

Stomach Cancer

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Key points

- Stomach cancer was the fifth most common malignant tumor in the world in 2020
- Genetics, environmental and lifestyle factors, H. pylori infection play part in its development
- Primary and secondary prevention strategies are the focus of stomach cancer prevention.

Stomach cancer was the fifth most common malignant tumor in the world in 2020 with approximately 1.1 million new cases, and is the fourth leading cause of cancer death, with around 800000 deaths.^{1,2} Over 85% of stomach cancer cases are registered in countries with high and very high Human Development Index (590000 and 360000 cases, respectively) ¹. The highest number of cases of stomach cancer (almost 820000 new cases and 580000 deaths) were registered in Asia (mainly in China).^{1,2,3} The estimated five-year survival rate is lower than 20%.^{2, 4,5}

Stomach cancer is a multifactorial disease including both lifestyle and environmental risk factors Helicobacter pylori (H. pylori) infection, low socioeconomic status, dietary factors.

Topographically, stomach cancer is classified into two subsites: cardiac stomach cancer (arising from the upper stomach) and non-cardiac stomach cancer (arising from the other parts of the stomach), which differ in epidemiologic patterns and etiology.⁶ The majority of all stomach cancers (approximately 90%) are adenocarcinomas, while other types (including lymphoma, sarcoma, neuro-endocrine tumors) are rare.^{7, 8} Two major histologic types of stomach cancer adenocarcinomas are diffuse and intestinal, which differ in epidemiological peculiarities, such as age at diagnosis, gender ratio, etc.^{9, 10}

Despite the strong declining trends in incidence and mortality, stomach cancer remains an important part of the global burden of cancer. Many of the risk factors remain insufficiently understood and need to be the focus of further research in order to achieve more specific and targeted preventive and curative measures.

Causes

Although differences in stomach cancer incidence in

different parts of the world are still not fully clear, most of the variation in stomach cancer incidence worldwide is due to variations in exposure to environmental or lifestyle related risk factors.^{11,12} Additionally, migrant studies¹³ and secular trends of gastric cancer rates also indicate that environmental factors have an important role in the etiology of gastric cancer.¹⁴ The most important risk factor for gastric cancer is H. pylori infection. Internationally, variations in H. pylori infection prevalence show similarities with variations in stomach cancer prevalence; in developing countries, H. pylori infection prevalence in adults is 76% vs 58% in developed countries.¹⁵ The prevalence was estimated to be 77.6% in South Africa, 55.8% in China, 52.2% in Mexico, 24.6% in Australia and 22.1% in Denmark.¹⁶ In the United States of America, the prevalence in non-Hispanic blacks was 53%, in Mexican Americans it was 62%, but was 26% among non-Hispanic whites.¹⁷ In part, the geographical variation of H. pylori infection rates correlates with the frequency of stomach cancer across populations. On the other hand, certain highly infected populations (e.g. in Africa and South Asia), unlike the East Asian countries, do not have a high incidence of stomach cancer, which can be explained, at least in part, by the differences in prevalence of genotypes of H. pylori (in East Asian the vacA m1 genotype is predominant, whereas the m2 genotype predominated in Africa, South Asia, and Europe).¹⁸

In addition, some research points to the role of aging, hereditary and genetic factors in stomach cancer burden. Some theories have suggested a protective role of female sex-specific hormones. A higher stomach cancer incidence in males than in females may be due to differences in the incidence of different subtypes of adenocarcinoma according to histology (intestinal or diffuse) and location (proximal or distal).^{6,7,19} Diffuse adenocarcinoma is more common in younger and female patients, whereas intestinal

adenocarcinoma is more common in males and the elderly.⁹ Intestinal adenocarcinoma dominates high-risk areas and is considered responsible for much of the international variation in incidence

Prevention and treatment

During the past century, Western developed countries experienced a major reduction in stomach cancer incidence and mortality, without the introduction of specific primary and secondary prevention measures. Generally, favorable trends in the frequency of stomach cancer are thought to be an important consequence of changes such as the reduction in the use of salt and an increase in the consumption of fruit and fresh vegetables due to improvements in food storage (refrigerators, freezers). This phenomenon has been dubbed the “unplanned triumph” of prevention.

Primary and secondary prevention strategies are the focus of stomach cancer prevention.

Primary prevention measures involve improvements in environment and lifestyle habits such as tobacco control/smoking cessation, reducing salt intake, increasing fruit and vegetable intake, developing other healthy behaviors (such as Mediterranean diet, higher intake of fiber, physical activity), *H. pylori* eradication, other medications (intake of non-steroidal anti-inflammatory drugs, statins), refraining from high alcoholic beverages, sanitation and hygiene improvements. The WHO has set a global goal of reducing the intake of salt to less than 5 g (2000 mg of sodium) per person per day by the year 2025. A meta-analysis of randomized trials (all trials were performed in areas with a high incidence of stomach cancer, mostly in Asia), in a total of 6695 participants followed from 4 to 10 years showed that the risk of stomach cancer can be reduced by 35% with the treatment of *H. pylori*. In addition to endoscopic and histological surveillance, the American and European guidelines recommend eradication of *H. pylori* in all persons who have atrophy and/or intestinal metaplasia and all persons who are first-degree relatives of stomach cancer patients. According to the Asian Pacific Gastric Cancer Consensus, population-based screening and treatment of *H. pylori* infection is recommended in regions which have an annual stomach cancer incidence of more than 20/100000. Eradication of *H. pylori* can be achieved with antibiotic therapy; but the treatment of asymptomatic carriers is not practical as many countries have a very high infection burden (e.g., over 75% of adult persons living in sub-Saharan Africa have *H. pylori* infection) and reinfection is relatively easy.

Japan has had a national endoscopic surveillance program since the early 1970s because of the high stomach cancer

risk. It is recommended that all people older than 40 years undergo screening with a double-contrast barium X-ray radiography and endoscopy every year. A study in China demonstrated that a preventive intervention which included eradication of *H. pylori*, nutritional supplements, and screening (with double-contrast radiography and endoscopy) resulted in a 49% reduction in relative risk for overall mortality in a high-risk group of individuals.

Upper gastrointestinal endoscopy is the gold standard for stomach cancer diagnosis and due to its high detection rate, it is used for stomach cancer screening in high-risk areas (such as Japan, Korea, Venezuela and other areas), but the available evidence shows that endoscopic surveillance of premalignant gastric lesions showed conflicting results.

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