ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Prateek Sharma, MD

Managing Recurrences Following Endoscopic Therapy for Barrett Esophagus



Prasad G. Iyer, MD, MSc Professor of Medicine Division of Gastroenterology and Hepatology Mayo Clinic Rochester, Minnesota

G&H What is the standard of care for the treatment of Barrett esophagus?

PI The treatment of Barrett esophagus depends on whether a patient has dysplasia or not. If dysplasia is present, the recommendation is to treat with endoscopic eradication therapy, which consists of resection of any visible abnormalities, followed by ablation. The most common ablation method is radiofrequency ablation. Some alternatives to radiofrequency ablation exist, such as cryoablation and argon plasma coagulation, but these methods are less commonly used. In the absence of dysplasia, endoscopic surveillance is recommended to detect the presence of dysplasia or carcinoma.

G&H What defines complete remission or eradication of intestinal metaplasia?

PI There are currently 2 schools of thought regarding the definition of complete remission or eradication of intestinal metaplasia. At the Mayo Clinic, we have always defined it as 2 negative successive endoscopies without intestinal metaplasia on biopsies from the tubular esophagus and the gastroesophageal junction. However, some centers define it as just 1 negative endoscopy without evidence of intestinal metaplasia.

G&H How common is recurrence following endoscopic therapy of Barrett esophagus?

PI Recurrence is fairly common. At least 2 meta-analyses have been published that show a rate of recurrence of

It is currently recommended that biopsies should be taken from the gastro-esophageal junction ... and then in a 4-quadrant fashion every 2 cm from the area where the Barrett segment used to be ...

approximately 8% to 9% for Barrett esophagus of any kind (with and without dysplasia), and approximately 1% to 2% for dysplastic Barrett esophagus.

G&H What factors are associated with recurrence?

PI Patients who have intramucosal cancer or high-grade dysplasia tend to recur more than patients who have low-grade or no dysplasia following ablation. Therefore, the grade of dysplasia for which a patient undergoes ablation is a major factor in determining the interval of surveillance following successful ablation. Other factors associated with recurrence are older age, male sex, longer Barrett segments, and presence of larger hiatal hernias.

G&H How is recurrent disease detected, and where is it most likely to be found?

PI At this time, recurrent disease is only detected endoscopically. Studies from our group and others have shown that most recurrences happen at the gastroesophageal junction followed by the distal esophagus (2-5 cm above the gastroesophageal junction).

Interestingly, most recurrences in the gastroesophageal junction are not visible, meaning they are detected only by random biopsies, whereas most recurrences in the tubular esophagus are visible and can be seen by an endoscopist. It appears that subsquamous or buried Barrett esophagus is rare. This has raised questions on whether there is any need to biopsy the normal-appearing neosquamous epithelium. Additionally, the long-term significance of nondysplastic intestinal metaplasia in the gastroesophageal junction is not known.

G&H How should biopsies be taken?

PI First and foremost, careful inspection of the tubular esophagus (in the area where Barrett esophagus was present) and the gastroesophageal junction (both in antegrade and close retroflexed views) is important. It is currently recommended that biopsies should be taken from the gastroesophageal junction (in a separate bottle), and then in a 4-quadrant fashion every 2 cm from the area where the Barrett segment used to be (the neosquamous epithelium). However, there is now evidence to suggest that most of the recurrences in the esophagus tend to occur distally (in the distal 5 cm), so biopsies taken in the distal esophagus are likely sufficient.

G&H What are the recommended surveillance intervals following endoscopic therapy?

PI Surveillance intervals depend on the preablation histology. For example, for patients who have high-grade dysplasia, surveillance is recommended every 3 months for a year, then every 6 months for a year, and then once

a year thereafter. For patients who have low-grade dysplasia, surveillance should occur every 6 months for a year and then once a year thereafter. It is likely that these

At this time, the only real tool that clinicians have to reduce the incidence of recurrence is antireflux treatment.

surveillance intervals will be widened as more evidence emerges.

