American Gastroenterological Association Technical Review on the Role of the Gastroenterologist in the Management of Esophageal Carcinoma

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The goal of this evidence-based review was to examine the clinical practice of the gastroenterologist in the management of patients with esophageal carcinoma. The methods for this review were to search and review the literature available on MEDLINE and PREMEDLINE on the topics of esophageal neoplasm, esophageal cancer, and Barrett's esophagus from 1968 to 2004. Bibliographies of significant reports were also reviewed to ensure that the pertinent literature was reviewed. Recommendations are graded as to the level of evidence available on a scale of I–V. Level I evidence is the presence of at least one prospective, randomized, controlled trial, level II evidence is based on well-designed cohort or case-controlled studies, level III evidence is based on case series or flawed clinical trials, level IV evidence is based on opinions of respected authorities or expert committees, and level V evidence is insufficient evidence to form any opinions.

Significance of Esophageal Cancer

Esophageal cancer is associated with one of the highest cancer mortality rates in the United States. In 2000, the last year of complete data available from the national cancer Surveillance, Epidemiology, and End Results database, the 5-year relative survival rates from esophageal cancer were the fifth lowest at 15.4%. In addition, the incidence of esophageal cancer is still significantly trending upward in white men with a 0.4% annual percentage increase from 1992 to 2000. This can be compared with colon cancer, which has actually had a significant decrease of 0.9% annual percentage change over the same period. Esophageal cancer is a predominantly male condition with a male/female incidence of 3.6:1. Esophageal cancers affect older patients, with the peak incidence in those 65–74 years old. It is estimated that, in 2003, there were 13,900 new cases of esophageal cancer and 13,000 deaths due to esophageal cancer. The mortality rate of esophageal cancer is significantly higher in minority populations than in white people.

There are 2 major types of esophageal cancer: adenocarcinoma and squamous cell cancer. The primary known risk factors for adenocarcinoma of the esophagus are smoking, chronic gastroesophageal reflux disease, and Barrett's esophagus. Known risk factors for squamous cell cancer of the esophagus include smoking, alcohol use, exposure to nitrosamines, ingestion of lye, Fanconi's anemia, achalasia, Plummer–Vincent webs, and tylosis.

Screening and Surveillance for Esophageal Cancer

Screening for Esophageal Cancer

Adenocarcinoma. Screening for esophageal cancer depends on the determination of the patient's risk for cancer, the cost and efficacy of the screening procedure, the stage at which the cancer can be diagnosed, and the treatment options available. At the current time, there is no direct evidence that has validated the use of screening for esophageal cancer in the United States. Screening for esophageal adenocarcinoma has been primarily focused on the detection of Barrett's esophagus with subsequent surveillance. Although screening for Barrett's esophagus has not been proven to decrease the risk of cancer, it has become accepted that surveillance for Barrett's esophagus can detect disease at earlier stages.[1–3] Barrett's esophagus has traditionally been found to be associated with chronic gastroesophageal reflux disease, and case series have found increasing incidences of Barrett's esophagus depending on the number of years of reflux symptoms.[4] However, a single-center study of 110 subjects found that 7% of asymptomatic individuals had long-segment

Abbreviations used in this paper: CI, confidence interval; CT, computed tomography; EUS, endoscopic ultrasonography; FDA, Food and Drug Administration; Nd:YAG, neodymium:yttrium-aluminum-garnet; OCT, optical coherence tomography; PAR, population attributable risk; PDT, photodynamic therapy; PET, positron emission tomography; QALY, quality-adjusted life year; SEMS, self-expanding metal stents.

