

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Barrett Esophagus and Life Expectancy: Implications for Screening?

Ernst J. Kuipers, MD, PhD
 Professor of Medicine
 Chair, Departments of Internal Medicine and
 Gastroenterology and Hepatology
 Erasmus MC University Medical Center
 Rotterdam, The Netherlands

G&H How prevalent is Barrett esophagus in the general population, and how prevalent is it in patients with gastroesophageal reflux disease?

EJK The incidence and prevalence of Barrett esophagus vary widely among populations, reflecting their prevalences of gastroesophageal reflux disease (GERD). In a study from Kaiser Permanente in California, the annual incidence of Barrett esophagus ranged from 6 cases per 100,000 blacks and 16 cases per 100,000 Asians to 22 cases per 100,000 Hispanics and 39 cases per 100,000 non-Hispanic whites. However, true population prevalence data are very scarce, as most prevalence studies are based on select populations undergoing endoscopy. In North American and European studies, the prevalence of Barrett esophagus has generally ranged from 2.4% to 13.2% in patients with dyspepsia or GERD symptoms who are undergoing endoscopy. In an attempt to obtain data from an asymptomatic population, some studies have focused on subjects undergoing colorectal cancer screening and have reported Barrett esophagus rates of 5.6–16.7%. However, because these populations were indicated for colonoscopy, they were comprised mainly of elderly individuals. A computer modeling study based on the incidence of esophageal adenocarcinoma and progression rates of Barrett esophagus to adenocarcinoma estimated that Barrett esophagus has a prevalence of 5.6% in the United States. In 2 European population-based

screening studies in which unselected subjects from a village all underwent endoscopy screening, the prevalence of Barrett esophagus was 1.6% in 1,000 Swedish subjects and 1.3% in 1,533 Italian subjects. From these studies, we can conclude that Barrett esophagus is a common condition, with a prevalence that most likely ranges from 2% to 6% in Western countries.

Interestingly, the incidence of Barrett esophagus has been increasing over time. In a Dutch study, the incidence of this condition increased from 14.3 cases per 100,000 individuals to 23.1 cases per 100,000 individuals per year between 1997 and 2002. This increase was not related to an increase in upper gastrointestinal endoscopies. The increase matches the increased incidence of esophageal adenocarcinoma in Western countries.

G&H How is Barrett esophagus usually detected in patients?

EJK Barrett esophagus is usually detected when patients undergo endoscopy for GERD symptoms. A considerable proportion of patients with Barrett esophagus is asymptomatic and remains undiagnosed unless an endoscopy is performed for other reasons. A small proportion of patients is diagnosed with Barrett esophagus when they present with alarm symptoms caused by esophageal adenocarcinoma. Most patients with esophageal adenocarcinoma were not previously diagnosed with Barrett esophagus.

G&H How often do patients with Barrett esophagus develop cancer?

EJK More than 50 cohort studies have reported on the incidence of esophageal adenocarcinoma in Barrett esophagus patients during follow-up. These study populations have ranged from less than a dozen patients to almost 3,000 patients who were followed long term. In a meta-analysis of these studies, the pooled estimate

for the incidence of esophageal adenocarcinoma was 6.3 cases per 1,000 patient-years of follow-up (95% confidence interval [CI], 4.7–8.4), the pooled estimate for the incidence of high-grade dysplasia and cancer was 10.2 cases per 1,000 patient-years of follow-up (95% CI, 7.5–14.0), and the pooled estimate for the incidence of fatal esophageal cancer was 3.0 cases per 1,000 patient-years of follow-up (95% CI, 2.2–3.9). These data were corroborated by a Dutch nationwide study of patients with histologically confirmed Barrett metaplasia. Among 42,207 subjects with 234,821 patient-years of follow-up, the annual incidence of esophageal adenocarcinoma was 4.3 cases per 1,000 patient-years (95% CI, 3.4–5.5).

Based on these cohort studies, clear distinctions can be made with respect to patient subgroups. The risk of cancer development is higher in men, patients with longer Barrett esophagus segments, and patients with dysplasia. In our Dutch cohort of 42,207 patients, the risk of progression to cancer was 3-fold higher among patients with low-grade dysplasia at baseline. The risk of cancer development was very high in patients with high-grade dysplasia.

G&H Has the risk of developing cancer been overestimated in patients with Barrett esophagus?

EJK The incidence of esophageal adenocarcinoma has rapidly increased over the past several decades. Although the mechanisms leading to cancer are insufficiently understood, the correlation between intestinal metaplasia in Barrett esophagus and adenocarcinoma has been well established. Furthermore, this metaplastic target lesion can be readily diagnosed and, nowadays, successfully treated, putting a strategic emphasis on the importance of diagnosis, surveillance, and intervention for the prevention of esophageal cancer. This has resulted in important developments, such as new endoscopic light techniques and intervention methods, such as mucosal resection techniques, that also have applications in other areas and are less invasive and cause less morbidity than previous surgical techniques. At the same time, patient-centered care requires that we have similar strategies for dealing with risk profiles of disease throughout the digestive system. Our approach should parallel efforts to screen and prevent colon and gastric cancers.

