortcomings of the competing strategies, mucosal ablation is appealing as a potential treatment strategy for dysplastic BE. Among the multiple endoscopic ablative strategies that have been studied in recent years, radiofrequency ablation (RFA) has shown promise because 2 prospective, multicenter clinical trials have shown it to be effective, safe, and well-tolerated. Further data are accumulating to determine whether RFA is durable and cost-effective. This article reviews the evidence behind RFA to differentiate it from other management strategies in terms of efficacy, durability, safety, tolerability, and cost-effectiveness. The role of RFA in the management of BE is described, including endoscopic resection. Future directions are identified for research that will help to better define the role of RFA in the management of BE.
3.14. Quality of life following radiofrequency ablation of dysplastic Barrett’s esophagus


*Endoscopy* 2010;42:790-9

**Background & study aims:** The impact of the diagnosis and treatment of dysplastic Barrett’s esophagus on quality of life (QoL) is poorly understood. This study assessed the influence of dysplastic Barrett’s esophagus on QoL and evaluated whether endoscopic treatment of dysplastic Barrett’s esophagus with radiofrequency ablation (RFA) improves QoL.

**Patients & methods:** We analyzed changes in QoL in the AIM Dysplasia Trial, a multicenter study of patients with dysplastic Barrett’s esophagus who were randomly allocated to RFA therapy or a sham intervention. We developed a 10-item questionnaire to assess the influence of dysplastic Barrett’s esophagus on QoL. The questionnaire was completed by patients at baseline and 12 months.

**Results:** 127 patients were randomized to RFA (n = 84) or sham (n = 43). At baseline, most patients reported worry about esophageal cancer (71% RFA, 85% sham) and esophagectomy (61% RFA, 68% sham). Patients also reported depression, impaired QoL, worry, stress, and dissatisfaction with the condition of their esophagus. Of those randomized, 117 patients completed the study to the 12-month end point. Compared with the sham group, patients treated with RFA had significantly less worry about esophageal cancer (P = 0.003) and esophagectomy (P = 0.009). They also had significantly reduced depression (P = 0.02), general worry about the condition of their esophagus (P ≤ 0.001), impact on daily QoL (P = 0.009), stress (P = 0.03), dissatisfaction with the condition of their esophagus (P ≤ 0.001), and impact on work and family life (P = 0.02).

**Conclusions:** Inclusion in the treatment group of this randomized, sham-controlled trial of RFA was associated with improvement in disease-specific health-related quality of life. This improvement appears secondary to a perceived decrease in the risk of cancer.
3.15. **Radiofrequency ablation is effective for the treatment of high-grade dysplasia in Barrett’s esophagus after failed photodynamic therapy**


*Endoscopy* 2011;43:627–30

Endoscopic radiofrequency ablation (RFA) is an effective treatment for high-grade dysplasia in Barrett’s esophagus in ablation-naïve patients, but no studies have evaluated its use in patients in whom ablative therapy has previously failed. We describe 14 patients with residual high-grade dysplasia following aminolevulinic acid or Photofrin (porfimer sodium) photodynamic therapy (PDT). An overall complete reversal of dysplasia was achieved in 86% with a combination of RFA and rescue endoscopic mucosal resection. The median total follow-up is 19 months. The rate of strictures was 7% (1/14) and there was a low rate of buried glands (0.5% follow-up biopsies). These data suggest RFA is both safe and effective for eradication of high-grade dysplasia in patients in whom PDT has failed.
3.16. Biopsy depth after radiofrequency ablation of dysplastic Barrett’s esophagus


Gastrointest Endosc 2010;72:490-6

**Background:** After endoscopic radiofrequency ablation (RFA) of dysplastic Barrett’s esophagus (BE), endoscopic biopsy samples are obtained to assess response to therapy. Whether these biopsies are of adequate depth to assess efficacy is unknown.

**Objective:** To compare the depth of endoscopic biopsy samples after RFA with those of untreated controls and to determine the prevalence of subepithelial structures in endoscopic biopsy fragments.

**Design:** Secondary analysis of the AIM Dysplasia Trial, a multicenter, randomized, sham-controlled study.

**Setting:** Nineteen treatment centers.

**Patients:** Subjects with dysplastic BE, either status post RFA or ablation naïve (sham).

**Main outcome measurements:** The proportion of biopsy samples demonstrating subepithelium, stratified by tissue type (columnar vs squamous) in sham- and RFA-treated subjects.

**Results:** A total of 5648 biopsy fragments were analyzed from 113 subjects (78 RFA, 35 sham; mean 50.0 fragments per subject). Most fragments (4653, 82.4%) contained subepithelium. Squamous biopsy samples from RFA and sham subjects demonstrated subepithelium at similar rates (78.4% vs 79.1%, respectively, *P* = not significant [NS]). Columnar biopsy samples from RFA and sham subjects also included subepithelium at similar rates (99.0% vs 98.8%, respectively, *P* = NS). Regardless of treatment assignment, more columnar than squamous biopsy samples demonstrated subepithelium (98.8% vs 78.5%, *P* < .001).

**Limitations:** Biopsy samples were not individually mounted.

**Conclusions:** In both squamous and columnar tissue, endoscopic biopsy samples after RFA were as likely to demonstrate subepithelium as untreated controls. Almost 80% of all biopsy samples were adequate to evaluate for subsquamous intestinal metaplasia. The primary determinant of biopsy depth is the type of epithelium that underwent biopsy, with squamous less likely to yield subepithelium than columnar. Biopsy samples after RFA appear to be of adequate depth to assess response to therapy. (Clinical trial registration number NCT00282672.)
3.17. Concomitant endoscopic radiofrequency ablation and laparoscopic reflux operative results in more effective and efficient treatment of Barrett esophagus

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*JACS* 2011;213:486-92

**Background:** Barrett esophagus (BE) caused by gastroesophageal reflux disease can lead to esophageal cancer. The success of endoscopic treatments with BE eradication depends on esophageal anatomy and post-treatment acid exposure.

**Study design:** Between January 2008 and December 2009, 10 patients were selected for combination treatment of BE using laparoscopic anti-reflux surgery and endoscopic radiofrequency ablation. Retrospective review of preoperative, procedural, and postoperative data was performed.

**Results:** Seven study patients had a pathologic diagnosis of nondysplastic BE and 3 patients had a diagnosis of low-grade dysplasia. Average length of BE lesions was $6.4 \pm 4.8$ cm. Procedure time averaged $154.4 \pm 46.4$ minutes. At the time of surgery, the mean number of ablations performed was $4.39 \pm 1.99$. Six patients were noted to have major hiatal hernias requiring reduction. Five patients (80%) had 100% resolution of their BE at their first postoperative endoscopy. The remaining 3 patients had a $\geq 50\%$ resolution and underwent subsequent endoscopic ablation. Symptomatic results revealed that 4 patients had substantial dysphagia to solids and other symptoms were minimal. Two patients were noted to have complications related to the ablative treatments. One stricture and 1 perforation were observed.

**Conclusions:** Endoscopic radiofrequency ablation of BE at the time of laparoscopic fundoplication is feasible and can effectively treat BE lesions. A single combined treatment can result in fewer overall procedures performed to obtain BE eradication.
3.18. The cost-effectiveness of radiofrequency ablation for Barrett’s esophagus

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*Gastroenterology* 2012 May 9 [Epub ahead of print]

**Background & Aims:** Radiofrequency ablation (RFA) reduces the risk of esophageal adenocarcinoma (EAC) in patients with Barrett’s esophagus (BE) with high grade dysplasia (HGD), but its effects in patients without dysplasia are debatable. We analyzed the effectiveness and cost-effectiveness of RFA for the management of BE.

**Methods:** We constructed a decision analytic Markov model. We conducted separate analyses of hypothetical cohorts of patients with BE with dysplasia (HGD or low-grade [LGD]) and without dysplasia. In the analysis of the group with HGD, we compared results of the initial RFA to endoscopic surveillance with surgery when cancer was detected. In analyzing the group with LGD or no dysplasia, we compared 3 strategies: endoscopic surveillance with surgery when cancer detected (S1), endoscopic surveillance with RFA when HGD detected (S2), and initial RFA followed by endoscopic surveillance (S3).

**Results:** Among patients with HGD, initial RFA was more effective and less costly than endoscopic surveillance. Among patients with LGD, when S3 was compared with S2, the incremental cost-effectiveness ratio (ICER) was $18,231/quality-adjusted life year (QALY), assuming an annual rate of progression rate from LGD to EAC of 0.5%/year. For patients without dysplasia, S2 was more effective and less costly than S1. In a comparison of S3 with S2, the ICERs were $205,500, $124,796, and $118,338/QALY using annual rates of progression of no dysplasia to EAC of 0.12%, 0.33%, or 0.5% per year, respectively.

**Conclusions:** Using updated data, initial RFA might not be cost-effective for patients with BE without dysplasia, within the range of plausible rates of progression of BE to EAC, and be prohibitively expensive, from a policy perspective. RFA might be cost effective for confirmed and stable LGD. Initial RFA is more effective and less costly than endoscopic surveillance in HGD.
3.19. The case for endoscopic treatment of non-dysplastic and low-grade dysplastic Barrett’s esophagus


*Dig Dis Sci* 2010;55:1918-31

Non-dysplastic mucosa (ND-) in Barrett’s esophagus (BE) shows clonal molecular aberrations, loss of cell cycle control, and other features of “neoplasia.” These changes occur prior to morphologic expression of neoplasia (dysplasia). Morphologic evaluation of dysplasia is fraught with error, and, as a result, often leads to false-negative and false-positive diagnoses. Early "crypt dysplasia" is difficult to detect, and is often missed in routine biopsy specimens. Some studies show substantial progression rates of low-grade dysplasia (LGD), and crypt dysplasia, to esophageal adenocarcinoma (EAC). Dysplasia, even when fully developed, may, in certain circumstances, be difficult to differentiate from non-dysplastic (regenerating) BE. Radiofrequency ablation (RFA) is a safe and effective method for removing mucosa at risk of cancer. Given the difficulties of dysplasia assessment in mucosal biopsies, and the molecular characteristics of ND-BE, this technique should be considered for treatment of all BE patients, including those with ND or LGD. Post-ablation neo-squamous epithelium reveals no molecular abnormalities, and is biologically stable. Given that prospective randomized controlled trials of ablative therapy for ND-BE aiming at reducing EAC incidence and mortality are unlikely to be completed in the near future, endoscopic ablation is a valid management option. The success of RFA in achieving safe, uniform, reliable, and predictable elimination of BE allows surgeons to combine fundoplication with RFA. Currently, there is no type of treatment for dysplastic or non-dysplastic BE that achieves a complete response in 100% of patients, eliminates all risk of developing cancer, results in zero adverse events, is less expensive in terms of absolute costs than surveillance, is durable for 20+ years, or eliminates the need for surveillance. Regardless, RFA shows established safety, efficacy, durability, and cost-effective profiles that should be considered in the management of patients with non-dysplastic or low-grade dysplastic BE.
3.20. Endoscopic ablation therapy for Barrett’s esophagus

