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Screening and Surveillance for Barrett Esophagus

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When Norman Barrett described columnar metaplasia in the esophagus in 1950, he could not have predicted the controversies that would arise from the condition that now bears his name. In response to chronic injury from reflux esophagitis, the normally squamous-lined lower esophagus becomes reepithelialized with intestinal-type (mucus-secreting) columnar epithelium, giving rise to Barrett esophagus. In a minority of cases, this metaplastic epithelium develops dysplasia, which, in turn, can progress to esophageal adenocarcinoma, a malignant neoplasm associated with substantial morbidity and a 5-year survival rate of less than 20%. Over the past 40 years, the incidence of esophageal adenocarcinoma has risen markedly in the United States, from 0.4 cases per 100 000 in 1975 to 2.6 cases per 100 000 in 2009.¹ Barrett esophagus and esophageal adenocarcinoma share similar epidemiologic risk factors, including gastroesophageal reflux disease (GERD), white race, male sex, increasing age, tobacco use, and central adiposity.

Barrett esophagus is typically asymptomatic and is usually only identified when macroscopic mucosal changes are observed incidentally at upper endoscopy, prompting biopsies for histologic confirmation. Because the diagnosis requires upper endoscopy, an invasive procedure that most people do not routinely undergo, the true prevalence is unknown. Endoscopic studies from Europe have suggested that Barrett esophagus affects less than 2% of asymptomatic individuals, although simulation modeling has generated a higher estimate of 5% to 6% for the United States.² Despite this modest prevalence, Barrett esophagus, as the only established precursor of esophageal adenocarcinoma, has become the focus of endoscopic screening and surveillance programs.

Several organizations, including the American Gastroenterological Association, recommend routine endoscopic surveillance for individuals with Barrett esophagus.³ The rationale is simple: if early invasive carcinoma can be identified, the patient may be offered potentially

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curative resection; or, if dysplasia is detected, the patient may be offered treatments, such as endoscopic ablation, that prevent further progression to invasive carcinoma. Data from randomized clinical trials (RCTs) of surveillance are awaited. However, several observational studies, including a recent report,⁴ have found that endoscopic surveillance is associated with an earlier stage of esophageal adenocarcinoma at diagnosis and more favorable survival. Observational data on cancer screening are notoriously susceptible to bias, notably lead-time bias (where a screening test is used to diagnose a cancer in advance of when it would present with symptoms, leading to an apparent increase in survival time), and length-time bias (screening tests tend to detect a greater proportion of indolent cancers that are associated with longer survival).

Another consideration that casts doubt on the potential benefit of surveillance is the low risk of esophageal adenocarcinoma associated with Barrett esophagus without dysplasia. A 2011 population-based study suggested that this risk maybe as low as 0.12% per year (1 case per 833 patient-years),⁵ considerably lower than the figure of 0.5% per year that is often quoted.⁶ The low risk of malignant progression in nondysplastic Barrett esophagus also raises concerns about whether ongoing RCTs have sufficient power to definitively confirm or refute the utility of endoscopic surveillance. Finally, even if endoscopic surveillance is shown to be efficacious, this approach is expensive, time-consuming for endoscopists and pathologists, and requires patients to undergo an invasive procedure. A 2014 cost-utility analysis of current surveillance protocols, incorporating progression estimates from large population-based studies, suggests that surveillance of patients with nondysplastic Barrett esophagus is unlikely to be cost-effective.⁷

Because it has not been shown that surveillance reduces the risk of death from esophageal adenocarcinoma, population-based screening for Barrett esophagus is a contentious issue. Less than 10% of patients with esophageal adenocarcinoma have a preceding diagnosis of Barrett esophagus. Thus, advocates of population-based screening argue that surveillance of patients with Barrett esophagus alone is unlikely to have a major impact on overall esophageal adenocarcinoma incidence or mortality. The American Gastroenterological Association recommends screening for Barrett esophagus in individuals older than 50 years with symptomatic GERD and at least 1 additional risk factor for esophageal adenocarcinoma.³ Given that up to 20% of people in Western nations experience GERD symptoms, the potential target population for screening is enormous. Conversely, about 40% of patients with esophageal adenocarcinoma do not report symptoms of GERD, and selecting individuals for screening based primarily on the presence of symptoms is likely to miss a substantial proportion of those at risk.

Randomized clinical trials demonstrate that radio-frequency ablation of dysplastic tissue reduces the risk of progression of Barrett dysplasia to esophageal adenocarcinoma.⁸ There is consensus that for patients with high-grade dysplasia, who are at greatly increased risk of esophageal adenocarcinoma, endoscopic eradication of the Barrett mucosa is the therapy of choice.³ In contrast, the natural history of low-grade dysplasia is poorly understood and confounded by a low rate of diagnostic agreement between different pathologists. The best treatment strategy for patients with low-grade dysplasia remains unclear; long-term data are

lacking for the comparison of outcomes following endoscopic ablation to those for intensive endoscopic surveillance.

Most individuals identified through screening and entering surveillance programs have Barrett esophagus without dysplasia. For such individuals, data are lacking on the risk of esophageal adenocarcinoma following endoscopic ablation. It is also not known whether endoscopic surveillance is still required after the ablation of Barrett mucosa. Proton pump inhibitors are widely prescribed for such patients, often irrespective of whether a patient has symptoms of GERD. There is no persuasive evidence, however, to support chemoprevention with proton pump inhibitors or any other agents, including nonsteroidal anti-inflammatory drugs, aspirin, or statins.

Population-based screening for Barrett esophagus using current endoscopic techniques would subject large numbers of individuals to a potentially unnecessary procedure with uncertain benefit, psychological morbidity, and substantial costs. Several technologic advances, however, could strengthen the rationale for screening. Less invasive, nonendoscopic screening methods, suitable for use in medical offices, are currently being evaluated in multicenter studies. For example, the “cytosponge,” an investigational device, is an ingestible capsule attached to a string. The device is swallowed, after which the capsule opens to release a compressed sponge. The sponge is then drawn back through the esophagus, where it collects a specimen of esophageal mucosal cells for cytologic and immunohistochemical examination.⁹ In addition, risk stratification of patients with Barrett esophagus based on demographics, clinical information, and diagnostic or predictive biomarkers of disease progression may facilitate more targeted screening, subsequent surveillance, and treatment.

Despite its increasing incidence and high mortality, esophageal adenocarcinoma is predicted to account for only 1.1% of new cancer cases in the United States in 2014. An important reason that endoscopic screening and surveillance for Barrett esophagus has become widespread is physicians' concerns about medical professional liability claims. A recent analysis of data from a professional liability claims database suggests that such fears may be unfounded.¹⁰ The number of claims for either “failure to screen for esophageal cancer in patients without alarm features” or “complications from esophagogastroduodenoscopies with questionable indications” were similarly low.¹⁰

Research should seek to resolve the many controversies surrounding Barrett esophagus, including the biology of low-grade dysplasia, the role of chemoprevention, and long-term outcomes following eradication therapy. Most importantly, studies should strive to establish whether screening and surveillance protocols for Barrett esophagus are associated with the desired benefits of reductions in esophageal adenocarcinoma incidence and mortality, and at what costs. Until these controversies are resolved, patients should be apprised of the limitations of the available evidence and encouraged to make informed choices about whether to participate in screening or surveillance programs.

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