



Racial/ethnic differences in survival among gastric cancer patients in california

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Abstract

Background Gastric cancer is an important cause of death among racial/ethnic minorities in the U.S. The objective of this study was to investigate racial disparities in survival among gastric cancer patients within demographic and disease subgroups.

Methods Patients diagnosed with invasive epithelial gastric cancer between 2006 and 2015 were identified from the California Cancer Registry. Cox proportional hazards regression was used to identify factors associated with survival among non-Hispanic whites (NHWs, $n = 7,475$), non-Hispanic blacks (NHBs, $n = 1,246$), Hispanics ($n = 6,274$), and Asians/Pacific Islanders (APIs, $n = 4,204$). Survival was compared across race/ethnicity within subgroups of demographic and disease factors. Five-year relative survival was also calculated within subgroups.

Results There were notable differences in patient characteristics by race/ethnicity, but predictors of survival were similar for each group. Overall, APIs (HR = 0.83, 95% CI: 0.79, 0.88, $p < 0.0001$) and Hispanics (HR = 0.94, 95% CI: 0.90, 0.99, $p = 0.0104$) had better survival than NHWs, but NHBs and NHWs did not have different prognosis (HR = 1.06, 95% CI: 0.98, 1.15, $p = 0.2237$). The survival advantage of APIs persisted in nearly every demographic and disease subgroup, but Hispanics and NHBs had similar survival as NHWs in most groups. Race was not a significant predictor of survival among those with public or no insurance and patients with cardia tumors.

Conclusions There are some differences in survival by race/ethnicity, but race/ethnicity alone cannot explain disparate outcomes in gastric cancer. Future studies, particularly ones that investigate the role of population-specific etiological factors and molecular tumor profiles, are needed to further understand factors associated with survival.

Keywords Gastric cancer · Survival · Disparities · Race · Epidemiology

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Introduction

In 2018, an estimated 26,240 American men and women were diagnosed with gastric cancer and 10,800 died from the disease [1]. Gastric cancer is an important cause of cancer death among racial and ethnic minorities in the U.S., with mortality rates for non-Hispanic blacks (NHBs), Hispanics, and Asians/Pacific Islanders (APIs) more than two times higher than rates for non-Hispanic whites (NHWs) [2], reflecting the significantly higher incidence rates of this cancer among nonwhite populations [3]. The reasons for such disparities in gastric cancer among nonwhites are not fully understood but may relate to higher prevalence of risk factors, including chronic infection with *Helicobacter pylori* [4–6], among these populations.

Survival from gastric cancer is low, with average five-year relative survival about 31% for all cases and only 5%

for patients diagnosed with metastatic disease [2]. Several studies suggest differential survival across race/ethnicity, with some reporting that APIs have more favorable prognosis [7–9] and that NHBs have poorer outcomes than other groups [8, 10]. Other demographic and clinical factors have been found to be associated with worse survival in gastric cancer patients, including older age [7], male sex [11], low socioeconomic status [12], cardia tumors [13], and late stage at diagnosis [14]. While there are notable differences in the distribution of these factors across race/ethnicity [7, 15, 16], it is not entirely clear if and how demographic and disease characteristics account for disparate survival in gastric cancer patients of different races.

This study sought to investigate racial disparities in survival among gastric cancer patients in California, the most diverse state [17]. Using a large population-based sample, we aimed 1) to determine factors associated with survival in gastric cancer patients in four major racial/ethnic groups, 2) to estimate the association of race/ethnicity with survival in gastric cancer patients, and 3) to examine differences in survival by race/ethnicity among subgroups of patients with shared demographic and clinical prognostic factors. A better understanding of these issues will give important insight into racial inequalities in survival, which is a necessary step to address and reduce disparate gastric cancer outcomes.

Methods

Patients with a cancer diagnosis in California are reported to the California Cancer Registry (CCR). Three regional registries from the Surveillance, Epidemiology, and End Results (SEER) program make up the CCR, which contains demographic, diagnostic, initial treatment, and outcome information on all reportable cancers diagnosed in California residents since January 1988. The registry was queried to select patients who were at least 20 years old when diagnosed with a first primary invasive epithelial gastric cancer (International Classification of Diseases for Oncology, 3rd edition [ICD-O-3] site codes C16.0–C16.9 and histology codes 8005–8799) in California between 2006 and 2015. Autopsy and death certificate diagnoses, patients with missing stage information, and patients with poorly specified (ICD-O-3 histology codes 8000–8004) or non-epithelial (codes 8800–9759) tumors were excluded. Patients from four major racial/ethnic groups were included in analysis: NHWs, NHBs, Hispanics and Latinos (any race, hereafter referenced as “Hispanics”), and APIs. Race information is identified from patient medical records, and classification of Hispanics and APIs was improved with the North American Association of Central Cancer Registries’ Hispanic Identification Algorithm [18] and Asian and Pacific Islander Identification Algorithm [19].

