Endoscopic management of Barrett’s esophagus with dysplasia
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CHAPTER 1

RADIOFREQUENCY ABLATION FOR BARRETT’S ESOPHAGUS

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INTRODUCTION

Barrett’s esophagus (BE) occurs when an abnormal, intestinal-type epithelium called “specialized intestinal metaplasia” replaces the stratified squamous epithelium that normally lines the distal esophagus. The condition develops as a consequence of chronic gastroesophageal reflux disease and predisposes to the development of adenocarcinoma of the esophagus.

Traditionally, high-grade dysplasia and intramucosal cancer arising from BE were treated with esophagectomy, while non-dysplastic BE and BE with low-grade dysplasia were managed with endoscopic surveillance. Problems associated with these approaches included significant morbidity and mortality from esophagectomy, and the risk of missed or interval development of cancer in patients undergoing surveillance. To address these issues, less invasive endoscopic treatments have been developed.

Radiofrequency ablation is an endoscopic treatment modality for eradication of BE. Primary circumferential ablation is performed using a balloon-based bipolar electrode, while secondary treatment of residual BE is performed using an endoscope-mounted bipolar electrode on an articulated platform. Studies suggest that this ablation technique is highly effective in removing Barrett’s mucosa and associated dysplasia and in preventing progression of disease, while minimizing the known drawbacks of photodynamic therapy and argon plasma coagulation, such as esophageal stenosis and subsquamous foci of BE (“buried Barrett’s”).

This topic will review the use of radiofrequency ablation for the treatment of Barrett’s esophagus. Other issues related to Barrett’s esophagus, including alternative treatments, are discussed separately.

INDICATIONS FOR RADIOFREQUENCY ABLATION

VISIBLE LESIONS CONTAINING HIGH-GRADE DYSPLASIA OR INTRAMUCOSAL CARCINOMA — Patients with visible abnormalities in a segment of Barrett’s esophagus (BE) that contains intramucosal carcinoma (IMC) or high-grade dysplasia (HGD) may be treated with radiofrequency ablation (RFA), but only after endoscopic mucosal resection (EMR) of the IMC or visible lesion.

EMR provides a relatively large tissue specimen that allows for histopathological staging of a lesion, enabling selection of patients for endoscopic treatment who have HGD or IMC and a low risk of lymph node involvement. Patients found to have submucosal invading lesions on histology (>T1sm1) have a 15 to 30 percent risk of positive local lymph nodes and should be referred for surgery. On the other hand, the risk of lymph node involvement is minimal in patients with IMC, making these patients candidates for endoscopic management.

A reason for combining ablative therapy with EMR is that EMR only removes a focal area from the BE, leaving the patient at risk for metachronous lesions arising from the residual Barrett’s mucosa. The addition of ablative therapy to EMR helps overcome this limitation.

In addition to staging a lesion, EMR is also done prior to RFA to provide a flat...
mucosa for RFA, which helps ensure that the ablation reaches the muscularis mucosae (picture 1).

Picture 1 Endoscopic and histological images of long-segment Barrett’s esophagus with early cancer treated with a combination of endoscopic resection and radiofrequency ablation using the Barrx system.

(A) Antegrade view of Barrett’s esophagus. (B) A lesion suspicious for early cancer is noted from the 2 to 4 o’clock positions. (C) View of the esophagus after endoscopic resection of the lesion in two pieces. (D) Histopathological evaluation of the specimens showed a radically resected adenocarcinoma infiltrating the muscularis mucosae (T1m3). (E) Same area six weeks after the endoscopic resection showing that the wound has healed completely with scarring. (F) Esophagus after primary circumferential ablation using the Barrx360 system (two applications at 12 J/cm²). (G) Residual Barrett’s mucosa six weeks after prior circumferential ablation. (H) After additional focal ablation of the residual islands of Barrett’s mucosa, complete ablation of the Barrett’s segment was achieved.

FLAT HIGH-GRADE DYSPLASIA — Patients with Barrett’s esophagus and HGD seem to be ideal candidates for RFA, since successful eradication of their dysplastic BE prevents the development of cancer. However, proper patient selection is critical. Patients should have no visible lesions, as these require endoscopic mucosal resection (EMR) for optimal staging and treatment.

To ensure that only patients with flat HGD are being treated with RFA monotherapy, several studies have required that patients undergo at least two high-resolution endoscopies with four-quadrant biopsies every 1 to 2 cm within two months prior to RFA to exclude cancer. The use of RFA for flat intramucosal carcinoma (IMC) has only been evaluated in retrospective cohort studies.
LOW-GRADE DYSPLASIA There are several arguments that favor the use of RFA for low-grade dysplasia (LGD) in BE:

• A confirmed histological diagnosis of LGD in BE represents a cancer-cell phenotype confined to the epithelium of the esophagus. For this reason, the World Health Organization has advised replacing the term “LGD” with the term “low-grade intraepithelial neoplasia.” The risk of neoplastic progression associated with dysplastic BE is high. In one study, patients with a consensus diagnosis of LGD had an 85 percent cumulative risk of progressing to high-grade dysplasia (HGD) during follow-up, with an annual incidence of 13.4 percent per patient per year.10 However, it is important to note that in the presence of inflammation, making an accurate diagnosis of LGD can be difficult; thus, RFA should only be considered in cases of confirmed LGD.

• Cost-utility models show that ablation is the preferred strategy for managing dysplastic BE over a wide range of conservative assumptions related to the efficacy of RFA. A cost-effectiveness analysis suggested that radiofrequency ablation is the preferred strategy for low-grade dysplasia, but only if the low-grade dysplasia was confirmed (ie, the diagnosis was agreed on by more than one pathologist) and stable (ie, LGD was seen on biopsies obtained at least six months apart).11

• RFA reduces the risk of malignant progression. In a randomized trial (the SURF-trial) that was conducted in nine European centers with 136 patients with a confirmed histological diagnosis of LGD, patients were assigned to treatment or standard endoscopic surveillance (at 6, 12, 24, and 36 months).12 The study was stopped after an interim analysis after two years of follow-up because of superiority of RFA over surveillance. RFA significantly reduced the risk of progression to high-grade dysplasia or esophageal adenocarcinoma compared with standard endoscopic surveillance (1.5 versus 27 percent), and RFA also significantly reduced the risk of progression to esophageal adenocarcinoma alone (1.5 versus 8.8 percent). The number needed to treat to prevent a single progression to HGD or esophageal adenocarcinoma was four. Given these considerations, many experts believe that the net health benefit (benefit minus risk) of RFA for LGD in BE is favorable, and thus RFA should be available to patients as a primary treatment option, provided that the diagnosis is confirmed by an expert pathologist and that the diagnosis has been confirmed on more than one occasion.

