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ORIGINAL PAPER

Disadvantages for non-Hispanic whites in gastric carcinoma survival in Florida

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Abstract

Purpose The prognosis for gastric carcinoma (GC) remains challenging with less than 35% of patients surviving 5 years. GC survival varies greatly by anatomical site, cardia and non-cardia. However, these important differences have not been thoroughly studied in relation to the increasing diversity in US populations such as Florida. In this study we examined, for the first time, the effect of race-ethnicity on risk of death from GC controlling for potential risk factors separately for cardia and non-cardia GCs.

Methods Data on GCs diagnosed in Florida from 2005–2016 were obtained from the statewide cancer registry. Age-standardized GC-specific 5-year survival was computed by anatomical site and race-ethnicity. In addition, a competing risk analysis was performed to assess prognostic factors and to estimate subdistribution hazard ratios of death from GC.

Results Whites had high proportions of cardia GC (43.9%) compared to all racial/ethnic minorities (10.9%, 19.6%, and 13.8% in Blacks, Hispanics, and Asians, respectively; $p < .0001$). Among 12,302 cases included, there were 7534 deaths from GC and 1179 from other causes. Age standardized GC-specific 5-year survival was significantly lower for Whites (28.0%) compared to Blacks (31.6%), Hispanics (37.6%), and Asians, (39.6%) and significantly lower for cardia GC (25.0%, 95% CI 23.4–26.6) compared to non-cardia GC (37.0%, 95% CI 35.5–38.4). Multivariable competing risk analysis in patients with non-cardia GC showed that Asians (sHR: 0.64, 95% CI 0.51–0.80), Hispanics (sHR 0.71, 95% CI 0.64–0.78), and Blacks (sHR 0.83, 95% CI 0.75–0.92) all had lower risks of death from GC compared to Whites. In patients with cardia GC, only Hispanics had statistically significant lower risk of death from GC than Whites (sHR 0.84, 95% CI 0.74–0.95, $p = 0.005$).

Conclusions The study of racial/ethnic survival disparities in patients with GC in Florida reveals Whites as the most disadvantaged group. Whites are more afflicted by cardia GC, which is associated with higher risk of death than non-cardia GC. However, even within non-cardia GC, Whites had higher risk of death than the other racial-ethnic groups. Commonly assessed survival determinants do not adequately explain these unusual disparities; thus, further investigation is warranted.

Keywords Cancer · Race · Gastric · Stomach · Disparities · Survival

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Introduction

Although gastric carcinoma (GC) incidence and mortality rates are declining in the United States at 1.5% and 2% [1] per year, respectively, it is still the third leading cause of cancer mortality worldwide [2] and the fifth leading cancer type in terms of new cases [2]. In 2019, there was an estimated 27,510 new cases and 11,140 deaths from GC in the U.S.[3].The prognosis remains poor, with the overall 5-year relative survival at 31.5% [1], ranging from 68.8% for those diagnosed at localized stage to a dismal 5.3% for distant stage [4].

Anatomical site for GC, i.e. cardia vs non-cardia, is an important factor to consider in population-based analyses due to their distinct etiology, distribution in the population and different prognosis. While cardia GC has consistently been related to obesity [5, 6] and gastroesophageal reflux disease [7, 8], non-cardia GC is associated with *Helicobacter pylori* infection [5, 9], low socioeconomic status [10], high consumption of processed meat, salty and smoked food, and low consumption of fruits and vegetables [7, 11]. By race-ethnicity, cardia GC is disproportionately more common among Whites [10, 12–14], while non-cardia GC is more common among minority populations including Hispanics [10, 12]. Cardia GC is associated with inferior survival, 22% of patients surviving 5 years [4] while for non-cardia GC, crude survival is higher, exceeding 30% after 5 years [4].

By race-ethnicity, ample disparities in GC survival have been documented, with majority foreign-born populations, especially Asians [15–18] but also Hispanics, showing higher survival for GC compared to all other racial/ethnic groups. In regards to secular differences in cancer survival between Whites and Blacks observed for a majority of cancers and often a result of different socio-economic status, access to healthcare, and different rates of earlier detection [19, 20], that has not been the case for GC with comparable 5-year net survival between U.S. Whites and Blacks [15, 21–25].

Florida is unique in the characteristics of Black race and Hispanic ethnicity [26]. A large proportion of the 5 million Hispanics in the state are Caribbean (Cubans, Puerto Ricans and Dominicans) [27] and their state-specific incidence and mortality rates for GC are distinct from Hispanics elsewhere in the country [28–30], in part because Cubans, the largest and oldest Hispanic subgroup in the state, present low rates of GC, more similar to Whites [28]. Additionally, Afro-Caribbeans, including those of Haitian and Jamaican descent [31], represent a substantial percentage of the 3.5 million Blacks in Florida. Patterns of GC vary also among Black subgroups both in Florida and elsewhere [32, 33]. Population-based analyses of these detailed-level populations are currently impossible due to incomplete Hispanic (and Black) subgroup cancer data. Nevertheless, research on survival disparities for the four main racial/ethnic groups (i.e. Whites, Blacks, Hispanics and Asians) which will contain the experience of these subgroups is needed to fully address GC disparities in Florida, especially taking into account the effect of anatomical site.

In this study we aim to examine the interplay between anatomical site and race-ethnicity in GC survival in the diverse state of Florida.