The primary association of interest was race/ethnicity with overall survival. The CCR database is linked annually to the National Death Index, hospital discharge data, Medicare files, the Department of Motor Vehicles, and other administrative databases to ensure accurate vital status and cause of death information. Covariates included age at diagnosis, sex, and neighborhood socioeconomic status (nSES), which was determined using data from the 2007–2011 American Community Survey and based on educational attainment, occupation type, employment rate, median household income, poverty level, median rent, and house values [20]. Marital status was dichotomized as married (married or domestic partner) or unmarried (single/never married, divorced, separated, or widowed). Insurance categories were based on primary payer at the time of diagnosis: 1) private insurance, 2) Medicare only or Medicare plus private insurance, 3) other public (Medicaid, military, other government-funded insurance), and 4) no insurance/self-pay.

Cancers were categorized based on anatomic location: cardia (ICD-O-3 site code 16.0), noncardia (codes 16.1–16.6), and overlapping/unspecified (codes 16.8–16.9). Histologic types were based on the Lauren classification [21] and categorizations used in several previous studies of gastric cancer [5, 22–25]; these included intestinal (ICD-O-3 histology codes 8010, 8140, 8144, 8211), diffuse (codes 8142, 8145, 8490), and other epithelial (all other codes except 8000–8004 and 8800–9759). Stage at diagnosis was based on SEER summary staging and was classified as localized, regional, and remote. First course of treatment was defined as cancer-directed therapy documented in a patient’s medical record and given before disease progression, recurrence, or treatment failure. Consistent with prior studies of survival in gastric cancer patients [7, 14], treatment was categorized as receipt of: (1) chemotherapy or radiation (no surgery), (2) chemotherapy and radiation (no surgery), (3) surgery only, (4) surgery plus single modality treatment (chemotherapy or radiation), (5) surgery, chemotherapy, and radiation, and (6) no treatment. Patients with missing data on any of the three treatments were classified as unknown.

Demographic and disease characteristics were summarized and compared by race/ethnicity using χ^2 tests. SEER*Stat Software version 8.3.5 was used to determine age-adjusted 5-year relative survival for each race/ethnicity. Relative survival was calculated within subgroups of sex, age at diagnosis, nSES, marital status, insurance status, anatomic site, histology type, stage at diagnosis, and treatment group. To allow for sufficient follow-up time, this part of the analysis was restricted to patients who were diagnosed between 2006 and 2010. For all patients diagnosed 2006–2015, Cox proportional hazards (PH) regression was used to estimate hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for overall survival, stratified by race/ethnicity. Models were adjusted for all variables found

to be significant prognostic factors in crude analysis. HRs were also calculated for each race/ethnicity within these same demographic and clinical subgroups, with NHWs serving as the reference for all comparisons. Follow-up time for survival was calculated as the number of months between the date of diagnosis and date of death through the end of the follow-up period (31 December 2015). Patients who were alive at the end of the follow-up date were censored. Survival analysis was conducted using SAS version 9.4 (Cary, NC).

Results

A total of 19,199 gastric cancer patients were identified for analysis, including 7,475 NHWs (38.9%), 1,246 NHBs (6.5%), 6,274 Hispanics (32.7%), and 4,204 APIs (21.9%). Patient characteristics by race/ethnicity are summarized in Table 1. There were highly significant differences across groups for all demographic and disease factors ($p < 0.0001$). While most patients were male, there were higher proportions of females among nonwhite patients. Hispanics were significantly younger than other race/ethnicity groups. The majority of NHWs and APIs were in middle and high nSES quintiles, while most NHBs and Hispanics were in the lowest and lower-middle SES neighborhoods. NHWs were more likely to have cardia tumors, while the majority of nonwhites had noncardia cancers. APIs were more likely to be diagnosed at earlier stages and to receive surgery, chemotherapy, and radiation as part of the first course of treatment.

Age-adjusted 5-year relative survival within each demographic and disease group by race/ethnicity are displayed in Table 2. Survival was poor for all groups, but overall, APIs had the most favorable survival at 38.1%, compared to 26.3, 25.6, and 22.7% for NHWs, Hispanics, and NHBs, respectively. For nearly all subgroups, APIs had significantly better relative survival than NHWs. Though Hispanics and NHBs generally had the lowest survival, there were no significant subgroup differences between Hispanics and NHWs and only four statistically significant differences between NHBs and NHWs. In general, for each race/ethnicity, male, older, poorer, unmarried, and uninsured patients had worse survival than their counterparts, though not all comparisons were statistically significant. For each race/ethnicity, patients with overlapping/unspecified tumors, cancers of diffuse histology, and remote stage diagnoses had the poorest prognosis.