NON-DYSPLASTIC BE The risk of progression to cancer in patients with non-dysplastic Barrett’s esophagus (BE) is small, and no objective markers are available to identify patients with an increased risk of developing cancer, though research looking at the risk-stratification of non-dysplastic BE has shown promising results. Whether to offer RFA to patients with non-dysplastic BE is highly controversial and is influenced by many factors. An argument against RFA in these patients is that the annual risk of malignant progression is low, and many patients with BE are elderly with significant comorbid conditions that limit their life-expectancy. Factors that favor treatment include the efficacy and safety profile of RFA and potential cost savings. For most patients with non-dysplastic BE, the net health benefit of RFA may be too low to justify its use. However, RFA could be considered for selected patients (eg, <50 years and a positive family history for esophageal adenocarcinoma).
Radiofrequency ablation (RFA) of Barrett’s esophagus (BE) generally starts with a stepwise circumferential ablation procedure, followed by focal ablation for any residual BE (figure 1). RFA is performed using the Barrx FLEX system (previously HALOFLEX system), which is comprised of two distinct ablation catheters: the Barrx\textsuperscript{360} ablation balloon for primary circumferential RFA and the Barrx\textsuperscript{90} device for secondary focal RFA of BE. Three alternative focal ablation devices have become available, the Barrx\textsuperscript{90} ULTRA, the Barrx\textsuperscript{60}, and the Channel RFA device.

Figure 1 Schematic illustration of primary circumferential and secondary focal radiofrequency ablation (RFA) of Barrett’s esophagus.

A) Pre-treatment image of a Barrett’s segment. (B, C) The esophageal diameter is measured at 1-cm intervals with a sizing balloon placed over a guidewire. (D) Introduction of the RFA balloon catheter over the guidewire. (E) The inflated RFA balloon positioned 1 cm above the top of the Barrett’s segment. (F) The RFA balloon repositioned for ablation of the second zone after ablation of the first zone with an overlap of 1 cm with the first ablation zone. (G) Image of the treated Barrett’s segment immediately after the RFA ablation with visible necrosis of the superficial mucosa. (H) Image of the healed distal esophagus three months after RFA treatment with regeneration with neosquamous mucosa and three small islands of residual Barrett’s mucosa. (I) Introduction of the endoscope with the Barrx\textsuperscript{90} cap for focal ablation. (J) Ablation of the third island of Barrett’s mucosa. The necrosis caused by ablation of the first two islands is visible proximally. (K) Image of the distal esophagus immediately after ablation of the three residual islands of Barrett’s mucosa. (L) Image of the healed distal esophagus, showing complete regeneration with neosquamous mucosa.
CIRCUMFERENTIAL ABLATION  Circumferential RFA with the Barrx\textsuperscript{360} catheter involves the inflation of a balloon ablation catheter within the esophagus at the site of the BE. The ablation catheter includes a coiled electrode array through which radiofrequency energy is applied, ablating the Barrett’s mucosa (picture 2). The Barrx\textsuperscript{360} catheter uses the Barrx FLEX energy generator (previously the HALO\textsuperscript{360} generator was used).

• Landmark determination – The first step in circumferential ablation is cleaning of the esophageal wall. In the past, this was done with 1 percent acetylcysteine and flushing with water to remove excessive mucus. Randomized trials have suggested that standard water rinses through the water jet channel of the endoscope are just as effective.\textsuperscript{13} We have therefore abandoned the cleaning with acetylcysteine. Next, the locations of the top of the gastric folds and the proximal extent of the BE (including islands) are recorded for reference during the sizing and ablation procedures. A stiff guide-wire or metal wire is then introduced, and the endoscope is removed, leaving the guide-wire in place.

• Esophageal sizing – Once the guide-wire is in place, a sizing catheter is connected to the Barrx FLEX generator, calibrated, and introduced over the guide-wire. The sizing catheter is used to measure the inner esophageal diameter prior to circumferential ablation. It consists of a 165-cm long shaft with 1-cm markings and a clear, 4-cm long non-compliant balloon at its distal end (picture 3). Upon activation via a footswitch, the sizing balloon is inflated to 4.3 psi (0.30 atm) by the generator using an integrated pressure:volume system. Based upon the baseline balloon volume and geometry, the mean esophageal inner diameter is calculated along the entire length of the 4-cm long balloon.

Picture 2 Endoscopic images of a primary circumferential ablation of Barrett’s esophagus using the Barrx\textsuperscript{360} system
(A) Long-segment Barrett’s esophagus with high-grade dysplasia. (B) The Barrx360 catheter is introduced and inflated at the upper end of the Barrett’s segment. (C) The whitish coagulum resulting from ablation. (D) After ablation of the whole Barrett’s segment and cleaning of the electrode and ablation zone, the catheter is reintroduced for a second ablation pass. (E) The second ablation pass results in a tan-colored ablation zone. (F) Treatment effect after two circumferential ablation passes.
The sizing procedure can be performed as a “blind” procedure, using the 1-cm scale on the catheter shaft for reference. For the first measurement, the distal end of the balloon is placed 6 cm above the proximal extent of the Barrett’s mucosa. After the first measurement cycle, the catheter is advanced 1 cm, and the sizing process is repeated. This sequence is reiterated until an increase in measured diameter indicates the transition into a hiatal hernia or the stomach.

- **Ablation catheter selection** – Based on the esophageal inner diameter measurements, an appropriate Barrx™ ablation catheter is selected. The Barrx™ ablation catheter consists of a 165-cm long shaft with a balloon at its distal end that contains a 3-cm long bipolar electrode. The electrode contains 60 electrode rings that alternate in polarity and completely encircle the balloon (figure 2). The ablation catheter is available in five outer diameters (18, 22, 25, 28, and 31 mm once inflated).

