



Screening and surveillance for Barrett's esophagus

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Elements for analysis

Epidemiology of adenocarcinoma in the upper digestive tract

The annual incidence of esophageal adenocarcinoma is increasing in North America, where adenocarcinoma tends to be more frequent than squamous-cell cancer, and in northern European countries.

The annual incidence of cancer at the cardia is increasing in the same countries, but there is some bias in the recording of cases, with overregistration of the cardia as the site in cases in which the site is not recorded. In fact, the incidence in the proximal stomach is found to be stable when this bias is corrected.

Tumors in the esophagogastric region include adenocarcinoma in the distal esophagus and adenocarcinoma in the proximal stomach. Many tumors registered at this site correspond to short-segment Barrett's esophagus (BE) and have been classified as cancer at the cardia.

The annual incidence of cancer in the distal stomach is declining.

The risk of cancer in Barrett's esophagus

A precancerous lesion in the gastrointestinal mucosa is a localized benign tumor with a significant potential for malignant progression. A precancerous condition corresponds to the status of a nonneoplastic mucosal area that has an increased risk for the development of a precancerous lesion. This means that cancer will occur only in a small fraction of the cases.

BE is a precancerous condition in which the risk of cancer has been overestimated due to publication bias (with positive findings being accepted more easily than negative findings). A reasonable estimate is 0.5 cancers occurring per 100 patient-years. This risk is estimated for males of Caucasian descent. In addition, individual factors conferring a higher risk are smoking and a long history of reflux symptoms. At present, adenocarcinoma in the esophagus is less frequent than at the gastric cardia. The worldwide burden of esophageal adenocarcinoma is small in comparison with the burden of gastric and colorectal cancer, but if the trend towards an increase is sustained, the situation may justify a policy of prevention and early detection.

■ *Etiology of BE and epidemiology of GERD*

Barrett's esophagus is a complication of gastroesophageal reflux disease (GERD). Inflammatory stress, resulting in metaplastic transformation of the mucosa and the development of a precancerous condition, is attributed to the presence of acid and bile salts in the refluxate; however, factors other than reflux may be also be causally involved in the development of precancerous lesions. Ethnic origins, male sex, increased body weight during adolescence, and persistent smoking may play a role.

There has been an inverse relationship in recent decades between the prevalence of duodenal ulcers (decreasing) and of GERD (increasing). The prevalence of GERD is increasing not only in Western countries but also in Asia, where it was previously uncommon. It is therefore expected that an increased prevalence of BE both in Western countries and in Asia will be observed in the coming few years. If the inflammatory stress in the metaplastic mucosa of the BE plays a major role in esophageal carcinogenesis, a parallel increase in the risk of cancer can be expected, despite the multiplicity of etiological factors.

Strategy

■ *Prevention of adenocarcinoma in BE*

Most cases of adenocarcinoma in the esophagus are detected at an advanced stage in patients with obstructive symptoms. This means that the status of prevention is very poor. An improved policy requires early diagnosis in patients with BE who have confirmed precancerous lesions, or the development of methods of detecting precancerous BE.

The majority of patients with BE, a precancerous condition, are asymptomatic; however, the overall risk of adenocarcinoma is far too small to justify a policy of mass screening in the population, based on upper gastrointestinal endoscopy as the selection test for BE. The strategy for detecting BE therefore needs to focus on the usual indications for endoscopy, taking into account the fact that systematic examination of patients with reflux symptoms would miss a large proportion of the target lesions.

A diagnosis of BE during upper gastrointestinal endoscopy is made in two distinct conditions: firstly, when the indication is based on reflux symptoms; and secondly, when the indication is for ulcer or nonulcer dyspepsia, or for opportunistic screening for gastric cancer. In the latter situation, examination during passage of the endoscope through the esophagus is often neglected and BE often remains undiagnosed. It can therefore be concluded that the most appropriate policy for preventing esophageal adenocarcinoma must be based on systematic screening for BE during all upper gastrointestinal endoscopy examinations, for whatever indication.

■ *Prevention strategy: 1, detecting BE*

Guidelines should be developed for quality control during endoscopic detection of BE. The following points should be emphasized:

- Use a recent model of video endoscope.
- Identify the landmarks with precision: the squamocolumnar junction, the esophagogastric anatomical junction (gastric folds and palisade vessels).

- Classify as: negative for BE, positive for short-segment BE, or positive for long-segment BE.
- When the findings are positive for BE, chromoscopy and/or magnification endoscopy are highly recommended but cannot yet be considered as standard methods. Only a few randomized and controlled studies have been performed so far to evaluate these technologies, and these showed conflicting results. In the meantime, histological control using the Seattle protocol is still preferable to selectively targeted biopsies. However, systematically taking four-quadrant biopsies (Seattle protocol) from every other centimeter of the segment with metaplasia, plus biopsies in any suspect area, is time-consuming and not completely reliable.
- When the findings are positive for intestinal metaplasia, detect any areas with neoplasia.

■ *Prevention strategy: 2, surveillance*

- There are no data indicating that surveillance strategies are cost-effective. A recent model analysis showed that, even for men over 50 years of age, surveillance of nonneoplastic BE is not cost-effective even if performed at 5-year intervals, with an excessively high cost per quality-adjusted life-year (QALY).
- When the examination is negative for intraepithelial neoplasia, the surveillance recommended by scientific societies is based on case-controlled trials showing that the surgical results were better in patients with BE who were receiving surveillance than in those who were not.
- The latest guidelines recommend adapting the surveillance strategy for BE to the scale of the risk, provided that the inclusion endoscopy followed the required criteria for quality control. Surveillance is justified at 3-year intervals in those who have high-risk factors (men and smokers) and who are in good health. In women and non-Caucasians, who have a lower risk, surveillance is less cost-effective; however, it appears to be unethical to exclude these groups from a surveillance program. For individuals in poor health (e.g., the elderly and patients with respiratory or cardiovascular disease), surveillance is not justified.
- It has been suggested that patients with longer BE segments have a higher risk of progression towards cancer. A recent study has confirmed this tendency with increasing segment length; however, the difference is small, and the frequency of endoscopic surveillance should be selected without regard to segment length.

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The texts of all of these references are available at www.esge.com

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