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0016-5085/05/$30.00
doi:10.1053/j.gastro.2005.03.077

(>3 cm) Barrett's esophagus.[5] A multicenter study of 536 subjects found that long-segment Barrett's esophagus was only present in 0.36% of subjects, although short-segment Barrett's esophagus was found in 5.6%.[6] This study did find that patients with heartburn had a significantly higher prevalence of long-segment Barrett's esophagus than those who did not. This is significant because past studies have shown that the degree of neoplasia found in Barrett's esophagus appears to be correlated with the length of Barrett's esophagus.[7] Other groups that may be at risk would include those with familial occurrence of adenocarcinoma, but this has only been described in a limited number of families. The cost-efficacy of screening family members because of a history of Barrett's esophagus has not been demonstrated.[8–12]

Screening methods for detection of Barrett's esophagus have included standard endoscopy, unsedated endoscopy with ultrathin endoscopes, catheter-based cytology, and balloon cytology.[13–16] Although preliminary studies indicate some promise with these technologies in terms of screening for adenocarcinoma, there have not been any definitive trials to allow recommendation of these techniques.

Squamous cell cancer. Screening for squamous cell cancer in the general population of the United States cannot be justified because of the low incidence of this form of cancer. However, specific subgroups may be identified that warrant screening endoscopy for squamous cell cancer. The most likely to benefit from screening would be those who have tylosis, which is a genetic defect in the 17q25 region that is found in patients with thickened palms and soles.[17,18] This group is likely to develop cancer by the age of 65 years and should undergo screening for squamous cell cancer. Patients with lye-induced or caustic strictures develop cancers approximately 46 years after ingestion and have been described to have an 8% incidence of cancer.[19,20] The development of cancer in patients with long-standing achalasia is infrequent, especially in women, and it is unclear if surveillance is warranted in these patients.[21] Most patients with achalasia are found to have prevalent cancers because they are usually diagnosed when obstruction and esophageal dilation are found.[22] Fanconi's anemia has also been associated with the development of esophageal cancer and may become more common as patients survive longer after bone marrow transplantation.[23] Patients with existing aerodigestive tumors, especially those of the oral cavity, who have had long-term extensive exposure to alcohol and tobacco might benefit from screening for cancers of the esophagus, although the rationale for this is based on case series.[24] Screening for esophageal cancer should be performed at the time of diagnosis of the head-and-neck cancer. Extensive alcohol consumption alone has been found to be an important criterion for screening in Asian patient populations.[25] Partial gastrectomies have been associated with an increased incidence of squamous cell cancers of the esophagus; these reports stem from areas of the world where squamous cell cancer is commonly found, and there is no convincing evidence to support the screening of patients in the United States.[26] The occurrence of squamous cell cancer is not decreasing in minority populations in the United States and remains the most frequent form of esophageal cancer in black and Hispanic populations.[27,28] Other conditions such as Plummer–Vinson webs have also been identified as being associated with an increased risk for squamous cell cancers, but the decreasing frequency of these webs makes this almost a historical footnote in Western countries.[29]

Screening methods such as cytologic balloons or sponges for screening for squamous cell cancers have been extensively tested in Asia. Balloons appear to be better than sponges, with an increased sensitivity of 44% compared with 18% for sponges.[30] This technology has been used as the primary screening tool in high-risk areas of China.[31]

Summary of Evidence—There is level III evidence that endoscopic screening of male white patients older than 50 years of age with symptoms of gastroesophageal reflux may be cost-effective. Patients with tylosis, lye-induced strictures, or Fanconi's anemia would benefit from screening endoscopy for squamous cell cancers (level III evidence). In addition, patients with long-term tobacco and alcohol use, achalasia, or prior head-and-neck cancers could be considered for screening, depending on their other risk factors (level III evidence). The interval for surveillance of these patients has not been established, but yearly investigations would seem to be reasonable (level IV evidence).

Surveillance for Esophageal Cancer

Significance of surveillance. The importance of Barrett's esophagus derives from its association with esophageal adenocarcinoma.[32,33] Approximately 5%–10% of patients diagnosed with Barrett's esophagus may develop esophageal adenocarcinoma based on older studies.[32,34,35] The incidence of cancer will most likely decrease with the increasing detection of Barrett's esophagus through screening programs. Surveillance of Barrett's esophagus can detect dysplasia in Barrett's esophagus, which can predict the risk of future diagnosis of esophageal cancer in these patients.[36,37]

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