The outer diameter of the ablation balloon should be smaller than the narrowest measured esophageal diameter. In patients who underwent prior EMR, the ablation catheter should be selected conservatively (by taking an additional step down), keeping in mind that the sizing balloon calculates a mean inner diameter over a length of 4 cm, which might result in an overestimation of the esophageal inner diameter at the site of an EMR scar. For example, if the smallest measured diameter is 30 mm, a 28-mm balloon would be appropriate in a patient who had not undergone EMR, whereas a 25-mm balloon would be chosen for a patient who had undergone EMR. 2
• Ablation regimens – Two different ablation regimens for circumferential ablation are currently in use. The standard ablation regimen, consisting of two double applications of 12 J/cm² with a cleaning phase in between is the most widely used regimen and has been studied extensively. A simplified regimen without a cleaning phase has been proposed.

• “Standard circumferential ablation” – The ablation catheter is introduced over the guide-wire, followed by the endoscope, which is advanced alongside the ablation catheter. Under endoscopic visualization, the proximal margin of the electrode is placed 1 cm above the most proximal extent of the BE. The ablation catheter is then inflated to 3 psi. Upon activation, radiofrequency (RF) energy is delivered to the electrode. Energy delivery typically lasts less than 1.5 seconds, after which the balloon automatically deflates. Moving distally, the balloon is repositioned, allowing a small amount of overlap with the previous ablation zone (5 to 10 mm). Ablation is repeated until the entire length of BE has received one application of radiofrequency energy. We treat the entire BE segment in a single session, irrespective of its length.

After the entire length of BE has undergone one ablation cycle, the guide-wire, ablation catheter, and endoscope are removed. Once outside the patient, the catheter is inflated and any adherent coagulum on the electrode surface is removed using wet gauze. A soft distal attachment cap is then fitted on the tip of the endoscope, and the scope is reintroduced into the patient. The soft extending rim of the cap is used to gently slough off the coagulum from the esophageal wall in the ablation zone. After most of the coagulum has been removed with the cap, forceful spraying of water through a spraying catheter using a high-pressure pistol can be used to wash off residual coagulum. Although the cleaning procedure requires extra procedure time, previous studies suggested that it increases the efficacy of the ablation.²,²,¹⁴

After the cleaning procedure, the entire length of BE is ablated again using the same energy settings. A circumferential ablation treatment using the Barrx³⁶⁰ catheter takes approximately 30 to 40 minutes, depending on the length of the BE.

We would advise using the standard regimen in patients with a complex or tortuous Barrett’s esophagus (eg, a relative stenosis, narrowing at the ER site). The cleaning step of the standard regimen is a good way to assess the completeness of the first ablation pass and allows for necessary adjustments of the balloon position to treat skipped zones.

• “Simplified circumferential ablation” – A randomized trial demonstrated that circumferential radiofrequency ablation is easier and faster, but equally safe and effective, when the cleaning phase between ablations is omitted.¹³ By omitting the cleaning phase, the procedure time was reduced to 25 minutes. At three months after the circumferential ablation, the percentage of Barrett’s surface regression did not differ significantly between those who underwent a simplified ablation and those who underwent a standard ablation. In addition, complete eradication of neoplasia and intestinal metaplasia was similar in the two groups (100 and 90 percent, respectively).

Based on these results, we omit the cleaning phase between circumferential ablations in patients with uncomplicated Barrett’s esophagus (without scarring or stenosis).

• Follow-up circumferential ablation – Twelve weeks after the first circumferential ablation treatment, patients undergo a follow-up endoscopy, and additional
therapy is carried out if needed. A circumferential ablation is performed if:
- There is residual circumferential BE measuring 2 cm or more
- There are multiple islands or tongues of BE

- **Follow-up focal ablation** – At the 12-week follow-up endoscopy, patients are treated with secondary focal ablation using the Barrx™ catheter for:
  - Residual BE with a circumferential extent of less than 2 cm
  - Circular treatment of the Z-line (at least once)
  - Small tongues of BE
  - Scattered islands of BE

**FOCAL ABLATION** Focal RFA with the Barrx™ catheter also uses radiofrequency energy to ablate small areas of BE. For focal ablation, the electric current is delivered through an electrode array attached to the end of the endoscope (picture 4).

The electrode array is mounted on an articulated platform (figure 3), allowing the electrode to move front-to-back and left-to-right, ensuring optimal tissue contact. It can be attached with a flexible strap to the distal end of any endoscope with a diameter of 8.6 mm to 12.8 mm without impairing endoscopic view or function. The electrode array is 20.6 mm long and 13.2 mm wide with an active electrode-surface of 20 mm x 13 mm.

![Endoscopic images of a focal ablation procedure for residual Barrett’s esophagus using the Barrx™ system](image)

(A) Antegrade view of an esophagus that had contained long-segment Barrett’s esophagus, six weeks after primary circumferential ablation. (B) Residual islands of Barrett’s mucosa. (C) Corresponding image using narrow band imaging. (D) Ablation effect immediately after treatment with the Barrx™ system. The distal end of the catheter is visible at the 12 o’clock position in the endoscopic field. (E) Endoscopic appearance after the first ablation pass (two applications of 15 J/cm²) and cleaning of the ablation zones. (F) After the second ablation pass, the ablation zones have a tan-colored appearance.
The FLEX generator is used for both circumferential (Barrx®) and focal RFA. The first generation HALO® energy generator is used only with the Barrx® catheter.

- Electrode introduction – The Barrx® electrode array fits on the tip of the endoscope and is placed at the 12 o’clock position in the endoscopic video image.
- The device and endoscope are then introduced under visual guidance. When the laryngeal cavity is seen, the tip of the endoscope is deflected slightly downward. The endoscope is gently advanced into the esophagus, passing the leading edge of the catheter behind the arytenoids.

In about 10 percent of cases, introducing the electrode array may prove difficult. In those cases, a Zenker’s diverticulum should be excluded. Introduction of the device should never be forced due to the risk of perforation. In these cases, we will sometimes blindly pass a biopsy forceps or the spraying catheter into the esophagus to guide the endoscope into the proximal esophagus. In difficult cases, a CRE-balloon may be used to open the upper esophageal sphincter by manually inflating the balloon to a low pressure and then advancing the endoscope and Barrx® device along with the balloon.

- “Standard focal ablation” – Residual Barrett’s epithelium is positioned at the 12 o’clock position in the endoscopic video image, corresponding to the position of the electrode. The electrode is brought into close contact with the mucosa, deflected upward, and activated.

Without separating the electrode from the esophageal wall, the electrode array is immediately activated a second time, resulting in a “double” application of radiofrequency energy at 15 J/cm².

