

Guidelines for Managing Short-Segment Barrett's Esophagus

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Presentation Summary

The American College of Gastroenterology recently published guidelines on the diagnosis, surveillance, and therapy for Barrett's esophagus (BE). Although the guidelines also are recommended for short-segment BE, managing short-segment BE remains a challenge for several reasons: 1) the relative risk of its progressing to adenocarcinoma compared with long-segment BE has not been determined; 2) short-segment BE can be difficult to identify endoscopically; and 3) the appropriate place to biopsy is disputed.

In western countries there has been almost a quadrupling in the frequency of adenocarcinoma of the esophagus in the past 20 to 30 years, despite a decrease in squamous cell carcinoma since the mid 1980s.¹ Symptomatic gastroesophageal reflux disease (GERD) is a strong risk factor for esophageal adenocarcinoma. In fact, in a case-control study of 1412 participants (592 GERD patients and 820 controls), the investigators found that heartburn, regurgitation, or both, at least once a week increased the risk of cancer by a factor of 8. If the symptoms were frequent, severe, and long-standing (ie, more than 20 years), the cancer risk was increased by a factor of 44.²

The proposed mechanism of progression from GERD to adenocarcinoma is thought to be as follows: 1) gastroesophageal reflux of acid injures

the squamous epithelium; 2) the injured epithelium is replaced by specialized intestinal metaplasia, a condition known as Barrett's esophagus (BE). Even though intestinal metaplasia is more resistant to acid peptic attack, it is also predisposed to develop genetic changes that result in dysplasia and eventually adenocarcinoma.

Screening and Surveillance

It is important to understand the difference between screening and surveillance for BE. Screening uses tests to identify individuals with BE in a large population (ie, those who have reflux symptoms). Surveillance uses tests to identify curable neoplasia in patients already known to have BE. Therefore, performing endoscopy on patients with long-standing GERD symptoms, or on patients who have not responded well to antireflux ther-

apy, is screening for BE. During screening endoscopy, it is not necessary to take biopsy specimens from a distal esophagus that looks normal specifically to look for short-segment BE. Sufficient data do not exist to support such a procedure.

American College of Gastroenterology Practice Guidelines

In 1998, the American College of Gastroenterology (ACG) published practice guidelines on the diagnosis, surveillance, and therapy of BE. These guidelines should be applied to patients with short-segment and long-segment BE, however, screening for short-segment BE is not recommended.

Classic BE can be visualized endoscopically, because it is characterized by long segments (ie, at least 3 cm) of columnar epithelium extending well up into the esophagus. Biopsies from that mucosa will show intestinal metaplasia with prominent goblet cells. In regular endoscopic surveillance, procedures should be 4-quadrant biopsies taken every other centimeter from the Barrett's mucosa and in any grossly abnormal areas. The grade of dysplasia determines the interval for the subsequent endoscopy.³

In patients with BE but no dysplasia, the ACG recommends surveil-

lance endoscopy with biopsy every 2 to 3 years. If there is BE with low-grade dysplasia, the recommendation is for surveillance endoscopy at 6-month intervals for at least 1 year, followed by subsequent yearly endoscopy if there is no progression in the grade of dysplasia.³

Finally, if high-grade dysplasia is found in BE, the diagnosis should be confirmed by another expert pathologist because of the seriousness of the condition and the potential for strong disagreement among pathologists regarding how to grade this condition. If the diagnosis is confirmed and the patient is a good operative risk, the ACG discusses 2 options: either esophageal resection, which carries substantial morbidity and mortality, or continued intensive surveillance at unspecified intervals. Other groups have used 3-month intervals.

If the patient is a poor operative risk and a protocol for experimental therapies is available, one of these techniques may be considered.³

Where to Biopsy in Short-Segment BE

Where the biopsy should be taken in short-segment BE (ie, tongues less than 3 cm) is difficult to determine because specialized columnar epithelium, typically found in BE, cannot be distinguished endoscopically from normal gastric epithelium. In a study of 140 patients without endoscopically apparent BE but with short segments of specialized columnar epithelium at the gastroesophageal junction, biopsies were taken at the squamocolumnar junction. Of the 140 patients, 114 (81%) had no specialized intestinal metaplasia; 26 patients (18%) did.⁴

Several names for intestinal metaplasia in the gastroesophageal junction have been proposed (Table). This raises the question: Are there fundamental differences between intestinal metaplasia in the esophagus and intestinal metaplasia in the

Table. Proposed Names for Intestinal Metaplasia in the Gastroesophageal Junction Region

■ Barrett's esophagus
– Short segment
– Ultrashort segment
– No segment
■ Columnar-lined esophagus with metaplasia
■ Metaplasia at the gastroesophageal junction
■ Metaplasia of the gastric cardia

stomach? If so, then the name of the condition becomes even more important and will influence the decision regarding from where biopsy specimens are taken.