Univariable survival analysis showed that all variables of interest were significant prognostic factors for overall survival. However, treatment was excluded from adjusted analysis because of its dependency on other variables, namely stage at diagnosis, and because we could not distinguish between curative and palliative intent. The adjusted

associations of demographic and disease characteristics with overall survival for each race/ethnicity are shown in Table 3. Except for APIs, female sex appeared to be associated with better survival, but this only reached statistical significance for NHWs and Hispanics. For all race groups, patients in the oldest age group had the poorest survival. Neighborhood-level SES was a significant prognostic factor for NHWs and APIs only. Being single or uninsured was associated with worse survival for all patients, but these associations were not significant for NHBs. Patients with noncardia tumors appeared to have better survival than those with cardia cancers, though this was again not statistically significant for NHBs. For all races, diffuse histology was significantly associated with greater hazard of death compared to intestinal histology. Later stage at diagnosis was also predictive of poor survival, regardless of race.

Table 4 shows the adjusted HRs within subgroups for each race/ethnicity compared to NHWs. Each row of the table corresponds to a different Cox PH model conducted within the respective group, with HRs indicating the race-specific survival estimates relative to NHWs in the same subgroup. After adjustment for demographic and disease characteristics, APIs had about 17% less hazard of death than NHWs (HR = 0.83, 95% CI: 0.79, 0.88, $p < 0.0001$), and Hispanics had about 6% better survival than NHWs (HR = 0.94, 95% CI: 0.90, 0.99, $p = 0.0104$). However, there was no significant difference in survival between NHBs and NHWs (HR = 1.06, 95% CI: 0.98, 1.15, $p = 0.2237$). With few exceptions, APIs had significantly better survival than NHWs in each demographic and disease group. Conversely, there were few significant survival differences between NHBs and NHWs within subgroups, and Hispanics had similar survival as NHWs in most groups. Among young adults, survival did not significantly differ between NHWs and NHBs or Hispanics. However, among those aged 70 and older at diagnosis, Hispanics and APIs had significantly better prognosis than NHWs. Unmarried Hispanic and API patients also had better survival than unmarried NHWs. NHBs who were married had significantly worse survival than their NHW counterparts. There were significant differences between NHBs and NHWs in the highest and lowest nSES groups but combining the two lowest and the two highest nSES quintiles removed the association (data not shown). Among patients with cardia tumors, there were no significant differences with respect to race/ethnicity, though APIs with noncardia cancers had more favorable survival than NHWs with noncardia tumors (HR = 0.80, 95% CI: 0.75, 0.86). Hispanics and APIs with intestinal histology types also had better survival than NHWs with the same type (respectively, HR = 0.91, 95% CI: 0.86, 0.97 and HR = 0.81, 95% CI: 0.76, 0.87). For each stage at diagnosis, APIs had better survival than NHWs, but there were no significant differences for Hispanics. NHBs diagnosed with localized

Table 1 Comparison of patients diagnosed with epithelial gastric cancer in California by race/ethnicity, 2006–2015

