Stomach Cancer Disparity among Korean Americans by Tumor Characteristics: Comparison with Non-Hispanic Whites, Japanese Americans, South Koreans, and Japanese

Eunjung Lee1, Lihua Liu1, Juanjuan Zhang1, Mariana C. Stern1, Afsaneh Barzi2, Amie Hwang1, Andre E. Kim1, Ann S. Hamilton1, Anna H. Wu1, and Dennis Deapen1

Abstract

Background: Stomach cancer incidence shows substantial racial-ethnic disparity in the United States, with Korean Americans experiencing by far the highest incidence. We examined stomach cancer incidence trends in Korean Americans by tumor subsite, histology, and stage and compared them with incidence rates in racial-ethnic groups with the second highest rate (Japanese Americans) and the lowest rate (non-Hispanic whites; NHWs) as well as populations in South Korea and Japan.

Methods: We calculated age-adjusted incidence rates by racial-ethnic groups, sex, and tumor characteristics, using the 1988–2012 California Cancer Registry data. Data on South Korea and Japan were obtained from the literature and other resources.

Results: Between 1988 and 2012 in California, Korean Americans had about five times greater incidence than NHWs and twice that of Japanese Americans. Tumor characteristics differed by ethnic group and gender. The incidence in Korean Americans has declined during recent years, for both cardia and noncardia sites and for both intestinal- and diffuse-type histology. Although Korean Americans were diagnosed at an earlier stage than other Californians, the proportion with localized disease (43%) was much smaller than in South Korea (57%), where population-based screening is available.

Conclusions: Stomach cancer incidence declined in the highest risk ethnic groups. However, the persistent disparity between Korean Americans and other racial-ethnic groups warrants additional strategies for prevention and earlier diagnosis.

Impact: Analysis of California Cancer Registry data identified a racial-ethnic subgroup with stomach cancer disparity that may benefit from targeted prevention and screening efforts. Cancer Epidemiol Biomarkers Prev; 26(4); 587–96. ©2016 AACR.
increased between 1973 and 2000 in men and women, whites and nonwhites (15, 17). Incidence rates of most subtypes were higher in nonwhites than in whites, with the exception of higher incidence of cardia subtype in whites (15, 16). Given the differential etiology and epidemiology across subtypes and race groups (10), it is important to examine the incidence trend and ethnic disparity by tumor subtype as well as stage at diagnosis to plan efficient prevention strategies. However, such information has not been described separately for Asian American subgroups.

To examine more recent data and reasons of stomach cancer disparity in Korean Americans, which may warrant focused prevention and screening efforts, we investigated the time trends of overall and subtype-specific stomach cancer incidence in Korean Americans. In addition, as migrant studies may provide insight into environmental factors related to etiology, we also provide incidence rates for NHWs, Japanese Americans, and populations in South Korea and Japan for comparison. Population prevalence of known risk factors is discussed within these population subgroups to gain additional insights into the stomach cancer disparity.

Materials and Methods

Cancer incidence data

U.S. data. We used the population-based California Cancer Registry (CCR) data. Approximately one third of all Korean Americans in the United States reside in the state of California (18). Cases included all California residents diagnosed during 1988–2012 with primary invasive stomach cancer (International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) site codes C16.0-C16.9, histology codes 8000-8999; ref. 2). Among the patients with invasive stomach cancer, there were 32,549 NHWs, 2,455 Korean Americans, and 2,007 Japanese Americans.

