Research Square

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Gastrointestinal Cancers: Racial and Ethnicity Differences

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Abstract

Objective: The purpose of this study was to examine race and ethnicity for overall survival (OS) and percent survival after 5- and 10-years for patients diagnosed with one of the gastrointestinal (GI) cancers.

Method: We used national data for 12 types of GI cancers (esophagus, stomach, gallbladder, intrahepatic bile duct, extrahepatic bile duct, liver, pancreas, small intestine, colon, rectosigmoid, rectum, and anal) for the years 2004-2016.

Results: A total of 2,249,213 patients diagnosed with one of the GI tract cancers with median age of 67 years were included in this study. There were 55% male, 77% non-Hispanic White (NHW), 12% were non-Hispanic Black (NHB), 6% were Hispanic, and the rest were classified as 'Other' race (4%). OS was higher for the Hispanics, followed by the 'Other', NHW and NHB (P <0.001). After adjusting for sex, income, insurance status, grade differentiation, age, and for Charlson-Dayo index, Hispanics and 'Other' race category had lower mortality compared to NHW (HR=0.93, 0.92-0.94, p <0.001; HR=0.92, 0.91-0.93, p <0.001), whereas NHB had higher risk compared to NHW (HR=1.09,1.08-1.09 p <0.001). Hispanics had lower mortality than NHW for 11 or 12 types (except esophagus), and 'Other' race category had lower risk for 10 of 12 types (except anal and small intestine). Five- and 10-year survival rates were higher for Hispanic patients (47%, 36%) followed by 'Other' (42%, 31%), NHW (40%, 28%), and for NHB (38%, 28%).

Conclusion: Hispanics and the patients from 'Other' race category diagnosed with one of the GI cancers had longer survival probability and lower risk of mortality compared to NHW and NHB.

Introduction

Cancer from the gastrointestinal tract and its associated excretory organs collectively represent one of the greatest public health issues in the US and worldwide. According to the American Cancer Society report (www.cancer.org) gastrointestinal cancers (GI) have the highest incidence and are a leading cause of cancer death. The incidence and mortality from GI cancers show disparities in the population [1, 2]. For instance, it is well known that native Asians from specific countries have a high incidence of gastric cancer [3]. Racial disparities related to the incidence and mortality have been documented in most of the studies for one or the other GI cancers, though the studies vary in terms of the study population, methodology and the independent effect of race (adjusting for other factors). Moreover, socio-economic factors play a role in racial disparity, incidence, and in rate of mortality.

In general, Africans American may be in a low socio-economic group, including a low level or lack of health insurance, lower level of education, and have less access to medical care, particularly access to prevention programs. Additionally, there might be other factors that are more specific to individual types of gastrointestinal cancers. For example, esophageal adenocarcinoma is more frequent among non-Hispanic whites (NHW); esophageal squamous cell carcinoma and colorectal cancer are more frequent among African Americans and the reasons might be multifactorial, including socioeconomic and lack of health care access, treatment, and prevention [4–9]. Also, a lower rate of surgery among Hispanics for esophageal cancer was associated with a decreased survival rate when compared to whites, even when adjusted for relevant socioeconomic and tumor factors [10].

In one of the studies using Surveillance, Epidemiology, and End Results database higher mortality rates were reported in minority groups (blacks, Hispanics, and Asians/Pacific Islanders) compared to non-Hispanic whites among patients diagnosed with non-cardia gastric cancer, whereas for cardia gastric cancer mortality rates were marginally higher in middle aged non-Hispanic patients with advanced disease[11]. However, Japanese and Asian patients diagnosed with gastric cancer have been reported to have better overall survival compared to White patients[12]. For patients diagnosed with gallbladder cancer

Hispanic ethnicity, although, showed better overall survival, but after adjusting for covariates such as treatment at an academic facility and year of diagnosis, this effect turned out to be non-significant[13]. Furthermore, it has also been reported that whites when compared to African Americans experienced better survival in small intestinal and anal cancer survival [14].