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*Minerva Gastroenterol Dietol* 2010;56:405-20

Barrett’s esophagus (BE) is an important risk factor for esophageal carcinoma and its incidence is rising. Amongst the various available endoscopic ablative therapies, radiofrequency ablation (RFA) is currently regarded as the most promising one, since RFA achieves high eradication rates of dysplasia and intestinal metaplasia with minimal complications. Patients with BE are advised to undergo regular endoscopic surveillance for dysplasia or cancer and endoscopy with four quadrant biopsy sampling at intervals of 1-2 cm of the entire length of BE remains the current standard for the detection of dysplasia or cancer. The management of BE depends on the histology of the biopsy specimens obtained during endoscopy, which includes non-dysplastic BE (ND-BE), low grade dysplasia, high grade dysplasia and adenocarcinoma. However, histological evaluation of dysplasia is fraught with error because of inter-observer variability even amongst expert gastrointestinal pathologists, and as a result, it often leads to false-negative or false-positive diagnoses. Non-dysplastic mucosa in BE shows clonal molecular aberrations, loss of cell cycle control, and other features of “neoplasia”. These changes occur prior to morphologic expression of neoplasia (dysplasia). Given the difficulties of dysplasia assessment in mucosal biopsies, the molecular characteristics of ND-BE and LGD, and safe and effective profiles of RFA, this technique should be considered as a treatment option for the whole spectrum of BE patients.
3.21. Routine polypectomy for colorectal polyps and ablation for Barrett’s esophagus are intellectually the same

HB El-Serag, DY Graham

Gastroenterology 2011;140:386-8

Recently, there have been several reports about the safety and efficacy of endoscopic ablation of high-grade dysplasia and low grade dysplasia, as well as patients without dysplasia; it has been shown to be efficacious and safe. If Barrett’s ablation therapy is safe and efficacious, we predict it will and possibly should become a routine response to the discovery of Barrett’s esophagus, just as polypectomy is to the discovery of a colorectal polyp.
3.22. Detection of intestinal metaplasia after successful eradication of Barrett’s esophagus with radiofrequency ablation

Vaccaro BJ, Gonzalez S, Poneros JM, Stevens PD, Capiak KM, Lightdale CJ, Abrams JA


**Background:** Radiofrequency ablation (RFA) is an effective means of eradicating Barrett’s esophagus (BE), both with and without associated dysplasia. Several studies have documented high initial success rates with RFA. However, there is limited data on IM detection rates after eradication.

**Aims:** To determine the rate of detection of intestinal metaplasia (IM) after successful eradication of Barrett’s esophagus.

**Methods:** BE patients with and without dysplasia who had undergone RFA were retrospectively identified. Only those who had complete eradication as documented on the initial post-ablation endoscopy, and had minimum two surveillance endoscopies, were included in the analyses. Clinical, demographic, and endoscopic data were collected. Cumulative incidence of IM detection was calculated by the Kaplan–Meier method.

**Results:** Forty-seven patients underwent RFA and had complete eradication of Barrett’s epithelium. The majority of patients were male (76.6%), and the mean age was 64.2 years. The cumulative incidence of newly detected IM at 1 year was 25.9% (95% CI 15.1–42.1%). Dysplasia was detected at the time of recurrence in four patients, and all cases were detected at the GE junction in the absence of visible BE. Patients with recurrent IM had longer baseline segments of BE (median, 4 cm vs. 2 cm, p = 0.03).

**Conclusions:** The rate of detection of new IM is high in patients who have undergone successful eradication of BE by RFA. Additionally, dysplasia can recur at the GE junction in the absence of visible BE. Future studies are warranted to identify those patients at increased risk for the development of recurrent intestinal metaplasia.
3.23. Radiofrequency ablation for nondysplastic Barrett’s esophagus: Treat or not to treat?

Fernandez-Esparrach G, Panes J

*Gastroenterology* 2011;140:2130-2

In summary, the study by Fleischer et al shows that complete eradication of IM by using circumferential and focal ablation techniques with radiofrequency energy is technically feasible and well-tolerated by patients with nondysplastic Barrett’s esophagus and has long-term efficacy. However, it is premature to advocate ablation for every patient with nondysplastic IM outside a clinical trial or patient registry protocol. As suggested by the authors, an ideal management paradigm for a nondysplastic population in the future might be to risk stratify patients by assaying for genotypes associated with propensity for neoplastic progression, and then to eradicate the nondysplastic Barrett’s esophagus in those patients at highest risk, with surveillance or no action in those patients at lower or null risk.
3.24. Endoscopic resection and ablation versus esophagectomy for high-grade dysplasia and intramucosal adenocarcinoma

Jorg Zehetner, Steven R. DeMeester, Jeffrey A. Hagen, Shahin Ayazi, Florian Augustin, John C. Lipham, Tom R. DeMeester

*J Thorac Cardiovasc Surg* 2011;141:39-47

**Background:** Esophagectomy has been the traditional therapy for high-grade dysplasia and intramucosal adenocarcinoma. New endoscopic approaches allow treatment of these lesions with esophageal preservation. The aim of this study was to compare the outcome of endoscopic therapy with esophagectomy for high-grade dysplasia and intramucosal cancer.

**Methods:** A retrospective review was performed of all patients treated for high-grade dysplasia or intramucosal adenocarcinoma from 2001 to April 2010.

**Results:** Endoscopic therapy was performed in 40 patients (high-grade dysplasia = 22, intramucosal cancer = 18) and esophagectomy in 61 patients (high-grade dysplasia = 13, intramucosal cancer = 48). Endotherapy consisted of 102 endoscopic resections and 79 mucosal ablations (median 3 interventions per patient). In the endotherapy group, intramucosal cancer was completely resected in all patients. At last assessment, 10 patients have been converted to intestinal metaplasia without dysplasia and 21 to no residual intestinal metaplasia. Five patients have follow-up biopsy procedures pending after recent ablation, and esophagectomy was performed in 3 patients for failed endotherapy. A laparoscopic Nissen fundoplication has been performed in 8 patients after eradication of intestinal metaplasia. Esophagectomy resected the mucosal disease with negative margins in all patients. Compared with esophagectomy, endotherapy was associated with significantly lower morbidity (39% vs 0; *P* < .0001) and similar survival (94% at 3 years in both groups; median follow-up 34 months after esophagectomy vs 17 months after endotherapy; *P* = .0026).

**Conclusions:** Endoscopic therapy for high-grade dysplasia or intramucosal cancer has lower morbidity than an esophagectomy and similar survival during short-term follow-up, but required multiple procedures in most patients. Both therapies are appropriate options, but preservation of the esophagus allows the option of a fundoplication for reflux control, perhaps further improving long-term quality of life.
3.25. Endoscopic radiofrequency ablation combined with endoscopic resection for early neoplasia in Barrett’s esophagus longer than 10 cm

Herrero LA, van Vilsteren FG, Pouw RE, Ten Kate FJ, Visser M, Seldenrijk CA, van Berge Henegouwen MI, Fockens P, Weusten BL, Bergman JJ.

*Gastrointest Endosc* 2011;73,682-90

**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.
3.26. Effects of Nissen fundoplication on endoscopic endoluminal radiofrequency ablation of Barrett’s esophagus

O’Connell K, Velanovich V

Surg Endosc 2011;25:830-4

Background: Endoscopic endoluminal radiofrequency ablation is achieving increasing acceptance as a mode of eliminating Barrett’s metaplasia and, thus, reducing the risk of developing esophageal adenocarcinoma. It is believed that reducing exposure of the esophageal epithelium to acid is essential to achieve long-term ablation of Barrett’s esophagus. However, it is unclear whether use of proton pump inhibitors or antireflux operations are more effective to accomplish this goal.

Methods: All patients who underwent endoscopic endoluminal radiofrequency ablation with the BARRx device (BARRx Medical, Sunnyvale, CA) were reviewed for date of initial ablation, length of Barrett’s epithelium, presence or performance of Nissen fundoplication, all follow-up endoscopy and treatment, and post treatment biopsy results. Patients were categorized by presence of Nissen fundoplication and presence of Barrett’s metaplasia or dysplasia by biopsy at least 12 months following ablation and at last endoscopic follow-up. Data were analyzed by Fisher’s exact test and Mann–Whitney U-test.

Results: Of 77 patients ablated, 47 had documented endoscopic follow-up at 12 months or longer following the ablation. Of these, 19 patients had Nissen fundoplication before, at the same time, or after ablation. Median length of Barrett’s epithelium, with interquartile range (IQR), was 3 (2–12) cm in patients with fundoplication compared with 3 (2–7) cm without fundoplication (P = NS). Median follow-up was 15 (12–24) months in fundoplication patients compared with 12.5 (12–17) months without (P = NS). One of 19 patients with fundoplication had persistent or recurrent Barrett’s epithelium, compared with 7 of 28 without fundoplication (P = 0.03). Of patients without fundoplication, those who had persistent or recurrent Barrett’s had median Barrett’s length of 10 cm (6–12 cm) compared with 3 cm (2–5 cm) in patients who had ablated Barrett’s (P = 0.03). Follow-up length was similar in those with ablated epithelium, 15 months (12–19 months), compared with those with persistent or recurrent Barrett’s, 12 months (12–13 months) (P = NS).

Conclusions: Patients who had fundoplication in conjunction with endoluminal radiofrequency ablation were more likely to achieve durable ablation compared with patients who were treated with proton pump inhibitor therapy. It appears that patients with long-segment Barrett’s esophagus are at higher risk for persistent or recurrent Barrett’s metaplasia. Consideration should be given for an antireflux operation in patients with long-segment Barrett’s esophagus and planned endoluminal radiofrequency ablation.
3.27. A UK-based cost-utility analysis of radiofrequency ablation or oesophagectomy for the management of high-grade dysplasia in Barrett’s esophagus

Boger PC, Turner D, Roderick P, Patel P

*Aliment Pharmacol Ther* 2010;32:1332-42

**Background:** In the UK, oesophagectomy is the current recommendation for patients with persistent high-grade dysplasia in Barrett’s oesophagus. Radiofrequency ablation is an alternative new technology with promising early trial results.