Methods

Data source

All cases ($N = 12{,}822$) of a first primary GC diagnosed between 2005 and 2016 in Florida, with a primary site code of C16.X and morphology codes 8000–8746 according to the International Classification of Diseases for Oncology, third revision (ICD-O-3) were obtained from the population-based Florida Cancer Data System (FCDS). FCDS, the statewide cancer registry, has been continuously classified at the highest level for completeness of cancer reporting by the North American Central Cancer Registries Association (NAACCR) [34]. Demographic, tumor and socioeconomic prognostic characteristics including age, sex, anatomical site, morphology, grade, stage at diagnosis, socio-economic status, and race-ethnicity as well as follow-up data (date and cause of death) were obtained from FCDS. GC anatomical site was classified into: cardia (ICD-O-3 code C16.0), non-cardia (C16.1–16.6), and unspecified/overlapping (C16.8–16.9). Non-cardia GC cases were further classified by more detailed anatomical site into two categories: midstomach (C16.1, C16.2, C16.5, C16.6); antrum and pylorus (C16.3, C16.4). Histological types were classified according to previous research and Lauren's criteria [35, 36] into the following: intestinal type (includes mucinous and papillary carcinoma, tubular, and intestinal morphology types); diffuse type (includes signet ring cell carcinoma, diffuse adenocarcinoma, linitis plastica, and undifferentiated); and other, specified; and unclassified (see Supplementary Table 1 for ICD-O-3 codes). For stage at diagnosis, the Surveillance, Epidemiology and End Results (SEER) staging categories localized, regional, distant, and unknown, were used. Socioeconomic status (SES) was studied based on the proportion of population living below the poverty level in the census tract of residence. Those residents in tracts with 0% to < 5% was classified as 'very low' poverty level, 5% to < 10% as 'low', 10% to < 20% as 'intermediate', 20% to < 100% as 'high', and unknown poverty level. Type of insurance was categorized as private, Medicare, Medicaid, no insurance

and unknown. Lastly, race-ethnicity was classified into four mutually exclusive groups as: non-Hispanic White (referred in this study as White for simplicity), non-Hispanic Black (Black), non-Hispanic Asian and Pacific Islander (Asian), and Hispanics of any race (Hispanics). Hispanic subgroup (e.g. Cubans, Puerto Ricans) based on the NAACCR Hispanic Identification Algorithm (NHIA) [37] and Black subgroup (African Americans, Afrocaribbeans) based on place of birth as described elsewhere [32] were used to describe intra racial-ethnic differences in GC according to anatomical site. Out of all primary cases of GC, 10 patients were excluded from the analysis because of missing survival time, 335 were excluded because they were diagnosed at autopsy or by death certificate, and 175 were excluded because they had unspecified or missing race-ethnicity.

Statistical analysis

Frequency distributions for all prognostic factors were examined and compared. Chi-square tests were used to examine bivariate associations between potential survivor determinants by race-ethnicity and anatomical site. For cause-specific survival analysis, the event of interest was death from GC. The Surveillance, Epidemiology, and End Results Program (SEER) definition for GC cause of death was used [38]. Five-year cause-specific survival was calculated for the entire study population of GC cases, for four race/ethical groups (Whites, Blacks, Hispanics and Asians), and by specified anatomical site (cardia, non-cardia), using the lifetable method. Survival was age-standardized according to the International Cancer Survival Standards [39] and computed based on the presumed alive assumption [40]. Under this assumption cases that were not found as deceased on successive annual mortality linkages were assumed to be alive and censored on the last date covered, in this case December 31, 2016. Corresponding survival proportions under the same assumption were obtained from SEER in order to make valid comparisons between Florida and the rest of the US for the same racial-ethnic groups and period of diagnosis. Cause-specific survival time for each case was thus computed in months elapsed from the date of diagnosis to the date of death or December 31, 2016, whichever occurred first. Deaths from cause other than GC were censored at time of death.

Lastly, univariable and multivariable competing risk analyses were performed to estimate cumulative incidence rates of death from GC over time, with death from other cause as the competing risk. The Gray's test [41] was used to compare cumulative incidence functions (CIFs) of GC mortality by race-ethnicity or other prognostic factor. For multivariable analysis, the Fine and Gray sub-distribution hazard regression modelling approach [42] was used to estimate the effect of race-ethnicity on CIF of death from GC, with death from other causes as the competing risk. Models were developed for each subgroup defined by anatomical site (cardia and non-cardia GC), with adjustment for sex, age at diagnosis, SES, insurance status, histology, and stage at diagnosis. Conventional Cox regression analyses were also used to study cause-specific and all-cause mortality and assess if there were substantial differences from the multivariable competing risk model. Results from competing risk analysis were summarized in terms of subdistribution hazard ratio (sHR) estimates and corresponding 95% confidence intervals and Cox regression results were summarized in terms of hazard ratios (HR). Type I error was set at 5%, and all tests were two-sided. Analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). This study is in compliance with the Florida Department of Health Institutional Review Board.

Results

Overall, there were 12,302 GCs diagnosed in Florida between 2005 and 2016 meeting selection criteria. The majority of patients were White (59%) with Hispanics, Blacks and Asians accounting for 23%, 16% and 2% of cases, respectively. The overall majority were males (63%) with a median age at diagnosis of 69 years. Whites had high proportions of cardia GC (43.9%) compared to all racial/ethnic minorities (10.9%, 19.6%, and 13.8% in Blacks, Hispanics, and Asians, respectively; $p < 0.0001$). For histology, 67% of all GCs were of the intestinal subtype and 19% were diffuse. Asians had a significantly higher proportion of diffuse type (34%) compared to all other populations. By stage, 22% were diagnosed at localized stage, 31% in regional stage, and 34% in distant stage while 14% were of unknown stage. Blacks also had the greatest proportion of people living in the highest poverty-stricken areas (51%) while Whites and Asians had more patients living in areas of low or very low poverty level, 45.0% and 43.1% respectively (Table 1). Whites had the lowest proportion of patients without insurance (3%) compared to all other groups, among whom approximately 10% of GC cases lacked health insurance. Hispanics (23.3%) and Blacks (21.7%) had the highest proportion of Medicaid beneficiaries compared to 14.1% of Asians and 6.7% of Whites.