Liver cancer has been most frequent among Asian/Pacific Islanders and it is partly attributed to hepatitis B vertical transmission, but other racial groups also show increasing rates due to hepatitis C and emergence of cirrhosis from non-alcoholic fatty liver disease. Also, gastric cancer incidence is usually highest among Asian/Pacific Islanders likely due to gene-environment interaction [1]. Many GI cancers present with higher risk within westernized countries, and the observed risk is suggested to originate from the more abundant availability of calories, red meat, and fat, and subsequent interaction with the gut microbiome [15].

There might be differences in dietary preferences and composition of the gut microbiome, as well as biologic and genetic influences [16, 17]. These disparities in gastrointestinal cancer risk, could be reduced with the advancement of precision medicine methods when applied to populations with the increased risk [18].

Finally, some of these studies suggested that disparity in GI cancer risk and outcomes are mainly attributed to race, while other studies suggested that such a disparity is mainly due to biologic and genetic influences [1, 17]. Health inequalities such as socioeconomic and insurance status, access to health care, screening and treatments options do contribute to the racial disparities leading to the differences in the survival outcomes for the patients diagnosed with one of the GI cancers.

To best our knowledge a comprehensive epidemiological study for 12 GI cancers (esophagus, stomach, gallbladder, intrahepatic bile duct, extrahepatic bile duct, liver, pancreas, small intestine, colon, rectosigmoid, rectum, and anal cancer) using national database has not been done. Therefore, in this epidemiological study, our objective were two-fold (1) to find out the incidences of 12 different types of GI cancers across the four race categories (Hispanic, Non-Hispanic black (NHB), Non-Hispanic white (NHW) and all other races (such Asian, Pacific Islanders etc.); and (2) to find out racial differences in the outcomes (survival years and percent patient survival) while adjusting for patients' demographics, socioeconomic status (income and insurance status), tumor differentiation, comorbid scores and the treatment modalities using the largest national cancer database from 2004 through 2016.

Methods

The nationally recognized National Cancer Database (NCDB) is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The data used in the study are derived from a de-identified NCDB files. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

General geographic- and site-specific variations in NCDB case coverage and limitations have been documented elsewhere [19]. The patients without recorded survival status have been excluded from the statistical analysis. All statistical analyses were done without imputing missing values for all the variables. All category and continuous variables were described using appropriate descriptive statistics. For example, all category variables were described as frequency and percentage and all continuous numeric variables were described as mean and standard deviation. For survival analysis, Kaplan Meier method was used to show comparative survival for two or more groups. Multivariate Cox regression was used to find out hazard ratio predicting mortality. For all statistical tests, an alpha of 0.05 was used and all statistical analysis was done using SAS version 9.4, SAS Institute, Cary, NC.

Results

Descriptive statistics for study population across four-race categories

The study population included a total of 2,249,213 patients diagnosed with one of the GI tract cancers from 2004 to 2016. In the study population there were 55% male, 45% female, 77%, NHW, 12% were NHB, 6% were Hispanic, and the rest were classified as 'Other' race (4%) which mostly includes Asian, and Pacific Islanders. The median age at diagnosis was 67 years and interquartile range was 20 years. Colon cancer had highest number of patients (36.9%), followed by pancreas (15.1%), rectum (11.7%), stomach (8.1%), liver (7.6%), esophagus (6.2%), rectosigmoid (3.9%), small intestine (2.9%), anal (2.6%), gallbladder (1.4%), and intrahepatic bile (1.0%) (Fig. 1). There were higher percentage of male and uninsured patients in Hispanic and 'Other' group; low income bracket and higher Charlson-Deyo score [20] were among highest among NHB and Hispanics; invasive cancers was slightly higher among the 'Other' race category; well differentiated tumor was more common among NHB; and mortality rate was higher among NHB and NHW race categories (Table 1).

Median Survival and K-M curves

For all GI cancers overall survival in months was better for 'Other' race category compared to Hispanic ($p = 0.0018$), NHB ($p < 0.001$) and NHW ($p < 0.001$). Similarly, Hispanics had better survival than NHB (< 0.001), and NHW (< 0.001). Also, NHW had better survival than NHB ($P = 0.0026$). Within each GI cancer categories Hispanic and 'Other' race categories had better survival than NHB and NHW. Overall median survival for was lower for pancreatic cancer, gallbladder, intrahepatic bile duct, liver, extrahepatic bile duct, stomach and for esophagus cancers (Fig. 2). For all GI cancers Hispanics and patients in 'Other' race category had better survival. Unadjusted Kaplan-Meier curves for all GI Cancers are shown in Fig. 5–7.

