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One Size Does Not Fit All: Marked Heterogeneity in Incidence of and Survival from Gastric Cancer among Asian American Subgroups

Robert J. Huang[1], Nora Sharp[2], Ruth O. Talamoa[2], Hanlee P. Ji[3], Joo Ha Hwang[1], and Latha P. Palaniappan[4]

ABSTRACT

Background: Asian Americans are at higher risk for noncardia gastric cancers (NCGC) relative to non-Hispanic Whites (NHW). Asian Americans are genetically, linguistically, and culturally heterogeneous, yet have mostly been treated as a single population in prior studies. This aggregation may obscure important subgroup-specific cancer patterns.

Methods: We utilized data from 13 regional United States cancer registries from 1990 to 2014 to determine secular trends in incidence and survivorship from NCGC. Data were analyzed for NHWs and the six largest Asian American subgroups: Chinese, Japanese, Filipino, Korean, Vietnamese, and South Asian (Indian/Pakistani).

Results: There exists substantial heterogeneity in NCGC incidence between Asian subgroups, with Koreans (48.6 per 100,000 person-years) having seven-fold higher age-adjusted incidence than South Asians (7.4 per 100,000 person-years). Asians had generally earlier stages of diagnosis and higher rates of surgical resection compared with NHWs. All Asian subgroups also demonstrated higher 5-year observed survival compared with NHWs, with Koreans (41.3%) and South Asians (42.8%) having survival double that of NHWs (20.1%, $P < 0.001$). In multivariable regression, differences in stage of diagnosis and rates of resection partially explained the difference in survivorship between Asian subgroups.

Conclusions: We find substantial differences in incidence, staging, histology, treatment, and survivorship from NCGC between Asian subgroups, data which challenge our traditional perceptions about gastric cancer in Asians. Both biological heterogeneity and cultural/environmental differences may underlie these findings.

Impact: These data are relevant to the national discourse regarding the appropriate role of gastric cancer screening, and identifies high-risk racial/ethnic subgroups who many benefit from customized risk attenuation programs.

Introduction

In the United States, Asian Americans (AA) are the fastest growing minority group. In 2017, an estimated 22 million Americans were of Asian descent (1), and the AA population is expected to double by 2050 (2). The AA population is ethnically and linguistically heterogeneous, with 84% belonging to one of the seven largest subgroups: Asian Indians, Chinese, Filipinos, Japanese, Koreans, Pakistanis, and Vietnamese (3). Aggregation of AAs into a single population may mask substantial differences in disease epidemiology and outcomes. It has previously been shown that AA subgroups have marked differences in mortality from coronary heart disease (4), stroke (5), and multiple cancers (6, 7). A better understanding of race-specific disease risk may allow for targeted diagnostic or therapeutic interventions, a tenant of precision medicine.

Gastric cancer remains the fifth most common cancer diagnosis and the third leading cause of cancer-related mortality worldwide (8). There is marked heterogeneity in incidence of gastric cancer worldwide, with highest incidence in East Asia, Latin America, parts of Eastern Europe, and Africa. Within the United States, there is a much higher burden of gastric cancer among AAs relative to non-Hispanic Whites (NHW; ref. 9). Few studies, however, have analyzed both differences in incidence of and survival from gastric cancer between AA subgroups within the United States (10). As there are no recommendations for gastric cancer screening from any U.S. professional society, regulatory body, or task force, a better understanding of risk by racial groups may inform future policy decisions.

In this descriptive study utilizing a dataset containing granular racial subgroup information, we compare patterns of incidence and survivorship between disaggregated AA subgroups. We specifically restricted our analysis to noncardia gastric cancers (NCGC), as these cancers constitute the majority of gastric cancers and are believed to have a pathogenesis, natural history, and epidemiology distinct from cardia-type gastric cancers (11–13). Given the tremendous growth of the AA population, the addition of recent immigrants from high-incidence regions, and improved modalities for the diagnosis and management of digestive cancers, we analyzed data over a 25-year period (1990–2014) to determine if secular trends existed.

Materials and Methods

Study design and data sources

This study was designed as a descriptive study of the Surveillance, Epidemiology, and End Results Program (SEER) Detailed Asian/Pacific Islander subgroup incidence and population datasets (14). A data-use agreement was signed by all study team members who had

[1]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, California. [2]The Stanford Center for Asian Health Research and Education, Stanford, California. [3]Division of Hematology and Oncology, Stanford University School of Medicine, Stanford, California. [4]Division of Primary Care and Population Health, Stanford University School of Medicine, Stanford, California.