Variable	Non-Hispanic white <i>n</i> = 7,475 <i>n</i> (%)	Non-Hispanic black <i>n</i> = 1,246 <i>n</i> (%)	Hispanic <i>n</i> = 6,274 <i>n</i> (%)	Asian/Pacific Islander <i>n</i> = 4,204 <i>n</i> (%)	χ^2 <i>p</i> value
Sex					< 0.0001*
Male	5092 (68.1)	718 (57.6)	3581 (57.1)	2389 (56.8)	
Female	2383 (31.9)	528 (42.4)	2693 (42.9)	1815 (43.2)	
Age at diagnosis					< 0.0001*
20–49 years	605 (8.1)	154 (12.4)	1481 (23.6)	486 (11.6)	
50–69 years	3347 (44.8)	567 (45.5)	2758 (44.0)	1691 (40.2)	
70+ years	3523 (47.1)	525 (42.1)	2035 (32.4)	2027 (48.2)	
Neighborhood socioeconomic status					< 0.0001*
Lowest	733 (9.8)	372 (29.9)	2224 (35.4)	546 (13.0)	
Lower-middle	1316 (17.6)	332 (26.6)	1635 (26.1)	788 (18.7)	
Middle	1638 (21.9)	219 (17.6)	1125 (17.9)	830 (19.7)	
Upper-middle	1809 (24.2)	180 (14.4)	787 (12.5)	958 (22.8)	
Highest	1691 (22.6)	100 (8.0)	332 (5.3)	941 (22.4)	
Unknown	288 (3.9)	43 (3.5)	171 (2.7)	141 (3.4)	
Marital status					< 0.0001*
Single/divorced/widowed	2807 (37.6)	724 (58.1)	2419 (38.6)	1272 (30.3)	
Married/domestic partner	4392 (58.8)	444 (35.6)	3624 (57.8)	2797 (66.5)	
Unknown	276 (3.7)	78 (6.3)	231 (3.7)	135 (3.2)	
Insurance					< 0.0001*
Private	3318 (44.4)	484 (38.8)	2430 (38.7)	1638 (39.0)	
Medicare	3163 (42.3)	461 (37.0)	1761 (28.1)	1785 (42.5)	
Other public	724 (9.7)	248 (19.9)	1569 (25.0)	586 (13.9)	
None	106 (1.4)	25 (2.0)	354 (5.6)	135 (3.2)	
Unknown	164 (2.2)	28 (2.2)	160 (2.6)	60 (1.4)	
Site					< 0.0001*
Cardia	3538 (47.3)	183 (14.7)	934 (14.9)	519 (12.3)	
Noncardia	2588 (34.6)	743 (59.6)	3645 (58.1)	2822 (67.1)	
Overlapping/unspecified	1349 (18.0)	320 (25.7)	1695 (27.0)	863 (20.5)	
Histology					< 0.0001*
Intestinal	4922 (65.8)	781 (62.7)	3338 (53.2)	2679 (63.7)	
Diffuse	1533 (20.5)	298 (23.9)	2099 (33.5)	1166 (27.7)	
Other epithelial	1020 (13.6)	167 (13.4)	837 (13.3)	359 (8.5)	
Stage at diagnosis					< 0.0001*
Localized	1972 (26.4)	319 (25.6)	1433 (22.8)	1218 (29.0)	
Regional	2376 (31.8)	373 (29.9)	1923 (30.7)	1524 (36.3)	
Remote	3127 (41.8)	554 (44.5)	2918 (46.5)	1462 (34.8)	
First course of treatment					< 0.0001*
No treatment	1632 (21.8)	353 (28.3)	1418 (22.6)	752 (17.9)	
Chemotherapy or radiation	1524 (20.4)	265 (21.3)	1536 (24.5)	703 (16.7)	
Chemotherapy and radiation	784 (10.5)	66 (5.3)	318 (5.1)	192 (4.6)	
Surgery only	1705 (22.8)	318 (25.5)	1408 (22.4)	1345 (32.0)	
Surgery and single modality	723 (9.7)	116 (9.3)	706 (11.3)	543 (12.9)	
Surgery, chemotherapy, and radiation	970 (13.0)	115 (9.2)	734 (11.7)	590 (14.0)	
Unknown	137 (1.8)	13 (1.0)	154 (2.5)	79 (1.9)	

Two-tailed *p* values were generated from χ^2 tests

Table 2 Age-adjusted 5-year relative survival in patients with epithelial gastric cancer in California by race/ethnicity, 2006–2010

