ADVANCES IN GERD

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Risk of Cancer in Patients With Barrett Esophagus

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G&H How prevalent is esophageal cancer in the United States? What are the most common risk factors?

NS Esophageal cancer has 2 major subtypes, squamous cell carcinoma and esophageal adenocarcinoma. Squamous cell carcinoma has been relatively static in its incidence and may actually be trending down slightly. The main risk factors are drinking alcohol, smoking tobacco, and African American race. Esophageal adenocarcinoma, on the other hand, has a remarkably different epidemiology and trend, as it has been increasing dramatically in the last 40 years in the United States. Per capita, esophageal adenocarcinoma is one of the fastest-increasing cancers in the United States. The main risk factors include white race, male sex, and gastroesophageal reflux disease. Other risk factors are obesity and increased abdominal circumference, which may promote reflux but may also influence hormonal changes that go along with abdominal obesity. We use what is known about the epidemiology of these diseases to set up rational screening programs.

G&H How often do patients with Barrett esophagus progress to esophageal cancer?

NS Patients with Barrett esophagus who have no dysplasia have relatively low rates of progression to esophageal cancer. For example, if 1000 patients are followed for a year, approximately 3 of those 1000 can be expected to progress to esophageal cancer. However, patients who do have dysplasia are at markedly increased risk. Depending on the study, the risk of progression in patients with high-grade dysplasia varies between 6% and 19% per year. In patients with low-grade dysplasia, the risk of progression is highly variable, and has been reported to be almost as low as that of nondysplastic Barrett esophagus to as high as approximately 13% per patient year. A reasonable estimate in a US population is likely just under 1% per patient year.

G&H What is the value of biomarkers as predictors of progression?

NS Currently, the only biomarker that clinicians commonly use is the degree of dysplasia. Although the degree of dysplasia is indicative of the risk of Barrett esophagus, it is far from a perfect biomarker. Many patients who clinicians might expect to progress based on the advanced degree of dysplasia do not actually progress. Conversely, dysplasia may not be recognized in a substantial proportion of patients who do progress. For that reason, clinicians have looked for other biomarkers, and multiple promising biomarkers are currently undergoing study. Several biomarkers have been utilized in the clinic, and some biomarker tests are commercially available and appear to stratify risk better than the degree of dysplasia. It is not yet well described which biomarker(s) should be used beyond dysplasia and in which clinical scenarios,

although it is a topic that is likely to receive increasing clarity in the future. It is possible that 1 or more biomarkers will be paired with histologic reads going forward.

> Societal guidelines recommend that patients with Barrett esophagus and no dysplasia undergo surveillance at 3- to 5-year intervals.

Figuring out which biomarkers can either be added to or used instead of dysplasia is important to allow clinicians to identify who might progress to cancer.

G&H What steps can be taken to reduce or prevent Barrett cells from developing into cancer? How effective are these steps?

NS With respect to prevention of progression of Barrett cells into cancer, it appears that patients who are taking proton pump inhibitors may have lower rates of progression than those who use H2 blockers or no other medication. Additionally, some data suggest that aspirin may be useful as a chemopreventive agent; however, the potential side effects of aspirin should be recognized, and there are some patients in whom this treatment is not appropriate. Similarly, the use of statins is associated with a lower risk of progression of Barrett esophagus in some studies.

The most commonly used and likely most effective step in preventing cancer in patients with Barrett esophagus and dysplasia is endoscopic eradication therapy. In that situation, clinicians deliver endoscopic treatments to the esophagus to lower the rate of cancer. Multiple studies suggest that there is a greater than 90% risk reduction of developing cancer after successful ablation for Barrett esophagus. Thus, in patients with Barrett esophagus and unfavorable progression markers, ablation will be the optimal step.

G&H How often should patients undergo surveillance endoscopy with biopsies?

NS Societal guidelines recommend that patients with Barrett esophagus and no dysplasia undergo surveillance at 3- to 5-year intervals. Within that span of 3 to 5 years, clinicians may use multiple different predictors to decide whether they want to go on the early end or the late end. For instance, patients with a longer Barrett segment may be at higher risk and should be surveilled at a 3-year interval, whereas patients with relatively small segments might be surveilled at longer intervals. During those examinations, an adequate number of biopsies should be taken (for example, at least 4 biopsies per every 2 cm). Clinicians can also consider the addition of brush biopsies with wide-area transepithelial sampling (WATS, CDx Diagnostics), which sample the Barrett segment more globally and could detect dysplasia that forceps biopsies might miss due to sampling error.

G&H How effective is treatment for early- and late-stage esophageal cancer?

NS Endoscopic treatment for early-stage esophageal cancer is quite effective. In fact, most series show that patients with T1a or intramucosal adenocarcinoma treated endoscopically have rates of eradication of not just the cancer but of Barrett esophagus that exceed 85%. On the other hand, treatment of late-stage cancer is often unsuccessful. Survival of late-stage cancer is uncommon, with most studies showing a 5-year mortality rate of more than 90% associated with stages 3 and 4 adenocarcinoma. Given the fact that esophageal cancer metastasizes to lymph nodes relatively early, it is perhaps unsurprising that we do not have great success in curing these patients.

G&H How significant of a concern is recurrence of esophageal cancer?

NS Recurrence is a significant enough concern for both early- and late-stage cancer that has been cured that guidelines recommend periodic screening of patients after successful curing of early-stage cancer. Most of these patients are undergoing endoscopy annually to ensure that there is no recurrence of Barrett esophagus or cancer. In patients with late-stage cancer, endoscopic surveillance is usually coupled with cross-sectional imaging, such as positron emission tomography–computed tomography, for surveillance after successful treatment.

G&H How should recurrent disease be managed?

NS At least in early-stage cancer, most disease recurrences can be managed endoscopically in a manner similar to the treatment of the initial disease. Ablation using either radiofrequency or cryotherapy, or, if the disease is nodular, endoscopic mucosal resection, can be used to avert progression of recurrent disease. In later-stage disease, recurrence is often treated with chemotherapy.

G&H What are the optimal follow-up intervals for monitoring patients with esophageal cancer?

NS The general recommendation for patients who have had their esophageal cancer treated endoscopically is to ensure that the cancer has been completely removed and the residual Barrett esophagus completely eradicated before undergoing endoscopy every 3 months for the first year, every 6 months in the second year, and then annually thereafter. New data suggest that perhaps a less aggressive schedule may also be feasible, but for now this is what the guidelines recommend.

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

NS The definition and description of the utility of biomarkers is very important in this area. A better understanding of which biomarkers should be used and when is an effort that multiple centers throughout the country are undertaking. Developing nonendoscopic methods for diagnosing Barrett esophagus, such that clinicians may be able to perform wider screening for the disease and therefore recognize disease earlier, is going to be key in decreasing the incidence of esophageal adenocarcinoma. I think the main message to primary care physicians is to look for and actively screen high-risk individuals, specifically people over the age of 50 years with chronic symptoms of gastroesophageal reflux disease. Patients who are obese, who smoke, and who are male are especially high-risk groups.

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Suggested Reading

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