Non-cardia patients had a higher proportion of cases diagnosed at the localized stage (25.3%) in comparison to those with cardia GC (21.1%) (Table 2). Conversely, those with cardia GC had a higher proportion of cases diagnosed at distant stage (32.8%) compared to non-cardia (30.3%). Among Hispanics, Cubans had a significantly higher proportion of GCs located in the cardia (30.8%) compared to Puerto Ricans (21.4%) and Mexicans (14.8%). Among

Table 1 Characteristics of GC cases by race-ethnicity

	All-combined *N* (%)	Whites *N* (%)	Blacks *N* (%)	Hispanics *N* (%)	Asians *N* (%)	*P*
Total	12,302 (100)	7,241 (58.9)	2,021(16.4)	2,771 (22.5)	269 (2.2)	
Sex						< .0001
Male	7,736 (62.9)	4,775 (65.9)	1,196 (59.2)	1,615 (58.3)	150 (55.8)	
Female	4,566 (37.1)	2,466 (34.1)	825 (40.8)	1,156 (41.7)	119 (44.2)	
Age at diagnosis						< .0001
15–44	729 (5.9)	233 (3.2)	170 (8.4)	294 (10.6)	32 (11.9)	
45–54	1,479 (12.0)	695 (9.6)	310 (15.6)	437 (15.8)	37 (13.8)	
55–64	2,567 (20.9)	1,453 (20.1)	509 (25.2)	532 (19.2)	73 (27.1)	
65–74	3,222 (26.2)	1,978 (27.3)	479 (23.7)	694 (25.0)	71 (26.4)	
75+	4,305 (35.0)	2,882 (39.8)	553 (27.4)	814 (29.4)	56 (20.8)	
Site						< .0001
Cardia	3,975 (32.3)	3,175 (43.9)	220 (10.9)	543 (19.6)	37 (13.8)	
Non-cardia	5,375 (43.7)	2,537 (35.0)	1,240 (61.4)	1434 (51.7)	164 (61.0)	
Unspecified/overlapping	2,952 (24.0)	1,529 (21.1)	561 (27.7)	794 (28.6)	68 (25.3)	
Histology						< .0001
Intestinal	8,242 (67.0)	4,984 (68.9)	1,332 (66.0)	1,772 (63.9)	154 (57.2)	
Diffuse	2,369 (19.3)	1,248 (17.2)	413 (20.5)	616 (22.3)	92 (34.2)	
Unclassified	712 (5.8)	424 (5.8)	116 (5.6)	154 (5.6)	18 (6.7)	
Others	979 (8.0)	585 (8.1)	160 (7.9)	229 (8.3)	5 (1.9)	
SEER stage						< .0001
Localized	2,686 (21.8)	1,616 (22.3)	429 (21.2)	594 (21.4)	47 (17.5)	
Regional	3,748 (30.5)	2,121 (29.3)	615 (30.5)	899 (32.4)	113 (42.0)	
Distant	4,130 (33.6)	2,398 (33.1)	712 (35.2)	934 (33.7)	86 (32.0)	
Unknown	1,738 (14.1)	1,106 (15.2)	265 (13.1)	344 (12.4)	23 (8.6)	
In Cardia GC						0.30
Localized	839 (21.1)	686 (21.6)	40 (18.2)	107 (19.7)	6 (16.2)	
Regional	1,300 (32.7)	1,032 (32.5)	63 (28.6)	192 (35.4)	13 (35.1)	
Distant	1,304 (32.8)	1,027 (32.3)	85 (38.6)	176 (32.4)	16 (43.2)	
Unknown	532 (13.4)	430 (13.5)	32 (14.5)	68 (12.5)	2 (5.4)	
In Non-Cardia GC						
Localized	1,358 (25.3)	661 (26.1)	307 (24.8)	357 (24.9)	33 (20.1)	< .0001
Regional	1,788 (33.3)	768 (30.3)	420 (33.9)	520 (36.3)	80 (48.8)	
Distant	1,631 (30.3)	761 (30.0)	392 (31.6)	437 (30.5)	41 (25.0)	
Unknown	598 (11.1)	347 (13.7)	121 (9.8)	120 (8.4)	10 (6.1)	
SES						< .0001
Very low poverty	1,548 (12.6)	1,080 (14.9)	134 (6.6)	295 (10.6)	39 (14.5)	
Low poverty	3,019 (24.5)	2,168 (29.9)	221 (10.9)	553 (20.0)	77 (28.6)	
Intermediate poverty	4,428 (36.0)	2,706 (37.4)	598 (29.6)	1,015 (36.6)	109 (40.5)	
High poverty	3,155 (25.6)	1,205 (16.6)	1032 (51.1)	877 (31.6)	41 (15.2)	
Unknown	152 (1.2)	82 (1.1)	36 (1.8)	31 (1.1)	3 (1.1)	
Insurance						< .0001
Private	4,158 (33.8)	2,631 (36.3)	585 (28.9)	847 (30.6)	95 (35.3)	
Medicare and specials	4,946 (40.2)	3,410 (47.1)	649 (32.1)	806 (29.1)	81 (30.1)	
Medicaid	1,606 (13.1)	483 (6.7)	438 (21.7)	647 (23.3)	38 (14.1)	
No insurance	741 (6.0)	225 (3.1)	195 (9.6)	294 (10.6)	27 (10.0)	
Unknown	851 (6.9)	492 (6.8)	154 (7.6)	177 (6.4)	28 (10.4)	

Florida 2005–2016

P p-value from chi-square test, *NA* not applicable, *SES* Social economic status