Subgroup	5-year survival (95% CI)			
	Non-Hispanic white	Non-Hispanic black	Hispanic	Asian/Pacific Islander
Overall	26.3 (24.7, 27.9)	22.7 (19.2, 26.5)	25.6 (23.7, 27.5)	38.1 (35.8, 40.4)
Sex				
Males	24.7 (22.8, 26.7)	19.2 (14.9, 24.0)	25.2 (22.7, 27.8)	38.7 (35.6, 41.8)
Females	29.4 (26.5, 32.4)	26.1 (20.5, 32.0)	25.9 (23.1, 28.9)	37.0 (33.6, 40.4)
Age at diagnosis ^a				
20–49 years	28.4 (23.6, 33.5)	23.3 (14.4, 33.5)	21.7 (18.5, 25.1)	40.1 (33.9, 46.2)
50–69 years	28.3 (26.0, 30.7)	28.3 (22.7, 34.2)	28.1 (25.5, 30.8)	39.1 (35.6, 42.6)
70+ years	22.8 (20.5, 25.3)	17.0 (12.0, 22.6)	23.9 (20.7, 27.3)	36.2 (32.7, 39.7)
Neighborhood socioeconomic status				
Lowest	25.7 (20.7, 30.8)	16.3 (11.1, 22.4)	23.8 (20.5, 27.1)	31.4 (24.6, 38.4)
Lower-middle	21.2 (17.8, 24.8)	22.4 (15.5, 30.2)	23.2 (19.4, 27.2)	39.3 (33.9, 44.7)
Middle	25.2 (21.8, 28.7)	19.2 (11.9, 27.8)	29.0 (24.4, 33.8)	38.4 (33.1, 43.6)
Upper-middle	28.4 (25.0, 32.0)	33.7 (23.0, 44.8)	26.7 (21.6, 32.0)	35.8 (30.9, 40.8)
Highest	27.9 (24.4, 31.4)	29.2 (15.9, 43.9)	20.4 (13.7, 28.0)	40.8 (35.9, 45.6)
Marital status				
Single/divorced/widowed	20.9 (18.5, 23.5)	20.4 (16.1, 25.1)	22.7 (19.8, 25.7)	31.3 (27.2, 35.5)
Married/domestic partner	28.9 (26.8, 31.0)	26.4 (19.8, 33.5)	26.7 (24.1, 29.2)	40.5 (37.6, 43.3)
Insurance				
Private	26.5 (24.0, 29.0)	30.8 (24.0, 37.8)	26.7 (23.4, 30.0)	38.0 (33.8, 42.1)
Medicare	26.7 (22.9, 30.6)	15.2 (9.3, 22.4)	27.0 (22.7, 31.5)	38.7 (31.8, 45.5)
Other public	17.7 (12.7, 23.4)	18.9 (10.5, 29.3)	22.6 (17.3, 28.3)	29.5 (23.1, 36.1)
None	18.1 (7.6, 32.2)	7.3 (0.5, 28.1)	22.8 (16.2, 30.2)	27.1 (17.2, 38.0)
Site				
Cardia	23.7 (21.6, 26.0)	12.5 (6.4, 20.6)	20.1 (15.8, 24.8)	24.2 (18.4, 30.4)
Noncardia	33.7 (30.7, 36.7)	32.4 (27.1, 37.7)	30.9 (28.4, 33.6)	45.4 (42.5, 48.3)
Overlapping/unspecified	17.5 (14.5, 20.7)	5.8 (2.8, 10.4)	15.7 (12.8, 18.8)	21.5 (17.5, 25.9)
Histology				
Intestinal	25.3 (23.4, 27.3)	23.4 (18.8, 28.3)	25.9 (23.4, 28.4)	39.3 (36.3, 42.2)
Diffuse	16.6 (13.8, 19.7)	9.5 (5.5, 14.9)	13.8 (11.1, 16.9)	30.7 (26.5, 34.9)
Other epithelial	45.1 (40.1, 49.9)	37.5 (26.5, 48.5)	49.9 (43.7, 55.7)	47.4 (39.6, 54.7)
Stage at diagnosis				
Localized	64.7 (61.0, 68.2)	57.7 (48.7, 65.8)	61.1 (56.5, 65.4)	76.9 (72.9, 80.5)
Regional	28.2 (25.4, 31.0)	23.7 (17.4, 30.6)	29.5 (26.1, 33.0)	39.6 (35.8, 43.4)
Remote	3.8 (2.8, 4.9)	2.3 (0.9, 4.7)	4.0 (2.9, 5.4)	3.8 (2.5, 5.6)
First course of treatment				
No treatment	9.0 (6.8, 11.6)	2.8 (0.9, 6.7)	9.1 (6.7, 11.9)	8.4 (5.3, 12.5)
Chemotherapy or radiation	4.3 (2.8, 6.3)	3.2 (1.0, 7.4)	3.5 (2.0, 5.5)	3.8 (1.9, 6.7)
Chemotherapy and radiation	9.9 (6.7, 13.9)	8.7 (1.5, 24.2)	12.4 (6.4, 20.5)	6.3 (1.9, 14.3)
Surgery only	56.9 (53.1, 60.5)	52.5 (44.0, 60.3)	50.8 (46.5, 54.9)	65.5 (61.4, 69.3)
Surgery and single modality	33.3 (27.6, 39.1)	23.9 (11.6, 38.6)	29.1 (22.4, 36.2)	39.4 (32.7, 46.2)
Surgery, chemotherapy, and radiation	41.0 (35.1, 46.8)	35.1 (20.3, 50.3)	41.4 (34.7, 48.0)	49.0 (42.4, 55.2)

CI confidence interval

Bolded values indicate significantly different ($p < 0.05$) relative survival from non-Hispanic whites^aEstimates for age at diagnosis were not age-adjusted

Table 3 Adjusted hazard ratios for mortality among patients with epithelial gastric cancer in California by race/ethnicity, 2006–2015