After all residual BE has been ablated, the coagulum is carefully pushed off the esophageal wall with the leading edge of the electrode array. The electrode surface is then cleaned outside the patient. Finally, the ablation zone in the esophagus is rinsed with a spraying catheter and pressure pistol, as described above.

- Using the ablation zones from the first ablation pass as a guide, all ablated areas are treated with a second “double” application of radiofrequency energy at 15 J/cm² (for a total of four applications).

In addition to treatment of any visually apparent BE, ablation of the entire Z-line is recommended (even if no clear tongues of BE are observed) to ensure eradication of all BE at the gastroesophageal junction (picture 5).

- “Simplified focal ablation” – In a randomized trial, the standard treatment regimen
was compared with a simplified regimen consisting of three applications of RF energy at 15 J/cm², without a cleaning phase in between. This procedure requires only a single introduction of the Barrx® electrode. In 41 patients, the efficacy of both regimens was compared in pairs of BE areas or islands. Three applications of radiofrequency energy at 15 J/cm² were non-inferior to the standard regimen for treatment of smaller BE areas.

Potential indications for this simplified procedure are small residual islands, or in patients in whom introduction of the endoscope and the Barrx® electrode is difficult. However, the triple-application has not been evaluated over larger surface areas and may in theory induce stenosis when applied on a larger scale. For this reason, we currently use three applications of 12 J/cm² as our standard regimen.

NEW ABLATION DEVICES Three new ablation catheters have been added to the Barrx FLEX system: the Barrx® Ultra catheter, the Barrx® catheter, and a channel RFA device that can be advanced through the scope. All three catheters can be used alongside the Barrx® catheter for secondary focal RFA of BE; however, no studies have yet evaluated the use of these devices in clinical practice. Recommendations for the use of these catheters are therefore based on previous experiences with the Barrx® device.
• Barrx Ultra device – The electrode array is mounted on an articulated platform in a similar way as the Barrx90 device, allowing the electrode to move front-to-back and left-to-right, ensuring optimal tissue contact. It can be attached with a flexible strap to the distal end of any endoscope with a recommended diameter of 8.6 mm to 9.8 mm without impairing endoscopic view or function. The electrode array is 40 mm long and 13 mm wide with an active electrode-surface area of 520 mm², resulting in a 200 percent larger electrode surface as compared with the regular Barrx90 device. The Barrx Ultra is less well evaluated in terms of energy settings and safety when compared with the Barrx90 device.

To prevent potential stenosis after focal ablation, the recommended treatment regimen consists of two double applications of RF energy at 12 J/cm², which has been studied extensively since the introduction of the Barrx90 device. An alternative regimen for the Barrx Ultra device consists of three applications of 12 J/cm². Patients can be treated with secondary focal ablation using the Barrx Ultra device if there are large tongues of residual BE or if there is short segment BE.

• Barrx60 device – The electrode array is mounted on an articulated platform in a similar way as the Barrx90 device, allowing the electrode to move front-to-back and left-to-right, ensuring optimal tissue contact. It can be attached with a flexible strap to the distal end of any endoscope with a recommended diameter of 8.6 mm to 9.8 mm. The electrode array is 15 mm long and 10 mm wide; as a result, the active electrode surface area is 60 percent of the surface area of the Barrx90 device.

The recommended treatment regimen consists of two double applications of energy at 15 J/cm² or three applications of 12 J/cm². Patients can be treated with the Barrx60 device for small islands of BE in the presence of a stenosis.

• Channel RFA device – The channel device is a through-the-scope device and fits through the working channel of an endoscope with a recommended diameter of 2.8 mm or larger. The design of the shaft provides catheter maneuverability, and the translucence of the device provides visibility. The electrode array is 15.7 mm long and 7.5 mm wide and has approximately the same active electrode surface area as the Barrx60 device. Since the channel device has only been tested in animal studies, the recommended treatment regimen consists of two double applications of energy at 15 J/cm² with cleaning, or three applications of 12 J/cm².

POST-TREATMENT CARE After RFA, acid suppressive therapy is important, not only to minimize patient discomfort, but also to allow the esophagus to heal optimally and regenerate with squamous epithelium. Studies suggest that ongoing gastroesophageal reflux has an adverse effect on treatment outcome. All patients should, therefore, receive high-dose proton pump inhibitors as maintenance therapy. In addition, extra acid suppression after each treatment session is advisable. We prescribe all patients esomeprazole 40 mg twice daily, supplemented with ranitidine 300 mg at bedtime, and sucralfate suspension (5 mL of a 200 mg/mL suspension) four times a day for two weeks after each ablation session. The proton pump inhibitor is continued as maintenance therapy.

After RFA, patients should adhere to a liquid diet for 24 hours. After 24 hours, patients may gradually advance to a soft and then normal diet at their own discretion, generally guided by their symptoms. Patients may experience symptoms of chest discomfort, sore throat, difficulty or pain with swallowing, and/or nausea, which usually improve daily.

For patients who have pain following the procedure, acetaminophen 500 to
1000 mg up to four times per day may be given as needed. Acetaminophen can be supplemented with diclofenac supplements 50 mg up to twice daily if the acetaminophen does not provide adequate relief. Other analgesic regimens include an antacid/lidocaine slurry and liquid acetaminophen with or without codeine. Some patients may also require antiemetic medication.

For patients presenting with severe chest pain and fever following their procedures, observation and conservative management with maximal acid suppression and an analgesic regimen will usually suffice. Only in rare cases, when there is a clear suspicion of severe complications, is additional testing (eg, computed tomography) required.

**EFFICACY**

The efficacy of radiofrequency ablation (RFA) has been studied in porcine models, pre-esophagectomy human subjects, and human subjects undergoing surveillance for Barrett’s esophagus (BE). Because the focal ablation device became available after the circumferential device, earlier studies focused on outcomes of circumferential RFA alone. More recent trials have included a stepwise approach of circumferential and focal RFA, as well as combining endoscopic mucosal resection with RFA.

Evidence from a number of well-designed studies, including a randomized, sham-controlled trial, suggests that RFA is highly effective at removing all BE at both the endoscopic and histologic level with a favorable safety profile. Although long-term follow-up studies are still limited, the five-year follow-up data suggest that eradication of the Barrett’s mucosa is maintained in more than 90 percent of patients. In addition, studies of the properties of the neosquamous mucosa that regenerates after RFA show the absence of the pre-existing oncogenetic abnormalities, suggesting a permanent transition to a low-risk epithelium.