**Aim:** To undertake a cost–utility analysis comparing these two strategies.

**Methods:** We constructed a Markov model to simulate the natural history of a cohort of patients with high-grade dysplasia in Barrett’s oesophagus undergoing one of two treatment options: (i) oesophagectomy or (ii) radiofrequency ablation followed by endoscopic surveillance with oesophagectomy for high-grade dysplasia recurrence or persistence.

**Results:** In the base case analysis, radiofrequency ablation dominated as it generated 0.4 extra quality of life years at a cost saving of £1902. For oesophagectomy to be the most cost-effective option, it required a radiofrequency ablation treatment failure rate (high-grade dysplasia persistence or progression to cancer) of >44%, or an annual risk of high-grade dysplasia recurrence or progression to cancer in the ablated oesophagus of >15% per annum. There was an 85% probability that radiofrequency ablation remained cost-effective at the NICE willingness to pay threshold range of £20 000–30 000.

**Conclusion:** Radiofrequency ablation is likely to be a cost-effective option for high-grade dysplasia in Barrett’s oesophagus in the UK.
3.28. Blitzkrieg for Barrett’s esophagus containing early neoplasia

G Triadafilopoulos

*Clin Gastroenterol Hepatol* 2010;8:7-9

“Endoscopic” blitzkrieg, the multicenter European effort by Pouw RE et al., described in the current issue of *Clinical Gastroenterology and Hepatology*, sought to assess the safety and efficacy of radiofrequency ablation (RFA) in conjunction with baseline endoscopic resection (ER) for high-grade intraepithelial neoplasia (HGIN) and early cancer (EC) in patients with Barrett’s esophagus (BE). The authors used ER and RFA to eradicate not only the neoplasia manifested as a visible lesion(s) (the *Schwerpunkt*) but also -and very importantly - the accompanying field of residual neoplasia and metaplasia in all cases. In this way, the most active and biologically dangerous areas of HGIN and EC were resected and histologically assessed *en bloc*, while the remaining areas of enemy soil (aka metaplasia) carrying the potential of future assault on the patient were then carpet-bombed into oblivion. More plainly stated, visible (nodular or irregular) early neoplastic lesions were endoscopically resected, followed by serial (circumferential or focal) RFA sessions until complete eradication of visible Barrett’s tissue was achieved (reported by the authors as a complete histological response for IM (CR-IM)).
3.29. When to consider endoscopic ablation therapy for Barrett’s esophagus

Shaheen NJ, Frantz DJ

*Curr Opin Gastroenterol* 2010;26:361-6

**Purpose of review:** To evaluate timing and patient selection for endoscopic ablative therapy in Barrett’s esophagus.

**Recent findings:** There has been an explosion in the literature describing ablative therapy in Barrett’s esophagus. Most recent data describe radiofrequency ablation (RFA), but other data pertain to photodynamic therapy (PDT) and other modalities. Most studies are cohort or case series. Reversion to squamous epithelium is the most common primary outcome. Cancer incidence data are scarce. RFA appears well tolerated. The main side-effect is chest pain, which can be managed with oral analgesics. Stricture occurs in 0–8% and is amenable to endoscopic dilatation. Infrequent side-effects include bleeding and perforation. Complete reversion to squamous epithelium occurs in more than 90% of nondysplastic and low-grade dysplasia and more than 80% in high-grade dysplasia patients, and the treatment appears durable for at least 2–5 years of available follow-up. Treatment of low-grade or nondysplastic disease may be cost-effective. PDT data suggest that all-cause mortality is similar to surgery for dysplastic Barrett’s esophagus. The stricture rate appears higher, and rates of complete reversion to neosquamous epithelium are lower than that of RFA, although definitive comparisons are lacking.

**Summary:** The excellent efficacy, side-effect profile, and cost-effectiveness appear to make RFA the intervention of choice in cases of high-grade dysplasia. RFA for low-grade dysplasia may be of value in young patients and/or those with long segment or multifocal disease. Treatment of nondysplastic Barrett’s esophagus is of uncertain value. PDT appears to have a higher stricture rate and to be more expensive than RFA.
3.30. Does ablative therapy for Barrett’s esophagus affect the depth of subsequent esophageal biopsy as compared with controls?

Overholt BF, Dean PJ, Galanko JA, Lightdale CJ

*J Clin Gastroenterol* 2010;44:676-81

**Background:** Photodynamic therapy (PDT) and radiofrequency ablation (RFA) are associated with high rates of complete eradication of Barrett esophagus (BE). However, if ablation were to induce fibrosis in the regenerated squamous epithelium, then postablation biopsies may not penetrate deeply enough to detect sub-squamous intestinal metaplasia (SSIM) and, therefore, complete response rates could be over-estimated.

**Goals:** To assess the depth of esophageal biopsies from the squamous epithelium of ablation-naive controls and from the neosquamous epithelium of post-PDT and post-RFA patients to determine if prior ablation results in a reduced proportion of biopsies containing lamina propria (LP) as compared with controls.

**Study:** Review of archived esophageal specimens from a prospective multicenter cohort study (post-RFA) and 2 retrospective consecutive case series (ablation-naive controls, post-PDT).

**Setting:** Eight US centers and 1 US gastrointestinal pathology laboratory.

**Patients:** Ablation-naive controls with GERD, dyspepsia, and/or BE. Post-PDT and post-RFA BE patients with biopsies more than 6 months after achieving complete eradication of BE.

**Interventions:** Review of endoscopic biopsies from ablation-naive controls, post-PDT patients, and post-RFA patients.

**Main outcome measurements:** One GI pathology lab processed all tissue and slides. One expert GI pathologist, blinded to cohort, graded the depth of each esophageal specimen as: partial epithelium, full epithelium, LP, muscularis mucosae, or submucosa. Each specimen was also evaluated for SSIM.

**Results:** There were 82 patients [ablation-naive (12), post-PDT (10), post-RFA (60)] with 899 biopsy specimens. The proportion of specimens containing “LP or deeper” was similar between groups: ablation-naive (88%), post-PDT (88%), post-RFA (91%) (P>0.05). No SSIM was detected in any group.

**Conclusions:** There is no difference in esophageal biopsy depth between ablation-naive squamous epithelium and post-PDT/post- RFA neo-squamous epithelium, thus refuting the concern of ablation-induced mucosal resistance to procurement of adequate biopsy specimens. Most biopsies (88% to 91%) from both ablation cohorts were deep enough to detect SSIM, in that they included “LP or deeper.”
3.31. A systematic review of the evidence for radiofrequency ablation for Barrett’s esophagus

Semlitsch T, Jeitler K, Schoefl R, Horvath K, Pignitter N, Harnoncourt F, Siebenhofer A

*Surg Endosc* 2010;24:2935-43

**Background:** Radiofrequency ablation with the HALO system is a new option for the treatment of patients with Barrett’s esophagus. This systematic review summarizes the results of all relevant publications on this topic to answer patient-relevant clinical questions and to evaluate the potential benefit and harm of this new therapy.

**Methods:** A systematic literature search of MEDLINE and CENTRAL up to May 2009 was performed. To identify the relevant literature, references were evaluated by two reviewers independently. The inclusion criteria for the review required that studies investigated patients with Barrett’s esophagus, used radiofrequency ablation as the intervention, and had a minimum follow-up period of 12 months.

**Results:** A total of nine relevant observational studies (involving 429 patients) were identified. Complete eradication of Barrett’s esophagus dysplasia and metaplasia was achieved respectively for 71–100% and for 46–100% of the patients. Only six cases of stenosis and one case of buried intestinal metaplasia were reported among all the patients. Only a few mild adverse events were reported.

**Conclusions:** Based on the evidence of observational studies, the summary of the current data suggests that radiofrequency ablation with the HALO system could be a promising method associated with a low complication rate, low risk of stricture formations, and a minor probability of buried glands. To evaluate the potential benefit at a higher level of evidence, randomized controlled trials (RCTs) involving a direct comparison with other more established endoscopic methods such as photodynamic therapy are necessary.
3.32. Endoscopic therapy using radiofrequency ablation for esophageal dysplasia and carcinoma in Barrett’s esophagus

Frederike G.I. Van Vilsteren, Jacques J.G.H.M. Bergman

_Gastrointest Endoscopy Clin N Am_ 2010;20:55–74

RFA is a novel and promising treatment modality in the treatment of BE with HGD or mucosal cancer, and is not associated with stenosis or buried glandular mucosa, which are known side effects from other ablation techniques such as PDT and APC. The combination of ER followed by RFA for removal of the residual flat BE is a powerful management strategy. Several clinical trials have shown that RFA is safe and highly effective for the removal of dysplasia and complete conversion of the BE into normal-appearing squamous esophagus. Although no long-term results are available yet, RFA should be regarded as the treatment of choice in patients with early neoplasia in BE with or without a prior ER. Future research will focus on the natural course of dysplastic and nondysplastic BE, biomarkers predicting disease progression, and cost-effectiveness plus quality of life to assess if RFA treatment is justified for patients with nondysplastic BE.
3.33. Properties of the neosquamous epithelium after radiofrequency ablation of Barrett’s esophagus containing neoplasia

RE Pouw, JJ Gondrie, AM Rygiel, CM. Sondermeijer, FJ ten Kate, RO Odze, M Vieth, KK Krishnadath, JJ Bergman

*Am J Gastroenterol* 2009;104:1366-73

**Objectives:** Endoscopic radiofrequency ablation (RFA) eradicates intestinal metaplasia and intraepithelial neoplasia associated with Barrett’s esophagus (BE), restoring an endoscopically normal neosquamous epithelium (NSE). We evaluated the post-RFA NSE for genetic abnormalities and buried glandular mucosa.

**Methods:** Eligible patients underwent RFA for BE containing early cancer and/or high-grade intraepithelial neoplasia with subsequent complete histological reversion to normal NSE. At baseline, the BE was sampled by brush cytology and biopsies. At least 2 months after RFA, the NSE was sampled by brush cytology, keyhole biopsies, and endoscopic resection. The untreated squamous epithelium was biopsied as a control. The baseline BE and post-RFA NSE were evaluated for immunohistochemical expression of Ki-67 and p53, and genetic abnormalities (DNA–fluorescent in situ hybridization: chromosome 1 and 9, p16 and p53). In addition, biopsy depth was compared for biopsies from the NSE and untreated squamous epithelium. The presence of buried glandular mucosa in NSE was assessed with primary and keyhole biopsy, and endoscopic resection.