Variable	Non-Hispanic white HR (95% CI)	Non-Hispanic black HR (95% CI)	Hispanic HR (95% CI)	Asians/Pacific Islander HR (95% CI)
Sex				
Male	Ref	Ref	Ref	Ref
Female	0.91 (0.86, 0.97)**	0.87 (0.75, 1.01)	0.91 (0.85, 0.97)**	1.04 (0.96, 1.14)
Age at Diagnosis				
20–49 years	Ref	Ref	Ref	Ref
50–69 years	1.15 (1.03, 1.28)*	1.09 (0.86, 1.39)	1.06 (0.98, 1.15)	1.20 (1.04, 1.38)*
70+ years	1.95 (1.74, 2.19)**	1.85 (1.43, 2.40)**	1.60 (1.45, 1.77)**	2.05 (1.76, 2.40)**
Neighborhood socioeconomic status				
Lowest	1.23 (1.11, 1.37)**	1.11 (0.85, 1.46)	1.03 (0.89, 1.19)	1.21 (1.05, 1.39)**
Lower-middle	1.32 (1.21, 1.44)**	1.00 (0.76, 1.32)	1.03 (0.89, 1.19)	1.16 (1.02, 1.31)*
Middle	1.21 (1.11, 1.31)**	0.96 (0.72, 1.28)	0.91 (0.78, 1.06)	1.13 (1.00, 1.28)*
Upper-middle	1.12 (1.03, 1.21)**	0.81 (0.60, 1.10)	0.96 (0.82, 1.12)	1.08 (0.96, 1.22)
Highest	Ref	Ref	Ref	Ref
Marital status				
Single/divorced/widowed	1.33 (1.25, 1.41)**	1.10 (0.95, 1.28)	1.17 (1.09, 1.25)**	1.18 (1.08, 1.29)**
Married/domestic partner	Ref	Ref	Ref	Ref
Insurance				
Private	Ref	Ref	Ref	Ref
Medicare	0.98 (0.92, 1.04)	1.19 (1.00, 1.41)	1.09 (1.00, 1.18)	1.02 (0.92, 1.13)
Other public	1.04 (0.94, 1.15)	1.16 (0.95, 1.42)	1.15 (1.06, 1.25)**	1.13 (1.00, 1.28)
None	1.39 (1.11, 1.74)**	1.32 (0.85, 2.06)	1.17 (1.01, 1.35)*	1.32 (1.03, 1.68)*
Site				
Cardia	Ref	Ref	Ref	Ref
Noncardia	0.91 (0.85, 0.97)**	0.83 (0.68, 1.01)	0.89 (0.82, 0.98)*	0.80 (0.71, 0.90)**
Overlapping/unspecified	1.19 (1.10, 1.28)**	1.13 (0.91, 1.41)	1.14 (1.03, 1.26)*	1.06 (0.92, 1.22)
Histology				
Intestinal	Ref	Ref	Ref	Ref
Diffuse	1.18 (1.10, 1.27)**	1.21 (1.02, 1.43)*	1.19 (1.11, 1.28)**	1.12 (1.02, 1.23)*
Other epithelial	0.79 (0.72, 0.86)**	0.82 (0.65, 1.04)	0.70 (0.62, 0.79)**	0.83 (0.71, 0.98)*
Stage at diagnosis				
Localized	Ref	Ref	Ref	Ref
Regional	1.72 (1.57, 1.87)**	1.56 (1.26, 1.92)**	1.84 (1.65, 2.05)**	2.42 (2.14, 2.73)**
Remote	4.87 (4.49, 5.30)**	4.46 (3.63, 5.47)**	5.52 (4.97, 6.12)**	8.48 (7.48, 9.62)**

Estimates are adjusted for all other variables in the table

HR hazard ratio, CI confidence interval

*Significantly different at $p < 0.05$

**Significantly different at $p < 0.01$

stage disease had significantly worse survival than NHWs diagnosed at this stage.

Discussion

In this large population-based study of patients with epithelial gastric cancer, we sought to better understand the association of race/ethnicity and survival by comparing demographic and disease-specific mortality risk across

four major racial/ethnic groups in California. We determined that APIs and Hispanics overall had significantly better prognosis than NHWs, but there was no survival difference between NHBs and NHWs. When comparing survival within homogenous subgroups, the survival advantage of APIs persisted. However, there were few groups in which NHBs and Hispanics had different survival than NHWs. Our results suggest that APIs with gastric cancer have significantly better prognosis than other race/ethnic

Table 4 Adjusted hazard ratios for mortality in non-Hispanic blacks, Hispanics, and Asian/Pacific Islanders versus non-Hispanic whites (reference) with epithelial gastric cancer in California, 2006–2015