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

Corresponding Author: Robert J. Huang, Stanford University School of Medicine, Stanford, CA 94305. Phone: 650-725-0634; E-mail: rjhuang@stanford.edu

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direct access to the data. Incidence data during the 25-year period between January 1, 1990, and December 31, 2014, were obtained from 13 U.S. regional SEER cancer registries, which record detailed subgroup populations (California, Connecticut, Hawaii, Iowa, New Jersey, New Mexico, Utah, Atlanta, Detroit, and Seattle). Collectively, these registries account for over 54% of the AA population (15). Population data were derived from the SEER detailed population databases, a specialized AA population file derived from the U.S. Census (16). For decennial census years (1990, 2000, 2010), AA population estimates were derived from the U.S. Census; for intercensus years (1991–1999, 2001–2009, 2011–2014), estimates were derived by linear interpolation or extrapolation of U.S. Census estimates (15). SEER submissions are checked for quality and completeness prior to release for public use (17).

Linkage of incident cases with county of diagnosis were performed utilizing the Federal Information Processing Standard (FIPS) code. County FIPS codes were then linked to county-level attributes derived from the Census Bureau's American Community Survey file for the year 2010 (1). Estimates for the percentage of families whose income is below the Federal poverty limit as based on Department of Health and Human Services criteria (County Poverty), and the percentage of persons 16 years and older who are unemployed (County Unemployment) were recorded for each county (1).

AA subgroups and inclusion/exclusion criteria

Analysis was restricted to the six largest (by population) AA subgroups which are reported on the U.S. Census: Chinese (2010 U.S. Census population 3,137,061), Indian or Pakistani (3,207,090), Filipino (2,555,923), Vietnamese (1,548,499), Korean (1,423,784), and Japanese (763,325; ref. 18). Notably, for incidence and survival analysis, Indians or Pakistanis (South Asians) were aggregated as they were not disaggregated in the incidence datasets until January 1, 2010. NHWs (2010 U.S. Census population 202,229,636) served as the reference population. AAs were included in this analysis regardless of Hispanic ethnicity. Cases of NCGC were identified based upon International Classification of Disease for Oncology, third edition (ICD-O-3) anatomic location codes (C16.1–C16.9). From these cases, only tumors with a histology consistent with adenocarcinoma (ICD-O-3 histology codes 801x, 802x, 814x, 821x, 822x, 823x, 825x, 826x, 831x, 848x, 849x) were included. The anatomic location of each NCGC was recorded (antrum, body, fundus, or unspecified). Diffuse-type NCGCs are believed to have a natural history and epidemiology distinct from other NCGCs, and feature early submucosal invasion and diffusion ("Linitis plastica"), and signet ring cells on histology. Tumors with histology codes 8142 ("Linitis plastic"), 8145 (carcinoma, diffuse-type type), and 8490 (signet ring cell carcinoma) were coded as diffuse-type NCGCs; all other tumors were non-diffuse-type NCGCs. Cases diagnosed in patients <30 years of age were excluded.

Patient demographic and tumor characteristics

Additional demographic covariates captured from the data sets included age at time of diagnosis, sex, year of diagnosis, and county of diagnosis. Tumor-level data captured included tumor histology, NCI-derived summary stage (localized, regional, distant, or unknown; ref. 19), and performance of surgical resection of the primary tumor (surgery codes 30, 31, 32, 33, 40, 41, 42, 50, 51, 52, 60, 61, 62, 63, 80). Health insurance coverage was available from 2007 onward, and was classified as insured with Medicaid, insured with non-Medicaid insurance, uninsured, or unknown. As cancer diagnosis, management, and survival has evolved over the study period, the time period of diagnosis was stratified (1990–2000 or 2001–2014) and utilized for adjustment.

Analysis of incidence

Age-adjusted incidence rates and 95% confidence intervals (CI) for NCGC in each AA subgroup and NHWs were expressed as cases per 100,000 persons, and age-adjusted to the 2000 U.S. standard population using SEER*Stat software (16). Rates were suppressed for case counts <10. Differences in rates between groups were assessed using RRs assuming a Poisson distribution. Annual percentage change (APC) with two-sided P values were used to characterize the magnitude and direction of trends (20, 21). Joinpoint regression is a Monte Carlo permutation-based method used to identify significant changes in the trend of cancer incidence rates over time (21). Joinpoint regression was performed for each AA subgroup on age-standardized incidence rates over time to identify inflection points, using a prespecified significance level of $P = 0.05$ with an uncorrelated errors model utilizing the Joinpoint Regression Program (22).