Predictors of All-cause mortality

For individual GI cancers hazards ratios (HR) for mortality adjusting for age, sex, insurance status, income level, comorbidity score, hospital type, location of residence, histology of tumor, and treatments such as surgery, chemotherapy, hormonal therapy, immunotherapy and radiation, Hispanics had lower risk of all-cause mortality compared to NHW (HR = 0.85, 0.84–0.86, $p < 0.001$). Similarly, 'Other' race category had lower risk compared to NHW (HR = 0.88, 0.87–0.89, $p < 0.001$). Whereas NHB had higher risk compared to NHW (HR = 1.03,1.03–1.04 $p < 0.001$). Within each of the GI cancers Hispanics had lower risk for mortality than NHW for all 12 types of GI cancers (HR ranges from 0.78 to 0.85) and 'Other' race category had lower risk for 10 of 12 types (except small intestine and anal cancer), whereas NHB compared NHW had higher risk 6 of 12 types (esophagus, small intestine, colon, rectosigmoid duct, rectum and anal) and lower risk for pancreas cancer (Table 2).

Five and 10-year survival for GI cancers across four race categories

Overall five-year and 10-year survival rates were higher for Hispanic patients (47%, 36%) followed by 'Other' (42%, 31%), NHW (40%, 28%), and for NHB (38%, 28%). For all GI cancers 5- and 10-year survival are shown in Fig. 2 and Fig. 3.

Discussion

All GI cancers are specific to organ sites and have very different etiologies. These cancers vary in terms of incidence; may have been caused by infections such as hepatitis B or C, or Helicobacter Pylori; might be affected by gene-environment interactions; may have associations with blood groups [16]; vary in terms of preventive vaccination, screening, and treatments as well as for their outcomes. Despite differences it seems that race and ethnicity disparity exist in survival for the patients diagnosed with any of the gastrointestinal cancers. The explanations for the

disparities are not often clear. One of the reasons may be that factors such as socioeconomic status including health care access, access to treatment, access to prevention (vaccination and screening), dietary factors and composition of the gut microbiome, and biologic and genetic influences might have some interactive effects.

In the present study median survival in months for most of the GI cancers showed advantage for Hispanics and for 'Other' race category compared to NHB and NHW. Similarly, five and ten-years survival percentage of patients were also higher for Hispanics and for 'Other' race category compared to NHB and NHW.

Even after adjusting for covariates such as income, insurance status, age, tumor differentiation, score of comorbid conditions, and treatments such as chemotherapy, hormonal therapy, immunotherapy, radiation, and surgery, the results showed a clear advantage for patients with Hispanic ethnicity/race, and for 'Other' race category compared to NHB and NHW for the patients diagnosed with any of the 12 types of GI cancers. These results are in conformity with other smaller studies [1, 2, 7, 10, 14]. Genetic makeup and dietary preferences might be potential factors that provide advantages to Hispanics and for 'Other' race category (mainly Asians) [15].

Many of studies described in GI cancer literature used smaller study population. Whereas larger studies using larger database focused more either upon common type of cancers such colon and pancreas cancer, or on stomach and esophageal cancers which has somewhat better survival outcomes. Less common cancers such as rectosigmoid, small intestine, gallbladder, and intrahepatic bile had not been studied extensively. Furthermore, racial disparity for 12 types of GI cancer using largest database, to best of our knowledge, has not been studied.

To contrast in the present study, we not only used of the largest cancer registry in the world and most used data resource for cancer in the United States, but we presented most compressive comparison across four categories of race in terms of (1) the incidences of the 12 type of GI Cancer; (2) 5- and 10-year patient percent survival an d for (3) risk for mortality while adjusting for most of the available covariates using largest national database. We concluded that there is an advantage for Hispanics and for 'Other (Asian and Pacific Islanders) race category in terms of the outcomes for the patients diagnosed with one of the 12 types of GI cancers (esophagus, stomach, gallbladder, intrahepatic bile duct, extrahepatic bile duct, liver, pancreas, small intestine, colon, rectosigmoid, rectum, and anal cancer).