Table 2 Stage (A) and racial-ethnic group (B) by anatomical site of GC. Florida 2005–2016

SEER Stage	Cardia	Non-cardia	Unspecified/overlapping	All GC combined
	N (column %)	N (column %)	N (column %)	N (column %)
A. Distribution of stage by anatomical site of GC				
Localized	839 (21.1)	1358 (25.3)	489 (16.5)	2686 (21.8)
Regional	1300 (32.7)	1788 (33.3)	660 (22.3)	3748 (30.4)
Distant	1304 (32.8)	1631 (30.3)	1195 (40.5)	4130 (33.6)
Unknown	532 (13.4)	598 (11.1)	608 (20.6)	1738 (14.2)
Total GC	3975 (100)	5375 (100)	2952 (100)	12,302 (100)
Race-ethnicity by subgroup	Cardia	Non-cardia	Unspecified/overlapping	All GC combined
	N (row %)	*N* (row %)	*N* (row %)	*N* (row %)
B. Distribution of anatomic site of GC by racial-ethnic subgroups				
All hispanics combined	543 (19.6)	1434 (51.7)	794 (28.7)	2771 (100)
Mexican	16 (14.8)	58 (53.7)	34 (31.5)	108 (100)
Puerto Rican	70 (21.4)	180 (55.0)	77 (23.5)	327 (100)
Cuban	206 (30.8)	284 (42.5)	178 (26.6)	668 (100)
Dominican	10 (15.9)	37 (58.7)	16 (25.4)	63 (100)
Central American	30 (12.6)	129 (54.2)	79 (33.2)	238 (100)
South American	68 (13.9)	261 (53.5)	159 (32.6)	488 (100)
Hispanics unspecified	143 (16.3)	485 (55.1)	251 (28.6)	879 (100)
All blacks combined	220 (10.9)	1240 (61.3)	561 (27.8)	2021 (100)
African Americans	138 (12.1)	678 (59.4)	326 (28.5)	1142 (100)
Afro-Caribbeans	55 (10.3)	329 (61.5)	151 (28.2)	535 (100)
Blacks Unspecified	27 (7.8)	233 (67.7)	84 (24.5)	344 (100)

Blacks, Asians and all non-Cuban Hispanics the majority of tumors were non-cardia GCs (Table 2).

Among 12,302 cases eligible for this study, there were 7534 deaths from GC and 1179 from other causes. Causes-of-death other than GC were multiple (more than 160 different diseases) with the most common ones being Ischaemic Heart Disease (14.6% of all non-GC deaths), Acute Myocardial Infarction (8.1%), and Chronic Obstructive Pulmonary Disease (6.7%). For all GC cases combined, age-standardized GC-specific 5-year survival was significantly lower among Whites (28.0%, 95% CI 26.8–29.2) compared to all other racial-ethnic groups: Blacks (31.6%, 95% CI 29.2–33.9) ($p=0.008$), Hispanics (37.6%, 95% CI 35.5–39.7) ($p<0.0001$), and Asians (39.6%, 95% CI 33.1–46.1) ($p=0.001$)(Table 3). By anatomical site, the age-standardized 5-year cause-specific GC survival for all races combined in Florida was significantly higher for non-cardia (37.0%) than cardia (25.0%), $p<0.0001$ (Table 3). In comparison to their counterparts in SEER, Whites showed lower 5-year survival for non-cardia GC in Florida (33.8%, 95% CI 31.7–35.8) compared to SEER Whites (37.2%, 95% CI 36.1–38.3) ($p=0.003$), but no significant difference for cardia GC (28% in FL vs. 28.8% in SEER, $p=0.919$). Conversely for both cardia and non-cardia GC, 5-year survival for Black (20.4% and 36.1% respectively) and Hispanics (28.9% and 42.2% respectively) in Florida were seemingly higher than in the remaining US, although the differences were not significant ($p>0.05$) (Table 3 and Fig. 1). For all GCs combined, age-standardized GC-specific 5-year survival among Blacks ($p=0.025$) and Hispanics ($p=0.0005$) in Florida was significantly higher than in the SEER population. More detailed age-specific survival and age-adjusted cause-specific survival by stage and racial-ethnic group estimates are shown in Supplementary Table 2.

Table 4 shows the subdistribution hazard ratios (sHRs) by specified anatomical site including cardia and non-cardia GC. Amongst those with cardia GC, after adjusting for sex, age, histology, stage, SES, and insurance, there was no significant difference between Whites (reference) and Blacks (sHR 0.92, 95% CI 0.76–1.12) or Asians (sHR 0.84, 95% CI 0.52–1.37) while Hispanics had a 16% lower risk of death from GC (sHR 0.84, 95% CI 0.74–0.95) in comparison to Whites. Amongst non-cardia GC patients, a more detailed anatomical site (mid-stomach vs. antrum and pylorus) did not show an effect on risk of death from GC. Yet, by race-ethnicity all groups showed an advantage in relation to Whites: the risk of death from GC was 17% lower in Blacks (sHR 0.83, 95% CI 0.75–0.92), 29% lower in Hispanics (sHR 0.71, 95% CI 0.64–0.78), and 36% lower in Asians (sHR 0.64, 95% CI 0.51–0.80), taking into account

Table 3 Events (A) and 5-year age-standardized GC-specific survival by anatomical site (B) by race-ethnicity. Florida and SEER 2005–2016