Patients with stomach cancer were further classified according to stage, anatomic subsite, and histologic type. Tumor stage was grouped into localized, regional, and distant according to the Surveillance, Epidemiology, and End Results Program (SEER) Summary Stage 2000 definition (19). Histology codes were categorized into intestinal type and diffuse type (20) on the basis of ICD-O-3 histology codes (intestinal-type: 8010, 8140, 8144, 8211; diffuse-type: 8490, 8142, 8145). This histologic type classification has been used in previous investigations (2, 15, 17). We considered changes in histology coding between ICD-O-2 and ICD-O-3: “8255” (mixed type; ICD-O-3) was coded as “8490” (i.e., diffuse type) prior to 2001 (15). Results remained similar when considering “8255” as diffuse type due to the small number of cases with “8255.” Tumor subsite was categorized into cardia (C16.0), noncardia (C16.1–C16.6), and unknown, which includes overlapping or unspecified (C16.8, C16.9). Overlapping subsite code (C16.8) indicates not only an overlap between cardia and noncardia sites but also an overlap between 2 or more noncardia subsites. Because the overlapping subsite code was noted for only 7% to 10% of cases across race/ethnic groups and does not necessarily indicate cardia and noncardia overlap, we decided to combine overlapping and unspecified sites together. The main findings did not change when separating overlapping (C16.8) and unspecified (C16.9) subtypes.

South Korea data. We used 1999–2012 cancer incidence data collected by the Korea Central Cancer Registry (KCCR; ref.8). Since 1999, KCCR has covered the entire population of South Korea with a completeness of 97.7% in 2012 (8). Subsite-specific incidence data were obtained from 2003–2008 data reported in Cancer Incidence in Five Continents (CI-5), Vol. X (5). Stage distribution was reconstituted from 2006–2010 data (21).

Japan data. We used 1975–2010 national estimates of cancer incidence data published by the Cancer Information Service on the basis of 25 population-based cancer registries in Japan (7, 22). Subsite-specific incidence data were obtained from the 2003–2008 Miyagi Prefecture data reported in CI-5, Vol. X (5). Miyagi prefecture had an incidence rate close to the median of all registries in Japan contributing the incidence rates to CI-5 and had a proportion of “overlapping or unspecified sites” comparable to those from U.S. registries. Stage distribution for Japan was reconstituted using 2003–2005 data presented in Japan Cancer Statistics 2014 (23).

Annual population estimates

We used the annual population estimates for NHWs in California provided in the 1990–2012 National Cancer Institute (NCI) SEER’Stat software package. We extended the 1990–2000 linear growth trends by sex and age to obtain the NHW population estimates for 1988–1989.

Annual population estimates for Asian subgroups were based on the Asian ethnic-specific population counts from the 1990, 2000, and 2010 population censuses for California. Because of the multiracial scheme used in the 2000 and 2010 census, population counts for each Asian subgroup by age and sex were represented by the simple average between the count for one race alone and the count for one race alone or 2 or more races for each sex-age-ethnicity–specific combination in each census year, respectively. Annual population estimates for Asian subgroups in California during 1988–2012 were obtained by linear interpolation of sex-age-specific population counts between census years for 1990–2000 and 2000–2010 and extrapolation of the linear trend in the adjacent decade for 1988–1989 and 2011–2012, respectively.

Statistical methods

Annual age-adjusted incidence rates (AAIR) per 100,000 population were calculated by direct standardization to the world standard population (24, 25) for the time periods of 1988–1990, 1991–1995, 1996–2000, 2001–2005, and 2006–2012, by sex and race/ethnicity. We also calculated AAIRs for each period specifically by tumor stage, histologic type, and anatomic subsite.

Jointpoint Regression Program Version 4.1.0 (National Cancer Institute; ref. 26) was used to describe changes in incidence trends and estimate the average annual percent change (AAPC) in AAIRs during 1988–2012 by race/ethnicity and sex. AAPC is a summary measure of a trend over a fixed period of time, which uses a single number to describe the average trend over a period of multiple years (27).