**Results:** All pretreatment specimens from all 22 patients showed abnormalities on immunohistochemical staining and fluorescent in situ hybridization, whereas all post-RFA NSE specimens were normal. All the post-RFA biopsies from the NSE contained full epithelia, whereas 37% contained lamina propria, a finding no different from biopsies from untreated squamous epithelium (36% lamina propria). Deeper keyhole biopsies contained lamina propria in 51%. All endoscopic resection specimens contained submucosa, whereas no biopsy or endoscopic resection specimen contained buried glandular mucosa.

**Conclusions:** Rigorous evaluation of the post-RFA NSE in patients who, at baseline, had BE containing early cancer high-grade intraepithelial neoplasia, showed neither persistent genetic abnormalities nor buried glandular mucosa.
3.34. Endoscopic versus surgical therapy for early cancer in Barrett’s esophagus: A decision analysis

Heiko Pohl, Amnon Sonnenberg, Sebastian Strobel, Alexander Eckardt, Thomas Roesch

Gastrointest Endosc 2009;70:623-31

Background: Esophagectomy for early esophageal adenocarcinoma is associated with increased operative mortality and morbidity, but possibly a decreased recurrence rate compared with endoscopic therapy when using EMR and radiofrequency ablation.

Objective: To compare the cost-effectiveness of esophagectomy and endoscopic therapy in the treatment of early esophageal adenocarcinoma.

Design: Decision analysis model.

Main outcome measurements: Incremental cost-effectiveness ratio.

Results: During the 5-year study period, endoscopic therapy cost $17,000.00 and yielded 4.88 quality-adjusted life years, compared with $28,000.00 and 4.59, respectively, for esophagectomy. Varying the recurrence rates of cancer or Barrett’s esophagus metaplasia after endoscopic therapy did not change the overall outcome. The sensitivity analysis demonstrated, however, that the outcome depended on the rate of lymph node involvement and operative mortality. Under the best of circumstances in favor of esophagectomy, such as 2% operative mortality, no reduced quality of life after esophagectomy, and a low 5-year survival rate after recurrence of endoscopic ablation, the risk of positive lymph nodes still needed to exceed 25% before esophagectomy became the preferred treatment option. This threshold is twice as high as the values reported for early submucosal cancer invasion.

Limitations: Limited data are available about the long-term outcome of EMR and radiofrequency ablation.

Conclusions: Endoscopic therapy for early Barrett’s esophagus adenocarcinoma is more effective and less expensive than esophagectomy. Even in early esophageal adenocarcinoma with submucosal invasion, endoscopic therapy is a cost-effective alternative to esophagectomy, especially in patients with a high operative risk.
3.35. An economic analysis of endoscopic ablative therapy for management of nondysplastic Barrett’s esophagus


*Endoscopy* 2009;41:400-8

**Background & aims:** Advances have occurred in the development of safe and effective ablative therapies for Barrett’s esophagus. The aim of the current study was to perform an economic analysis evaluating the cost-effectiveness of endoscopic ablation of nondysplastic Barrett’s esophagus.

**Methods:** A Markov model evaluated three competing strategies in a hypothetical 50-year-old cohort with nondysplastic Barrett’s esophagus from a societal perspective. Strategy I – natural history of Barrett’s disease (without surveillance); Strategy II – surveillance performed according to the American College of Gastroenterology practice guidelines; Strategy III – endoscopic ablative therapy. The model was biased against ablative therapy with a conservative estimate of complete response and continued standard surveillance even after complete ablation. All potential complications were accounted for, and an incomplete histological response after ablation was presumed to have the same risk of progression as untreated Barrett’s. Transitional probabilities, discounted cost, and utility values to estimate quality-adjusted life-years (QALY) were obtained from published information. Direct costs were used in our analysis.

**Results:** In baseline analysis, the ablative strategy yielded the highest QALY and was more cost-effective than endoscopic surveillance. In a Monte Carlo analysis, the relative risk of developing cancer in the strategy based on endoscopic ablation was decreased compared with the other strategies. In threshold analysis, the critical determinants of cost-effectiveness of the ablative strategy were rate of complete response to ablation, total cost of ablation, and risk of progression to dysplasia.

**Conclusions:** Within the limits of the model, ablation for nondysplastic Barrett’s esophagus is more cost-effective than endoscopic surveillance. Clinical trials of ablative therapy in nondysplastic Barrett’s esophagus are needed to establish its effectiveness in reducing cancer risk.
3.36. A cost-utility analysis of ablative therapy for Barrett’s esophagus

John M Inadomi, Ma Somsouk, Ryan D Madanick, Jennifer P Thomas, Nicholas J Shaheen

*Gastroenterology* 2009;136:2101-14

**Background & aims:** Recommendations for patients with Barrett’s esophagus (BE) include endoscopic surveillance with esophagectomy for early-stage cancer, although new technologies to ablate dysplasia and metaplasia are available. This study compares the cost-utility of ablation with that of endoscopic surveillance strategies.

**Methods:** A decision analysis model was created to examine a population of patients with BE (mean age 50), with separate analyses for patients with no dysplasia, low-grade dysplasia (LGD), or high-grade dysplasia (HGD). Strategies compared were: no endoscopic surveillance; endoscopic surveillance with ablation for incident dysplasia; immediate ablation followed by endoscopic surveillance in all patients or limited to patients in whom metaplasia persisted, and esophagectomy. Ablation modalities modeled included radiofrequency, argon plasma coagulation, multipolar electrocoagulation and photodynamic therapy.

**Results:** Endoscopic ablation for patients with HGD could increase life expectancy by 3 quality adjusted years at an incremental cost of < $6,000, compared with no intervention. Patients with LGD or no dysplasia can also be optimally managed with ablation, but continued surveillance after eradication of metaplasia is expensive. If ablation permanently eradicates at least 28% of LGD or 40% of non-dysplastic metaplasias, ablation would be preferred to surveillance.

**Conclusions:** Endoscopic ablation could be the preferred strategy for managing patients with BE with HGD. Ablation might also be preferred in subjects with LGD or no dysplasia, but the cost-effectiveness depends on the long-term effectiveness of ablation and whether surveillance endoscopy can be discontinued following successful ablation. As further post-ablation data become available, the optimal management strategy will be clarified.
3.37. Radiofrequency ablation for Barrett’s esophagus and low-grade dysplasia in combination with an antireflux procedure: A new paradigm

dos Santos RS, Bizekis C, Ebright M, DeSimone M, Daly BD, Fernando HC

*J Thorac Cardiovasc Surg* 2010;139:713-6

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

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

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

**Conclusions:** Radiofrequency ablation performed either before or after an antireflux procedure is safe. This approach is effective for reducing or eliminating metaplasia and dysplasia. Long-term studies will be necessary to determine whether this approach can provide durable control of both reflux and Barrett’s esophagus.
3.38. Radiofrequency ablation of Barrett’s esophagus

Thomas J Watson

*J Gastrointest Surg* 2010;14:S88-S93

**Introduction:** Barrett’s esophagus (BE) is known to be due to chronic gastroesophageal reflux disease and is a precursor of esophageal adenocarcinoma.

**Discussion:** The ability to eliminate BE is appealing, given the neoplastic potential of this condition and the continued increase in incidence of adenocarcinoma involving the esophagus and esophagogastric junction, a highly lethal disease. While a number of endoscopic technologies targeting metaplastic or neoplastic esophageal mucosa have been introduced into the clinical marketplace, most have not been widely adopted. Radiofrequency ablation recently was developed and holds appeal as a reliable, minimally invasive, inexpensive, and well-tolerated technique to destroy pathologic esophageal epithelium.

**Conclusion:** The available data show its efficacy and safety in the short-term, though more mature follow-up is needed to demonstrate its durability in the long-term and its cost-effectiveness in ultimately saving lives.
3.39. Treatment of ultralong-segment Barrett’s using focal and balloon-based radiofrequency ablation

Melina C. Vassiliou, Daniel von Renteln, Daniel C. Wiener, Stuart R. Gordon, Richard I. Rothstein

*Surg Endosc* 2010;24:786-91

**Introduction:** Endoscopic radiofrequency ablation (ERFA) is being evaluated as definitive treatment for patients with Barrett’s esophagus (BE). Guidelines have yet to be developed for the application of this technology to patients with ultralong-segment BE (ULBE, C8 cm). This study reports a single institution’s experience with ERFA of ULBE.

**Methods:** A retrospective review of patients with ULBE undergoing ERFA from August 2005 to February 2009 was conducted. The entire segment of intestinal metaplasia (IM) was treated at each session using balloon- and/or plate-based devices (BARRX Medical, Inc., Sunnyvale, CA). Retreatments, endoscopic mucosal resection (EMR), dilations, and biopsies were performed based on endoscopic findings. Surveillance was conducted according to standard guidelines.

**Results:** Twenty-five patients (22 male) with a median age of 66 years [interquartile range (IQR) 57–74 years] were included. The length of BE treated was 10 cm (median; IQR 8–12 cm). Intramucosal carcinoma (IMC) was present in 3 patients, 15 had high-grade dysplasia (HGD), 6 had low-grade dysplasia (LGD), and 1 had IM without dysplasia. Complications for all 25 patients included hemorrhage (n = 1), stricture (n = 2), and nausea and vomiting (n = 2). Time from the initial procedure was such that 15 patients had post-ablation biopsies at least once. One patient with biopsies elected to undergo esophagectomy. Of these patients, 78.5% (11/14) had complete response (CR; no residual IM), two patients regressed from HGD to IM, and one patient with IMC had residual HGD and was treated with repeat EMR. The number of ablations in this group was 2.5 (median, IQR 2–3) during a median follow-up time of 20.3 months (IQR 10.4–29.2 months).

