

# Endoscopic Eradication Therapy for Neoplastic Barrett's Esophagus Demonstrates 94% Treatment Success and Long-term Durability



Jennifer M. Kolb, MD, MS  
Associate Editor

Sachin Wani, MD  
Guest Contributor

Jennifer M Kolb MD, MS<sup>1</sup> and Sachin Wani, MD<sup>2</sup>

<sup>1</sup>Assistant Professor of Medicine, Division of Gastroenterology, Hepatology and Parenteral Nutrition, VA Greater Los Angeles Healthcare System, David Geffen School of Medicine at UCLA, Los Angeles, California

<sup>2</sup>Professor of Medicine, Division of Gastroenterology and Hepatology, University of Colorado Anschutz School of Medicine, Aurora, Colorado

This article reviews Sanne van Munster, Esther Nieuwenhuis, Bas L A M Weusten, et al. Long-term Outcomes after Endoscopic Treatment for Barrett's Neoplasia with Radiofrequency Ablation ± Endoscopic Resection: Results from the National Dutch Database in a 10-year Period. *Gut* 2022; 71: 265-76. PMID: 33753417. <http://www.doi.org/10.1136/gutjnl-2020-322615>.

Correspondence to Jennifer M. Kolb, MD, MS, Associate Editor. Email: [EBGI@gi.org](mailto:EBGI@gi.org)

## STRUCTURED ABSTRACT

**Question:** What are the short- and long-term outcomes of endoscopic eradication therapy (ablation ± resection) for patients with Barrett's esophagus (BE) related neoplasia?

**Design:** Nine centralized, expert centers in the Netherlands where endoscopists and pathologists adhere to a standardized protocol for BE care.

**Patients:** The study included 1,386 patients with BE and confirmed low-grade dysplasia (LGD), high-grade dysplasia (HGD), or low-risk esophageal cancer (EAC; mucosal or superficial submucosal sm1, well-moderately differentiated, no lymphovascular invasion, R0 resection) who underwent at least 1 radiofrequency ablation (RFA) between January 1, 2008, and December 31, 2018 in the RFA treatment cohort. There were 1,154 patients in the RFA durability cohort who had successful endoscopic eradication therapy and achieved complete eradication of BE with at least 1-year of follow up.

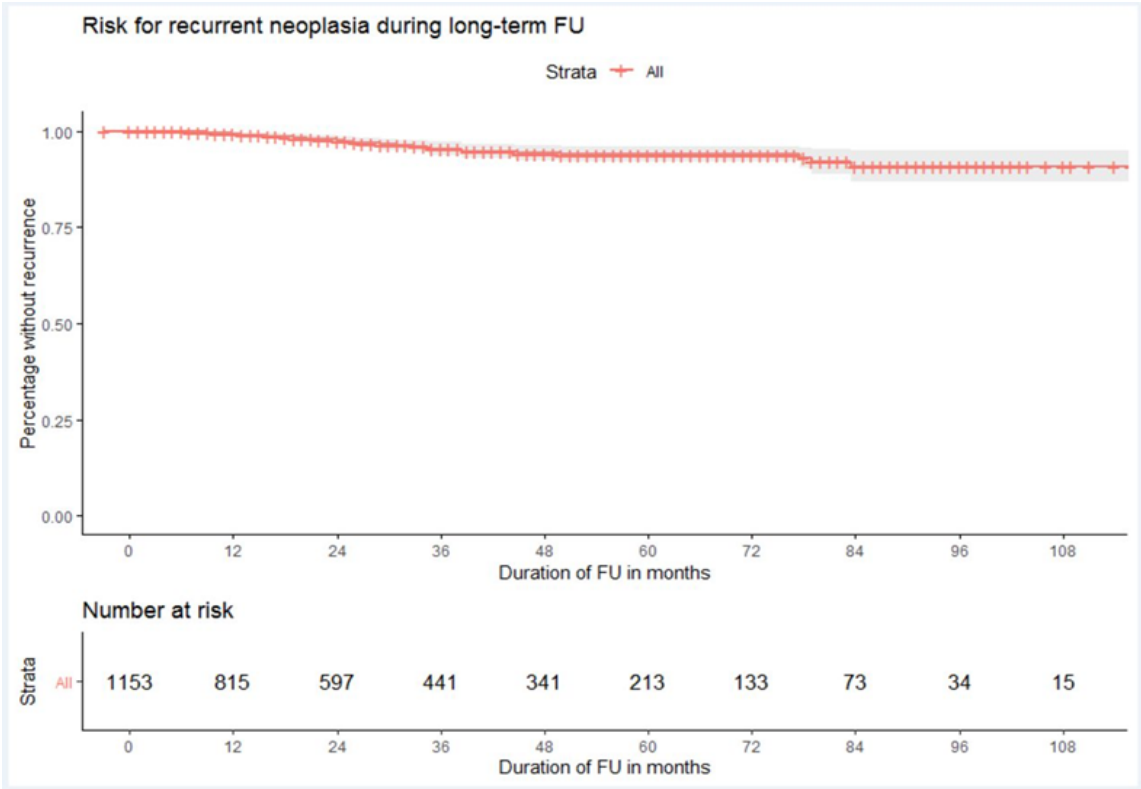
**Interventions/Outcomes:** Patients in the RFA treatment cohort underwent endoscopic resection of any visible lesions followed by RFA at 3-4 month intervals (or straight to ablation if all flat dysplasia). This was followed by touch up for residual non-neoplastic BE that persisted with resection, argon plasma coagulation, or RFA of the gastroesophageal junction. The RFA