In this article, we refer to Koreans and Japanese living in California as Korean Americans and Japanese Americans, respectively, and the populations in South Korea and Japan as South Koreans and Japanese, respectively.
Results

Comparison of overall stomach cancer incidence and time trends across racial-ethnic groups

Between 1988 and 2012 in California, Korean Americans had the highest stomach cancer incidence of any racial-ethnic group both among men and women, with an AAIR that was about 5 times higher than that of NHWs and about twice that of Japanese Americans (Fig. 1 and Supplementary Table S1). The AAIRs for Korean Americans and Japanese Americans are much lower than the rates in South Korea and in Japan. In 2006–2012, the Korean American AAIRs were only 40% (for men) and 50% (for women) of the rates in South Korea. The same proportion for Japanese Americans in comparison to Japanese was 17% for men and 30% for women, respectively (Fig. 1). Nearly all (~98%) of Korean American patients with stomach cancer included in this study were born in Korea, whereas about 50% of Japanese American patients were born in the United States. In all population subgroups, the rates were much higher in men than in women. Among men, incidence rates in all subgroups in the United States significantly and steadily declined between 1988 and 2012. The rates in Japanese men also substantially declined during this time period. However, the rates in South Korean men declined only slightly, and the decline was not apparent until 2010. Among women, incidence rates declined continuously in Japanese Americans and NHWs between 1988 and 2012. The rates in Korean American women also declined during this time period, although the decline was not clearly observed until the most recent years. As in South Korean men, the decline in South Korean women were observed only during the most recent years.

Comparison of tumor characteristics and time trends by tumor characteristics across racial-ethnic groups

By tumor subsite. Tumor subsite distributions varied widely across ethnic groups and by sex, and this pattern was consistent over the 25-year period (Fig. 2). The proportion of cardia stomach cancer was highest among NHWs (40–49% in men; 16–24% in women) and lowest among Korean Americans (2–7% in men; 3–8% in women) and South Koreans (4% in men; 3% in women). The cardia proportions in Japanese Americans were slightly higher than (for men) or similar to (for women) the proportions in Japanese. Over the 25 years, the proportion of cardia cancer has increased, especially among NHWs. Reflecting the substantial ethnic difference in subsite distribution, incidence of cardia cancer was higher in NHWs and Japanese Americans than in Korean Americans among men (Supplementary Fig. S1 and Supplementary Table S2). The

Figure 1.
incidence rates of cardia cancer generally decreased in all subgroups during this period, except for NHW women. Incidence rates of other parts of the stomach (e.g., noncardia, overlapping/unspecified) also decreased in all population subgroups, although the decrease in Korean American women was less clear and appeared to be limited to the most recent years.

Figure 2.

Stomach Cancer Disparity in Korean Americans

By stage at diagnosis. The proportion of localized stage disease increased over the past 25 years in all ethnic groups, with the largest increase being observed between late 1980s and early 1990s among Korean and Japanese Americans (Fig. 3). There was no sex difference in stage distribution within each ethnic subgroup (data not shown). Of all ethnic groups, Korean Americans consistently had the highest proportion of localized disease throughout the study period. In 2006–2012, 43% of Korean American patients were diagnosed with a localized disease, which is much higher than those in other ethnic groups (~30%). The proportion of localized disease in South Korea and in Japan was even higher (57% and 55%, respectively). When examining the incidence trends by stage (Supplementary Fig. S2 and Supplementary Table S3), incidence of localized disease in Korean American men and Japanese American men substantially increased during the first half of the 25 years, consistent with the stage conversion during this time period. A similar pattern was observed for women, although the magnitude of change was smaller than in men. More advanced stage disease decreased over the 25 years in all ethnic groups both in men and in women.

By histology type. When examining intestinal- and diffuse-type using the ICD-O-3 histology codes as described in the Materials and Methods, males had a higher proportion of intestinal type than females; the difference across ethnic groups within each sex was smaller (Supplementary Table S4). When examining the incidence trends, incidence of intestinal type substantially decreased across all ethnic groups regardless of sex (Fig. 4 and Supplementary Table S4). Incidence of diffuse type decreased in general in all ethnic groups among men and women during the more recent years.

Discussion

To our knowledge, this is the first population-based investigation of stomach cancer disparity in Korean Americans examining tumor characteristics. Our results demonstrate a persistent stomach cancer disparity in Korean Americans and demonstrate for the first time that the incidence in Korean Americans has started to decline in recent years. Tumor characteristics with respect to subsite and histology showed difference by ethnicity and sex: the proportion of cardia stomach cancer was highest among NHW men and lowest among Korean American and South Korean men and women, and the intestinal type histology was more frequent among men than in women for all racial-ethnic groups. Although Korean Americans had an earlier stage at diagnosis than others in California, the proportion with localized disease was still much smaller than in South Korea.