The limitation of this study mostly pertains to the data elements in the database such as exclusion of some of the cancer etiology variables (tumor size, cancer stages) due to substantial missing values, and race categories were derived from the combination of race and ethnicity variable. The database only includes approximately 70% of all newly diagnosed cases of cancer. Also, this database has undergone some significant changes from 2004 through 2016 that may affect its completeness and the types of available data elements. Finally, NCDB database does not accurately represent the cause of the patient's death and this limits the calculation of cancer-specific survival.

Conclusion

With a very large study population the survival for Hispanic patients as well as for the 'Other" race category (Asians/Pacific Islanders) had a higher overall survival probability, higher percentage of patients for five- and ten-year survival, even after adjusting for most of the available covariates, had lower risk of mortality compared to NHB and NHW. Possible hypotheses include dietary preferences, underlying genetic profile and environmental factors. Further studies are needed to confirm these hypotheses.

Declarations

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Conflict of Interest: None

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The National Cancer Database (NCBD) is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The data used in the study are derived from a de-identified NCDB files. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

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Tables

Table 1: Descriptive statistics for the patients diagnosed with gastrointestinal cancer across the four race categories from 2004 through 2016 (N= 2,249,213)

Characteristic	Hispanic (N=136,409)		NHB (N=276,497)		NHW (N=1741709)		Others (N= 94,598)		P value
Age (Median, IQR)	63.0	20	63.0	18.0	68.0	20	65.0	20	<0.001
Gender (N, %)									<0.001
Male	77,303	56.7	142,099	51.4	962,892	55.3	52,969	56.0	
Female	59,106	43.3	134,398	48.6	778,817	44.7	41,629	44.0	
Insurance Type (N, %)									<0.001
	74,950	56.7	163,693	60.6	899,118	62.1	51,036	55.4	
Medicaid/Medicare/other	13,978	10.6	17,487	6.5	38,081	2.6	5,137	5.6	
public	43,296	32.7	88,696	32.9	510,826	35.3	35,960	39.0	
None									
Private									
Income (2008-2012) (N, %)									<0.001
<$38,000	38,388	28.3	122,458	44.5	248,737	14.4	10,962	11.6	
$38,000-$47,999	32,907	24.2	61,385	22.3	418,682	24.2	15,016	15.9	
$48,000-$67,999	35,578	26.2	50,323	18.3	483,690	27.9	24,307	25.8	
≥ $68,000	28,920	21.3	41,017	14.9	581,474	33.6	43,880	46.6	
Type of hospital (N, %)									<0.001
Community Cancer	10,489	8.1	20,723	7.7	176,402	10.3	9,610	10.6	
Comprehensive	45,685	35.4	87,097	32.6	730,835	42.8	30,226	33.3	
Community Cancer	56,001	43.4	120,655	45.1	559,689	32.8	41,196	45.3	
Academic/Research	16,873	13.1	39,094	14.6	239,365	14.0	9,822	10.8	
Integrated Network									
Cancer									
Location of Residence (N, %)									<0.001
	126,574	94.6	247,170	90.9	1,395,810	82.4	86,440	93.7	
Metro	455	0.3	2,984	1.1	35,901	2.1	923	1.0	
Rural	6,767	5.1	21,681	8.0	262,180	15.5	4,917	5.3	
Urban									
Charlson/Deyo Score (N, %)									<0.001
	94,312	69.1	184,127	66.6	1,206,474	69.3	70,183	74.2	
0	28,692	21.0	62,863	22.7	367,836	21.1	17,675	18.7	
1	6,706	4.9	17,384	6.3	106,722	6.1	3,776	4.0	
2	6,700	4.9	12,123	4.4	60,677	3.5	2,964	3.1	
≥ 3									
Behavior (N, %)									<0.001
In Situ/Carcinoma in	3,864	2.8	10,640	3.8	59,299	3.4	2,368	2.5	
Situ	132,545	97.2	265,857	96.2	1,682,410	96.6	92,230	97.5	
Invasive									
Histology (N, %)									<0.001
Well differentiated	12,794	9.4	27,774	10.0	163,772	9.4	8,332	8.8	
Moderately	47,071	34.5	104,008	37.6	692,934	39.8	34,909	36.9	
differentiated	27,205	19.9	46,558	16.8	332,527	19.1	19,084	20.2	
Poorly differentiated	1,924	1.4	3,011	1.1	28,414	1.6	1,432	1.5	
Undifferentiated	47,415	34.8	95,136	34.4	524,062	30.1	30,850	32.6	
Not determined									
Mortality (N, %)									<0.001
Dead	73,528	53.9	168,726	61.0	1,070,869	61.5	49,728	52.6	
Alive	62,881	46.1	107,771	39.0	670,840	38.5	44,870	47.4	
Surgery (N, %)	76,168	57.8	158,119	59.25	1,089,308	64.5	56,691	62.0	<0.001
Chemotherapy (N, %)	61,162	47.2	114,874	43.5	747,144	44.5	41,321	45.9	<0.001
Hormonal therapy (N, %)	469	0.4	798	0.3	3944	0.2	231	0.3	<0.001
Immunotherapy (N, %)	1,411	1.0	3,082	1.1	18,566	1.1	1,009	1.1	<0.001
Radiation (N, %)	22,972	17.1	44,257	16.2	339,282	19.7	16,299	17.5	<0.001
Gastrointestinal Cancer (N, %)									<0.001
	4,848	3.6	13,410	4.9	118,541	6.8	3,199	3.4	
Esophagus	17,634	12.9	27,710	10.0	124,307	7.1	13,190	13.9	