durability cohort underwent endoscopic surveillance every 3 months in year 1, followed by annual endoscopy in years 2-5, and then endoscopy every 2-3 years. However, after 2015, the protocol was changed to 1 endoscopy in the first year. Surveillance biopsies were taken from the cardia and the neosquamous epithelium, according to the Seattle protocol from 2008-2013, but both were abandoned (neosquamous in 2013, cardia 2016) and replaced with close examination and only targeted biopsies. **Outcome:** Rate of complete eradication of intestinal metaplasia (CE-IM) after treatment, rate of sustained eradication of LGD/HGD/EAC during long-term follow up, rate of progression to advanced EAC not amenable to endoscopic resection, and complications. Additional outcomes included diagnostic yield of surveillance endoscopy and random biopsies.

**Data Analysis:** Durability of dysplasia eradication was estimated using Kaplan-Meier, Hazard Ratio for recurrence dysplasia using Cox proportional hazards model.

**Funding:** None.

**Results:** A total of 1,386 patients were in the RFA treatment cohort (62% underwent resection of a visible lesion), and 1,270 achieved complete eradication of intestinal metaplasia (94%, 95% CI 93-95). Treatment failure occurred in only 6% of the cohort. Of the 1,154 patients in the RFA durability cohort (median follow-up 43 months, 4 endoscopies), recurrence of LGD/HGD/EAC occurred in 3% of patients (annual risk 1%, 95% CI 0.8-1.4) and of HGD/EAC in 2% (annual risk 0.7%; **Figure 1**). Recurrences occurred in 38 patients at a median of 31 months. Most were associated with visible lesions and amenable to endoscopic eradication therapy although 5 were advanced EAC that could not be managed endoscopically. Complications included stenosis requiring dilation (15%), bleeding (2%), and perforation after endoscopic resection or dilation (1%). The less frequent surveillance strategy post complete eradication of intestinal metaplasia (after 2015, annually compared to every 3 months the first year) had similar rates of dysplasia recurrence and progression to advanced neoplasia. Additionally, outcomes were the same after abandoning random sampling from the neosquamous epithelium (post-2013) and random cardia biopsies (post-2016).



**Figure 1.** Long-term outcomes. Kaplan-Meier curve for the risk for recurrent dysplasia during follow-up (FU) based on the RFA durability cohort. Recurrence of LGD/HGD/EAC occurred in 3% of patients (annual risk 1%, 95%CI 0.8-1.4) and of HGD/EAC in 2% (annual risk 0.7%). Figure from van Munster et al. CC BY 4.0 license.

COMMENTARY

*Why Is This Important?*

Professional society guidelines worldwide recommend endoscopic eradication therapy for BE-related neoplasia with endoscopic resection of visible lesions followed by ablation of the residual flat BE segment over repeated sessions until complete eradication of intestinal metaplasia is reached. Landmark studies such as AIM dysplasia<sup>1</sup> and the SURF trial<sup>2</sup> demonstrate the effectiveness of RFA in achieving complete eradication of intestinal metaplasia in 77-88% of patients. Despite innovation in ablative technologies and meaningful progress creating optimal treatment algorithms, the long-term durability of endoscopic eradication therapy is unknown.

This is the first study to characterize long-term outcomes after RFA in a large cohort and provides important updates to our understanding of the timing and detection of recurrence. Endoscopic therapy was highly effective with low rates of recurrence when performed at centralized care centers by expert endoscopists and pathologists utilizing a standardized protocol. These results emphasize the importance of a high-quality examination as was performed at these Barrett expert centers- use of high-definition endoscopy, standardized reporting systems (Prague C&M criteria), and documentation of any visible lesions.