Analysis of survival

Differences in patient and tumor attributes between AA subgroups were analyzed using Student t test for normally distributed variables, the Wilcoxon rank-sum test for nonnormally distributed variables, and the chi-squared test for categorical variables. Cause of death and survival time in months were captured for each patient in the cohort. The primary endpoint was observed, all-cause survival at 5 years. Univariable and multivariable Cox regression was performed to evaluate the association between AA subgroup and NCGC-specific survival. The proportional hazards assumption was tested by assessing the log(−log) plot of the survival function. Patient demographics, tumor characteristics, and county-level attributes were analyzed as potential confounders. Interactions between covariates was assessed by including an interaction term in the multivariable model. For the purposes of hazards regression, all variables were considered time-independent.

A priori sensitivity analyses were performed to assess the robustness of the hazards regression. To control for differences in noncancer mortality between racial groups, sensitivity analysis was performed restricting the endpoint to cancer-specific deaths. Some recent AA immigrants may choose to return to their country of origin following a cancer diagnosis, as shown by Pinheiro and colleagues (23). Therefore, sensitivity analysis was conducted by considering any censoring event within 12 months of cancer diagnosis as a mortality event. Additional sensitivity analyses were performed restricting analysis to patients diagnosed at a local cancer stage, restricting analysis to patients with known tumor stage and histology, and restricting to patients with known insurance status (available for years 2007–2014 only).

All models estimated the HR and CI, with two-sided $P < 0.05$ considered as statistically significant. There was a small degree of missing data for categorical covariates (<5% for all covariates); these observations were excluded from analysis in the hazards regression model. Incidence and APC were analyzed using SEER*Stat software (16). Survival analysis was conducted using SAS version 9.4 (SAS Institute Inc.).

Results

Crude incidence by subgroup

Age-adjusted incidence of NCGC over the study period, stratified by sex and years of diagnosis (1990–2000 vs. 2001–2014) are depicted

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Table 1. Age-adjusted incidence of NCBC by race.

Year of diagnosis	NHW	Chinese	Japanese	Filipino	Korean	Vietnamese	South Asian
	Age-adjusted rate per 100,000 (95% CI)						
	Males and females combined						
Total	6.4 (6.4–6.5)	16.8 (16.2–17.4)	26.3 (25.5–27.2)	8.7 (8.2–9.1)	48.6 (46.9–50.4)	22.8 (21.4–24.1)	7.4 (6.6–8.2)
1990–2000	8.1 (7.9–8.2)	20.7 (19.5–21.9)	35.7 (34.1–37.4)	11.5 (10.6–12.3)	58.6 (54.8–62.5)	33.2 (29.8–36.9)	8.5 (6.7–10.7)
2001–2014	5.3 (5.2–5.4)	15.2 (14.5–15.8)	20.5 (19.6–21.5)	7.3 (6.9–7.9)	45.1 (43.1–47.1)	19.9 (18.5–21.3)	7.2 (6.4–8.1)
	Males						
Total	8.3 (8.2–8.4)	21.2 (20.2–22.2)	36.7 (35.1–38.4)	11.0 (10.3–11.8)	67.0 (63.8–70.4)	27.4 (25.3–29.7)	8.1 (7.0–9.4)
1990–2000	10.9 (10.7–11.1)	26.4 (24.4–28.5)	48.1 (25.3–51.2)	14.7 (13.2–16.3)	85.2 (77.6–93.3)	42.8 (36.8–49.5)	10.4 (7.7–14.6)
2001–2014	6.7 (6.5–6.8)	19.1 (18.0–20.2)	28.7 (26.9–30.6)	9.2 (8.3–10.1)	61.1 (57.6–64.8)	23.4 (21.2–25.7)	7.6 (6.4–9.0)
	Females						
Total	5.0 (5.0–5.1)	13.3 (12.6–14.0)	20.0 (19.0–21.0)	7.0 (6.5–7.5)	35.7 (33.8–37.7)	18.5 (16.9–20.2)	6.6 (5.6–7.7)
1990–2000	6.2 (6.1–6.3)	16.1 (14.7–17.6)	26.8 (25.0–28.8)	8.8 (7.8–10.0)	41.7 (37.7–46.0)	25.3 (21.4–29.6)	6.6 (4.6–9.2)
2001–2014	4.2 (4.1–4.3)	12.1 (11.3–12.9)	16.1 (15.0–17.2)	6.2 (4.7–6.8)	33.4 (31.3–35.7)	16.5 (14.9–18.4)	6.6 (5.5–7.9)