**Conclusions:** ERFA is safe and feasible in patients with ULBE and can be applied to the entire length of IM during one session. Eradication of BE can be achieved with few repeat ablations and continued, vigilant surveillance.
3.40. **Endoscopic ablation of Barrett’s esophagus using the Halo System**

David E. Fleischer, Virender K. Sharma

*Dig Dis* 2008;26:280-4

There is increasing interest in the endoscopic treatment of Barrett's esophagus. Endoscopic treatment has been utilized for many years, but in the past, no specific method has emerged as an appealing treatment option with appropriate safety, efficacy and ease of treatment for both patients and physicians. Recently there has been a growing literature related to the endoscopic ablation of Barrett's esophagus using radiofrequency ablation (RFA) (Halo® system). In order to discuss when RFA is indicated for Barrett's, one needs to know: (1) What is the 'histology' of the Barrett's? Does the patient have intestinal metaplasia, low-grade dysplasia, high-grade dysplasia or intramucosal carcinoma? (2) What are the endoscopic options to be considered as opposed to RFA? What are the advantages and disadvantages of each? (3) What additional variables need to be examined?
3.41. Radiofrequency ablation of Barrett’s esophagus

G Arora, S Basra, AK Roorda, G Triadafilopoulos

Eur Surg 2009;41:19-25

Summary: Background: Barrett’s esophagus (BE) is an important risk factor for esophageal carcinoma and its incidence is likely rising. Amongst the various available endoscopic ablative therapies, radiofrequency ablation (RFA) is a very promising new one.

Methods: We performed a comprehensive review of the literature on the treatment of BE using RFA. We searched for published articles on Pubmed and also reviewed the abstracts from the major gastroenterological society meetings of 2007 and 2008.

Results: RFA is an effective option in treating BE, especially when dysplastic changes are present, achieving high eradication rates with minimal complications. Prior control of intra-esophageal pH by either pharmacologic therapy or fundoplication is important in maximizing efficacy and preventing relapse.

Conclusions: RFA is a very well tolerated therapy for non-dysplastic and dysplastic BE and will likely become a first-line treatment. More data, however, will be needed to compare the various existing modalities of endoscopic ablative and resection therapies for BE.

J Lenglinger, FM Riegler

_Eur Surg_ 2009;41:132-5

The study demonstrates the danger of dysplasia. 19% of persons in the sham group developed cancer within one year. This indicates that the cancer probably has already developed at the time of the diagnosis of dysplasia. RFA is a safe procedure. Why not consider RFA earlier in the sequence? Let us consider RFA to eliminate intestinal metaplasia, followed by an effective fundoplication around the dilated end stage esophagus. Thus modern management of Barrett’s esophagus and dysplasia will include RFA and fundoplication. This in turn requires the open minds for the interdisciplinary approach. RFA can be conducted by surgeons and gastroenterologists. On the basis of these considerations and the thoughts presented within the Editorial, RFA has been introduced at the Vienna Medical School, Vienna General Hospital as an interdisciplinary treatment including a highly motivated team of gastroenterologists (Michael Hafner, Andreas Puspok), surgeons (Johannes Zacherl, Sebastian Schoppmann) and nurses serving for the patient. For the benefit of our patients we should fulfill this challenge.
3.43. Endoscopic endoluminal radiofrequency ablation of Barrett’s esophagus: Initial results and lessons learned

Vic Velanovich

*Surg Endosc* 2009;23:2175-80

**Background:** Ablating Barrett's epithelium may reduce the risk of developing esophageal adenocarcinoma. This study reports the experience of a single surgeon using an endoscopic endoluminal device that delivers radiofrequency energy (the BARRX device) to ablate Barrett's esophagus.

**Methods:** All patients who underwent ablation of Barrett's epithelium with the BARRX system were reviewed for length of Barrett's metaplasia, presence of high-grade dysplasia, postprocedure complications, completeness of ablation at first follow-up endoscopy, need for additional ablation, completeness of ablation at second follow-up endoscopy, and concomitant performance of a Nissen fundoplication.

**Results:** Sixty-six patients underwent Barrett's ablation. The median length of the Barrett's esophagus was 3 (range, 1-14) cm. Twelve patients (18%) had high-grade dysplasia. There were no immediate procedure-related complications. Four strictures occurred: three in patients with >/=12-cm segments of Barrett's and one in a 6-cm segment. Twenty-nine of 49 patients (59%) who had planned 3-month follow-up endoscopy had complete ablation. Five patients had planned two-stage ablation. Twenty patients with incomplete ablation had additional ablation. Twenty-seven patients had planned follow-up endoscopy at >/=1 year; 25 of 27 (93%) had biopsy-proven normal esophageal mucosa. The median length of Barrett's esophagus in patients with initially incomplete ablation was 6 cm, compared with 2 cm in the initially complete ablation patients. Seven Nissen fundoplications were present at the time of ablation, whereas six were performed concomitantly with the ablation without increased difficulty.

**Conclusions:** Complete ablation of Barrett's esophagus with radiofrequency endoluminal ablation is achievable in >90% of patients. Patients with longer segments are likely to require additional ablation. Patients with very long segments are at risk for stricture and should be approach cautiously. Performance of a fundoplication is not hindered by concomitant ablation.
3.44. **Radiofrequency ablation of Barrett’s esophagus: Short-term results**

Shady M. Eldaif, MD, Edward Lin, DO, Kimberly A. Singh, MD, Seth D. Force, MD, Daniel L. Miller, MD

*Ann Thorac Surg* 2009;87:405–11

**Background:** The presence of Barrett’s esophagus (BE) increases the risk of esophageal cancer. Total regression of BE is uncommon with medication or laparoscopic fundoplication, and endoscopic techniques to obliterate BE have varied results. This study evaluated the early results of a balloon-based catheter radiofrequency ablation (RFA) system in patients with medically refractory reflux symptoms and biopsy-proven BE.

**Methods:** The medical records of 27 consecutive patients who underwent RFA for BE from March 2005 through January 2007 were reviewed. Esophagogastroduodenoscopy was performed before ablation to document presence of BE and no cancer and at 8 weeks after the RFA to assess the presence of residual BE.

**Results:** Mean patient age was 53.6 ± 12.5 years; 16 (59%) were men. The average length of the Barrett segment treated was 4.6 ± 4.7 cm. Two patients (7.4%) had low-grade dysplasia. No patient had high-grade dysplasia and cancer. There was no periprocedural morbidity or at follow-up, no postprocedure dysphagia or stricture. In all patients, the BE was completely replaced with normal squamous epithelium. Symptoms regressed in 16 patients (60%) with RFA and proton pump inhibitor therapy. Eleven required an anti-reflux procedure for persistent symptoms.

**Conclusions:** Short-term results show that RFA for BE is safe and achieves 100% replacement of intestinal metaplasia. RFA of BE combined with fundoplication may be offered to patients with BE and medically refractory reflux symptoms. Long-term endoscopic surveillance is needed to determine if the risk of cancer is reduced with this bimodality therapy.
3.45. Circumferential and focal ablation of Barrett's esophagus containing dysplasia

Virender K Sharma, H Jae Kim, Ananya Das, Christopher D Wells, Cuong C Nguyen, David E Fleischer

*Am J Gastroenterol* 2009;104:310-7

**Objectives:** The finding of dysplasia in a Barrett's esophagus (BE) is associated with an increased risk for developing esophageal adenocarcinoma. Ablation using the HALO system has shown promise for the treatment of BE with dysplasia. The objective of this study was to assess the safety and efficacy of a stepwise regimen of circumferential and focal ablation using the HALO system for the treatment of BE with dysplasia.

**Methods:** Patients with BE containing low-grade dysplasia (LGD) or high-grade dysplasia (HGD) were enrolled. Primary circumferential ablation was followed every 3 months by further circumferential ablation or focal ablation until complete endoscopic eradication of BE was achieved. At 3- or 6-month intervals, depending on baseline grade, targeted and four quadrant random biopsies were obtained to assess the histological response to ablation. A complete response (CR) is defined as all biopsies negative for intestinal metaplasia (IM) (CR-IM) or dysplasia (CR-D) at last available follow-up.

**Results:** A total of 63 patients were treated (57 men; median age 71 years; median BE length 5 cm), with worst grade of dysplasia being LGD (n=39) and HGD (n=24). Follow-up is available for 62 patients (median 24 months). Overall, CR-IM is 79% and CR-D is 89%. For the LGD cohort, CR-IM is 87% and CR-D is 95%. For the HGD cohort, CR-IM is 67% and CR-D is 79%.

**Conclusions:** Stepwise circumferential and focal ablation of BE containing dysplasia appears to be a safe and effective intervention, achieving a CR for dysplasia in 95% and 79% of LGD and HGD patients, respectively.
3.46. Stepwise radiofrequency ablation of Barrett’s esophagus preserves esophageal inner diameter, compliance, and motility


*Endoscopy* 2009;41:2-8

**Background & aims:** Stepwise endoscopic circumferential and focal radiofrequency ablation is safe and effective for the eradication of Barrett’s esophagus. In contrast to other techniques, radiofrequency ablation appears to avoid significant esophageal scarring or stenosis. Our aim was to evaluate whether radiofrequency ablation has an adverse effect on esophageal function in patients treated for Barrett’s esophagus containing intramucosal cancer and/or high grade dysplasia.

**Methods:** Twelve patients with Barrett’s esophagus containing intramucosal cancer or high grade dysplasia were included in the study. After endoscopic resection of visible abnormalities, stepwise circumferential and focal ablation were performed every 2 months up to a maximum of five sessions. Measurement of the inner diameter was performed at 1-cm intervals in the distal esophagus. Manometry was performed using a water perfused sleeve catheter. Compliance was evaluated using the functional lumen imaging probe (FLIP), measuring eight cross-sectional areas within a saline filled bag with two pressure side holes, one proximal to and one inside the bag. Esophageal sizing, manometry, and compliance were recorded in patients at baseline and at least 2 months after the final ablation session. In addition, FLIP and manometry measurements were performed in 10 healthy volunteers.

**Results:** All patients achieved complete eradication of dysplasia and Barrett’s esophagus, without severe complications or ablation related stenoses. The esophageal diameter was unchanged by the ablation. Lower esophageal sphincter pressure and length and esophageal contraction amplitude before and after ablation were not significantly different. Baseline compliance was significantly different between healthy volunteers and Barrett’s esophagus patients. Compliance was not, however, significantly changed by ablation.

**Conclusions:** Stepwise circumferential and focal ablation of Barrett’s esophagus is an effective and safe treatment modality for early Barrett’s neoplasia that appears to preserve the functional characteristics of the esophagus.
3.47. **Endoscopic ablation of Barrett's esophagus: A multicenter study with 2.5-year follow-up (AIM-II long-term follow-up)**

David Fleischer, Bergein Overholt, Virender Sharma, Alvaro Reymunde, Michael Kimmey, Ram Chuttani, Kenneth Chang, Charles Lightdale, Nilda Santiago, Doug Pleskow, Patrick Dean, Kenneth Wang

*Gastrointest Endosc* 2008;68:867-76

**Background:** For patients with Barrett's esophagus (BE), life-long surveillance endoscopy is recommended because of an elevated risk for developing dysplasia and esophageal adenocarcinoma. Various endoscopic therapies have been used to eradicate BE. Recently circumferential radiofrequency ablation has been used with encouraging short-term results.