**ERADICATION OF NON-DYSPLASTIC BARRETT’S MUCOSA** Studies have shown that RFA is effective for eradicating BE: 17,20-23

- In a series that included 448 patients with Barrett’s esophagus with variable degrees of dysplasia, complete remission was achieved in 26 percent of patients by one year, 56 percent of patients by two years, and 71 percent of patients by three years. 20 This study was not performed in expert centers and therefore reflects the results of RFA in a community setting. The study lacks a strict ablation protocol, as ablation could be stopped before complete endoscopic and histological eradication of BE was achieved, with a mean of 0.9 cm residual BE after treatment.

The incidence of recurrence two years after achieving complete remission was 33 percent, 78 percent of which were non-dysplastic. It should be noted that in this study, complete remission was defined as the absence of intestinal metaplasia from both esophageal and gastro-esophageal junction biopsies. Similarly, recurrence included isolated intestinal metaplasia of the cardia/gastro-esophageal junction, and this accounted for almost half of the reported recurrences.

- In the Ablation of Intestinal Metaplasia Trial-II (AIM-II) trial, complete eradication of Barrett’s mucosa at 12 months was achieved in 48 out of 70 subjects (70 percent) with non-dysplastic BE using only the Barrx system for circumferential ablation. 21
• In a follow-up study, the Barrx device was used for additional ablation in patients from the AIM-II trial who had residual BE. At 30-month follow-up, complete remission of BE was found in 97 percent of patients by intention to treat analysis. None of the patients presented with esophageal stenosis and no buried Barrett’s glands were found in any of the more than 4000 biopsies obtained during follow-up.

• Fifty of the patients who had complete remission of BE at 30 months in the AIM-II trial were reevaluated at five years. Complete remission of BE was noted in 46 patients (92 percent), whereas four patients (8 percent) had focal nondysplastic BE. The four patients with nondysplastic BE were all successfully treated with a single session of focal RFA.

EFFECT ON DYSPLASTIC BE. RFA has been shown to decrease the risk of malignant progression in patients with dysplastic BE. RFA eradicates all Barrett’s mucosa in 66 to 100 percent of patients and eradicates dysplasia in 79 to 100 percent. In a meta-analysis of 20 studies, complete eradication of dysplastic Barrett’s mucosa was achieved in 91 percent of patients. Similarly, in a systematic review that included 12 studies of RFA for the eradication of high-grade dysplasia (HGD) or early cancer (EC) in patients with BE, RFA (preceded by endoscopic resection of nodular disease if necessary) resulted in eradication of HGD or EC in 92 percent and complete eradication of BE in 88 percent.
A large, European randomized trial (SURF-trial) further demonstrated that RFA reduces the risk of malignant progression among patients with a confirmed diagnosis of low-grade dysplasia in BE. The trial was conducted in nine centers and included 136 patients: 68 patients were allocated to RFA (ablation) and 68 patients were allocated to surveillance (control). Patients in the ablation arm could receive up to five treatment sessions in the first year and were followed annually thereafter. Patients in the control arm were seen at 6, 12, 24 and 36 months. The trial was stopped after all patients were followed for at least 24 months (instead of the projected 36 months) due to superiority of ablation over surveillance. Ablation significantly reduced the risk of progression to HGD or cancer (1.5 versus 27 percent), and ablation also significantly reduced the risk of progression to cancer alone (1.5 versus 8.8 percent).

In the ablation arm, 93 percent of the patients were free of dysplasia, and 88 percent of patients were free of intestinal metaplasia after treatment. This was maintained during follow-up in 98 percent and 90 percent of patients, respectively. In the control arm, 28 percent of patients were free of dysplasia during follow-up, and 0 percent of patients were free of intestinal metaplasia. All recurrences in the ablation arm were small islands or tongues less than 10 mm and were effectively managed endoscopically.

In a community-based study, 429 patients (primarily with non-dysplastic BE) underwent RFA using a stepwise approach with both circumferential and focal RFA. Follow-up biopsies were obtained in 338 patients. In the patients who had follow-up biopsies, BE was eradicated in 72 percent, and dysplasia was eradicated in 89 percent (median of follow-up of nine months). Safety data were available for all 429 patients. There were no serious adverse events or deaths, and strictures occurred in 2 percent of the patients.

One year follow-up data were available for 137 patients (32 percent). In that cohort, the BE and dysplasia eradication rates were 77 and 100 percent, respectively (median follow-up of 20 months). However, given the large number of patients who lacked long-term follow-up, these results should be viewed with caution.

In a cohort study from the Netherlands, 54 patients with HGD or EC were followed for five years after RFA. Seventy-two percent of patients in this study were treated with endoscopic resection prior to RFA. Follow-up biopsies were obtained in 54 patients and after five years, endoscopic ultrasound and endoscopic resection of neosquamous epithelium were performed. Quality of follow-up was ensured by using a rigorous and unique follow-up protocol, with high-resolution endoscopy scheduled at pre-defined time points, and by obtaining a large number of samples (both biopsies and endoscopic resection specimens). Kaplan-Meier analysis demonstrated sustained eradication of dysplasia and intestinal metaplasia in more than 90 percent of patients after five years of follow-up.

In a prospective cohort study that included 63 patients with LGD and HGD, after a median follow-up of 24 months, 79 percent of patients were free of BE, and 89 percent were free of dysplasia. For the subset of 39 patients with LGD, 87 percent were free of BE, and 95 percent were free of dysplasia; whereas for the subset of 24 patients with HGD, the rates were 67 and 79 percent, respectively.

A retrospective series examined 112 patients with dysplastic BE who had complete eradication of dysplasia and intestinal metaplasia following RFA and were then followed with endoscopic surveillance for a median of 397 days (13.3 months). Disease recurrence was seen in eight patients (7 percent) and included progres-
sion to intramucosal cancer (one patient), progression to esophageal adenocarcinoma (two patients), HGD (one patient), LGD (one patients), and nondysplastic BE (three patients).

**COMBINING ENDOSCOPIC MUCOSAL RESECTION AND RFA FOR HIGH-GRADE DYSPLASIA AND INTRAMUCOSAL CARCINOMA** Patients with visible abnormalities in a segment of Barrett’s esophagus (BE) that contains intramucosal carcinoma (IMC) or high-grade dysplasia (HGD) may be treated with radiofrequency ablation (RFA), but only after endoscopic resection of the IMC or visible lesion.

