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## Gastric Cancer in Korean Americans: Risks and Reductions

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### Abstract

Gastric cancer is one of the leading causes of cancer worldwide. However, Koreans have the highest reported incidence of this deadly disease. Risk factors predisposing to the formation of gastric cancer include a combination of environmental risks, such as diet and infection (*Helicobacter pylori*), and, in some cases, genetic predisposition. Early screening and detection is essential to reduce gastric cancer mortality. The low prevalence and late onset of gastric cancer in Americans, compared to Korean Americans, however, has hindered our ability to risk stratify, screen, and improve early detection in Korean Americans, thereby contributing to the increasing mortality in this group. Gastric cancer control must focus on improved medical technology, in combination with community outreach, education, and awareness. Korean community services, church-based groups, media campaigns, medical communities, both academic and community based, and industry collaborations are essential to heighten awareness about gastric cancer in Korean Americans. Efforts to reduce the burden of gastric cancer in Korean Americans must focus on the dissemination of information to those most affected by the disease and those serving this community.

### Introduction

This presentation focuses on gastric cancer in Korean Americans and risk reduction for this often fatal disease. Many disparities exist in the prevalence, incidence, and mortality of gastric cancer. In the United States, it is the 14<sup>th</sup> most common cancer and the seventh leading cause of cancer death. It occurs in 1 to 3 per 100,000 women and in 5 to 8 per 100,000 men. Unfortunately, only about 10 to 20% of all gastric cancers are found in early stages. The 5-year survival rate, therefore, is between 10 and 20%. Worldwide, however, gastric cancer is the second most common cancer and one of the top five leading causes of cancer death, occurring in 35 per 100,000 women and in 80 per 100,000 men. It accounts for 10% of all cancers and 12% of all cancer deaths. The prevalence, however, varies by region. It is highest in Asia, Latin America, and Eastern Europe. In regions with higher prevalence, 10 to 40% occur in early stages, with the 5-year survival rate between 10 and 50%. Early detection has been found to decrease mortality. Japan, where mass screening for gastric cancer is practiced, has the lowest mortality worldwide.

Because current guidelines for cancer screening and prevention focus on common cancers, gastric cancer in the United States has often been overlooked and therefore diagnosed at a later stage. The American Cancer Society 2002 guidelines for early detection include the detection of breast cancer, cervical cancer, colorectal cancer, endometrial cancer, prostate cancer, and lung cancer, but not gastric cancer. Furthermore, national goals have been set forth as follows: Healthy People 2015 has a goal of a 50% reduction in cancer mortality and a 25% reduction in cancer incidence by the year 2015. The Department of Health and Human Services would like to eliminate health disparities by the year 2010. Although these goals are commendable, there are many barriers to overcome.

First, there has been a rapid increase in ethnic minority populations in this country. In the health field, these growing populations are often overlooked, resulting in insufficient data and a lack of awareness of host-country diseases. Data on foreign-born populations by region of birth

indicate that between 1950 and 2000, immigration of Europeans declined markedly, while both Latin American and Asian American populations increased steadily. Specifically, there was a logarithmic increase in the Asian American Pacific Islander (AAPI) population in the United States between 1970 and 1990. In fact, the AAPI growth rate as of 1990 was 20 times that of non-Hispanic whites, six times that of African Americans, and two times that of Hispanics. By the year 2050, the AAPI population should reach 10% of the entire population in this country. Looking directly at Asian subgroups in the year 2000, we see that Koreans account for a little more than 1 million of the AAPI population, and this subgroup continues to grow.

Meanwhile, cancer death rates for people older than 65 reveal discrepancies between different AAPI subgroups and Caucasians. In the Caucasian and Japanese populations, more than 75% of cancer deaths occur in people older than 65 years of age. In contrast, Filipino, Korean, and Chinese populations have cancer deaths occurring at a younger age. This, in part, can be explained by the younger age of the immigrating population. Data published by the Illinois Department of Public Health in 1990 indicate that 13.6% of the Caucasian population in Illinois was older than 65 years of age, versus 5.3% in the AAPI population. This migrant effect may partly explain the age discrepancy.