**Objective:** To provide longer follow-up and to assess the long-term safety and efficacy of step-wise circumferential ablation with the addition of focal ablation for BE.

**Design:** Prospective, multicenter clinical trial (NCT00489268).

**Setting:** Eight U.S. centers, between May 2004 and February 2007.

**Patients:** Seventy subjects with 2 to 6 cm of BE and histologic evidence of intestinal metaplasia (IM).

**Interventions:** Circumferential ablation was performed at baseline and repeated at 4 months if there was residual IM. Follow-up biopsy specimens were obtained at 1, 3, 6, 12, and 30 months. Specimens were reviewed by a central pathology board. Focal ablation was performed after the 12-month follow-up for histological evidence of IM at the 12-month biopsy (absolute indication) or endoscopic appearance suggestive of columnar-lined esophagus (relative indication). Subjects received esomeprazole for control of esophageal reflux.

**Main outcome measurements:** Complete absence of IM per patient from biopsy specimens obtained at 12 and 30 months, defined as complete remission–IM (CR-IM).

**Results:** At 12 months, CR-IM was achieved in 48 of 69 available patients (70% per protocol [PP], 69% intention to treat [ITT]). At 30 months after additional focal ablative therapy, CR-IM was achieved in 60 of 61 available patients (98% PP, 97% ITT). There were no strictures or buried glandular mucosa detected by the standardized biopsy protocol at 12 or 30 months, and there were no serious adverse events.

**Limitations:** This was an uncontrolled clinical trial with 2.5-year follow-up.

**Conclusion:** Stepwise circumferential and focal ablation resulted in complete eradication of IM in 98% of patients at 2.5-year follow-up.
3.48. Radiofrequency ablation for total Barrett’s eradication: A description of the endoscopic technique, its clinical results and future prospects


*Endoscopy* 2008;40:1033-40

Stepwise circumferential and focal radiofrequency ablation using the HALO system is a novel and promising ablative modality for Barrett’s esophagus. Primary circumferential ablation is performed using a balloon based bipolar electrode, while secondary treatment of residual Barrett’s epithelium is performed using an endoscope mounted bipolar electrode on an articulated platform. It has been used as a single modality treatment or in combination with other therapies. Recent studies suggest that this ablation technique is highly effective in removing Barrett’s mucosa and its associated dysplasia without the known drawbacks of photodynamic therapy or argon plasma coagulation, such as esophageal stenosis and subsquamous foci of intestinal metaplasia (also known as “buried Barrett”). In this review paper we will explain the technical background of radiofrequency ablation using the HALO system, give a summary of its current status, and speculate on possible future applications.
3.49. Eradication of Barrett esophagus with early neoplasia by radiofrequency ablation, with or without endoscopic resection

Ross E. Pouw, Joep J. Gondrie, Carine M. Sondermeijer, Fiebo J. ten Kate, Thomas M. van Gulik, Kausilia K. Krishnadath, Paul Fockens, Bas L. Weusten, Jacques J. Bergman

*J Gastrointest Surg* 2008;12:1627-37

**Background:** Radiofrequency ablation is safe and effective for complete eradication of nondysplastic Barrett esophagus (BE). The aim was to report the combined results of two published and two ongoing studies on radiofrequency ablation of BE with early neoplasia, as presented at SSAT presidential plenary session DDW 2008.

**Methods:** Enrolled patients had BE ≤12 cm with early neoplasia. Visible lesions were endoscopically resected. A balloon based catheter was used for circumferential ablation and an endoscope-based catheter for focal ablation. Ablation was repeated every 2 months until the entire Barrett epithelium was endoscopically and histologically eradicated.

**Results:** Forty-four patients were included (35 men, median age 68 years, median BE 7 cm). Thirty-one patients first underwent endoscopic resection [early cancer (n=16), high-grade dysplasia (n=12), low-grade dysplasia (n=3)]. Worst histology remaining after resection was high-grade (n=32), low-grade (n=10), or no (n=2) dysplasia. After ablation, complete histological eradication of all dysplasia and intestinal metaplasia was achieved in 43 patients (98%). Complications following ablation were mucosal laceration at resection site (n=3) and transient dysphagia (n=4). After 21 months of follow-up (interquartile range 10–27), no dysplasia had recurred.

**Conclusions:** Radiofrequency ablation, with or without prior endoscopic resection for visible abnormalities, is effective and safe in eradicating BE and associated neoplasia.
3.50. Circumferential and focal radiofrequency ablation for the treatment of Barrett’s esophagus

AK Roorda, G Triadafilopoulos

*Expert Rev Gastroenterol Hepatol* 2008;2:627-34

This invited profile summarizes the technical aspects and clinical trial results related to the use of circumferential and focal radiofrequency ablation in the management algorithm for Barrett’s esophagus. What makes this relatively new endoscopic intervention unique is its promising safety and efficacy profile reported in published clinical trials. This technology appears to have overcome many of the limitations of prior endoscopic ablative modalities, and is thus garnering a role in the management of this disease state.
3.51. Circumferential ablation of Barrett’s esophagus that contains high-grade dysplasia: A U.S. multicenter registry


Gastrointest Endosc 2008;68:35-40

Background: The management strategies for Barrett’s esophagus (BE) that contains high-grade dysplasia (HGD) include intensive endoscopic surveillance, photodynamic therapy, thermal ablation, EMR, and esophagectomy.

Objective: To assess the safety and effectiveness of endoscopic circumferential balloon-based ablation by using radiofrequency energy for treating BE HGD.

Design: Multicenter U.S. registry.


Patients: Patients with histologic evidence of intestinal metaplasia (IM) that contained HGD confirmed by at least 2 expert pathologists. A prior EMR was permitted, provided that residual HGD remained in the BE region for ablation.

Intervention: Endoscopic circumferential ablation with follow-up esophageal biopsies to assess the histologic response to treatment.

Outcomes: Histologic complete response (CR) end points: (1) all biopsy specimen fragments obtained at the last biopsy session were negative for HGD (CR-HGD), (2) all biopsy specimens were negative for any dysplasia (CR-D), and (3) all biopsy specimens were negative for IM (CR-IM).

Results: A total of 142 patients (median age 66 years, interquartile range [IQR] 59-75 years) who had BE HGD (median length 6 cm, IQR 3-8 cm) underwent circumferential ablation (median 1 session, IQR 1-2). No serious adverse events were reported. There was 1 asymptomatic stricture and no buried glands. Ninety-two patients had at least 1 follow-up biopsy session (median follow-up 12 months, IQR 8-15 months). A CR-HGD was achieved in 90.2% of patients, CR-D in 80.4%, and CR-IM in 54.3%.

Limitations: A nonrandomized study design, without a control arm, a lack of centralized pathology review, ablation and biopsy technique not standardized, and a relatively short-term follow-up.

Conclusions: Endoscopic circumferential ablation is a promising modality for the treatment of BE that contains HGD. In this multicenter registry, the intervention safely achieved a CR for HGD in 90.2% of patients at a median of 12 months of follow-up.
3.52. **Stepwise circumferential and focal ablation of Barrett’s esophagus with high-grade dysplasia: Results of the first prospective series of 11 patients**

JJ Gondrie, RE Pouw, CMT Sondermeijer, FP Peters, WL Curvers, WE Rosmolen, KK Krishnadath, F Ten Kate, P Fockens, JJ Bergman

*Endoscopy* 2008;40:359-69

**Background & study aims:** Stepwise circumferential and focal ablation of nondysplastic Barrett’s esophagus has proven safe and effective. This study assessed the efficacy and safety of ablation for Barrett’s esophagus with high-grade dysplasia (HGD), and residual Barrett’s esophagus with dysplasia after prior endoscopic resection for visible lesions.

**Patients & methods:** This was a prospective cohort study. All visible abnormalities were resected prior to ablation. Persistence of dysplasia and absence of invasive cancer was confirmed with biopsies after endoscopic resection. A balloon-based electrode was used for primary circumferential ablation and an endoscope-mounted electrode was used for secondary focal ablation. Eradication of dysplasia and Barrett’s esophagus was the main outcome measure.

**Results:** Eleven patients (eight men; median age 60 years) were treated (median Barrett’s length 5 cm). Visible abnormalities were removed with endoscopic resection in six patients. The worst pathological grade of residual Barrett’s esophagus after endoscopic resection and prior to ablation was LGD (n = 2) and HGD (n = 9). Patients underwent a median of two circumferential and two focal ablation sessions. Complete remission of dysplasia and complete endoscopic and histological removal of Barrett’s esophagus was achieved in 11/11 patients (100%). There were no adverse events or strictures, and in none of the 473 biopsies of neo-squamous mucosa was subsquamous Barrett’s esophagus (“buried Barrett’s”) observed. During a median follow-up period of 14 months after the last treatment session and a median number of two follow-up endoscopies, none of the patients showed recurrence of dysplasia or endoscopic signs of recurrent Barrett’s mucosa.

**Conclusions:** Stepwise circumferential and focal ablation appears to be a safe and effective treatment for complete removal of Barrett’s esophagus containing HGD, and can be safely performed after prior endoscopic resection for endoscopically visible abnormalities.
3.53.  **Effective treatment of early Barrett’s neoplasia with stepwise circumferential and focal ablation using the HALO system**

JJ Gondrie, RE Pouw, CMT Sondermeijer, FP Peters, WL Curvers, WE Rosmolen, F Ten Kate, P Fockens, JJ Bergman

*Endoscopy* 2008;40:370-9

**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).

**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. 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.

**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.
3.54. A prospective pilot trial of ablation of Barrett’s esophagus with low-grade dysplasia using stepwise circumferential and focal ablation (HALO system)


Endoscopy 2008;40:380-7

**Background & study aims:** Yearly surveillance endoscopy is carried out for Barrett’s esophagus with low-grade dysplasia (LGD) so that progression to high-grade dysplasia and adenocarcinoma can be detected at the earliest stage. The aim of the study was to assess the long-term safety and effectiveness of circumferential ablation followed by focal ablation (HALO system) for eliminating Barrett’s esophagus and LGD.