GC	All-combined	Whites	Blacks	Hispanics	Asians
A. Events, *n (%)*					
Deaths from GC	7534 (61.2)	4687 (64.7)	1200 (59.4)	1505 (54.3)	142 (52.8)
Deaths from other cause	1179 (9.6)	730 (10.1)	213 (10.5)	218 (7.9)	18 (6.7)
Alive	3589 (29.2)	1824 (25.2)	608 (30.1)	1048 (37.8)	109 (40.5)
Total GC cases	12,302 (100)	7241 (58.9)	2021(16.4)	2771 (22.5)	
B. Age-standardized GC-specific 5-year survival and 95% confidence interval					
Florida					
Cardia ($N=3975$)	25.0%[x] (23.4, 26.6)	24.4% (22.7, 26.2)	20.4% (13.3, 27.6)	28.9% (24.4, 33.5)	–
Non-Cardia ($N=5375$)	37.0%[x] (35.5, 38.4)	33.8%[b,c,y] (31.7, 35.8)	36.1%[d] (33.0, 39.2)	42.2%[b,d] (39.3, 45.1)	46.1%[c] (37.6, 54.6)
All combined[a] ($N=12302$)	31.0% (30.0, 31.9)	28.0%[e,f,g] (26.8, 29.2)	31.6%[e,h,v] (29.2, 33.9)	37.6%[f,h,z] (35.5, 39.7)	39.6%[g] (33.1, 46.1)
SEER					
Cardia ($N=17,093$)	24.6% (23.9–25.4)	24.5%[i,j] (23.6, 25.4)	18.5%[i,k,l] (15.7, 21.5)	25.8%[k] (23.2, 28.4)	31.3%[j, l] (28.1, 34.6)
Non-Cardia ($N=26,041$)	38.0% (37.4–38.7)	37.2%[m,n,o,y] (36.1, 38.3)	33.4%[m,p,q] (31.8, 35.0)	38.9%[n,p,r] (37.5, 40.4)	47.0%[o,q,r] (45.5, 48.5)
All combined[a] ($N=56,808$)	28.9% (28.5–29.4)	28.8%[s,t] (28.1, 29.4)	28.6%[v,u] (27.4, 29.8)	33.5%[s,u,w,z] (32.4, 34.5)	40.4%[t,v,w] (39.2, 41.6)

–: Suppressed due to numbers less than 10 in at least one age group

[a]Includes cardia, non-cardia and unspecified/overlapping GC

[b–z]Same letter indicates significant pairwise difference at $p<0.05$ as follows:

Row pairwise comparisons: b-w

Column pairwise comparisons: *x*, *y*, *z*

Deaths from other cause were censored

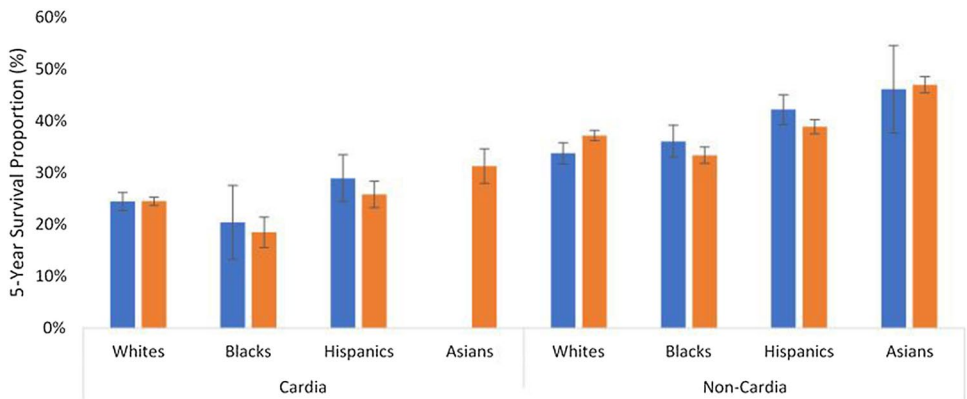

Fig. 1 Age-Standardized GC-specific 5-year survival by race-ethnicity and anatomical site. Florida and SEER 2005–2016. Blue represents FL, yellow represents SEER. *FL* Florida, *SEER* surveillance, epidemiology and end results

as competing risk death from other cause. Those living in census tracts with the highest level of poverty also had a higher risk of death from GC amongst non-cardia (HR 1.17, 95% CI 1.02–1.35) GCs compared to those in the lowest level of poverty.

In examining differences between the multivariable competing risk Fine-Gray models (Table 4) and more conventional methods, we fit multivariable Cox Regression models for cause-specific mortality (censoring deaths from other causes) and for all-cause mortality (Supplementary Table 3). The magnitude of the main estimates in these additional analyses were not substantially different from those in the multivariable competing risk model in Table 4.

Figure 2a shows the cumulative incidence of death from GC over time by anatomical site, with non-cardia GC experiencing lower mortality than cardia GC. Figure 2b shows that the cumulative incidence of GC death was highest for Whites and lowest for Asians. Figures 2c and d depict the cumulative incidence of GC death by race-ethnicity for cardia and non-cardia GC. The cumulative incidence of death

Table 4 Effect of potential prognostic factors on risk of death from GC, with death from other cause as the competing risk (Fine-Gray model). Analyses by GC anatomic site, Florida, 2005–2016