Subgroup	NHB vs. NHW HR (95% CI)	Hispanic vs. NHW HR (95% CI)	API vs. NHW HR (95% CI)
Overall	1.06 (0.98, 1.15)	0.94 (0.90, 0.99)*	0.83 (0.79, 0.88)**
Sex			
Male	1.08 (0.98, 1.19)	0.95 (0.90, 1.01)	0.80 (0.75, 0.86)**
Female	1.03 (0.91, 1.16)	0.92 (0.85, 0.99)*	0.86 (0.80, 0.94)**
Age at diagnosis			
20–49 years	1.08 (0.85, 1.37)	0.99 (0.86, 1.14)	0.81 (0.69, 0.96)**
50–69 years	1.04 (0.92, 1.17)	0.96 (0.89, 1.03)	0.87 (0.80, 0.94)**
70+ years	1.08 (0.97, 1.21)	0.89 (0.83, 0.96)**	0.82 (0.76, 0.88)**
Neighborhood socioeconomic status			
Lowest	1.20 (1.03, 1.40)*	0.98 (0.87, 1.09)	0.86 (0.74, 0.99)*
Lower-middle	0.96 (0.83, 1.12)	0.91 (0.82, 1.00)*	0.77 (0.69, 0.87)**
Middle	1.01 (0.85, 1.20)	0.86 (0.77, 0.95)**	0.80 (0.71, 0.89)**
Upper-middle	0.94 (0.77, 1.15)	0.97 (0.87, 1.08)	0.85 (0.77, 0.94)**
Highest	1.32 (1.03, 1.70)*	1.15 (1.00, 1.34)	0.88 (0.79, 0.98)*
Marital status			
Single/divorced/widowed	1.00 (0.90, 1.11)	0.89 (0.83, 0.96)**	0.79 (0.73, 0.86)**
Married/domestic partner	1.15 (1.02, 1.30)*	0.97 (0.91, 1.04)	0.86 (0.80, 0.92)**
Insurance			
Private	1.00 (0.88, 1.14)	0.92 (0.85, 0.99)*	0.82 (0.76, 0.89)**
Medicare	1.13 (1.01, 1.28)*	0.94 (0.87, 1.02)	0.82 (0.76, 0.89)**
Other public	0.87 (0.53, 1.43)	0.85 (0.62, 1.16)	0.79 (0.55, 1.12)
None	0.87 (0.53, 1.43)	0.85 (0.62, 1.16)	0.79 (0.55, 1.12)
Site			
Cardia	1.13 (0.94, 1.35)	0.97 (0.88, 1.06)	0.92 (0.82, 1.03)
Noncardia	1.03 (0.93, 1.15)	0.94 (0.87, 1.00)	0.80 (0.75, 0.86)**
Overlapping/unspecified	1.06 (0.92, 1.23)	0.91 (0.83, 1.00)	0.84 (0.76, 0.93)**
Histology			
Intestinal	1.01 (0.92, 1.11)	0.91 (0.86, 0.97)*	0.81 (0.76, 0.87)**
Diffuse	1.11 (0.95, 1.29)	1.00 (0.92, 1.10)	0.82 (0.74, 0.90)**
Other epithelial	1.19 (0.94, 1.51)	0.94 (0.80, 1.09)	0.90 (0.75, 1.07)
Stage at diagnosis			
Localized	1.21 (1.01, 1.46)*	0.95 (0.84, 1.08)	0.63 (0.55, 0.72)**
Regional	1.07 (0.92, 1.23)	0.95 (0.87, 1.04)	0.84 (0.77, 0.92)**
Remote	1.03 (0.93, 1.15)	0.94 (0.88, 1.00)	0.91 (0.85, 0.98)**

Each row of the table corresponds to a different Cox proportional hazards model conducted within the respective group. NHW estimates are the reference for all comparisons

Estimates are adjusted for all other variables in the table

NHW non-Hispanic white, NHB non-Hispanic black, API Asian/Pacific Islander, HR hazard ratio, CI confidence interval

*Significantly different from NHWs at $p < 0.05$

**Significantly different from NHWs at $p < 0.01$

groups, but that factors other than race/ethnicity may play a larger role in gastric cancer survival.

We observed that patients in each racial/ethnic group presented with different disease characteristics, and that gastric cancer afflicted a different demographic within each race/ethnicity. There were higher proportions of female patients among nonwhite groups, and Hispanics and blacks were

significantly more likely than NHWs and APIs to have low nSES. In addition, NHWs were more likely to have cardia tumors, and diffuse histology was more common among Hispanics. Similar distributions of these factors by race have been reported previously [22, 26]. Interestingly, while there were notable differences in patient characteristics, prognostic factors were generally similar among each race group.

For example, though nonwhite patients were much more likely to have noncardia cancers, having a noncardia tumor was associated with better survival among both nonwhite and NHW patients. This finding is supported by studies indicating that cardia cancers are associated with worse mortality than noncardia tumors [13]. In addition, though the distribution of disease characteristics varied by race, we found that diffuse histology and later stage at diagnosis had similar impacts on survival in each race/ethnic group. Together, our findings suggest that prognostic factors for gastric cancer are similar regardless of race.

Though predictors of survival were similar for each race, there were some differences in risk of death across race. For example, older age and singlehood were generally associated with worse survival for all races, but Hispanics and APIs within these groups had better survival than their NHW counterparts. Indeed, we found that overall, Hispanics had slightly better prognosis than NHWs, and APIs had the most favorable survival of all race/ethnic groups. Moreover, the survival advantage of APIs in the whole population was observed in nearly every subgroup, consistent with previous reports [6, 8, 27–29]. Contrary to other studies [10], however, we did not observe a general survival disparity between NHBs and NHWs, though NHBs diagnosed with localized disease were more likely to die than NHWs diagnosed at the same stage. The reasons for this difference are not clear but may reflect unequal access to or utilization of treatment.

