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How useful is histologic confirmation of intestinal metaplasia in patients with long-segment Barrett's esophagus?

Chin Hur and Patrick Yachimski

C Hur is Director of GI Health Outcomes Research at the Massachusetts General Hospital, and an Assistant Professor of Medicine at Harvard Medical School, and P Yachimski is a Fellow in Gastroenterology at the Massachusetts General Hospital, Boston, MA, USA.

SYNOPSIS

BACKGROUND—Controversy exists regarding the usefulness of histologic confirmation of intestinal metaplasia in patients with long-segment Barrett's esophagus (LSBE).

OBJECTIVES—To determine the frequency of intestinal metaplasia in patients with LSBE and to establish an optimal biopsy protocol to detect intestinal metaplasia in these patients.

DESIGN AND INTERVENTION—This retrospective, single-center study included consecutive patients with LSBE (defined as ≥ 1 cm of columnar-lined esophagus). Exclusion criteria included previous surgical repair of the lower esophageal sphincter. Patients were arbitrarily allocated to one of two endoscopic biopsy procedures: endoscopy with 1–4 biopsies taken, or endoscopy with >4 biopsies taken. The number of biopsies taken in the >4 biopsies group was influenced by clinician judgment. All biopsy specimens were histologically assessed using hematoxylin and eosin staining. At least three gastrointestinal pathologists examined each specimen to determine the mucosa type (intestinal metaplasia, cardiac type, fundic type, glandular not otherwise specified, or squamous). Intestinal metaplasia was diagnosed by the presence of goblet cells. Further histologic assessment with standard alcian blue-periodic acid–Schiff staining was performed in a subset of patients who had >6 biopsies taken during endoscopy. At least two pathologists assessed these specimens. Patients were stratified by the number of biopsies taken per endoscopy: 1–4, 5–8, 9–12, 13–16 and >16 .

OUTCOME MEASURES—The main outcome measures were the detection of intestinal metaplasia, and the frequency of intestinal metaplasia detected according to the number of biopsies taken.

RESULTS—In total, 125 patients (mean age 65 years [range 41–85 years]) were included, in whom 296 endoscopies were performed and 1,646 biopsies were taken. Mean follow-up was 25 months. The mean length of a Barrett's esophagus segment was 4 cm (range 1–11 cm). Intestinal metaplasia was present in 80 patients (64%); 150 endoscopies (51%) revealed intestinal metaplasia and 557 biopsies (34%) contained foci of intestinal metaplasia. The mean percentage of patients in whom intestinal dysplasia was detected was significantly greater in the group that had 5–8 biopsies taken per endoscopy than the group that had 1–4 biopsies taken per endoscopy: 67.9%

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Correspondence Massachusetts General Hospital Gastrointestinal Unit & the Institute for Technology Assessment 101 Merrimac Street Boston MA 02114 USA chur@partners.org.

Competing interests

The authors declared no competing interests.

PRACTICE POINT

Multiple biopsies should be taken in systematic fashion in patients with suspected Barrett's esophagus on endoscopic examination to maximize the diagnostic yield and accuracy of Barrett's esophagus screening

(95% CI 64–71.8%) and 34.6% (95% CI 32–37.6%), respectively; $P < 0.001$. There was no significant difference in the mean percentage of intestinal metaplasia detected between patients who had 5–8 biopsies taken per endoscopy, and those who had 9–12, and 13–16 biopsies taken per endoscopy; the diagnostic yield of intestinal metaplasia was 100% if >16 biopsies were taken per endoscopy. Standard alcian blue-periodic acid–Schiff staining resulted in a change in diagnosis for 5 of 92 patients (5.4%) who underwent this assessment. Increasing age was associated with a significant reduction in the risk of detecting intestinal metaplasia.

CONCLUSION—A minimum of eight random biopsies are required to be taken per endoscopy to diagnose intestinal metaplasia in patients with LSBE.

Keywords

Barrett's esophagus; biopsy; detection; endoscopy; intestinal metaplasia

COMMENTARY

Although population prevalence data are limited, more than 3 million individuals in the US are estimated to harbor Barrett's esophagus.¹ American consensus criteria for the diagnosis of Barrett's esophagus require biopsy-proven intestinal metaplasia,² although this viewpoint is not universally endorsed.³ Agreement exists that intestinal metaplasia is a precursor to esophageal adenocarcinoma; however, much of the rationale for not requiring evidence of intestinal metaplasia to diagnose Barrett's esophagus centers on the relatively high error rate of biopsy for detecting intestinal metaplasia within columnar-lined epithelium. The high false-negative rate of biopsy means that Barrett's esophagus can be missed in some patients if the stringent diagnostic requirement of histologic evidence of intestinal metaplasia is not met. This concern might be further heightened in health-care settings where logistical constraints limit the number of biopsies that can be obtained during endoscopic examinations.

The goal of endoscopic screening in patients with Barrett's esophagus is to identify individuals who are at risk for disease progression to esophageal adenocarcinoma, and to tailor management, namely endoscopic surveillance, to improve clinical outcomes. The use of Barrett's esophagus screening and surveillance is, however, not without controversy. If it is assumed that individuals diagnosed with Barrett's esophagus (with or without intestinal metaplasia) will undergo endoscopic surveillance; the effect of not requiring histologic evidence of intestinal metaplasia for diagnosis will be to increase the size of the surveillance pool. The theoretical benefit of 'liberalizing' the definition of Barrett's esophagus could be to diminish the chance of a false-negative diagnosis; however, this benefit would come at the cost of increasing the number of false-positive diagnoses. Individuals with a false-positive diagnosis, inappropriately labeled as having an increased risk of esophageal adenocarcinoma, would needlessly incur the burden of diagnosis including, but not limited to, the risks and cost of endoscopic surveillance.

In selected diseases, minimizing the number of false-negative results from diagnostic testing or maximizing test sensitivity should be the primary aim; however, this is not the case in Barrett's esophagus. Cost-effectiveness analyses constructed on the basis of mathematical disease models have found that Barrett's esophagus (confirmed by histologic evidence of intestinal metaplasia) screening and surveillance can be cost-effective,⁴ albeit substantially less cost-effective than other widely accepted health programs, such as colorectal cancer screening. Broadening the definition of Barrett's esophagus would increase the proportion of false-positive diagnoses, which would significantly increase cost with only a marginal gain in health outcomes. From a public health standpoint, these events would render Barrett's

esophagus endoscopic screening and surveillance cost-ineffective and prohibitively expensive.

Harrison *et al.* begin with the premise that intestinal metaplasia detection is an important goal in Barrett's esophagus screening, and then ask whether an optimal or threshold number of biopsies are required for detection. The study's finding that diagnostic yield increases with more extensive biopsy sampling makes intuitive sense—the more one looks, the more one is likely to find. On the basis of their analysis, the authors recommend that a minimum of eight biopsies should be taken to maximize the diagnostic yield and accuracy of Barrett's esophagus screening. Alcian blue-periodic acid–Schiff staining led to a marginal increase in diagnostic yield and is not routinely indicated.

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