Two recent reports based on 1990–2008 SEER data (3) and 1988–2007 data from Los Angeles County (9) showed that stomach cancer rates were not decreasing in Korean American men and women. Our updated data from California suggest that Korean American rates have started to decline both in men and in women. Despite this encouraging trend, our data show that Korean Americans still experience the highest incidence, consistent with previous reports of higher stomach cancer incidence in Korean Americans compared with all other ethnic groups in the United States, including Hispanics and other Asian Americans (2–4, 9). The high incidence rates among Korean Americans mirror those of South Koreans, who have the highest incidence in the world (6, 28) and about twice the incidence of Korean Americans (9, 29). It is noteworthy that stomach cancer incidence in Korean Americans declined much earlier than in South Koreans. This is in line with the well-documented observation that Asian immigrants experience lifestyle changes and divergence in cancer incidence patterns after migration (30, 31). Interestingly, Japanese Americans have a much lower stomach cancer incidence than Korean Americans, even though the incidence in Japan is high (5). This likely reflects the difference in the immigration history: more recent immigration of Korean Americans compared...
with Japanese Americans. The majority of Korean Americans immigrated after 1965 (32, 33), and only about 25% of Korean Americans in California in 2014 (and ~15% of adult Korean Americans) were born in the United States (34). In contrast, Japanese American immigration was highest between the 1900s and mid-1920s and then continued in a relatively smaller volume since the 1950s (35), and 71% of California Japanese Americans are U.S.-born second-, third-, or even fourth-generation immigrants (34). Lifestyle changes among immigrants are larger in subsequent generations than in the first generation (30, 31). At present, we do not have sufficient power to examine stomach cancer incidence by birthplace for these Asian American subgroups. Additional efforts in monitoring stomach cancer disparity are warranted given the continuing immigration from these 2 countries.

Understanding cancer risk factors in ethnic subgroups and comparing the risk factor prevalence between immigrants and their population of origin and the U.S. population is helpful in identifying prevention strategies. The strongest risk factor for stomach cancer is H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic H. pylori infection. Analysis of preneoplastic stomach cancers from a large national pathology database (36) showed that H. pylori prevalence in Korean Americans was about 2 times that of NHWs (19% vs. 10%). Similarly, analysis of blood samples from large nationwide surveys in the United States (37) and South Korea (38) found H. pylori seroprevalence (detecting H. pylori immunoglobulin G) among South Koreans to be about 3 times higher than that of U.S. NHWs (67% vs. 21%), which is in line with the difference in the stomach cancer rates. However, when considering H. pylori prevalence in other ethnic groups in the United States, H. pylori prevalence itself does not completely explain the stomach cancer disparity in Korean Americans. For example, while Chinese Americans have similar H. pylori prevalence to Korean Americans (36), their stomach cancer incidence is only about 30% that of Korean Americans (3). Likewise, U.S.-born non-Hispanic blacks and Mexican Americans have similar seroprevalence rates (52% and 64%, respectively) to South Koreans (37, 38) but experience stomach cancer rates that are only 15% to 30% of the incidence in South Koreans (3, 5). Increased pathogenicity of East Asian strains of H. pylori has been proposed as an additional contributing factor (39–41). The interplay between H. pylori and environmental factors, and possibly host genetic factors, may also play a role (11, 12, 42, 43).