The racial differences in survival observed in the whole population were not detected in all patient groups. Indeed, Hispanics and NHBs had similar survival as NHWs among most subgroups, and among several subgroups, race was not a significant prognostic factor. For instance, race was not a predictor of survival among patients with public or no insurance and patients with cardia tumors. While diffuse histology had a significantly negative impact on survival among all race groups, we found that NHWs, NHBs, and Hispanics with diffuse tumors had similar survival. These findings may indicate that race alone does not have as large of a role in explaining disparate gastric cancer outcomes as previously reported [7], at least among NHWs, NHBs, and Hispanics. Researchers are finding that genetics, tumor biology, environmental factors, and underlying physiology may contribute to disparities in gastric cancer morbidity and mortality [6]. For example, the Cancer Genome Atlas (TCGA) project has identified four molecular subtypes of gastric cancer, and one study found that survival varied across these subtypes [30]. Differential distribution of molecular subtypes may explain some of the survival differences observed in our study.

It is also possible that differences in *H. pylori* infection status may contribute to disparate gastric cancer survival, as several studies have found an association between *H. pylori* infection and better survival [31–33]. In addition, racial/

ethnic groups vary significantly with respect to strain of *H. pylori* infection, as strains tend to cluster according to geographic origin [34, 35]. Genomic differences in *H. pylori* may affect outcomes, though the association of different strains with gastric cancer prognosis is not yet well understood. Interestingly, a meta-analysis evaluating the impact of *H. pylori* infection on survival in 7,191 gastric cancer patients found that infection was associated with improved survival in European patients but was not associated with survival in patients in Asia or the United States [36]. While beyond the scope of the present study, these findings suggest a need to further investigate differences in genetics and *H. pylori* infection to better understand variation in gastric cancer outcomes.

There are a few proposed explanations as to why APIs appear to have better survival from gastric cancer, including stage migration and the extent of lymphadenectomy [6, 7]. In addition, we observed that APIs were more likely to be diagnosed early and to receive treatment, consistent with previous reports that APIs were more likely to have surgical resection [7] and were more likely to undergo curative intent surgery than non-Asians [8]. Because of the comparatively high prevalence of gastric cancer and screening campaigns in several Asian countries [37], certain API populations may be more aware of gastric cancer risk and thus be more likely to be proactive about gastric cancer screening and treatment [27, 38]. While earlier stage at diagnosis may explain some survival differences, we observed that APIs fared better than other race/ethnic groups even when diagnosed at the same stage. In addition, we demonstrated that APIs also consistently had better survival than other races within groups of the same histology and anatomic site, which may suggest important differences in tumor biology. Racial/ethnic differences in tumor biology may have important implications for therapeutic response and subsequent survival. Researchers should continue to investigate the underlying epidemiologic, biologic, and genetic factors that may contribute to APIs' superior survival, as this knowledge may be key to understanding and improving gastric cancer outcomes.

There are notable limitations of this study. While more than a quarter of California's population was born outside of the U.S. [39], we were unable to adequately determine which study participants were foreign-born due to large amounts of missing data about birth country in the registry. Gastric cancer risk varies by place of birth [40], which may have implications for survival. We also lacked data on other factors that may impact prognosis, including smoking, obesity, comorbidities, and *H. pylori* infection. While histology categorizations are consistent with many previous studies, the inclusion of ICD-O-3 code 8010 (carcinoma, NOS, 2.1% of study sample) in the intestinal category is not unanimously agreed upon. Despite these limitations, this study adds a novel contribution to the existing literature.

This large, diverse population-based sample allowed us to investigate survival within and across four major racial/ethnic groups. By comparing racial differences in survival within subgroups of demographic and disease characteristics, we were able to assess which factors may drive the survival differences observed across groups.

In summary, this study investigated racial differences in survival among gastric cancer patients. Though there were significant differences in patient characteristics by race/ethnicity, predictors of survival were similar for each group. After comparing survival across race/ethnicity, APIs and Hispanics overall had better survival than NHWs, and the survival advantage of APIs persisted in nearly every demographic and disease subgroup. However, in most subgroups, Hispanics and NHBs had similar survival as NHWs. Further, race was not a significant predictor of survival among those with public or no insurance and patients with cardia tumors. Together, these findings indicate that there are some differences in survival by race/ethnicity, but race/ethnicity alone cannot explain disparate outcomes in gastric cancer. Given that survival in gastric cancer patients is dismal for all races, future studies, particularly ones that investigate the role of population-specific etiological factors and molecular tumor profiles, are needed to further understand and address factors associated with survival.

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