Stomach	3,532	2.6	4,572	1.7	22,511	1.3	1.814	1.9	
Gallbladder	1,774	1.3	1,927	0.7	18,244	1.1	1,364	1.4	
Intrahepatic bile duct	4,232	3.1	4,780	1.7	42,104	2.4	3,178	3.4	
Extrahepatic bile duct	20,335	14.9	25,824	9.3	110,149	6.3	14,992	15.9	
Liver	17,124	12.6	41,015	14.8	271,177	15.6	11,158	11.8	
Pancreas	3,010	2.2	10,191	3.7	49,714	2.9	1,652	1.8	
Small intestine	40,179	29.5	104,210	37.7	657,837	37.8	27,442	29.0	
Colon	5,299	3.9	8,540	3.1	70,224	4.0	4,233	4.5	
Rectosigmoid	15,425	11.3	27,384	9.9	208,734	12.0	11,384	12.0	
Rectum	3,017	2.2	6,934	2.5	48,167	2.8	992	1.1	
Anal									

Table 2. Adjusted hazard ratio of mortality for the patients diagnosed with GI cancers from 2004-2016.

Gastrointestinal Cancer	Reference	Hispanic (HR, 95% CI)		NH Black (HR, 95% CI)		Other (HR, 95% CI)	
Esophagus	NH White	0.85*	0.82 -0.88	1.07*	1.04 - 1.09	0.84*	0.81 - 0.88
Stomach	NH White	0.84*	0.82 – 0.86	0.99	0.97 – 1.03	0.80*	0.78 – 0.82
Gallbladder	NH White	0.79*	0.75 - 0.83	0.98	0.95 -1.03	0.86*	0.81 - 0.92
Intrahepatic bile duct	NH White	0.82*	0.77- 0.88	0.97	0.92 - 1.03	0.91*	0.85 -0.98
Extrahepatic bile duct	NH White	0.86*	0.82 - 0.89	1.01	0.97-1.05	0.88*	0.84 - 0.93
Liver	NH White	0.80*	0.79- 0.82	1.01	1.00 – 1.03	0.82*	0.80 – 0.84
Pancreas	NH White	0.84*	0.83 - 0.86	0.98*	0.97 – 0.99	0.88*	0.86 -0.90
Small intestine	NH White	0.83*	0.77 - 0.89	1.07*	1.03 – 1.11	0.98	0.89 – 1.05
Colon	NH White	0.85*	0.84 - 0.87	1.10*	1.08 -1.11	0.88*	0.84 - 0.87
Rectosigmoid	NH White	0.80*	0.76 - 0.85	1.13*	1.09 – 1.18	0.82*	0.78 - 0.87
Rectum	NH White	0.81*	0.78 - 0.83	1.04*	1.02 - 1.07	0.86*	0.82 – 0.89
Anal	NH White	0.78*	0.72 - 0.82	1.13*	1.08 -1.12	1.03	0.92 - 1.16
All GI Cancers	NH White	0.85*	0.84- 0.86	1.03*	1.03-1.04	0.88*	0.87-0.89