Note: Age-adjusted (to year 2000 U.S. Census) incidence of NCGCs per 100,000 person-years. NHW, non-Hispanic White.

in **Table 1**. Among males, all AA racial subgroups with the exception of South Asians demonstrated higher age-adjusted incidence in both 1990–2000 and 2001–2014 periods compared with NHWs (rate ratio $P < 0.001$ for all racial subgroups except South Asians). Koreans demonstrated the highest incidence among males in both 1990–2000 and 2001–2014, with age-adjusted incidence roughly 8-fold higher than South Asians.

Similar patterns were found among females, where all AA racial subgroups with the exception of South Asians demonstrated higher age-adjusted incidence in both 1990–2000 and 2001–2014 periods compared with NHWs (rate ratio $P < 0.001$ for all racial subgroups except South Asians). Koreans also demonstrated the highest incidence among females in both 1990–2000 and 2001–2014, with age-adjusted incidence nearly 6-fold higher than South Asians.

Secular changes in age-adjusted incidence

Age-adjusted incidence of NCGC by racial group over the study period, stratified by sex, is depicted in **Fig. 1**. Among males, all racial groups demonstrated decreasing incidence of NCGC over the study period: NHW APC −3.8% (CI: −4.0% to −3.7%), Chinese APC −2.3% (CI: −2.9% to −1.8%), Japanese APC −4.2% (CI −4.9% to −3.6%), Filipino APC −3.1% (CI: −4.2% to −2.0%), Korean APC −2.9% (CI: −3.8% to −2.1%), and Vietnamese APC −4.3% (CI: −5.4% to −3.2%). Similarly, among females, all racial groups demonstrated decreasing incidence of NCGC over the study period: NHW APC −2.9% (CI: −3.2% to −2.6%), Chinese APC −2.3% (CI: −3.0% to −1.6%), Japanese APC −4.2% (CI: −4.9% to −3.3%), Filipino APC −3.0% (CI: −4.1% to −1.9%), Korean APC −2.5% (CI: −3.5% to −1.4%), and Vietnamese APC −3.5% (CI: −5.0% to −1.9%). South Asian APC could not be calculated due to small sample sizes. No joinpoints were identified for any racial group in either sex.

Patient demographic characteristics

Patient demographic characteristics by racial subgroup are depicted in **Table 2**. AAs in aggregate constituted a higher proportion of the 2001–2014 cohort compared with the 1990–2000 cohort, consistent with the growth of the U.S. AA population over the study period. There were differences in age at diagnosis between subgroups, with NHWs having the oldest age at diagnosis, followed by Japanese; South Asians, Vietnamese, and Korean patients tended to have younger ages of diagnosis ($P < 0.001$). There were small differences in sex distribution between groups, although in all groups males outnumbered females. There were differences in county-level measures of poverty and unemployment between subgroups. Japanese in particular tended to

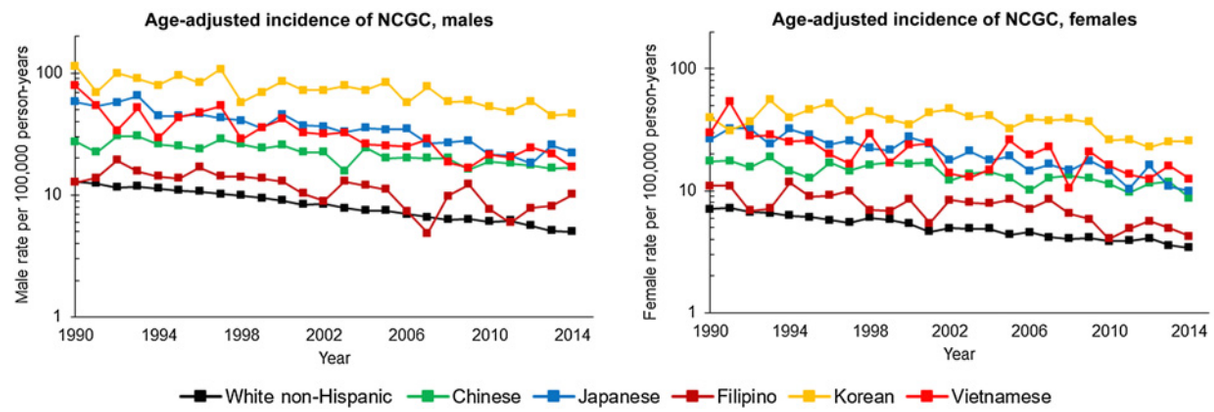

Figure 1.