Prognostic factors	Univariable Fine-Gray models				Multivariable Fine-Gray model			
	Cardia GC		Non-Cardia GC		Cardia GC		Non-Cardia GC	
	sHR (95% CI)	*P*	sHR (95% CI)	*P*	sHR (95% CI)	*P*	sHR (95% CI)	*P*
Sex								
Female	Reference		Reference		Reference		Reference	
Male	0.97 (0.88, 1.06)	0.48	1.07 (1.00, 1.15)	0.07	0.98 (0.89, 1.09)	0.74	1.02 (0.94, 1.10)	0.66
Age								
15–44	Reference				Reference		Reference	
45–54	1.07 (0.84, 1.36)	0.57	1.09 (0.92, 1.29)	0.34	1.19 (0.94, 1.51)	0.15	1.06 (0.89, 1.25)	0.51
55–64	1.10 (0.88, 1.38)	0.40	1.11 (0.94, 1.30)	0.22	1.32 (1.05, 1.66)	0.02	1.08 (0.92, 1.27)	0.34
65–74	0.94 (0.75, 1.18)	0.61	1.15 (0.98, 1.35)	0.09	1.20 (0.95, 1.52)	0.12	1.12 (0.95, 1.32)	0.20
75+	1.43 (1.14, 1.78)	0.002	1.55 (1.33, 1.81)	< .0001	1.83 (1.45, 2.32)	< .0001	1.59 (1.35, 1.88)	< .0001
Race								
Whites	Reference		Reference		Reference		Reference	
Blacks	1.04 (0.87, 1.24)	0.68	0.85 (0.78, 0.93)	.0004	0.92 (0.76, 1.12)	0.42	0.83 (0.75, 0.92)	0.0003
Hispanics	0.86 (0.77, 0.97)	0.01	0.74 (0.68, 0.80)	< .0001	0.84 (0.74, 0.95)	0.005	0.71 (0.64, 0.78)	< .0001
Asians	0.94 (0.60, 1.47)	0.77	0.61 (0.49, 0.77)	< .0001	0.84 (0.52, 1.37)	0.48	0.64 (0.51, 0.80)	< .0001
Histology								
Intestinal	Reference		Reference		Reference		Reference	
Diffuse	1.28 (1.14, 1.44)	< .0001	1.01 (0.93, 1.09)	0.86	1.23 (1.08, 1.40)	0.002	1.04 (0.95, 1.14)	0.38
Unclassified	1.64 (1.32, 2.04)	< .0001	1.39 (1.13, 1.71)	0.002	1.34 (1.06, 1.68)	0.01	1.08 (0.86, 1.35)	0.54
Others	1.12 (0.94, 1.34)	0.22	0.28 (0.23, 0.35)	< .0001	1.15 (0.97, 1.38)	0.12	0.43 (0.35, 0.52)	< .0001
SEER stage								
Localized	Reference		Reference		Reference		Reference	
Regional	1.83 (1.61, 2.07)	< .0001	2.76 (2.45, 3.12)	< .0001	1.88 (1.66, 2.14)	< .0001	2.68 (2.37, 3.03)	< .0001
Distant	4.63 (4.08, 5.26)	< .0001	6.69 (5.92, 7.57)	< .0001	4.84 (4.24, 5.51)	< .0001	6.67 (5.88, 7.58)	< .0001
Unknown	3.07 (2.63, 3.58)	< .0001	3.57 (3.05, 4.17)	< .0001	2.74 (2.33, 3.21)	< .0001	3.17 (2.70, 3.71)	< .0001
Primary site								
Mid-Stomach	NA		Reference		NA		Reference	
Antrum and Pylorus	NA		1.07 (1.00, 1.15)	0.052	NA		1.01 (0.94, 1.09)	0.81
SES								
Very low poverty	Reference		Reference		Reference		Reference	
Low poverty	1.05 (0.93, 1.19)	0.44	1.16 (1.01, 1.32)	0.03	1.04 (0.92, 1.18)	0.54	1.12 (0.97, 1.28)	0.11
Intermediate poverty	1.11 (0.98, 1.25)	0.09	1.06 (0.93, 1.20)	0.39	1.05 (0.93, 1.19)	0.42	1.07 (0.94, 1.22)	0.30
High poverty	1.15 (1.00, 1.31)	0.05	1.17 (1.03, 1.33)	0.02	1.14 (0.99, 1.30)	0.08	1.17 (1.02, 1.35)	0.03
Unknown	1.21 (0.78, 1.87)	0.40	0.71 (0.49, 1.05)	0.08	0.99 (0.61, 1.60)	0.96	0.78 (0.52, 1.15)	0.21
Insurance								
Private	Reference		Reference		Reference		Reference	
Medicare and specials	1.13 (1.04, 1.24)	0.004	1.27 (1.16, 1.38)	< .0001	1.11 (1.01, 1.23)	0.03	1.12 (1.02, 1.23)	0.02
Medicaid	1.14 (0.99, 1.33)	0.075	1.19 (1.06, 1.33)	0.003	1.17 (0.99, 1.38)	0.06	1.16 (1.03, 1.31)	0.01
No insurance	1.40 (1.15, 1.70)	0.0007	1.09 (0.93, 1.28)	0.30	1.35 (1.10, 1.65)	0.004	0.98 (0.82, 1.17)	0.81
Unknown	1.39 (1.19, 1.63)	< .0001	1.10 (0.93, 1.29)	0.27	1.32 (1.10, 1.57)	0.002	1.10 (0.94, 1.30)	0.24

sHR Subdistribution hazard ratio from univariable or multivariable Fine-Gray models for death from GC, accounting for death from other causes as the competing risk

95% CI 95% confidence interval. *P* p-value. *NA* Not applicable, *SES* social economic status