There is concern that patients undergoing RFA following endoscopic resection may be at increased risk for complications. However, one study with 90 patients (44 who underwent RFA following endoscopic resection and 46 who only underwent RFA) did not find a difference in the rate of stricture formation between the groups. Patients who underwent RFA following endoscopic resection had a stricture rate of 14 percent, compared with 9 percent for those who underwent RFA alone (odds ratio 1.53; 95% confidence interval 0.26-9.74).

An advantage of RFA over other ablation methods is that it does not appear to interfere with subsequent endoscopic resection for residual lesions. Studies suggest that it is possible to resect areas of Barrett’s mucosa that persist after multiple RFA sessions using the ligate-and-cut technique, without the need for submucosal lifting. Other endoscopic ablation techniques typically result in submucosal scarring, which complicates subsequent treatment with endoscopic resection.

The ability to perform endoscopic resection for residual dysplastic tissue may explain the higher success rates in studies that incorporated endoscopic resection for residual BE (83 to 100 percent) compared with other RFA studies that did not.

**EFFECT ON QUALITY OF LIFE** — Patients in the AIM-dysplasia trial were also evaluated to see if RFA had an effect on their quality of life. At baseline, similar numbers of patients assigned to RFA and sham procedures reported worry about esophageal cancer (71 versus 85 percent, respectively) and worry about esophagectomy (61 versus 68 percent, respectively). Patients were also similar with regard to the presence/severity of depression, impaired quality of life, worry, stress, and dissatisfaction with the condition of their esophagus.

After undergoing an endoscopy 12 months following RFA or a sham procedure, patients were informed of their biopsy results (but not of their randomization group) and completed a second questionnaire. At follow-up, patients in the RFA group were less likely to be worried about esophageal cancer compared with those in the sham group (22 versus 66 percent) and were less likely to be worried about esophagectomy (17 versus 47 percent). They also showed significantly more improvement with regard to the presence/severity of depression, impaired quality of life, worry, stress, and dissatisfaction with the condition of their esophagus.

Interestingly, patients in the RFA group who did not achieve eradication of their BE still showed improvement in many of the quality of life domains, including worry about esophageal cancer and worry about esophagectomy, compared with those who underwent the sham procedure.
There is concern that residual Barrett’s esophagus (BE) could be hidden beneath the neosquamous epithelium following ablation, but the clinical relevance of “buried” Barrett’s is still uncertain.

The possibility of occult malignant progression of the buried glands has been suggested by cases of adenocarcinoma arising underneath neosquamous epithelium after ablation therapy with radiofrequency ablation, photodynamic therapy, or argon plasma coagulation. However, because the Barrett’s mucosa is protected from gastroesophageal refluxate by the neosquamous epithelium, the malignant potential of the buried glands may be lower than that seen with normal Barrett’s mucosa.

Buried Barrett’s prior to RFA — Some of the clinical uncertainty is due to the observation that buried Barrett’s glands may be seen in up to 28 percent of patients in the absence of treatment, suggesting that buried glands found following RFA may have been present prior to treatment.

In a retrospective study of 112 patients who completed treatment with RFA, 15 percent of the subjects had evidence of buried glands before or during RFA treatment. Importantly, 71 percent of cases showed buried glands during RFA treatment. A finding of buried glands was always concomitant with the presence of Barrett’s mucosa visualized on endoscopy or biopsy. At the final evaluation, none of the patients showed evidence of buried glands, and all patients were classified as being in complete remission.

In a sham-controlled study of 127 patients, 25 percent of the subjects had buried glands at baseline. At follow-up, only 5 percent of those treated with RFA were found to have buried glands, compared with 40 percent of subjects in the sham group (p<0.001). Overall, in a systematic review that included 1004 patients who underwent RFA, buried metaplasia was found in only 1 percent.

FALSE-NEGATIVE RESULTS Another concern is that buried Barrett’s following RFA is under-recognized because the biopsies do not sample the neosquamous epithelium deeply enough. A study of 16 patients examined the sampling depth and presence of buried glands in biopsies and endoscopic resection specimens from neosquamous epithelium after RFA. Four-quadrant routine biopsies were obtained every 2 cm from the neosquamous epithelium. Immediately after each routine biopsy, a second “keyhole” biopsy was taken from the same biopsy site to obtain a deeper sample. In addition, one set of four-quadrant routine biopsies was obtained from the untreated squamous epithelium of the proximal esophagus. Finally, a tissue sample from the neosquamous epithelium was obtained using endoscopic resection.

The study showed:

- No difference in primary biopsy depth when comparing specimens obtained from the post-RFA neosquamous epithelium with specimens obtained from the untreated squamous epithelium (lamina propria present in 37 versus 36 percent of samples), suggesting that the post-RFA neosquamous epithelium is not more resistant to biopsy than untreated tissue.
- Keyhole biopsies and endoscopic resection sampled more deeply than routine biopsies (55 and 100 percent contained lamina propria, respectively).
- No buried Barrett’s glands were detected in any of the primary, keyhole, or endoscopic resection specimens.
This study shows that biopsies obtained from squamous mucosa following RFA are similar to those obtained from normal squamous mucosa and that the low rate of buried glands reported after RFA compared with other ablation techniques is not a reflection of a sampling error specific to RFA. The absence of buried glands in all the specimens obtained in this study (including endoscopic resection specimens that sampled deep into the submucosa) is consistent with most clinical studies, in which buried glands are a rare finding. This suggests that RFA may be associated with complete eradication of all Barrett’s epithelium.

FALSE-POSITIVE RESULTS Tissue artifacts and residual BE may also lead to an incorrect diagnosis of buried Barrett’s glands. Biopsies from neosquamous epithelium near the neosquamocolumnar junction may lead to sampling of the transition from neosquamous to columnar epithelium, leading to a histologic finding of glandular mucosa beneath the neosquamous epithelium, which may mistakenly be interpreted as buried Barrett’s glands. In the case of a residual island of BE that was not treated with RFA, tangential sampling of the island combined with tangential sectioning of the biopsy may result in an erroneous finding of buried Barrett’s. 46

A diagnosis of buried Barrett’s glands should only be made if the endoscopist is positive that there were no residual BE islands after detailed inspection with narrow band imaging, and if the biopsies were not obtained at the level of the neosquamo-columnar junction. 47