**Patients & methods:** Patients with 2 - 6 cm of Barrett’s esophagus with histology demonstrating LGD on their last two sequential endoscopies over the previous 2 years and confirmed by two pathologists were enrolled in this prospective, single-center trial. Circumferential ablation was carried out at baseline and at 4 months (if residual Barrett’s esophagus present). Endoscopy with 4-quadrant biopsies every 1 cm was performed at 1, 3, 6, 12, and 24 months. After 1 year, focal ablation was applied to any visible Barrett’s esophagus or irregularity of the squamocolumnar junction. Patients received lansoprazole 30 mg bid. Complete responses for dysplasia (CR-dysplasia) and intestinal metaplasia (CR-IM) at 2-year follow-up, with complete response defined as “all biopsies negative for dysplasia or intestinal metaplasia” were the main outcomes.

**Results:** Ten patients (nine men, mean age 66.9 years, range 48 - 79) with confirmed LGD (median 4.4 cm, range 3 - 6) underwent circumferential ablation with focal ablation after 1 year as necessary. At 2 years, CR-dysplasia was 100 % and CR-IM was 90 %. There were no strictures or buried intestinal metaplasia at follow-up.

**Conclusion:** A stepwise regimen of circumferential ablation followed by focal ablation appears to eradicate intestinal metaplasia (90 % CR-IM) and dysplasia (100 % CR-dysplasia) at 2-year follow-up in this trial, without stricture formation or buried intestinal metaplasia.
3.55. **Pilot series of radiofrequency ablation of Barrett’s esophagus with or without neoplasia**

J. C. Hernandez, S. Reicher, D. Chung, B. V. Pham, F. Tsai, G. Disibio, S. French, V. E. Eysselein

*Endoscopy* 2008;40:388-92

**Background & study aims:** Radiofrequency ablation is a rapidly evolving therapeutic modality for Barrett’s esophagus. The aim of this ongoing 12-month trial is to assess Barrett’s esophagus eradication after radiofrequency ablation using a balloon-based (HALO-360) and a plate-based (HALO-90) device. We report here our experience with the first 10 patients (out of 40) who have completed 12 months of follow-up.

**Patients & methods:** Following radiofrequency ablation using the HALO-360 device all patients were maintained on double-dose proton pump inhibitor therapy. Endoscopic evaluation was performed at 3 and 12 months postablation. Patients with residual Barrett’s esophagus at 3 months underwent repeat ablation. Ten patients, seven with nondysplastic Barrett’s esophagus, two with low-grade and one with high-grade dysplasia have completed the study to date.

**Results:** Complete Barrett’s esophagus eradication was achieved in seven patients, and partial eradication was achieved in three. There were no major complications. One case of buried Barrett’s metaplasia was encountered and successfully re-ablated, with complete Barrett’s esophagus eradication achieved at 12 months.

**Conclusions:** In this study, Barrett’s eradication rates were comparable to previously published reports. One case of buried Barrett’s metaplasia was identified out of 247 biopsies and was eradicated with repeat ablation.
3.56. **Balloon-based electrode for the ablation of non-dysplastic Barrett’s esophagus: ablation of intestinal metaplasia**

A. Aviles, A. Reymunde, N Santiago

*Boletin* 2006;98:270-5

**Introduction:** Barrett’s esophagus (BE) is a condition in which an abnormal intestinal-type epithelium called specialized intestinal metaplasia (SIM) replaces the stratified squamous epithelium that normally lines the distal esophagus. This occurs as a consequence of chronic gastroesophageal reflux disease (GERD) which is present in more than 20% of adults. It is present in 1-2% of the United States population with an estimated prevalence as high as 25% in white males older than 50 yrs without GERD. This intestinal metaplasia predisposes patients to esophageal adenocarcinoma, the most rapidly rising tumor incidence over the last 30 years, with an annual incidence of 0.5% in patients with BE and a survival rate less than 10% in 5 years. The objective of the study was to assess the safety and efficacy of circumferential endoscopic ablation of Barrett’s esophagus using the HALO\textsuperscript{360} System.

**Methods:** Patients with non-dysplastic Barrett’s esophagus confirmed within the previous year were treated twice per session with a balloon-based, bipolar radiofrequency ablation device with a pre-selected energy of 10 J/cm\textsuperscript{2} at 260 W for 10 secs, achieving full thickness ablation of epithelium followed by Omeprazole 40 mg PO BID for 1 month and then, daily. Patients were followed at 1, 3, 6 and 12 months with EGD with biopsy and a 2\textsuperscript{nd} re-treatment at 4 months if IM persisted.

**Results:** A total of 21 Hispanic patients underwent treatment with a gender distribution of 9 female and 10 male, at a mean age of 59.6 years old (SD ± 12.9) and mean weight of 161 lbs (SD ± 26.1). There was a complete response of 66.7%, 61.9%, 76.2% at 1, 3, 6, and 12 months respectively and a biopsy clearance rate (BCR) of 84.6% and 92.3% at 6 and 12 months with single treatment and 62.5% and 50.0% at 6 and 12 months in retreated patients. No complications from the procedure such as strictures or ulcer were reported at 1 year after treatment.

**Conclusions:** In spite of the multiple treatment options for BE, especially among ablation techniques, radiofrequency ablation therapy is achieving promising results with a full thickness ablation of Barrett’s epithelium in 76.2% of patients without direct injury to the submucosa, avoiding formation of stricture and minimal side effects from treatment.
3.57. Endoscopic ablation of intestinal metaplasia containing high-grade dysplasia in esophagectomy patients using a balloon-based ablation system

C.D. Smith, P.A. Bejarano, W.S. Melvin, M.G. Patti, R. Muthusamy, B.J. Dunkin


**Background:** This study aimed to determine the optimal treatment parameters for the ablation of intestinal metaplasia (IM) containing high-grade dysplasia (HGD) using a balloon-based ablation system for patients undergoing esophagectomy.

**Methods:** Immediately before esophagectomy, patients underwent ablation of circumferential segments of the esophagus containing IM-HGD using the HALO360 system. The treatment settings were randomized to 10, 12, or 14 J/cm² for two, three, or four applications. After esophagectomy, multiple sections from ablation zones were microscopically evaluated. Histologic end points included maximum ablation depth (histologic layer) and complete ablation of all IM-HGD (yes/no).

**Results:** Eight men with a mean age of 57 years (range, 45–71 years) were treated, and 10 treatment zones were created. There were no device-related adverse events. At resection, there was no evidence of a transmural thermal effect. Grossly, ablation zones were clearly demarcated sections of ablated epithelium. The maximum ablation depth was the lamina propria or muscularis mucosae. The highest energy (14 J/cm², 4 applications) incurred edema in the superficial submucosa, but no submucosa ablation. Complete ablation of IM and HGD occurred in 9 of 10 ablation zones (90%), defined as complete removal of the epithelium with only small foci of "ghost cells" representing nonviable, ablated IM-HGD and demonstrating loss of nuclei and cytoarchitectural derangement. One focal area of viable IM-HGD remained at the margin of one ablation zone (12 J/cm², 2 applications) because of incomplete overlap.

**Conclusion:** Complete ablation of IM-HGD without ablation of submucosa is possible using the HALO360 system. Ablation depth is dose related and limited to the muscularis mucosae. In one patient, small residual foci of IM-HGD at the edge of the ablation zone were attributable to incomplete overlap, which can be avoided. This study, together with non-esophagectomy IM-HGD trials currently underway, will identify the optimal treatment parameters for IM-HGD patients who would otherwise undergo esophagectomy or photodynamic therapy.
3.58. **Endoscopic endoluminal radiofrequency ablation of Barrett’s esophagus in patients with fundoplications**

N. Hubbard, V. Velanovich


**Background:** Endoscopic endoluminal radiofrequency ablation using the BARRX device is a new technique to treat Barrett’s esophagus. This procedure has been used in patients who have not had antireflux surgery. This report presents an early experience of the effects of endoluminal ablation on the reflux symptoms and completeness of ablation in post-fundoplication patients.

**Methods:** Seven patients who have had either a laparoscopic or open Nissen fundoplication and Barrett’s esophagus underwent endoscopic endoluminal ablation of the Barrett’s metaplasia using the BARRX device (BARRX Medical, Sunnyvale, CA). Pre-procedure, none of the patients had significant symptoms related to gastroesophageal reflux disease. One to two weeks after the ablation, patients were questioned as to the presence of symptoms. Pre-procedure and post-procedure, they completed the GERD-HRQL symptom severity questionnaire (best possible score, 0; worst possible score, 50). Patients had follow-up endoscopy to assess completeness of ablation 3 months after the original treatment.

**Results:** All patients completed the ablation without complications. No patients reported recurrence of their GERD symptoms. The median pre-procedure total GERD-HRQL score was 2, compared to a median postprocedure score of 1. One patient had residual Barrett’s metaplasia at 3 months follow-up, requiring re-ablation.

**Conclusions:** This preliminary report of a small number of patients demonstrates that endoscopic endoluminal ablation of Barrett’s metaplasia using the BARRX device is safe and effective in patients who have already undergone antireflux surgery. There appears to be no disruption in the fundoplication or recurrence of GERD-related symptoms. Nevertheless, longer-term follow-up with more patients is needed.
3.59. **Balloon-based, circumferential, endoscopic radiofrequency ablation of Barrett’s esophagus: 1-year follow-up of 100 patients**


*Gastrointest Endosc* 2007;65:185-95

**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 (HALO360 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 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$^2$ (x2) 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 (4,306 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.
3.60. Early experience with radiofrequency energy ablation therapy for Barrett’s esophagus with and without dysplasia

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Dis Esophagus 2007;20:516-22

Background: Radiofrequency (RF) ablation using the HALO360 system combined with proton pump inhibitor (PPI) therapy is a new treatment for Barrett’s esophagus (BE).

Methods: We assessed the safety and effectiveness of this combination therapy at a community-based, BE referral center. After symptom evaluation, endoscopy and histologic assessment, esophageal motility, pH monitoring on PPI, computed tomography, endoscopic ultrasonography and mucosal resection for nodules, we performed HALO360 ablation followed by twice daily PPI and 3-monthly surveillance for up to 12 months. If metaplasia or dysplasia were present at follow-up, the patients received a second ablation.