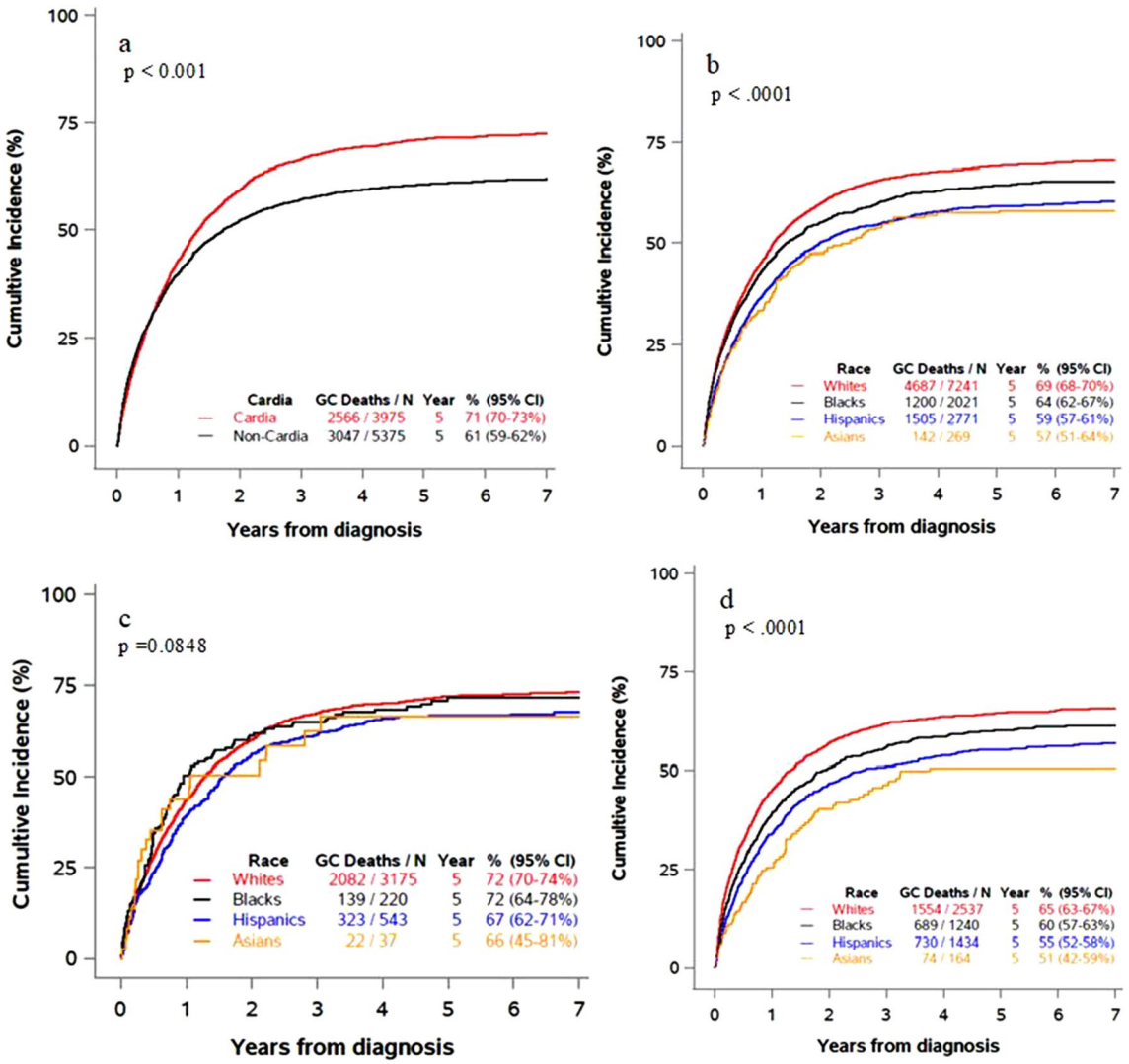

Fig. 2 Cumulative incidence of death from GC, with death from other causes treated as a competing risk by anatomical site (**a**), by race-ethnicity in all GCs combined (**b**), by race-ethnicity in cardia GC (**c**), and by race-ethnicity in non-cardia GC (**d**). *P* P-value from Gray's test. Censored observations not shown. Maximum follow-up truncates at 7 years

for cardia GC does not appear different between Whites and Blacks while for non-cardia GC mortality was highest for Whites and lowest for Asians, with cumulative incidence of GC death exceeding 60% for Whites at 7 years.

Discussion

This study provides the first population-based examination of GC cause-specific survival in multi-racial and multi-ethnic Florida. We demonstrated that although the overall GC prognosis remains a challenge with survival barely exceeding 30% after 5 years, marked differences by anatomical site and race-ethnicity may be indicative of opportunities for improvement in specific populations. By anatomical site, cardia GCs were associated with worse survival outcomes compared to non-cardia GCs. According to race-ethnicity, and contrary to the majority of cancer disparities studies, Whites showed the lowest GC survival of all major racial-ethnic groups.

GC survival was associated with all the known prognostic factors: those diagnosed at distant stage, with diffuse histological type, as well as patients living in areas of low SES (high poverty) showed a higher risk of death from GC in relation to those with localized stage, intestinal types, and high SES. Of all the significant predictors of survival, SES and especially anatomical site, cardia versus non-cardia, were the most unevenly distributed by race-ethnicity. The preponderance of cardia GCs was particularly evident for Whites (in excess of 40% of all GCs) and is in

agreement with previous research [2, 7, 10]. Reasons for this may include a higher prevalence of risk factors such as gastroesophageal reflux disease (GERD) and its complications among Whites [43–45]. Among Hispanics, Cubans are known to have a cancer profile closer to Whites [30], so it is not surprising their higher proportion of cardia GCs in relation to other Hispanics. In turn, non-cardia GC is associated with *Helicobacter pylori* infection [5, 9, 10, 12], which is less commonly found among Whites and more common in minorities [46, 47]. The lower survival for those with cardia GC can be due to various causes. Cardia GC is more often of diffuse histologic subtype [48, 49], which is harder to detect early and results in a poorer prognosis [48, 50]. Additionally, tumors located at the proximal (cardia) part of the stomach may require total gastrectomy or esophagogastrectomy, if extending into the lower esophagus, resulting in a relatively worse prognosis [7, 8, 51, 52]. Moreover, the nutritional consequences of post-gastrectomy syndrome manifested by early satiety, maldigestion of food products, and/or malabsorption may also contribute to poor outcomes in individuals with more extensive stomach resections.[53, 54].