* $p < 0.05$
Hazards ratios adjusted for age, sex, insurance status, income level, comorbidity score, hospital type, location of residence,
histology of tumor, and treatments such as surgery, chemotherapy, hormonal therapy, immunotherapy and radiation.
Variable TNM clinical stage group was not included in the regression model as there were more than 35% of the patients had
missing data.

Figures

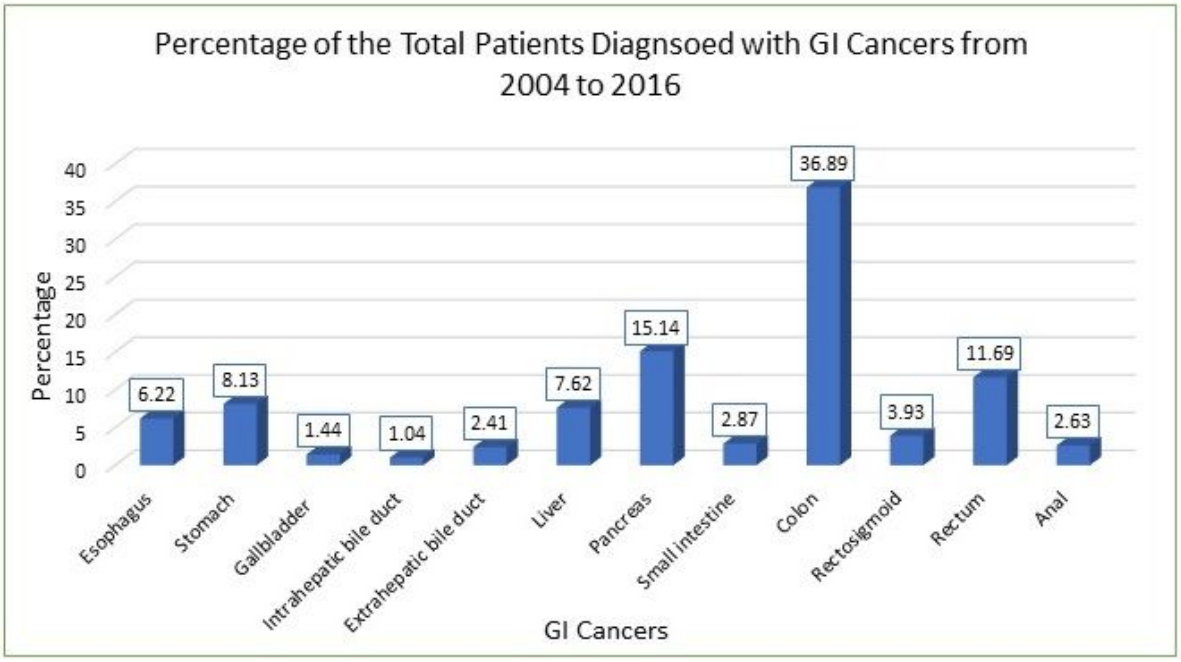

Figure 1. Percentage of patients diagnosed with each of each of the GI cancers from 2004-2016.