Age-adjusted (to year 2000 U.S. Census) incidence of NCGCs per 100,000 person-years, as stratified by racial subgroup over the study period (1990–2014). Data presented with logarithmic *Y*-axis. Left panel depicts data for males, and right panel for females. Data for South Asians not depicted due to small sample sizes.

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Table 2. Patient demographic characteristics by race.

Covariate	Frequency (%) NHW (*N* = 32,996)	Chinese (*N* = 3,085)	Japanese (*N* = 3,495)	Filipino (*N* = 1,378)	Korean (*N* = 3,029)	Vietnamese (*N* = 1,162)	South Asian (*N* = 463)	*P* value
Year of diagnosis								<0.001
1990–2000	12,257 (37.2)	979 (31.7)	1,588 (45.9)	475 (34.5)	796 (26.3)	283 (24.4)	64 (13.8)	
2001–2014	20,739 (62.9)	2,106 (68.3)	1,871 (54.1)	903 (65.5)	2,233 (73.7)	879 (75.7)	399 (86.2)	
Age								<0.001
<50	2,098 (6.4)	330 (10.7)	126 (3.6)	145 (10.5)	385 (12.7)	190 (16.4)	99 (21.4)	
50–59	3,536 (10.7)	373 (12.1)	256 (7.4)	202 (14.7)	528 (17.4)	201 (17.3)	91 (19.7)	
60–69	6,166 (18.7)	621 (20.1)	616 (17.8)	308 (22.4)	799 (26.4)	259 (22.3)	114 (24.6)	
70–79	9,923 (30.1)	913 (29.6)	1,227 (35.5)	411 (29.8)	839 (27.7)	288 (24.8)	103 (22.3)	
≥80	11,272 (34.2)	847 (27.5)	1,234 (35.7)	312 (22.6)	477 (15.8)	224 (19.3)	56 (12.1)	
Female	15,025 (45.5)	1,346 (43.6)	1,561 (45.1)	658 (47.8)	1,270 (41.9)	497 (42.8)	206 (44.5)	
County poverty level (quartiles)[a]								<0.001
Lowest poverty	13,830 (42.1)	1,660 (55.2)	1,381 (53.3)	620 (49.6)	815 (27.5)	425 (36.8)	227 (49.0)	
Second	9,798 (29.8)	256 (8.5)	288 (11.1)	234 (18.7)	572 (19.3)	384 (33.3)	81 (17.5)	
Third	6,928 (21.1)	1,070 (35.6)	888 (34.3)	370 (29.6)	1,545 (52.2)	328 (28.4)	119 (25.7)	
Highest poverty	2,288 (7.0)	22 (0.7)	33 (1.3)	26 (2.1)	27 (0.9)	17 (1.5)	36 (7.8)	
County unemployment (quartiles)[b]								<0.001
Lowest unemployment	3,530 (10.8)	141 (4.7)	799 (30.9)	149 (11.9)	145 (4.9)	34 (3.0)	17 (3.7)	
Second	10,092 (30.7)	1,540 (51.2)	738 (28.5)	462 (37.0)	946 (32.0)	648 (56.2)	207 (44.7)	
Third	13,997 (42.6)	1,182 (39.3)	911 (35.2)	502 (40.2)	1,712 (57.9)	380 (32.9)	150 (32.4)	
Highest unemployment	5,225 (15.9)	145 (4.8)	142 (5.5)	137 (10.9)	156 (5.3)	92 (8.0)	89 (19.2)	
Insurance status (2007–2014 only)	*N* = 11,032	*N* = 1,276	*N* = 854	*N* = 517	*N* = 1,303	*N* = 537	*N* = 250	<0.001
Insured, non-Medicaid	9,139 (82.8)	810 (63.5)	862 (90.4)	355 (68.7)	767 (58.9)	276 (51.4)	164 (65.6)	
Insured, Medicaid	1,121 (10.2)	394 (30.9)	30 (3.1)	127 (24.6)	383 (29.4)	240 (44.7)	61 (24.4)	
Uninsured	200 (1.8)	32 (2.5)	[c]	23 (4.5)	98 (7.5)	[c]	12 (4.8)	
Unknown status	572 (5.2)	40 (3.1)	[c]	12 (2.3)	55 (4.2)	[c]	13 (5.2)	

[a]County poverty level is defined as percentage of families living below Federal poverty line.
[b]County unemployment defined as the percentage of individuals 16 or older who are unemployed. NHW, non-Hispanic White.
[c]Denotes unreported due to low cell count.

live in counties of low poverty and low unemployment. There were also differences in insurance status between subgroups; Japanese tended to have high rates of non-Medicaid insurance. Chinese, Filipinos, Koreans, Vietnamese, and South Asians had higher levels of Medicaid-insurance or non-insurance relative to NHWs ($P < 0.001$).

