Screening and Preventive Strategies in Esophagogastric Cancer

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KEYWORDS

• Screening • Prevention • Gastric adenocarcinoma • Barrett esophagus
• Esophageal adenocarcinoma • Esophageal squamous cell carcinoma

KEY POINTS

- Gastric adenocarcinoma, esophageal adenocarcinoma, and esophageal squamous cell carcinoma are among the most prevalent and deadly of malignancies.
- Screening in high-risk populations has significantly reduced the mortality of gastric adenocarcinoma; however, screening efficacy for high-risk individuals within low-risk populations is unclear.
- Although esophageal adenocarcinoma has a clear precursor lesion (Barrett esophagus), clearly effective screening techniques and programs are still being developed.
- Screening for esophageal squamous cell carcinoma is not cost-effective; however, avoidance of environmental risk factors (smoking, alcohol abuse) can prevent the disease.

INTRODUCTION

Gastric and esophageal cancers are among the most common tumors that cause significant mortality worldwide, although their incidence is much higher in specific geographic locations. Unfortunately, although new treatment protocols have improved the outcome of most major malignancies, prognosis in gastric and esophageal cancer remains poor. Screening and prevention programs offer the hope of reducing morbidity and mortality from these diseases.

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GASTRIC CANCER

Gastric cancer is among the most common cancers in the world with more than 900,000 cases in 2012, making it the fifth most common cancer in the world.[1,2] The incidence of gastric cancer, however, is much higher in the developing world, particularly in East Asia where more than 50% of cases occur.[3] Although screening programs have been developed in Asian countries, particularly Japan and Korea, significantly improving outcomes through early detection,[4–6] mortality rates in the West have remained high.[7,8]

Risk Factors

There are numerous risk factors for developing gastric cancer. These risks can be broken down into modifiable and nonmodifiable (**Table 1**).

Nonmodifiable risk factors

Race and ethnicity are nonmodifiable risk factors for gastric cancer. Although environmental factors likely play a role, they alone cannot explain the high incidence of disease in East Asia; particularly because this increased incidence persists in immigrants and their offspring from East Asia to the West.[9,10] Age is also important, with more than 90% of cases occurring after the age of 45 years.[8] Family history also contributes to risk, with studies from both the West and East showing a first-degree relative with gastric cancer increases a person's risk 2- to 4-fold.[11–13] Gender also plays a role, with men having a 2- to 5-fold increased risk of gastric cancer.[14] Higher estrogen levels seem to protect women from the disease. Increased rates of gastric cancer in women on estrogen-blocking therapies (tamoxifen) and after menopause demonstrate this effect.[15,16] In fact, women seem to develop gastric cancer at a similar rate to men but with a 10 to 15 year lag.[17]

Although gastric cancer is usually sporadic, about 10% of cases seem linked to genetic syndromes.[18] The most common syndrome is hereditary diffuse gastric cancer (HDGC), recently defined by the International Gastric Cancer Linkage Consortium.[19] HDGC is characterized by autosomal dominant inheritance, with about a 60% to 80% increase in the risk of gastric cancer and a 40% to 50% increase in breast cancer. About 40% of HDGC is due to mutations in E-cadherin (CDH1). Mutations in CTNNA1 have also recently been found in a subset of patients with the condition.[18] Other cancer syndromes have been associated with increased risk of gastric cancer, including Lynch syndrome (DNA mismatch repair gene mutation), familial adenomatous polyposis (APC gene mutation), Peutz-Jeghers syndrome (STK11 gene mutation), juvenile-polyposis syndrome (SMAD4 or BMPR1A mutation), hereditary breast and ovarian cancer syndrome (BRCA 1 or BRCA 2 mutation), and Li-Fraumeni syndrome (p53 mutation). However, gastric cancer still remains very uncommon in these syndromes, with rates of occurrence less than 5%.[20]

Table 1
Risk factors for developing gastric cancer

Nonmodifiable Risk Factors	Modifiable Risk Factors
Race or ethnicity (East Asian or Pacific Islander)	*H pylori* infection
Age (>45 y)	Tobacco smoking
Family history	Obesity (body mass index >30)
Sex (Male) Genetics	High salt diet
	Low fruit or vegetable diet