Figure 1

(caption in Figure)

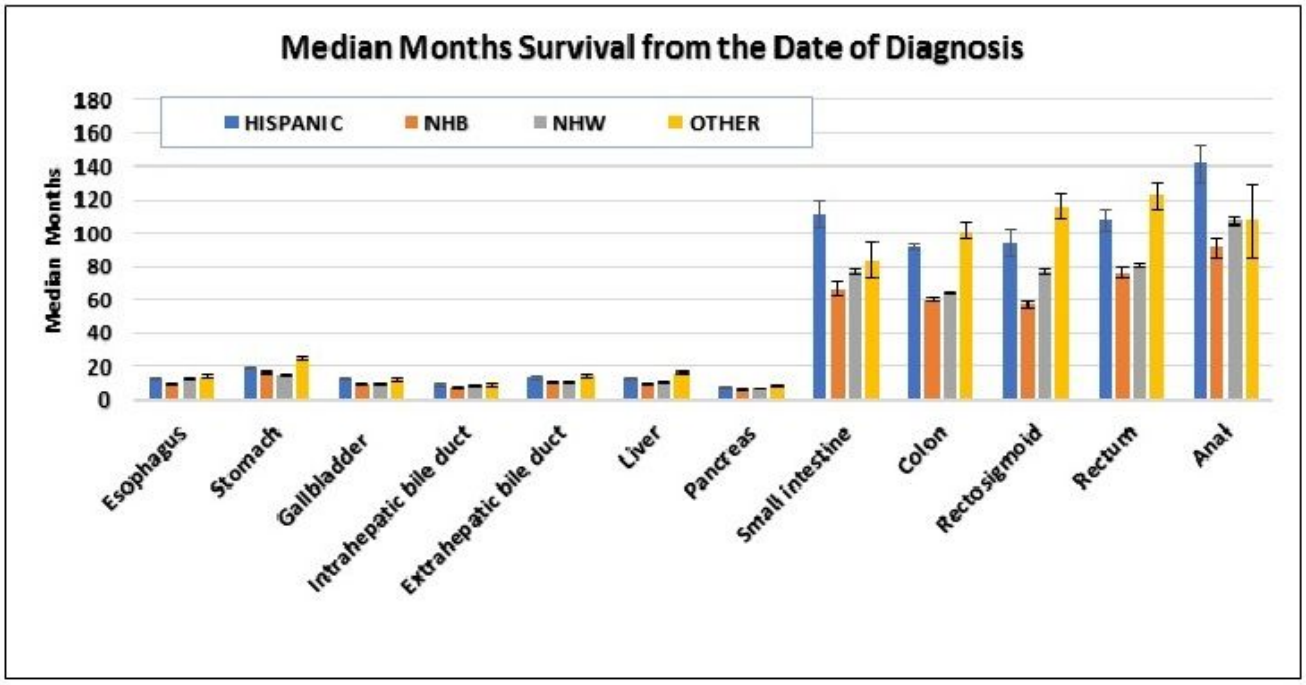

Figure 2. Median survival in months with 95% CI across the four race categories for the patients diagnosed with one of the 12 types of GI cancers from 2004 through 2016.

Figure 2

(caption in Figure)