Signature cancers for AAPIs include nasopharyngeal cancer, hepatobiliary cancer, and stomach or gastric cancer. These cancers, however, are often not reflected in United States-based cancer incidence or mortality data and therefore are not used to effect screening recommendations. Yet Surveillance, Epidemiology, and End Results (SEER) data from 1988 to 1992, broken down by AAPI subgroup for gastric cancer incidence, show that gastric cancer ranks second among Korean men, third among Korean women, and first among Vietnamese women. Korean Americans in the age groups of 35 to 54 and 55 to 69 have the highest incidence of gastric cancer, with the incidence of this cancer between the ages of 35 and 54, as reported by the SEER data, being especially striking. It is important, therefore, that we separate Koreans or AAPIs from the rest of the population when deciding priorities in cancer awareness.

## Biology of Gastric Cancer

In order to reduce the risk of gastric cancer, we need to understand its biology. Its pathogenesis can be modeled after colon cancer carcinogenesis, with a stepwise progression from normal mucosa to cancer. There are two basic types of gastric cancer: intestinal type, which accounts for the majority of gastric cancers in this country, and diffuse type. In the intestinal type, there is a progression from normal mucosa to chronic inflammation, leading to chronic gastritis. This can develop into atrophic gastritis to intestinal metaplasia to dysplasia and finally to cancer. Intestinal metaplasia may be irreversible, although it is unclear how to manage and follow this histologic pattern. The second type of gastric cancer is the diffuse type, where normal mucosa progresses directly to chronic gastritis and eventually to cancer. This type of gastric cancer is much more difficult to diagnose and treat. Studies have shown that *Helicobacter pylori* (*H. pylori*), a unique gastric organism, is often responsible for the development of chronic gastritis, initiating the stepwise progression to cancer.

The discovery of *H. pylori* has not only revolutionized our understanding of peptic ulcer disease but is also changing our understanding of gastric cancer. This unique organism lives in only one place - the human stomach. It is able to create its own microenvironment, resistant to gastric acid, and is therefore difficult to eradicate. The World Health Organization in 1984 classified *H. pylori* as a class 1 carcinogen. It is found in 70 to 95% of all gastric cancers. When infected with *H. pylori*, the relative risk for the development of gastric cancer is 2.1. If we assume that approximately 50% of the world is infected with this organism, then this bacteria may be

responsible for 42% of gastric cancers worldwide. Obviously, more research on this bacteria and its effect on cancer needs to be done.

Studies have shown that treatment of *H. pylori* infection can decrease recurrent disease and early treatment may stop the progression of some of the stepwise changes that lead to the development of gastric cancer. The prevalence of *H. pylori* infection varies by age and country of origin. In the United States, France, and Australia, less than 10% of children are infected by the age of 10, and infection rates increase with age. In areas with a higher prevalence of gastric cancer, such as in Algeria, the Ivory Coast, Thailand, and Korea, the prevalence of *H. pylori* infection is dramatically different. By the age of 10 in these countries, up to 50% of children are already infected. We think that one source of the infection may be the drinking water. We also know that the infection clusters in families. Among children who are positive, 87% of their siblings and 83% of their mothers will also be infected. With *H. pylori*-negative children, family prevalence rates are less than 40 to 50%. This is an organism that is easily spread among family members and, in fact, from unrelated persons to others as well; gastroenterologists, for example, have a very high rate of *H. pylori* infection owing to their constant exposure to gastric contents.

## Prevention and Treatment of Gastric Cancer

What are signs and symptoms of gastric cancer? For the most part, this is an asymptomatic disease, but the most frequently reported symptoms are indigestion, heartburn, nausea or vomiting, bloating, loss of appetite, weakness, and fatigue. With advanced disease, blood in the stool or vomit is possible. It is important to risk stratify patients based on both symptoms and risk factors. Besides *H. pylori* infection, many other risk factors have been identified. For Asians, one of the major risk factors is diet — in particular, diets high in smoked foods, salted fish and meats, and pickled foods, including Kim-chi. Because the need for smoking, salting, and pickling foods decreased once refrigeration became readily available, this risk factor has lessened in some populations. However, it has continued to be a significant risk factor among Asians owing to cultural dietary habits. Other risk factors include tobacco and alcohol use, previous stomach surgery, pernicious anemia, blood type A, male sex, and age. In addition, there are high-risk groups for gastric cancer, specifically those with genetic or regional predispositions. Those with a genetic predisposition may have a personal or family history of gastric polyps or cancer. Familial cancer syndromes include familial adenomatous polyposis or hereditary non-polyposis colorectal cancer syndrome. Regional high-risk groups are those from countries with high gastric cancer prevalence, in particular Koreans and AAPIs.