Results: Thirteen patients (12 male) were treated, three with high-grade dysplasia, four with low-grade and six with non-dysplastic intestinal metaplasia. The mean baseline BE length was 6 cm (range 2–12); nine patients had a hiatal hernia and two had a prior fundoplication. Esophageal pH < 4.0 for < 4% of time was achieved only in 5/13 patients. A mean of 1.4 ablation sessions were performed, without serious adverse events or strictures. Complete eradication of BE was achieved in 6/13 (46%) patients. The mean endoscopic surface regression was 84% (from a mean length of 6 ± 1 cm to 1.2 ± 0.5 cm, \( P < 0.001 \)). Complete elimination of dysplasia was achieved in 5/7 (71%) patients.

Conclusions: Ablation efficacy was better in those patients who had maximal pH control (\( P < 0.05 \)). HALO360 ablation of BE with or without dysplasia is safe, well-tolerated and effective in the community setting. Follow-up ablation further reverses residual BE or dysplasia.
3.61. Barrett’s esophagus and new therapeutic modalities

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_Therapy_ 2007;4:825-40

Barrett’s esophagus is a metaplastic change of the epithelium of the esophagus, caused by injury and inflammation related to gastroesophageal reflux disease. Metaplasia is defined as the transformation from one cell type to another cell type. In the case of Barrett’s esophagus, the normal squamous epithelium is replaced by a columnar epithelium-containing goblet cells, deemed intestinal metaplasia (IM). Owing to a significantly elevated risk for the development of esophageal adenocarcinoma associated with the presence of IM, patients with this diagnosis undergo surveillance endoscopy with multiple biopsies of the diseased tissue every 2–3 years, in order to detect adenocarcinoma at the earliest possible tumor stage. Development of dysplastic cellular changes within the Barrett’s epithelium often precedes the development of cancer. In cases of IM containing dysplasia, surveillance endoscopy is performed more frequently (every 3–12 months). For many patients with high-grade dysplasia, the esophagus may be removed surgically in order to preempt the development of cancer.
3.62. Changing attitudes toward endoluminal therapy

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Background: As with new laparoscopic techniques, the ability to convince surgeons and gastroenterologists to embrace endolumenal techniques and the additional training required to perform the new procedures will correlate with how rapidly endolumenal therapies are adopted. The authors measured their ability to change attitudes among surgeons, who may or may not perform endoscopy as a part of their practice, toward endolumenal therapies.

Methods: As part of the endolumenal therapy postgraduate course presented at the annual Society of American Gastrointestinal Endoscopic Surgeons (SAGES) meeting in Ft. Lauderdale, Florida 2005, experts presented current literature and data on new endolumenal techniques. The participants, primarily of surgeons, were polled electronically about a number of case scenarios before and after their presentation. Each scenario was relevant to the topic presented and chosen to reflect potentially controversial disease processes with traditional or endolumenal treatment options. The responses were collected in real time and displayed to course participants.

Results: A panel of 10 experts presented data on a range of endolumenal therapies including endolumenal treatment for gastroesophageal reflux disease (GERD), endoscopic stenting, endoscopic treatments in bariatric surgery, intraoperative endoscopy, endoscopic mucosal resection (EMR), transanal endoscopic microsurgery (TEM), mucosal ablation for Barrett’s esophagus, intraluminal resection, transluminal endoscopic surgery, and how to educate surgeons in new endolumenal techniques. Demographic data showed that 83.6% of the participants performed endoscopy as part of their practice. A comparison with traditional surgical options showed a statistically significant positive attitude change (p < 0.05) toward adoption of most endolumenal techniques after expert presentation. Only EMR and TEM did not show a statistically significant change in the participants willingness to adopt these techniques. There was no significant change in the attitudes of how best to train surgeons. After presentation of the training options, 76% of the respondents believed that these techniques should be taught in residency.

Conclusions: The education of surgeons in new endolumenal therapeutic techniques can have a significant impact in terms of changing practice attitudes and may accelerate adoption of new endoscopic techniques.
3.63. Thin-layer ablation of human esophageal epithelium using a bipolar radiofrequency balloon device

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*Surg Endosc* 2006;20:125-30

**Background:** The goal of this study was to determine the optimal treatment parameters for the ablation of human esophageal epithelium using a balloon-based bipolar radiofrequency (RF) energy electrode.

**Methods:** Immediately prior to esophagectomy, subjects underwent esophagoscopy and ablation of two separate, 3-cm long, circumferential segments of non-tumor bearing esophageal epithelium using a balloon-based bipolar RF energy electrode (BARRX Medical, Inc., Sunnyvale, CA, USA). Subjects were randomized to one of three energy density groups: 8, 10, or 12 J/cm². RF energy was applied one time proximally and two times distally. Following resection, sections from each ablation zone were evaluated using H&E and diaphorase. Histological endpoints were complete epithelial ablation (yes/no), maximum ablation depth, and residual ablation thickness after tissue slough. Outcomes were compared according to energy density group and 1 vs 2· treatment.

**Results:** Thirteen male subjects (age, 49–85 years) with esophageal adenocarcinoma underwent the ablation procedure followed by total esophagectomy. Complete epithelial removal occurred in the following zones: 10 J/cm² and 12 J/cm². The maximum depth of injury was the muscularis mucosae: 10 and 12 J/cm². A second treatment did not significantly increase the depth of injury. Maximum thickness of residual ablation after tissue slough was only 35 microns.

**Conclusions:** Complete removal of the esophageal epithelium without injury to the submucosa or muscularis propria is possible using this balloon-based RF electrode at 10 J/cm² or 12 J/cm². A second application does not significantly increase ablation depth. These data have been used to select the appropriate settings for treating intestinal metaplasia in trials currently underway.
3.64. Complete ablation of esophageal epithelium with a balloon-based bipolar electrode: A phased evaluation in the porcine and in the human esophagus

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*Gastrointest Endosc* 2004;60:1002-10

**Background:** The aim of this study was to evaluate the endoscopic and the histologic effects of a balloon-based bipolar radiofrequency electrode for ablation of porcine and human esophageal epithelium.

**Methods:** All procedures were performed with a balloon based, bipolar radiofrequency system that creates a circumferential, thin-layer epithelial ablation zone within the esophagus. In Phase I, multiple ablations were created in 10 farm swine, followed by acute euthanasia and histologic assessment for completeness of epithelial removal and ablation depth. In Phase II, multiple ablations were created in 19 farm swine, with varying power and energy density, followed by endoscopy at 2 and 4 weeks to assess stricture formation. In Phase III, 3 ablations were created in 12 farm swine, with varying energy density (5, 8, 10, 12, 15, or 20 J/cm²) at 350 W. Animals were euthanized at 48 hours. Histologic examination determined the percentage of epithelium removed and the ablation depth. In Phase IV, 3 patients underwent esophageal epithelial ablation before esophagectomy, creating separate lesions proximal to the tumor. Completeness of epithelial ablation and ablation depth was quantified histologically.

**Results:** In Phase I, complete removal of esophageal epithelium was achieved at energy density settings of 9.7 to 29.5 J/cm². In Phase II, 9.7 and 10.6 J/cm² produced no stricture, whereas more than 20 J/cm² produced a stricture in every case. In Phase III, 8-20 J/cm² resulted in 100% epithelial ablation. Five and 8 J/cm² spared the muscularis mucosae, whereas 10 J/cm² caused injury to the muscularis mucosae but preserved the submucosa. In Phase IV, histologic examination demonstrated full thickness epithelial removal in areas of electrode contact. Ablation extended only to the muscularis mucosae, without injury to submucosa.

**Conclusions:** In the porcine and the human esophagus, circumferential, full-thickness ablation of epithelium without direct injury to the submucosa is possible and was well tolerated. In all cases, depth of ablation was linearly related to energy density of treatment.
4. SELECT PEER-REVIEWED ABSTRACTS OF RFA FOR BE

4.1. Safety outcomes of balloon-based circumferential radiofrequency ablation after focal endoscopic resection of early Barrett’s neoplasia in 118 patients: Results of an ongoing European multicenter study


Gastrointest Endosc 2010;71:AB126

Background: In patients with a Barrett’s esophagus (BE) containing high-grade dysplasia (HGD) or early cancer (EC), endoscopic resection (ER) of visible lesions followed >6 weeks later by step-wise radiofrequency ablation (RFA) for residual BE is highly effective, however, limited data is available related to the adverse event profile of this approach.

Aims: Evaluate the frequency and severity of adverse events related to balloon-based circumferential RFA of BE >6 weeks after ER.

Methods: This prospective European trial is conducted at 13 tertiary referral centers with expertise in BE neoplasia. Investigators were trained at the coordinating site and the first 4 RFA cases were supervised on-site by the principal investigator. The coordinating study team attended all treatment sessions and first follow-up at each site to maximize protocol compliance and to standardize technique. A single expert pathologist interpreted all ER specimens, post-ER/pre-RFA and post-RFA biopsies. Eligibility criteria: BE ≤12cm with HGD/EC; ER of visible lesions pre-RFA (ER <2cm length; <50% circumference); no invasion >T1sm1; no N+ on EUS; 2 endoscopies post-ER/pre-RFA with 4-quad/2cm biopsies to exclude residual EC. At least 6 weeks after ER, balloon based circumferential RFA was performed, followed every 2-3 months by additional RFA until clearance of BE achieved.

Results: 118 patients (96 male, mean age 65yrs, median BE length 6cm) underwent en-bloc (n=57) or piecemeal ER (n=61, median 3 (IQR 2-4) pieces/session). Worst ER histology: EC (n=75), HGD (n=55), LGD (n=5), no dysplasia (n=3). Worst histology post-ER/pre-RFA: HGD (n=30), LGD (n=50), no-dysplasia (n=38, all had HGD/EC in ER). Acute adverse events included superficial mucosal laceration evident after inflation of the RFA balloon: at the ER scar (n=10, 8.5%) or at a reflux stenosis (n=2, 1.7%), none required intervention. One delayed adverse event occurred: melena (n=1, 0.8%), no intervention was required. All adverse events were categorized on the protocol case report forms as “mild”. By November 2009, 55 patients completed treatment: complete eradication of neoplasia (CR-N) and intestinal metaplasia (CR-IM) was achieved in 55/55 (100%) and 53/55 (96%) patients, respectively.

Conclusion: This is the largest prospective multicenter study combining ER and RFA for treatment of HGD/EC in BE. Our safety outcomes suggest that when performed by trained, expert endoscopists in carefully selected patients after limited ER for staging purposes, adverse events related to balloon-based RFA are infrequent and mild. Interim efficacy outcomes from 55 patients (CR-N 100%, CR-IM 96%) are very favorable and comport with those from other studies.