

Screening and surveillance for gastric cancer in the United States: Is it needed?

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Background and Aims: Although the incidence of gastric cancer in the United States is relatively low, the incidence of gastric cancer is higher than for esophageal cancer, for which clear guidelines for screening and surveillance exist. With the increasing availability of endoscopic therapy, such as endoscopic submucosal dissection, for treating advanced dysplasia and early gastric cancer, establishing guidelines for screening and surveillance of patients who are at high risk of developing gastric cancer has the potential to diagnose and treat gastric cancer at an earlier stage and improve mortality from gastric cancer. The aims of this article were to review the data regarding the risk factors for developing gastric cancer, methods for gastric cancer screening, and results of national screening programs.

Methods: A review of the existing literature related to the aims was performed.

Results: Risk factors for gastric cancer that were identified include race/ethnicity (East Asian, Russian, or South American), first-degree relative diagnosed with gastric cancer, positive *Helicobacter pylori* status, and presence of atrophic gastritis or intestinal metaplasia. Endoscopy has the highest rate of detecting gastric cancer compared with other gastric cancer screening methods. The national screening program in Japan has demonstrated a mortality reduction from gastric cancer based on cohort data.

Conclusions: Gastric cancer screening with endoscopy should be considered in individuals who are immigrants from regions associated with a high risk of gastric cancer (East Asia, Russia, or South America) or who have a family history of gastric cancer. Those with findings of atrophic gastritis or intestinal metaplasia on screening endoscopy should undergo surveillance endoscopy every 1 to 2 years. Large prospective multicenter studies are needed to further identify additional risk factors for developing gastric cancer and to assess whether gastric cancer screening programs for high-risk populations in the United States would result in improved mortality. (Gastrointest Endosc 2016;84:18-28.)

Gastric cancer is one of the world's leading causes of morbidity and mortality from malignant disease. An estimated 1 million cases of gastric cancer (952,000 cases; 6.8% of all

Abbreviations: AG, atrophic gastritis; CI, confidence interval; EGC, early gastric cancer; IM, intestinal metaplasia; OR, odds ratio; PG, pepsinogen; UGI, upper GI.

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cancers) occurred globally in 2012, making it the fifth most-common malignancy in the world, after lung, breast, colorectal, and prostate cancers.^{1,2} More than 70% of gastric cancer cases occur in the developing world, and approximately 50% occur in East Asia.³ Gastric cancer is less common in the United States, with the incidence of gastric cancer among males and females in the United States at 12.3 and 6.0 per 100,000/year, respectively; however, there is a disproportionately higher incidence in Asians.⁴ The estimated number of new cases of gastric cancer in the United States in 2015 was 24,590 (1.5% of all cancers) and 10,720 deaths (1.8% of all cancer deaths).⁵ It should be noted that the estimated number of new cases of esophageal cancer in the United States for 2015 was 16,980 (1.0% of all cancers), which is less than the number of new cases of gastric cancer. Guidelines for esophageal cancer screening and surveillance of Barrett's esophagus exist; however, guidelines for gastric cancer screening and surveillance of gastric intestinal metaplasia (IM) are lacking.

TABLE 1. Main risk factors for gastric cancer according to the tumor location

	Risk estimates (95% CI)		Reference
	Noncardia cancer	Cardia cancer	
<i>H pylori</i> infection	RR 2.97 (2.34-3.77)	RR .99 (.72-1.35)	Helicobacter and Cancer Collaborative Group ²³
Cigarette smoking	RR 1.60 (1.41-1.80)	RR 1.87 (1.31-2.67)	Ladeiras-Lopes et al ⁹⁷
Alcohol	RR 1.07 (.91-1.26)	RR .94 (.78-1.13)	Tramacere et al ⁹⁸
Obesity (BMI > 30)	RR 1.26 (.89-1.78)	RR 2.06 (1.63-2.61)	Yang et al ⁹⁹
Vegetables	RR .75 (.59-.95)	RR .63 (.50-.79)	Lunet et al. ¹⁰⁰
Fruit	RR .61 (.44-.84)	RR .58 (.38-.89)	Lunet et al. ¹⁰⁰
High salt intake	OR 2.05 (1.60-2.62)		Ge et al. ¹⁰¹
Family history of gastric cancer	OR 2.82 (1.83-4.46)		Shin et al. ²⁷
Intestinal metaplasia	RR 6.4 (2.6-16.1)*		Uemura et al. ³⁷

CI, Confidence interval; RR, relative risk; BMI, body mass index; OR, odds ratio.

*In *H pylori*-positive individuals.

Since the 1970s there have been notable improvements in the 5-year relative survival rates for gastric cancer in the United States, from 15% in 1975 to 29% in 2009.⁶ However, these low survival rates suggest that most cases (over 65%) are still diagnosed at an advanced stage.⁵ The overall 5-year relative survival rate is about 20% in most parts of the world, but in Japan and Korea 5-year survival rates above 70% for stage I and II gastric cancer have been reported.⁷⁻⁹ A multicenter retrospective study of 2191 patients with gastric cancer undergoing surgical resection showed that early gastric cancer (EGC) comprised approximately 20% of all surgically resected cancers in North America compared with 50% of resected cancers in Japan.¹⁰ Although these differences can be explained by multiple factors, one of most plausible reasons is the implementation of a screening program for detection of EGC in Japan and Korea.

Identification of risk factors involved in carcinogenesis and interventions to address these risk factors may reduce the incidence of gastric cancer. Reducing gastric cancer mortality also requires early identification of patients who are at high risk for gastric cancer and management strategies to slow or prevent progression of gastric cancer. It is likely to be more cost-effective to detect and treat early-stage gastric cancer with endoscopic resection rather than surgical resection. In this review we discuss risk factors for gastric cancer, define high-risk groups, and summarize current guidelines for screening and surveillance strategies for these high-risk groups. Finally, we propose an algorithm for screening and surveillance of individuals who are at high risk for gastric cancer in the United States.

RISK FACTORS FOR GASTRIC CANCER

Gastric cancer is a multifactorial disease involving both genetic and environmental risk factors. Its risk factors differ depending on whether cancers arise in the proximal cardia

region or in the distal noncardia region. Advanced age, male sex, smoking, and family history are common risk factors for both cardia and noncardia cancers. In terms of race/ethnicity, whites tend to develop cardia cancer, whereas Hispanics and Asians tend to develop noncardia cancer. *Helicobacter pylori* infection and dietary factors, such as high intake of salt, increase the risk of noncardia cancer. On the other hand, obesity and GERD are mainly associated with cancers arising from the cardia. The estimates of risk factors for gastric cancer are summarized in Table 1.

Age

The incidence of gastric cancer increases with age. Between 2007 and 2011 only 6% of cases occurred in individuals younger than age 45 in the United States, whereas approximately 70% of cases were diagnosed in individuals aged 55 to 84.

Sex

Compared with women, men have a higher risk of both cardia (5-fold) and noncardia (2-fold) gastric cancer.¹¹ The reason for this difference is unclear, but environmental or occupational exposures may play a role. Men have historically tended to smoke more than women, whereas estrogens may protect against the development of gastric cancer.¹² Delayed menopause and increased fertility may lower the risk of gastric cancer, whereas antiestrogen drugs such as tamoxifen may increase the rates of gastric cancer.^{13,14} These hormones may protect against gastric cancer among women of childbearing age, but their effect is diminished after menopause. Consequently, women develop gastric cancer in a manner similar to men, albeit with a 10- to 15-year lag period.¹⁵

Race/ethnicity

There is significant variability in the gastric cancer incidence across different ethnicities in the United States.

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