According to data from 2005 to 2007, men and women born now in the United States are estimated to have a lifetime risk of esophageal cancer (adeno and squamous cancer combined) of 0.50%; thus, their risk for esophageal adenocarcinoma is approximately 0.40%. These subjects also have a lifetime risk of stomach cancer that is 2-fold higher (0.88%), a lifetime risk of pancreatic cancer that is 3-fold higher (1.41%), and a lifetime risk of colorectal cancer that is more than 10-fold higher (5.12%). These differences reflect the prevalence of precursor lesions, such as Barrett

metaplasia, atrophic gastritis and intestinal metaplasia of the stomach, and colorectal adenoma. For each of these precursors, the risk of progression to cancer depends on severity, yet the overall risk is very similar among precursor lesions. For example, the progression to cancer among subjects with intestinal metaplasia and low-grade dysplasia of the stomach is very similar to the progression to cancer in patients with intestinal metaplasia and low-grade dysplasia of the esophagus, yet our approach to these patients differs widely.

G&H Does the presence of Barrett esophagus in a patient shorten his or her life expectancy?

EJK Barrett esophagus patients appear to have a decreased life expectancy, although this finding is not consistently noted in all studies. Potential explanations include a true correlation due to shared risk factors such as obesity and smoking, as well as the possibility that subjects with comorbidities are more likely to undergo endoscopy and, thus, be diagnosed with Barrett metaplasia.

Despite this uncertainty, it is clear that esophageal cancer is the cause of death in a minority of Barrett esophagus patients. In most cohort studies, esophageal cancer accounted for 4–8% of mortality. In contrast, cardiovascular and respiratory conditions accounted for more than 50% of mortality. In our Rotterdam cohort of 133 long-segment Barrett esophagus patients who have been followed since they were diagnosed between 1973 and 1986, 109 (82%) patients have died; in only 6 (5.5%) patients, death was related to esophageal adenocarcinoma due to either end-stage cancer or surgery. Their mean age at death was 81 years (range, 70–96 years). This cohort study showed that the incubation period from Barrett esophagus to invasive cancer is likely more than 30 years.

G&H What are the screening guidelines for Barrett esophagus in Europe and the United States?

EJK There are several guidelines on the management of patients with Barrett esophagus. The recent American Gastroenterological Association position statement on the management of Barrett esophagus recommends the screening of patients with multiple risk factors associated with esophageal adenocarcinoma (50 years of age or older, male gender, white race, chronic GERD symptoms, and an elevated body mass index); this was classified as a weak recommendation with moderate-quality evidence. The committee recommends against screening all patients with GERD; this was classified as a strong recommendation with low-quality evidence. These statements agree with the American Society for Gastrointestinal Endoscopy guidelines. According to guidelines from the American College of Gastroenterology, the use of screening in the general population cannot be recom-

mended, and the benefit of screening select populations with higher risks of esophageal cancer remains to be established. The committee remarked that screening remains controversial in the absence of documented impact on mortality from cancer; furthermore, the large number of Barrett esophagus patients who lack reflux symptoms provides a diagnostic challenge. British Society of Gastroenterology guidelines recommend against screening and do not make exceptions for any subgroups of patients.

G&H Are there data on how many people are screened and how many cases of Barrett esophagus are detected each year?

EJK Although a number of studies have reported on the incidence of Barrett esophagus, we do not know how many people undergo screening. Some researchers have questioned gastroenterologists both in the United States and Europe regarding imaginary cases, but it is difficult to translate these data into the real number of cases being screened each year. These surveys do suggest that screening is applied more widely than is recommended by guidelines.

G&H Do you think that any additional patient groups should be screened for Barrett esophagus?

EJK The existing guidelines are quite clear in their recommendation to exercise restraint when screening patients for Barrett esophagus. The guidelines are also clear in explaining the uncertainties surrounding screening. At the moment, there is no evidence that screening should be performed more widely than recommended by these excellent guidelines. GERD is a very common condition. Many patients with Barrett esophagus do not have GERD symptoms. Esophageal cancer remains a relatively rare condition. Most importantly, there is, at present, insufficient proof from prospective studies that screening has a significant impact on mortality from esophageal cancer, as well as on overall mortality.

G&H Are there any disadvantages to screening individuals who may not need it?

EJK Screening for Barrett esophagus—like screening for any other disease—is not harmless. Screening requires significant resources, in terms of costs and endoscopy capacity. Furthermore, even though the risks associated with upper gastrointestinal endoscopy, biopsy sampling, and sedation are very small, they become important when applied to large populations in a screening setting. In addition, patients diagnosed with Barrett esophagus may overestimate their cancer risk, contributing to a decreased quality of life as well as increased insurance premiums.

G&H What are the next steps for research in this area?

EJK There is much excellent ongoing research on new detection methods for Barrett esophagus, optimization of diagnostic techniques for the detection of dysplastic foci within Barrett mucosa, and endoscopic treatment methods. Apart from this ongoing research, we greatly need more solid data to determine whether Barrett esophagus screening reduces mortality due to esophageal cancer as well as overall mortality. The same question pertains to surveillance for dysplasia in patients with known Barrett esophagus. With the newer ablative treatment methods, we need to know which patients benefit most in terms of morbidity and mortality and at which burden and costs. Given the low frequency of relevant disease endpoints, such studies need to be carefully designed and should include multiple centers. Furthermore, we need more data on the incubation period from the establishment of metaplasia to the development of invasive cancer. If the average incubation period is very long, this would imply that subjects who develop Barrett metaplasia after 50 years of age have a low risk of developing esophageal adenocarcinoma. Finally, there is a need for more information on the impact of drugs such as proton pump inhibitors, aspirin, nonsteroidal anti-inflammatory drugs, and statins on the progression of Barrett metaplasia.

Suggested Reading

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