INTESTINAL METAPLASIA OF THE CARDIA

There are limited data available on the natural history of recurrent intestinal metaplasia (IM) of the cardia/gastroesophageal junction. After RFA treatment, the gastro-esophageal junction is frequently biopsied given the known increased risk of recurrences in this area, as endoscopic differentiation between gastric mucosa and IM is nearly impossible. 48 However, the clinical relevance of IM, when detected in this area is uncertain because focal IM in this area may reflect insufficient treatment, recurrence of disease, or an irrelevant normal finding. Several studies have reflected on the relevance of IM at the cardia/gastroesophageal junction:

• A Netherlands cohort study of 54 patients followed patients for five years after RFA, obtaining four-quadrant biopsies at every follow-up endoscopy (median 20 biopsies per patient) immediately below the gastro-esophageal junction. 15 In 35 percent of patients, focal IM of the cardia was detected during follow-up. In 89 percent of these patients, focal IM of the cardia was only diagnosed on a single occasion. In total, 53 of 1,43 biopsies contained focal IM. All of the patients with focal IM of the cardia had a normal endoscopic appearance of the neo-squamocolumnar junction, and none of these patients developed dysplasia after a median of 61 months of follow-up. None of these patients was retreated endoscopically. 15

In this study, IM of the cardia was mostly observed in a single biopsy, this diagnosis was generally not reproduced during further follow-up, and there was no increased incidence over time. If IM of the cardia reflects residual disease, one would expect to find IM more than once in a single patient. If IM of the cardia
results from ongoing reflux after treatment, one would expect an increased incidence over time. It should be noted that all patients in this study received high-dose maintenance therapy with esomeprazole 40 mg twice daily. Studies have shown that IM of the cardia can be detected in biopsies of 25 percent of the normal population, and this is generally not considered a premalignant condition. The clinical relevance of focal IM of the cardia after RFA is therefore unknown, but these long-term data do not suggest that this is related to residual BE or recurrent disease.

- In a United States series that included 448 patients with BE with variable degrees of dysplasia, 17 patients developed recurrence of BE at the gastroesophageal junction only, after having achieved complete remission after RFA. Of these, 72 percent of patients had IM. Forty-seven percent of patients with IM or dysplasia at the cardia had a normal endoscopic appearance of the neo-squamous columnar junction. Follow-up results after detection of focal IM are not available.

These studies show that the management of focal IM of the gastroesophageal junction varies widely, as formal guidelines are lacking. The gastroesophageal junction remains an area at risk after endoscopic treatment and should be carefully inspected during follow-up with high-resolution endoscopy combined with advanced imaging techniques, and biopsies should be obtained immediately distal to the junction. Focal IM without dysplasia diagnosed on a single occasion does not appear to warrant treatment, as the majority of patients do not develop dysplasia during follow-up. If dysplasia is detected at the gastroesophageal junction, this can usually be managed endoscopically.

ADVERSE EVENTS — Adverse events reported with radiofrequency ablation (RFA) include esophageal strictures, upper gastrointestinal hemorrhage, and chest pain. Stricture rates of 0 to 56 percent have been described with other endoscopic ablation techniques. Overall, studies of radiofrequency ablation (RFA) for Barrett’s esophagus (BE) have shown lower rates of stricturing (0 to 6 percent). The stricturing seen with RFA has generally been associated with either prior endoscopic resection or a narrow esophagus at baseline due to underlying reflux disease.

- A study of 12 patients that compared measurements of esophageal inner diameter, motility, and compliance before RFA treatment and two months after the last ablation session showed no significant differences, suggesting that RFA does not impair the functional integrity of the esophagus.

- In a sham-controlled study of 127 patients, 6 percent of the RFA cohort experienced a stricture, but all resolved with a mean of 2.6 dilations. There were no perforations or deaths.

- In a randomized trial with 136 patients, 12 percent of the ablation cohort (8 of 68 patients) experienced a stricture, but these appeared generally mild in nature as all resolved with a median of one dilation.

- In a community-based registry of 429 patients, nine strictures occurred following 788 procedures (1 percent of cases, 2 percent of patients). All of the strictures resolved after a median of three dilations. There were no cases of bleeding (other than one patient who vomited blood-tinged mucus), perforation, or death.

Performing endoscopic resection prior to RFA may increase the risk of complications. In a study of 65 patients, there were no complications in the 18 patients who
had not previously undergone endoscopic resection. In the 47 patients who had undergone endoscopic resection prior to circumferential RFA, mucosal lacerations were observed in patients who underwent RFA with a catheter that exceeded the smallest measured inner esophageal diameter and in patients whose endoscopic resection involved more than one-third of the esophageal circumference and was greater than 2.5 cm in length. Five cases of esophageal stenosis after RFA occurred, all in patients whose endoscopic resection involved more than 50 percent of the esophageal circumference and was longer than 2 cm in length.

Based on these observations, it is advisable to choose the size of the ablation catheters carefully in cases of prior EMR.

**FOLLOW-UP ENDOSCOPY**

Three months after the last treatment, the absence of residual Barrett’s epithelium should be confirmed by endoscopic inspection. Techniques available to detect residual BE include:

- High-quality white light endoscopy for detailed endoscopic inspection of the treatment area.
- Narrow band imaging or comparable technologies (eg, FICE, i-scan).

Detailed inspection of the neosquamous mucosa after RFA is important for two reasons: first, to detect even small areas of BE that can be additionally treated, as any residual BE puts the patient at risk of developing esophageal adenocarcinoma (picture 4); second, if random biopsies are obtained and accidentally small residual islands of Barrett’s are sampled, this can result in a histological finding of buried Barrett’s, causing doubts on the efficacy of the treatment and resulting in a missed opportunity to treat endoscopically visible remnants of Barrett’s mucosa. In a study evaluating the incidence of buried Barrett’s in biopsies obtained after RFA, buried glands were found in 0.1 percent of biopsies from endoscopically normal neosquamous epithelium. However, when small islands of columnar mucosa were intentionally biopsied, buried glands were detected in 21 percent of biopsies. The low percentage of buried Barrett’s in biopsies from neosquamous mucosa found in this study is similar to the 0 to 5 percent found in over 1000 patients from other studies on RFA for BE.

We recommend follow-up with high-resolution endoscopy and narrow band imaging, or a comparable technique, to carefully inspect the neo-squamocolumnar junction in antegrade and retroflexed positions to rule out the presence of small islands of Barrett’s mucosa. We also obtain biopsies immediately distal (<5 mm) to the neosquamocolumnar junction to evaluate for residual intestinal metaplasia.