G&H How effective is endoscopic therapy for treating recurrent disease?

PI Over 95% of recurrences can be managed endoscopically; thus, this type of therapy is very effective.

G&H When is recurrence most likely to occur? Is late recurrence a concern?

PI Not much is known regarding the timing of recurrence. Earlier studies claimed that recurrence was rare, but this claim was quickly countered by studies showing that recurrence was a fairly common phenomenon. A systematic review and meta-analysis reported that most recurrences occur in the initial 12 months after achieving remission. However, when the definition of recurrence was modified to 2 negative surveillance histologic examinations, this observation was not seen. Indeed, my colleagues and I published an article in Gut last year that combined data from 5 tertiary care centers (3 from the United States and 2 from the United Kingdom). The data showed that the incidence of recurrence continued to increase over time and did not flatten. Thus, late recurrences can certainly happen. The incidence of recurrence beyond 5 years is not clearly defined yet in most studies and needs to be carefully researched. At this time, it is likely premature to recommend widening surveillance intervals beyond 12 to 18 months after 5 years of remission.

G&H What measures can be taken to help reduce or prevent the risk of recurrence?

PI This is an important question, but unfortunately, good data are lacking. At this time, the only real tool

that clinicians have to reduce the incidence of recurrence is antireflux treatment. Proton pump inhibitors are typically used to control reflux as tightly as possible. There are not enough data to suggest whether aspirin or any other treatment can reduce recurrence. Some clinicians believe that correcting a hiatal hernia may reduce recurrence, but data on that regard are not very strong.

G&H What are the priorities of research in this area?

PI One of the top priorities is being able to identify a high-risk group, or individuals who are most likely to recur. Detecting recurrence is another major goal. Volumetric laser endomicroscopy allows clinicians to look beneath the surface of the esophagus, and research is ongoing to determine if clinicians can predict who will recur vs who may not recur. If we know who will recur, we may be able to monitor them closely and perhaps use treatments (such as aspirin, a statin, or some other novel compound) that can reduce the risk of recurrence. Lastly, it is unclear whether certain ablation techniques, such as cryotherapy, are less susceptible to recurrence. More research is needed in this area.

Dr Iyer has received research funding from Exact Sciences, C2 Therapeutics/Pentax Medical, and Medtronic. He serves as a consultant for Medtronic, C2 Therapeutics/Pentax Medical, CSA Medical, and Symple Surgical.

Suggested Reading

Fujii-Lau LL, Cinnor B, Shaheen N, et al. Recurrence of intestinal metaplasia and early neoplasia after endoscopic eradication therapy for Barrett's esophagus: a systematic review and meta-analysis. *Endosc Int Open.* 2017;5(6):E430-E449.

Gupta M, Iyer PG, Lutzke L, et al. Recurrence of esophageal intestinal metaplasia after endoscopic mucosal resection and radiofrequency ablation of Barrett's esophagus: results from a US multicenter consortium. *Gastroenterology*. 2013;145(1):79-86.e1.

Kahn A, Shaheen NJ, Iyer PG. Approach to the post-ablation Barrett's esophagus patient [published online January 3, 2020]. *Am J Gastroenterol.* doi:10.14309/aig.000000000000514.

Krishnamoorthi R, Singh S, Ragunathan K, Katzka DA, Wang KK, Iyer PG. Risk of recurrence of Barrett's esophagus after successful endoscopic therapy. *Gastrointest Endosc.* 2016;83(6):1090-1106.e3.

Sami SS, Ravindran A, Kahn A, et al. Timeline and location of recurrence following successful ablation in Barrett's oesophagus: an international multicentre study. *Gut.* 2019;68(8):1379-1385.

Sawas T, Iyer PG, Alsawas M, et al. Higher rate of Barrett's detection in the first year after successful endoscopic therapy: meta-analysis. *Am J Gastroenterol*. 2018;113(7):959-971.