The prevention of gastric cancer requires two steps: primary prevention, consisting of lifestyle modifications or chemoprevention, including the treatment of *H. pylori* infection; and secondary prevention, which includes screening and surveillance. The rationale for chemoprevention of gastric cancer is that between 50 and 80%, or more, of all cases of gastric cancer are associated with diet. Many studies have shown this link. Pickled foods, smoked foods, and highly salted and preserved foods can all release carcinogens once they are metabolized in the stomach. Constant exposure of the lining of the stomach to such foods allows for the production of carcinogens, which result in mutations and histologic changes. In addition to food products, the way in which food is consumed may also impact the risk of gastric cancer; for example, very hot-temperature foods and rapid food consumption may be detrimental.

At the same time, some foods may reduce the risk of gastric cancer. Diets high in fresh fruits and yellow and green vegetables have been shown to be effective in cancer reduction by reducing food-derived carcinogens. The roles of green tea and garlic are unclear. Nutritional supplements with beta carotene (30 milligrams/day) or vitamin C (1 gram/day) have shown a 5-fold regression of atrophic epithelium, while the treatment of *H. pylori* infection in the same

studies showed a 4.8-fold regression. Many potential chemoprevention agents are being studied. Cox-2 inhibitors, which are commonly used for arthritis management, rofecoxib, celecoxib, other nonsteroidal anti-inflammatory agents such as ibuprofen, and aspirin may all be important in the prevention of gastric cancer.

Secondary prevention of gastric cancer is less clear cut. No randomized control trials have been done to show a decrease in mortality by screening for gastric cancer. Failure to identify early gastric cancer in the United States is most likely due to several factors, including low incidence in the majority population, the lack of risk stratification, and the lack of aggressive screening. Japan, on the other hand, has the lowest mortality rates for gastric cancer worldwide. In 1960, Japan instituted a national, mass gastric cancer screening program in which everyone older than 40 was screened for gastric cancer by x-ray. Most studies showed a two-fold decrease in mortality for those who were screened versus those who were unscreened, largely owing to the early detection of disease. Unfortunately, in the United States, less than 10 to 20% of all gastric cancers are found in the early stages, and the 5-year survival rate is equally low. In Japan, however, where mass screening is done, 40 to 50% of all gastric cancers are found in the early stages, with a 5-year survival rate of 53%. My conclusion is that, in the right setting, screening seems to make a big difference.

## Recommendations

I firmly believe, therefore, that the risk of gastric cancer and its mortality rate can be reduced. To do so involves risk stratification and education, together with continued research on the pathogenesis of gastric cancer and on the development of optimal screening and prevention programs. In AAPI communities, we need aggressive education regarding the signs and symptoms of gastric cancer. We also need to continue research on chemoprevention and to include data from the AAPI community in national databases. The good news is that in the United States, there was a steady decline in the adjusted death rates in both men and women for gastric cancer between 1930 and 1997. But it is important that our AAPI communities reflect the same decrease in incidence. To work toward that goal, I strongly recommend that we develop strategies for change. It is important that we continue to do aggressive community outreach, identifying gastric cancer as being a problem that should be addressed. The community needs to form a partnership with physicians and public health, state, and national agencies to promote health issues and to continue lobbying for funding for community-based research and the collection of health data for education. We need to utilize multiple modalities for education including faith-based and media directed education. Chicago, for example, has approximately 250 churches, and we know that about 70% of first-generation Koreans attend church, thus providing a valuable community resource for education.

Physician outreach is also important, to ensure that physicians understand risk stratification for gastric cancer and to provide up-to-date information for patient education. We must encourage physicians to work with community liaisons to consider strategies for implementing screening, to address insurance issues, and to provide culturally sensitive education. In addition, cultural competency training should be mandated for all health professionals.

Research is paramount if we wish to reduce the risk of gastric cancer. We need to lobby for increased allocation of funding for gastric cancer, including community-based research and AAPI-specific funding, and to improve data collection on AAPIs as individual subgroups. *H. pylori* vaccines, which are being developed, need to be strongly considered for all AAPIs. Research is needed on chemoprevention, the identification of biomarkers for gastric cancer, and improved and consistent pathologic ratings for premalignant disease such as intestinal metaplasia. Finally, we need to implement prevention and screening programs for AAPI communities as we strive to close the gap and lessen health disparities.

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