Given the very low incidence of buried Barrett’s reported in multiple studies, extensive biopsies from the neosquamous mucosa are, in our opinion, not necessary, provided that detailed inspection with high-resolution endoscopy with narrow band imaging did not show any columnar mucosa or mucosal irregularities.

If residual BE is found, ablation can be repeated every 12 weeks until it has been eradicated both visually and histologically. Most patients will need one circumferential ablation session and one to two focal ablation sessions to eradicate all dysplasia.
and Barrett’s mucosa. We suggest a maximum number of two circumferential and three focal ablation sessions, which should be sufficient in most patients.

The recommended follow-up interval depends on the initial grade of dysplasia:
• For patients with IMC/HGD, we recommend follow-up endoscopy at 6 and 12 months and annually thereafter. Others perform surveillance endoscopies every three months for the first year, every six months for the second year, and annually thereafter. 53
• For patients with LGD/nondysplastic BE, we recommend follow-up endoscopy at 12 months. If there is complete eradication of IM at that stage, we stop surveillance. The published literature on the durability of RFA shows that the risk of progression in these patients is small. 53

COST-EFFECTIVENESS

Cost-effectiveness models have found radiofrequency ablation (RFA) to be cost-effective if certain assumptions are met:
• One study used a Markov model in a hypothetical 50-year-old cohort with non-dysplastic Barrett’s esophagus (BE) to evaluate three competing strategies: (1) no intervention (natural history), (2) surveillance alone, and (3) RFA. The assumptions were conservative and used an estimate of BE eradication rate with RFA of 50 percent, which was intentionally lower than rates reported in published studies. They concluded that patient age, cost of RFA, and BE eradication rates were critical determinants of the cost-effectiveness of RFA. Within a range of these parameters, RFA was a cost-effective strategy for non-dysplastic BE. 54
• A second model was designed to simulate the natural history of a cohort of patients with BE followed from age 50 until age 80 years or death. 55 It compared the incremental cost-effectiveness between three competing strategies: (1) surveillance, (2) esophagectomy, and (3) RFA. Endoscopic ablation for patients with high-grade dysplasia increased life expectancy by three quality-adjusted years at an incremental cost of less than $6000 compared with no intervention. RFA was also the most cost-effective strategy in patients with low-grade dysplasia or no dysplasia if ablation permanently eradicated low-grade dysplasia in more than 28 percent of patients or non-dysplastic BE in more than 40 percent of patients. However, in order for RFA to be cost-effective, surveillance needed to stop after successful ablation.
• A third model used a hypothetical cohort of 50-year-old patients with BE either with or without dysplasia followed until the age of 80 years or death. 11 The model compared three strategies: endoscopic surveillance with surgery when cancer was detected; endoscopic surveillance with RFA when dysplasia was detected; or initial RFA followed by endoscopic surveillance.

The study found that among patients with baseline high-grade dysplasia, initial RFA followed by endoscopic surveillance was more effective and less costly than the other approaches.

For patients with baseline low-grade dysplasia, initial RFA had an incremental cost effectiveness ratio (ICER) of $18,231 per quality-adjusted life year (QALY).
compared with endoscopic surveillance followed by RFA for HGD, assuming an annual rate of progression to cancer of 0.5 percent. Several studies have reported progression rates for LGD that are significantly higher.

For patients without baseline dysplasia, endoscopic surveillance followed by RFA for high-grade dysplasia was more effective and less costly than endoscopic surveillance followed by surgery once cancer developed. Compared with surveillance and RFA when HGD developed, initial RFA had unacceptably high ICERs per QALy of $205,500, $124,796, and $118,338 for annual rates of progression to cancer of 0.12, 0.33, and 0.5 percent, respectively.

**SUMMARY AND RECOMMENDATIONS**

Radiofrequency ablation (RFA) is an endoscopic treatment for Barrett’s esophagus (BE), which studies suggest is highly effective at removing Barrett’s mucosa and associated dysplasia.

- RFA is an option for the treatment of patients with dysplastic (low-and high-grade dysplasia) BE since RFA decreases their risk of malignant progression. Short to intermediate-term follow-up is promising, and five-year follow-up data suggest that the eradication of BE following RFA is maintained in more than 90 percent of patients.
- For most patients with non-dysplastic BE, the net health benefit of RFA may be too low to justify its use. However, RFA can be considered for selected patients (eg, <50 years old and a positive family history for esophageal adenocarcinoma).
- RFA can be used in conjunction with endoscopic resection for raised high-grade dysplasia or intramucosal carcinoma.
- RFA is performed with the Barrx FLEX system, which uses a balloon-based catheter for primary circumferential RFA and focal catheters for secondary focal RFA of BE.
- Circumferential RFA involves inflation of a 3-cm long balloon ablation catheter (Barrx™ device) within the esophagus at the site of the BE. The balloon contains an electrode array through which an electric current is applied, ablating the Barrett’s mucosa.
- Secondary focal RFA to ablate small areas of BE also uses electrical energy to ablate the tissue, and the electrode array is attached to the end of the endoscope (Barrx™ device). New catheters have been developed that may serve as an adjunct to the Barrx™ device.
- Adverse events reported with radiofrequency ablation (RFA) include esophageal strictures, upper gastrointestinal hemorrhage, and chest pain. These complications are generally mild, and severe complications are rare.
- After RFA, acid suppressant therapy is important, not only to minimize patient discomfort, but also to allow the esophagus to heal optimally and regenerate with squamous epithelium. All patients should receive high-dose proton pump inhibitors as maintenance therapy. In addition, extra acid suppression after each treatment session is advisable. We prescribe all patients esomeprazole 40 mg twice daily, supplemented with ranitidine 300 mg at bedtime, and sucralfate suspension (200 mg/mL) 5 mL four times a day for two weeks after each ablation session. The proton pump inhibitor is continued as maintenance therapy.
• Three months after the last treatment, the absence of residual Barrett’s epithelium is confirmed by endoscopic inspection. The use of high-resolution endoscopes with narrow band imaging is important to detect even small areas of residual intestinal metaplasia. Close inspection of the gastroesophageal junction is warranted, and biopsies should be obtained immediately below the GEJ (<5 mm).
• For patients with initial intramucosal carcinoma/high-grade dysplasia, we perform follow-up endoscopy 6 and 12 months after the last treatment and then annually. For patients with initial low-grade dysplasia/nondysplastic BE, we perform follow-up endoscopy 12 months after the last treatment. If complete eradication of intestinal persists at that time, surveillance can be stopped.


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