Cancer characteristics and survival

NCGC characteristics and observed 5-year survival by subgroup are depicted in **Table 3**. There existed notable differences in stage of diagnosis between racial groups. In particular, Koreans (31.4%) and South Asians (29.2%) had significantly higher rates of diagnosis at local stage compared with NHWs (21.8%) and Filipinos (18.2%, $P < 0.001$). With regards to histology, all AA subgroups had a higher proportion of diffuse-type cancers compared with NHWs ($P < 0.001$), with Filipinos (33.5%) and Vietnamese (31.1%) having the highest proportion of diffuse-type cancers. There were notable differences in the anatomic location of cancers, with all AA subgroups having a higher frequency of cancers originating from the antrum compared to NHWs ($P < 0.001$). In particular, Vietnamese (45.6%), Koreans (42.0%), and Chinese (41.4%) had a very high percentage of antral cancers. There existed substantial differences in rates of surgical resection, with all AA subgroups undergoing surgical resection at higher rates compared with NHWs ($P < 0.001$). In particular, Koreans (54.3%) and Vietnamese (50.0%) had very high rates of surgical resection relative to other subgroups. With regards to observed 5-year survival, all AA subgroups had higher survival compared with NHWs ($P < 0.001$). In particular, Koreans (41.3%) and South Asians (42.8%) had survival over double that of NHWs (20.1%).

Cancer characteristics and survival were further stratified by sex (Supplementary Tables S1 and S2) and period of diagnosis (1990–2000, 2001–2014; Supplementary Tables S3 and S4). In all stratified analyses, the trends of AAs having earlier stage of diagnosis compared with NHWs, a higher proportion of cancers originating from the antrum compared to NHWs, a higher rate of surgical resection compared with NHWs, and better overall survival compared with NHWs was preserved.

Proportional hazards regression

To understand potential confounders of differences in survival, Cox regression was performed (**Table 4**). In the minimally-adjusted model (adjusted for age, sex, and time period of diagnosis), all AA subgroups demonstrated significantly better survival compared with NHWs. Following adjustment for stage of diagnosis, this survival advantage over NHWs slightly attenuated but remained significant for all AA subgroups ($P < 0.001$, for all subgroups). Following additional adjustment for performance of surgical resection and tumor histology, the HRs further attenuated but remained significant for all AA subgroups ($P < 0.001$, for all subgroups). Following further adjustment for regional socioeconomic attributes, the HRs remained significant for all subgroups.

To assess model sensitivity toward differences in noncancer mortality between races, sensitivity analysis was performed by restricting outcomes to cancer-specific deaths and treating noncancer deaths as points of censorship. Although the HR slightly attenuated for all AA subgroups, they remained significant in both minimally- and fully-adjusted models. To evaluate model sensitivity toward insurance

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Table 3. NCGC characteristics by race.