Additionally, results have been mixed regarding the timing of BE and dysplasia recurrence after eradicating the BE, which impacts surveillance strategies.<sup>3</sup> In this large cohort with long-term follow up, recurrence was rare and typically did not occur until after the first year. In fact, the authors were able to show that more frequent endoscopy every 3 months in the first year after complete eradication of intestinal metaplasia had no benefit over annual surveillance in years 1-5, suggesting less frequent surveillance in year one may be appropriate. Finally, this study addresses 2 key issues related to sampling strategy during surveillance. The current accepted method is 4 quadrant biopsies every 1-2 cm of the neosquamous epithelium (Seattle protocol) during surveillance. However, the investigators abandoned this strategy in 2013 due to presumed low diagnostic yield and indeed found no difference in dysplasia. This underscores the point that most recurrences are visible and can and should be identified with careful inspection. Furthermore, although random biopsies from the cardia showed non-dysplastic IM in 14% of patients, most could not be reproduced and none progressed to neoplasia, suggesting this practice is clinically useless.

### ***Key Study Findings***

Endoscopic eradication therapy is highly effective with 1,270/1,348 (94%) of patients achieving complete eradication of intestinal metaplasia. In 1,154 patients with long-term follow up, recurrence was uncommon and occurred in 38 patients (3%) for an annual recurrence risk of 1%. After achieving complete eradication of intestinal metaplasia, surveillance annually versus every 3 months for the first year was equivalent, and random sampling of the neosquamous epithelium and cardia provided no additional value.



***Caution***

This study was performed in expert high-volume centers in the Netherlands with centralized care. Therefore, results may not be generalizable to general practice settings in the US. The study design may have been selected for patients who were likely to be most successful with endoscopic eradication therapy as they did not enroll those who underwent resection alone without RFA or those who had limited life expectancy.

***My Practice***

We adhere to a 10-step approach to performing a high-quality endoscopic examination for all patients with BE<sup>4</sup> which includes careful inspection with a distal attachment cap, use of virtual chromoendoscopy, and description of the Barrett's segment and any lesions using standardized reporting systems (Prague, Paris). Any visible lesion, no matter how subtle, should be removed using endoscopic mucosal resection or endoscopic submucosal dissection. RFA is used for flat dysplasia or to eradicate the rest of the flat BE after resection. Although the present results suggest lengthening the surveillance interval to annually in the first year, we remain skeptical about whether these results can be applied to a US population where care is not always standardized or centralized and believe these results will need validation here. We continue to follow ASGE<sup>5</sup> and AGA<sup>6</sup> guidelines for surveillance endoscopies after complete eradication of intestinal metaplasia that suggests surveillance at 1 and 3 years for baseline LGD and 3, 6, and 12 months then annually for HGD based on modeling analyses.<sup>7</sup> We also continue to perform surveillance biopsies of the neosquamous epithelium using the Seattle biopsy protocol, typically focused on the gastroesophageal junction and distal 2cm of the esophagus. Abandoning random biopsies altogether is aspirational but should only be considered in expert hands with well-trained eyes to detect dysplasia.

***For Future Research***

More research is needed to determine the optimal surveillance interval after achieving complete eradication of intestinal metaplasia and whether results of this study should be incorporated into updated guidelines. Future studies

should develop risk prediction models to identify which individuals are most likely to have BE recurrence and whether surveillance schedules can be tailored to the individual. Additionally, more data is needed before we completely abandon random biopsies of the neosquamous epithelium post-ablation.

### ***Conflict of Interest***

The authors report no potential conflicts of interest.

### **REFERENCES**

1. Shaheen NJ, Sharma P, Overholt BF, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. *N Engl J Med* 2009;360:2277-88.
2. Phoa KN, van Vilsteren FG, Weusten BL, et al. Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial. *JAMA* 2014;311:1209-17.
3. Kolb JM, Davis C, Wani S. Durability of Endoscopic Eradication Therapy for Barrett's Esophagus-Related Neoplasia: A Call for Centralized Care. *Gastroenterology* 2022;162:343-345.
4. Kolb JM, Wani S. Barrett's esophagus: current standards in advanced imaging. *Transl Gastroenterol Hepatol* 2021;6:14.
5. Wani S, Qumseya B, Sultan S, et al. Endoscopic eradication therapy for patients with Barrett's esophagus-associated dysplasia and intramucosal cancer. *Gastrointest Endosc* 2018;87:907-931.e9.
6. Sharma P, Shaheen NJ, Katzka D, et al. AGA Clinical Practice Update on Endoscopic Treatment of Barrett's Esophagus With Dysplasia and/or Early Cancer: Expert Review. *Gastroenterology* 2020;158:760-769.
7. Cotton CC, Haidry R, Thrift AP, et al. Development of Evidence-Based Surveillance Intervals After Radiofrequency Ablation of Barrett's Esophagus. *Gastroenterology* 2018;155:316-326 e6.