Salted food intake, particularly salted fish intake, is an established stomach cancer risk factor (44–47). In Korea, the mean daily sodium intake was 4,546 mg (5,212 mg in men and 3,868 mg in women; ref.48). This is higher than that in U.S. adults (4,043 mg in men; 2,884 mg in women; ref.49). Even within Korean American immigrants, birthplace (U.S.-born vs. Korean-born) and length of residence in the United States are associated with decreased levels of salt intake (32) and consumption of a traditional Korean diet (50) which typically includes diverse types of salted fish. Thus, the ecologic comparison of levels of salt intake, and possibly salted fish intake, is compatible with the differences in the stomach cancer incidence across these populations. A synergistic effect between salt intake and H. pylori has been proposed by available, although limited, data from

Figure 4.
epidemiologic and laboratory studies (14, 51, 52). Therefore, prevention efforts to reduce salted food intake and *H. pylori* infection in high-risk populations are warranted.

Smoking and heavy alcohol drinking are additional stomach cancer risk factors (11, 53–55). In 2001, the prevalence of current smoking in South Korean, California *H. pylori* American, and California NHW men was 61%, 38%, and 20%, respectively, which corresponds with the differences in stomach cancer incidence (34, 56). The role of heavy drinking on the observed disparity is less clear. South Korean men consume nearly double the amount of alcohol and 4 times the amount of liquor than men in the United States (per capita; ref.57), consistent with the incidence difference between South Korean men and Korean American men. However, the prevalence of heavy drinking in Korean American men was similar to that of NHW men (34), although there may be ethnic differences in the amount and pattern of alcohol consumption and burden of heavy drinking on stomach cancer (58). Among women, smoking and heavy drinking were inconsistent with the stomach disparity in that South Korean and Korean American women have lower prevalence of smoking and drinking than NHW women (34, 56, 59).

The ethnic difference in subsite distribution was consistent with earlier reports showing that stomach cancer in the cardiopharyngeal region has been particularly high among white men (15) and scarce in South Koreans (60, 61). The reasons for this pattern are not clearly understood but may be related to the higher prevalence of erosive reflux disease in men than in women and in whites than in other ethnic groups (62). Obesity and reflux disease are key risk factors of cardia cancer in the United States (10). *H. pylori* infection is not associated with cardia cancer in Western countries and only weakly associated with cardia cancer in high-risk populations (10, 63). An earlier study reported a continued increase in cardia cancer up to 2005 among men of "other races," the majority of whom are Asians (15). Our results, together with an updated report focused on Hispanics in California (2), suggest a promising decrease in cardia cancer among many ethnic groups in men and also, at least since the late 1990s, in women.

The observed histology distribution is similar to that from one previous study in the United States, which reported a higher proportion of diffuse-type for women (~25%) than for men (~15%) (15). The incidence of diffuse-type stomach cancer increased up to the year 2000 (17) but since then decreased up to 2005 in all ethnic groups (i.e., whites, blacks, "others") regardless of sex (15). Our results extend earlier findings and show that diffuse-type incidence has decreased in NHWs, Korean Americans, and Japanese Americans in recent years. *H. pylori* is involved in carcinogenesis of both intestinal-type and diffuse-type with similar relative risks (64), although there are differences in their downstream or alternative events in each carcinogenic pathway (12, 13). Thus, it is possible that decreasing *H. pylori* prevalence to some extent contributed to the recent decreasing trend of diffuse-type stomach cancer. It is unclear why the decreasing trend of diffuse type was much more substantial in men than in women and warrants further research. The trends of "other" histologic types are difficult to interpret because it includes a diverse of types of rare forms of stomach cancer such as other types of adenocarcinoma, sarcoma, carcinoid tumor, squamous cell carcinoma.