For all GCs combined, a significant disadvantage was observed among Whites in comparison to all other racial-ethnic groups, including Blacks, a group that historically has had similar survival outcomes as Whites for GC [21]. However, because of the survival differences between cardia and non-cardia tumors and varying proportions by race-ethnicity, we proceeded with a stratified analysis with separate models for each of these anatomical sites. Each competing risk analysis model took into account all the commonly analyzed factors for GC survival on a population basis including sex, age, histology, stage, and poverty level [25, 55]. While significant racial-ethnic differences were not observed for cardia GC, important disparities became evident among non-cardia GCs with Blacks, Hispanics and Asians all having an important advantage in relation to Whites. While this relative vulnerability of Whites for GC has been observed in relation to Asians and Hispanics [25, 35]; the significant difference between Whites and Blacks in non-cardia GCs in this study is novel.

Several factors could explain this survival disadvantage. Previous cancer surveillance data have demonstrated an overestimation of survival for foreign-born populations [56]. This is particularly true for states like Florida, where patient follow-up is limited to passively collecting dates of death [56, 57]. This may lead to a less efficient capture of deaths for foreign-born populations who may die abroad, which therefore leads to inflated survival [56, 57]. The latter could in part help explain the relative disadvantage for Whites since a large proportion of Black and Hispanic cancer patients in Florida are foreign-born [29]. However, in absolute terms, when survival for Whites in Florida and SEER were compared directly, Whites in Florida showed significantly lower survival for non-cardia GC, which does suggest an actual disadvantage for Whites in this state for this anatomical site. This finding is unique and warrants further study, especially since the annual number of non-cardia GCs among Whites are in the hundreds in the Sunshine State.

In contrast to Florida Whites, Florida Blacks and Hispanics show a survival advantage, although not significant, in relation to their SEER counterparts for both cardia and non-cardia GC. The biology of gastric adenocarcinomas for individuals born outside the US may influence outcomes. It is known that the genomic signature of gastric adenocarcinomas in Hispanic patients differs from that in non-Hispanics [58]. Also, the countries of origin for Florida immigrants overlap with locations harboring the highest gastric cancer incidence rates, including Colombia, Venezuela, Honduras, Ecuador, Guatemala, and Peru [2]. Perhaps population awareness of disease or SES in country of origin may influence timely diagnosis or migration for treatments not available in their countries of origin, potentially influencing survival.

To clarify these findings, both in relative terms (Whites and other racial-ethnic groups) and within Whites in different parts of the US, several future research avenues are proposed. First, a detailed analysis regarding treatment patterns including receipt of neoadjuvant chemotherapy; second, improvements in FCDS follow-up procedures which could enable a better assessment of these disparities; third, the study of molecular subtypes of GC which may have an impact on survival [59–61] according to race-ethnicity. Moreover, the influence of gastric surgical volumes and distance from these high-volume centers with experienced surgeons is worthy of study.

There are some limitations present in our study in addition to the known follow-up data characteristics. First, information on comorbidities was not available for study. However, our choice of cause-specific survival as the main outcome of interest in our analyses greatly minimizes this limitation. Second, it is possible that residual confounding may partly account for some of the differences noted. It is possible that more granular categories than the ones used here for histology (e.g. proportion of signet-ring cell carcinomas currently included in diffuse type), and stage (different lymph node spread in more detailed AJCC stage versus the used SEER stage) could alter the estimates for the measures of association found in this study. Moreover, survival analyses by Hispanic (e.g. Cubans) and Black subgroups (e.g. Afro-Caribbeans) could be very useful to improve the understanding the survival differences in Florida and better characterize the cancer experience of these unique growing populations. However, these analyses are marred by the persistent problem of having a substantial proportion of cases with 'unspecified' subgroup, which causes important

biases in survival analysis [57]. In any case, our results indicate a heterogeneity in Hispanic subgroups in relation to proportions of cardia versus non-cardia GC. GC patterns among Cubans with higher proportion of cardia GC, are distinct from other Hispanics, while for Black subgroups, no substantial differences in the proportion by anatomical site were found between U.S.-born African Americans and Afro-Caribbeans.

Conclusions

Our study illustrates that stratification and/or adjustment by anatomical site should be carried out when comparing GC survival by racial-ethnic populations or across countries, which is not always the case in population-based studies [21, 62]. Moreover, the need for accurate follow-up data among the foreign-born is important when there is increased interest on the cancer experience of the large immigrant populations in the US who currently account for 16% of the population [63]. We found a survival advantage for minority populations in comparison to Whites: among Hispanics for cardia GC and among Blacks, Hispanics, and Asians for non-cardia GC. The overall GC disadvantage for Whites is a result of two main factors: first, a disproportionate weight of cardia GCs, and second, a lower survival for Whites observed for non-cardia GCs. As in other GC studies [35], the drivers behind these observed advantages for minorities and disadvantages for Whites are hard to pinpoint and remain elusive, despite adjustment for all commonly assessed prognostic factors. In this respect, further analyses are needed to examine racial-ethnic disparities in receipt of treatment and/or heterogeneity in molecular subtypes that may have a clinical impact on GC survival.

Author's Contribution JL: Methodology, Formal analysis, Writing—Original Draft, Writing—Review and Editing, Visualization. HM: Formal analysis, Writing—Review and Editing, Visualization. IR: Formal analysis, Writing—Review and Editing. DAS: Writing- Review and Editing. PSP: Conceptualization, Methodology, Formal analysis, Writing—Original Draft, Writing—Review and Editing, Supervision.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

Ethics approval This is the result of a secondary data analysis with deidentified data. The study is covered under Florida Department of Health IRB #2018-053, PI: PS Pinheiro.

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