	Frequency (%)							
Covariate	NHW (*N* = 32,996)	Chinese (*N* = 3,085)	Japanese (*N* = 3,495)	Filipino (*N* = 1,378)	Korean (*N* = 3,029)	Vietnamese (*N* = 1,162)	South Asian (*N* = 463)	*P* value
Stage of diagnosis[a]								<0.001
Local	7,181 (21.8)	673 (21.8)	794 (23.0)	251 (18.2)	952 (31.4)	266 (22.9)	135 (29.2)	
Regional	7,500 (22.7)	971 (31.5)	952 (27.5)	399 (29.0)	915 (30.2)	385 (33.1)	120 (25.9)	
Distant	9,446 (28.6)	786 (25.5)	761 (22.0)	450 (32.7)	654 (21.6)	337 (29.0)	128 (27.7)	
Unknown stage	8,869 (26.9)	655 (21.2)	952 (27.5)	278 (20.2)	508 (16.8)	174 (15.0)	80 (17.3)	
Histology[b]								
Diffuse	8,093 (24.5)	843 (27.3)	889 (25.7)	462 (33.5)	845 (27.9)	361 (31.1)	126 (27.2)	<0.001
Non-diffuse	24,903 (75.5)	2,242 (72.7)	2,570 (74.3)	916 (66.5)	2,184 (72.1)	801 (68.9)	337 (72.8)	
Anatomic location								<0.001
Antrum	9,005 (27.3)	1,276 (41.4)	1,199 (34.7)	439 (31.9)	1,271 (42.0)	530 (45.6)	130 (28.1)	
Body	9,507 (28.8)	927 (30.1)	1,193 (34.5)	441 (32.0)	947 (31.3)	335 (28.8)	132 (28.5)	
Fundus	2,357 (7.1)	115 (3.7)	119 (3.4)	68 (4.9)	81 (2.7)	24 (2.1)	32 (6.9)	
Unspecified	12,127 (36.8)	767 (24.9)	948 (27.4)	430 (31.2)	730 (24.1)	273 (23.5)	169 (36.5)	
Surgical resection performed	10,152 (30.8)	1,432 (46.4)	1,380 (39.9)	510 (37.0)	1,646 (54.3)	581 (50.0)	176 (38.0)	<0.001
Observed 5-year survival	20.1%	31.8%	27.6%	24.2%	41.3%	31.7%	42.8%	<0.001

[a]Defined based on National Cancer Institute–derived summary stage.
[b]Histology codes for diffuse-type cancers are ICD-O-3 codes 8142, 8145, 8490; all other tumors were classified as non-diffuse type. NHW, non-Hispanic White.

status, sensitivity analysis was performed, restricted to years 2007–2014 where insurance data was available (Supplementary Table S5); in this model, Chinese, Japanese, Korean, and South Asian race continued to associate inversely with hazard in the minimally-adjusted model. The HR of Japanese race attenuated significantly in the fully-adjusted model, whereas the HRs for Chinese, Korean, and South Asian race remained significant. To evaluate model sensitivity toward emigration of AAs following cancer diagnosis, all censored observations within 12 months of diagnosis among AAs were counted as deaths. There was no significant change in HR for any AA subgroup in either minimally- or fully-adjusted model in this analysis. Sensitivity analysis was also performed by restricting analysis to cases with known tumor location and cancer stage (Supplementary Table S6); in this analysis, the survival advantage of all groups except Filipinos persisted in both minimally- and fully-adjusted models.

Discussion

In this descriptive study capturing 25 years of longitudinal data from 13 U.S. regional SEER cancer registries which collectively represent over half of the AA population, we found substantial differences in incidence of and survival from NCGC between AA subgroups. Far from being a homogeneous group, we found that cancer incidence varied nearly eight-fold between Asian subgroups. We further found that Asian subgroups demonstrate unique patterns with regards to stage of diagnosis, rates of resection, and socioeconomic profile. We demonstrate that even after adjustment for patient characteristics, tumor staging, treatment, and socioeconomic factors, AA subgroups continue to demonstrate both better overall and cancer-specific survival compared with NHWs. These findings are novel, timely, and may help to direct future risk attenuation and educational efforts to reduce cancer mortality in the United States.

Although NCGC incidence has declined over the study period, Chinese, Japanese, Korean, and Vietnamese American populations remain at heightened risk. As screening for gastric cancer is not routinely performed in the United States, diagnosis is usually made upon symptom onset. This is especially tragic as gastric cancers are curable (through surgical or endoscopic resection) if diagnosed early. These disaggregated data may hold implications for cancer screening, as while mass screening of the general American population is not cost effective, targeted screening of high-risk ethnic and racial minorities may be (24). This study provides granular incidence data, which may

Table 4. HRs and 95% CIs of overall survival by racial group.

	Minimally adjusted		Adjusted for stage of diagnosis		Adjusted for stage, histology, and surgical resection[a]		Adjusted for stage, histology, resection, and county attributes[b]	
Racial group	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
NHW	1.00	Ref.	1.00	Ref.	1.00	Ref.	1.00	Ref.
Chinese	0.74 (0.70–0.77)	<0.001	0.75 (0.71–0.78)	<0.001	0.78 (0.75–0.82)	<0.001	0.79 (0.76–0.83)	<0.001
Japanese	0.77 (0.73–0.80)	<0.001	0.81 (0.77–0.84)	<0.001	0.84 (0.81–0.88)	<0.001	0.91 (0.87–0.96)	<0.001
Filipino	0.91 (0.86–0.97)	0.004	0.88 (0.82–0.93)	<0.001	0.88 (0.84–0.95)	<0.001	0.91 (0.85–0.97)	0.003
Korean	0.57 (0.54–0.60)	<0.001	0.65 (0.62–0.68)	<0.001	0.69 (0.66–0.73)	<0.001	0.70 (0.66–0.73)	<0.001
Vietnamese	0.74 (0.69–0.80)	<0.001	0.75 (0.70–0.81)	<0.001	0.79 (0.73–0.85)	<0.001	0.80 (0.74–0.85)	<0.001
South Asian	0.63 (0.56–0.71)	<0.001	0.65 (0.57–0.73)	<0.001	0.64 (0.57–0.73)	<0.001	0.64 (0.57–0.72)	<0.001