There are subtle but important fundamental differences between intestinal metaplasia in the esophagus and stomach. In the stomach, there is a positive association with *Helicobacter pylori* infection and intestinal metaplasia, but in the esophagus there is a negative correlation. There is obviously no association with GERD in the stomach, but there is a definite association with GERD in the esophagus and the presence of intestinal metaplasia. In the esophagus, the intestinal metaplasia tends to be incomplete, but in the stomach it tends to be complete (ie, to the pathologist it looks identical to the small intestine). There is also a cytokeratin pattern that may be characteristic of intestinal metaplasia in the esophagus compared with that in the stomach. Finally, the cancer risk appears to be higher with intestinal metaplasia in the esophagus than in the stomach.

These fundamental differences between metaplasia in the esophagus compared with the stomach were highlighted in a recent study that measured the frequency of dysplasia as a marker for the development of adenocarcinoma. Seventy-eight patients with short-segment BE and 34 patients with cardia intestinal metaplasia were followed prospectively for a mean of 24 months. Dysplasia developed in 9 patients with short-segment BE and in 1 patient with cardia intestinal metaplasia.⁵ The presence of such differences makes the location of the biopsy even more critical.

Short-Segment BE Endoscopic Landmarks

One way to better understand short-segment BE is to identify endoscopic landmarks. For example, the squamocolumnar junction, or Z-line,

is a visible line formed by the juxtaposition of pale squamous epithelium and the darker columnar mucosa. Conversely, the gastroesophageal junction is an imaginary line. It represents the anatomic junction of the esophagus and stomach, and it can be defined as the upper level of the gastric folds. If the gastroesophageal junction and the squamocolumnar junction are separated, a segment of columnar-lined esophagus lies between them. A biopsy can be taken from that segment to determine whether there is intestinal metaplasia. If the Z-line and the gastroesophageal junction coincide, there is no columnar-lined esophagus. However, the Z-line and the gastroesophageal junction may be more difficult to see in a live endoscopy, where the patient may be breathing and gagging; however, it is important to make the effort to identify them.⁶

Length of BE and Cancer Risk

How does the length of BE affect the risk of cancer? Intuitively, it would seem that the more cells (ie, the longer the segment of BE) that are available for mutation, the more likely a cancer will develop. A preliminary study indicates that patients with short-segment BE are not at a substantially lower risk than patients with longer segments, although a slight trend toward increased risk for neoplastic progression with increasing segment length has been noted. Further investigation is required to answer this question more definitively.⁷

Summary

Classic BE is easy to visualize endoscopically; however to detect short-segment BE, clinicians need to know their landmarks. Familiarity with the features of short-segment BE will affect where biopsy samples are taken because of the important differences between intestinal metaplasia of the esophagus and stomach. It is not clear whether short-segment BE

carries a lower risk of cancer than long-segment BE. The ACG guidelines for endoscopy should be followed for both short- and long-segment BE, but there is as yet no rationale to support screening for short-segment BE.

... REFERENCES ...

1. Devesa SS, Blot WJ, Fraumeni JF Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer* 1998;83:2049-2053.
2. Lagergren J, Bergstrom R, Lindgren A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999;340:825-831.
3. Sampliner RE. Practice guidelines on the diagnosis, surveillance, and therapy of Barrett's esophagus. The Practice Parameters Committee of the American College of Gastroenterology. *Am J Gastroenterol* 1998;93:1028-1032.
4. Spechler SJ, Zeroogian JM, Antonioli DA, Wang HH, Goyal RK. Prevalence of metaplasia at the gastro-oesophageal junction. *Lancet* 1994;344(8936):1533-1536.
5. Sharma P, Weston AP, Morales T, Topalovski M, Mayo MS, Sampliner RE. Relative risk of dysplasia for patients with intestinal metaplasia in the distal oesophagus and in the gastric cardia. *Gut* 2000;4:9-13.
6. Spechler SJ. The role of gastric carditis in metaplasia and neoplasia at the gastro-esophageal junction. *Gastroenterology* 1999;117:218-228.
7. Rudolph RE, Vaughan TL, Storer BE, et al. Effect of segment length on risk for neoplastic progression in patients with Barrett's esophagus. *Ann Intern Med* 2000;132:612-620.