Recent data suggest that endoscopy-based screening leads to earlier diagnosis (65) and improves gastric cancer survival (66). In South Korea, stomach cancer screening is offered as part of a national cancer screening program to persons aged ≥40 years with 2-year intervals using upper endoscopy (predominantly) or upper gastrointestinal series (67). The prevalence of endoscopy screening is widely available through opportunistic cancer screenings. As a result, 80% of the screen target population (age ≥ 40 years) has ever had stomach cancer screening, primarily through upper endoscopy (67), and the majority is following the program guidelines with regards to the procedure and screening interval. Unfortunately, in the United States, well-defined guidelines for stomach cancer screening are currently lacking (68), although guidelines from the American Society for Gastrointestinal Endoscopy pointed out the importance of race and ethnicity considerations and suggest that endoscopic stomach cancer screening be considered for first-generation immigrants from high-risk regions (69). The earlier stage at diagnosis in Korean Americans compared with other ethnic groups in the United States suggests that aggressive diagnostic work-up and/or opportunistic screening practices may be occurring in some part of the community medical practice. However, the unfavorable stage distribution in Korean Americans compared with South Koreans or Japanese suggests that additional strategies of prevention and early diagnosis are warranted to reduce stomach cancer disparity (28). It has been shown that nearly all early-stage stomach cancer would progress with time and lead to death if untreated (70). Endoscopy can also detect precancerous changes, creating prevention opportunities such as lifestyle changes and/or *H. pylori* eradication as well as opportunities for aggressive endoscopy surveillance for disease progression.

Thus, in addition to designing strategies to reduce prevalence of stomach cancer risk factors in high-risk populations, the medical community and policy makers should consider offering endoscopy screening in the absence of symptoms to Korean Americans and other high-risk Asian Americans such as Japanese and Vietnamese Americans (4) to detect stomach cancer at an early stage or to prevent the disease. Lung cancer screening in the United States provides a precedent for such targeted screening. Lung cancer screening through low-dose computed tomography is being recommended for selected asymptomatic high-risk populations with heavy smoking history and the cost is covered by the Centers for Medicare and Medicaid Services (CMS) and private insurance companies (71). Following a similar approach, it is timely to consider insurance/CMS coverage of stomach cancer screening for high-risk populations such as Korean Americans and other high-risk Asian Americans. A recently proposed ethnicity-based targeted screening algorithm comprising initial endoscopy screening of high-risk individuals such as immigrants from high-incident regions followed by subsequent treatment and periodic surveillance depending on *H. pylori* infection or other premalignant changes merits further discussion (68).

The strengths of the current study include the use of population-based CCR data and the fact that this is the first investigation of Korean American stomach cancer disparity considering tumor characteristics and comparing with South Korean incidence rates. The limitations include potential misclassification of race/ethnicity of cancer cases, primarily derived from medical records, and potential errors in population estimates (3), as in any studies based on United States cancer registries. However, these errors are likely to be minimal and nondifferential by tumor characteristics (72), thus unlikely to explain the 5-fold higher incidence in Korean Americans compared with NHWs and the difference in...
tumor characteristics by race/ethnicity and sex. Our data on intestinal- and diffuse-type classification were reconstituted from histology codes; however, we adopted classification methods used in previous investigations (2, 15, 17). Although comparisons of cardia stomach cancer were based on small sample sizes, the ethnic difference in tumor subsite distribution was sufficiently large. Finally, we were not able to examine stomach cancer incidence in second-generation Korean Americans because the majority (~98%) of Korean American patients with stomach cancer were first-generation immigrants.

In conclusion, our results show persistent stomach cancer disparity in Korean Americans and substantial ethnic difference in tumor characteristics. Comparisons of incidence rates and stage distribution between Korean Americans and South Koreans along with ecologic comparisons of risk factors indicate that additional prevention and screening strategies need to be implemented targeting high-risk immigrant populations such as Korean Americans.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

Disclaimer
The ideas and opinions expressed herein are those of the author(s) and endorsement by the State of California, Department of Public Health, the National Cancer Institute, and the CDC or their Contractors and Subcontractors is not intended nor should be inferred.

References

Authors’ Contributions
Conception and design: E. Lee, L. Liu, A. Barzi, D. Deapen
Development of methodology: L. Liu, D. Deapen
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): D. Deapen
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): E. Lee, L. Liu, J. Zhang, A. Barzi, A.E. Hwang, A.S. Hamilton, D. Deapen
Writing, review, and/or revision of the manuscript: E. Lee, L. Liu, M.C. Stern, A. Barzi, A.E. Hwang, A.E. Kim, A.S. Hamilton, A.H. Wu, D. Deapen
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): D. Deapen
Study supervision: E. Lee, D. Deapen

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