Barrett's Esophagus: Clinical Issues

Stuart Jon Spechler, MD[a,b,c,*]

KEYWORDS

• Barrett's esophagus • Gastroesophageal reflux disease
• Intestinal metaplasia • Esophageal adenocarcinoma

Barrett's esophagus has been defined conceptually as the condition in which any extent of metaplastic columnar epithelium that predisposes to cancer development replaces the stratified squamous epithelium that normally lines the distal esophagus.[1] The condition develops as a consequence of gastroesophageal reflux disease (GERD). Barrett's metaplasia has clinical importance primarily because of its malignant predisposition, and virtually all of the contentious clinical issues in Barrett's esophagus are related in some way to its cancer risk. This article considers some key clinical issues that impact the management of patients with Barrett's esophagus.

DIAGNOSIS

Although more than 60 years have passed since Barrett[2] published his original treatise on the condition that now bears his name, authorities still dispute the diagnostic criteria for Barrett's esophagus. The conceptual definition proposed in the introduction does not translate readily into clear-cut diagnostic criteria, in part because it is not clear which of the multiple columnar cell types that can be found in Barrett's esophagus have a malignant predisposition.

In 1976, Paull and colleagues[3] reported that patients with Barrett's esophagus could have up to three types of columnar epithelia lining the distal esophagus: (1) a junctional (also called "cardia-type") epithelium comprised of mucus-secreting cells; (2) a gastric fundic-type epithelium with parietal and chief cells; and (3) intestinal-type metaplasia (also called "specialized columnar epithelium" or "specialized intestinal metaplasia") with prominent goblet cells. By the early 1980s, it had been established that Barrett's esophagus was a risk factor for esophageal adenocarcinoma, and intestinal metaplasia was reported to be the esophageal epithelial type

Supported by the Office of Medical Research, Department of Veterans Affairs and the National Institutes of Health (DK63621 to R.F.S.)
[a] Department of Medicine, Veterans Affairs North Texas Healthcare System, Dallas, TX, USA
[b] University of Texas Southwestern Medical Center, Dallas, TX 75216, USA
[c] Division of Gastroenterology, Dallas Veterans Affairs Medical Center, 4500 South Lancaster Road, Dallas, TX 75216, USA
* Corresponding author. University of Texas Southwestern Medical Center, Dallas, TX 75216.
E-mail address: SJSpechler@AOL.com

Gastrointest Endoscopy Clin N Am 21 (2011) 1–7
doi:10.1016/j.giec.2010.09.012 giendo.theclinics.com
1052-5157/11/$ – see front matter. Published by Elsevier Inc.

most frequently associated with that cancer.[4] By the late 1980s, intestinal metaplasia was widely regarded as both the most common type of Barrett's epithelium and the one that predisposed to malignancy.[5] In addition, intestinal metaplasia was readily identified histologically by its distinctive goblet cells and, unlike the cardia-type and gastric fundic-type epithelia, intestinal metaplasia clearly was abnormal when found in the region of the gastroesophageal junction. Consequently, some authorities chose to define Barrett's esophagus by the presence of intestinal metaplasia, and this diagnostic criterion was adopted into clinical practice.[5] Since the 1990s, an esophageal biopsy specimen showing intestinal-type metaplasia with goblet cells has become virtually a sine qua non for the diagnosis of Barrett's esophagus.[6]

In 1994, Spechler and colleagues[7] reported that 18% of consecutive patients in a general endoscopy unit who had columnar epithelium that involved less than 3 cm of the distal esophagus had intestinal metaplasia. Before then, endoscopists infrequently took biopsy specimens from such short segments of esophageal columnar epithelium. Since then, Barrett's esophagus has been categorized as long-segment (when the metaplastic epithelium extends $\geq$3 cm above the gastroesophageal junction) or short-segment (when there is <3 cm of metaplastic epithelium lining the esophagus).[8] The Prague C and M classification, which calls for identifying both the circumferential extent (C) and the maximum extent (M) of Barrett's metaplasia, is an even more recent system for describing the extent of Barrett's esophagus endoscopically.[9] Although studies have demonstrated excellent interobserver agreement among endoscopists using the Prague C and M criteria (when columnar epithelium extends >1 cm above the gastroesophageal junction), the clinical benefit of using this system has not been established and, presently, patients with any extent of intestinal metaplasia in the esophagus are managed similarly.

When evaluating studies on Barrett's esophagus, physicians should consider how changes in diagnostic criteria over the years have impacted the conclusions of those investigations. For example, short-segment Barrett's esophagus was not widely recognized until 1994, and most studies reported before that year included only patients with long-segment disease. More recent studies, however, include a substantial proportion of short-segment Barrett's patients whose GERD severity and esophageal cancer risk may differ considerably from those for patients with long-segment disease. It may not be appropriate to extrapolate the results of older studies on the epidemiology and natural history of long-segment Barrett's esophagus to patients with short-segment disease.

Another recent issue that has caused considerable controversy is whether the diagnosis of Barrett's esophagus should be limited to patients who have an esophageal biopsy specimen demonstrating intestinal metaplasia (with goblet cells), or whether the finding of gastric cardia-type epithelium in the esophagus also warrants that diagnosis.[10] Cardia-type epithelium traditionally has been considered the normal lining of the proximal stomach (the gastric cardia). However, there are data to suggest that cardia-type epithelium might not be normal, but rather a metaplastic lining that develops as a consequence of GERD.[11] Histochemical and molecular studies of cardia-type epithelium have revealed abnormalities that could predispose to carcinogenesis,[12,13] and several limited clinical studies support the concept that cardia-type epithelium has malignant potential.[14–16] Consequently, some authorities have proposed that cardia-type epithelium in the esophagus should be considered Barrett's esophagus.[10]

Most studies of cancer risk in Barrett's esophagus have included patients with intestinal metaplasia, either primarily or exclusively. Therefore, the magnitude of the cancer risk associated with cardia-type epithelium in the esophagus is not clear.