Note: Minimally-adjusted model incorporates age, gender, and time period of diagnosis (1990–2000 vs. 2001–2014).
[a]Additionally adjusted for histology (diffuse type) and performance of surgical resection of primary tumor.
[b]Additionally adjusted for county unemployment and poverty.

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guide future cost-effectiveness studies focused on the highest-risk subgroups within the multiethnic U.S. population.

The relative survival advantage of Asians relative to NHWs is stark and in contrast to usual patterns of cancer inequality and disparity among minority groups (25–27). Some of these differences may be secular in nature, such as the increasing proportion of AAs in the 2001–2014 cohort (where survival was higher) due to the rapid growth of the AA population. Part of the survival gap may also be explained by differences in stage of diagnosis and rates of surgical resection. Notably, there appeared to be a strong correlation between rates of survival and rates of surgical resection, and the groups with highest rates of surgery (Koreans, Vietnamese, Chinese) also had the best overall survival. This is particularly interesting as early-stage gastric cancer is mostly asymptomatic and detected incidentally. Our previous work analyzing a multicenter database showed that 90% of gastric cancers in the United States are diagnosed during endoscopies for symptoms (such as anemia, weight loss, or bleeding), at which time disease has often progressed beyond a localized stage (28). In contrast to the United States, South Korea, Japan, and certain regions of China have implemented population-level mass screening programs for gastric cancer (29, 30). We hypothesize that some of the differences in early detection between AA subgroups reflect an increased cultural awareness of risk for NCGC among first- or second-generation immigrants from high-incidence regions with established screening programs. These patients may be more likely to request referral for surveillance from their primary care physicians, especially as knowledge of gastric cancer risk is low among the majority of American primary care providers (31).

Even after adjustment for differences in stage of diagnosis, therapy received, tumor characteristics, and demographic attributes, a distinct survival advantage existed for AAs compared to NHWs. This "survival gap" has been described comparing Asian-based and Western cohorts (32–34), as well as comparing Asians and NHWs within Western nations (10, 35, 36). This finding may suggest underlying differences in tumor behavior between racial groups, such as differences in somatic genetic alterations (37, 38). With comprehensive molecular characterization of NCGCs through the Cancer Genome Atlas Project (39), additional understanding of the biological underpinnings of this racial gap may emerge.

Several limitations to these data exist. Important risk factors for NCGC, such as *Helicobacter pylori* infection status, cigarette smoking, family history, and dietary patterns could not be captured from the SEER data sets. Although county-level attributes of poverty and unemployment were captured, patient-specific data regarding socioeconomic status (such as individual employment status, occupation, household income) could not be captured. Insurance status data was available only from 2007 and later. Immigrant generation and year of immigration could not be determined from these data sets. Emigration from the United States following diagnosis could not be captured, and there could be bias introduced by emigration which is not fully accounted for by sensitivity analysis.

In summary, this descriptive study capturing data from 13 U.S. regional SEER cancer registries found striking differences between AA subgroups in incidence, staging, histology, treatment, and survivorship from NCGC. These data add to a limited body of existing literature regarding cancer risk and outcomes between Asian subpopulations, and may hold implications for targeted early detection programs.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: R.J. Huang, L.P. Palaniappan
Development of methodology: R.J. Huang, L.P. Palaniappan
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): R.J. Huang, L.P. Palaniappan
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): R.J. Huang, L.P. Palaniappan
Writing, review, and/or revision of the manuscript: R.J. Huang, N. Sharp, R.O. Talamoa, J.H. Hwang, L.P. Palaniappan
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): L.P. Palaniappan
Study supervision: H.P. Ji, J.H. Hwang, L.P. Palaniappan

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One Size Does Not Fit All: Marked Heterogeneity in Incidence of and Survival from Gastric Cancer among Asian American Subgroups

Robert J. Huang, Nora Sharp, Ruth O. Talamoa, et al.

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