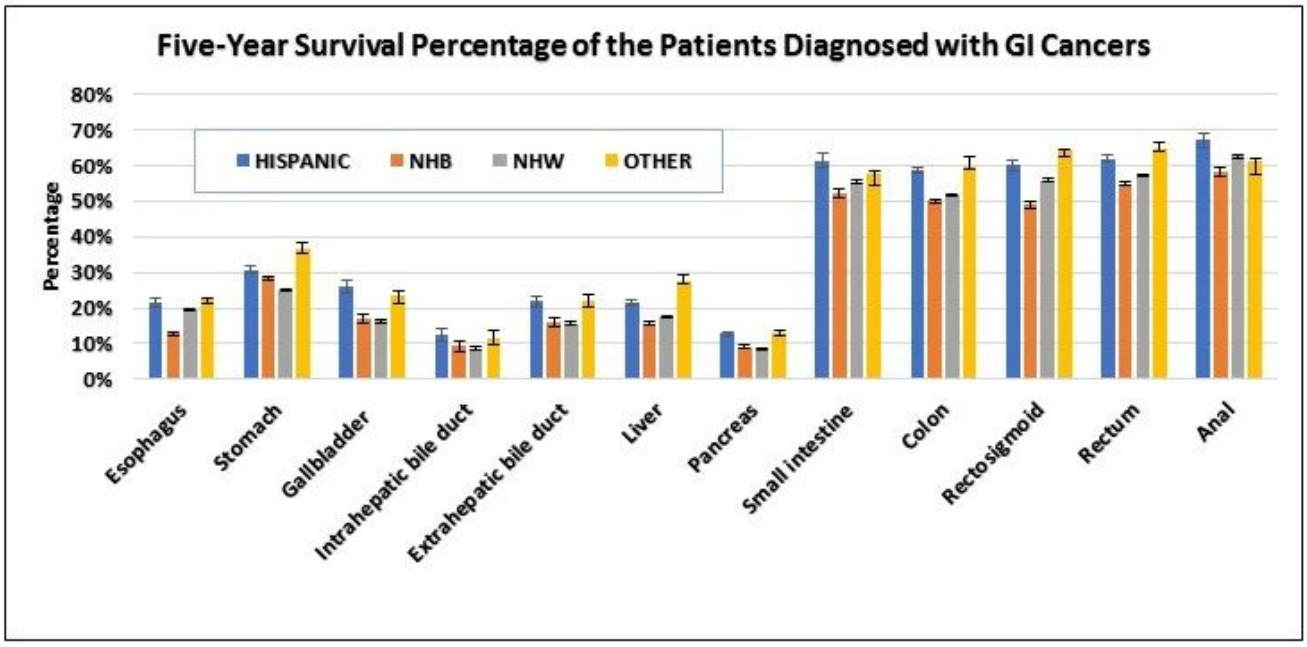

Figure 3. Five-year survival percentage with 95% CI across the four race categories for the patients diagnosed with one of the 12 types of GI cancers from 2004 through 2016.

Figure 3

(caption in Figure)

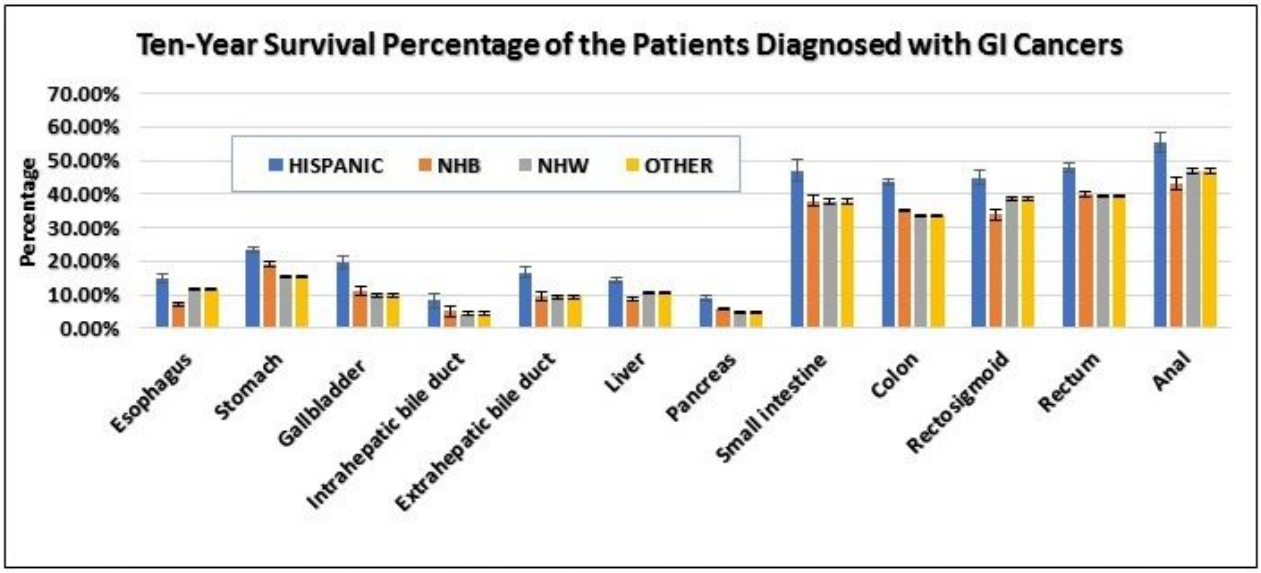

Figure 4. Ten-year survival percentage with 95% CI across the four race categories for the patients diagnosed with one of the 12 types of GI cancers from 2004 through 2016.

Figure 4

(caption in Figure)

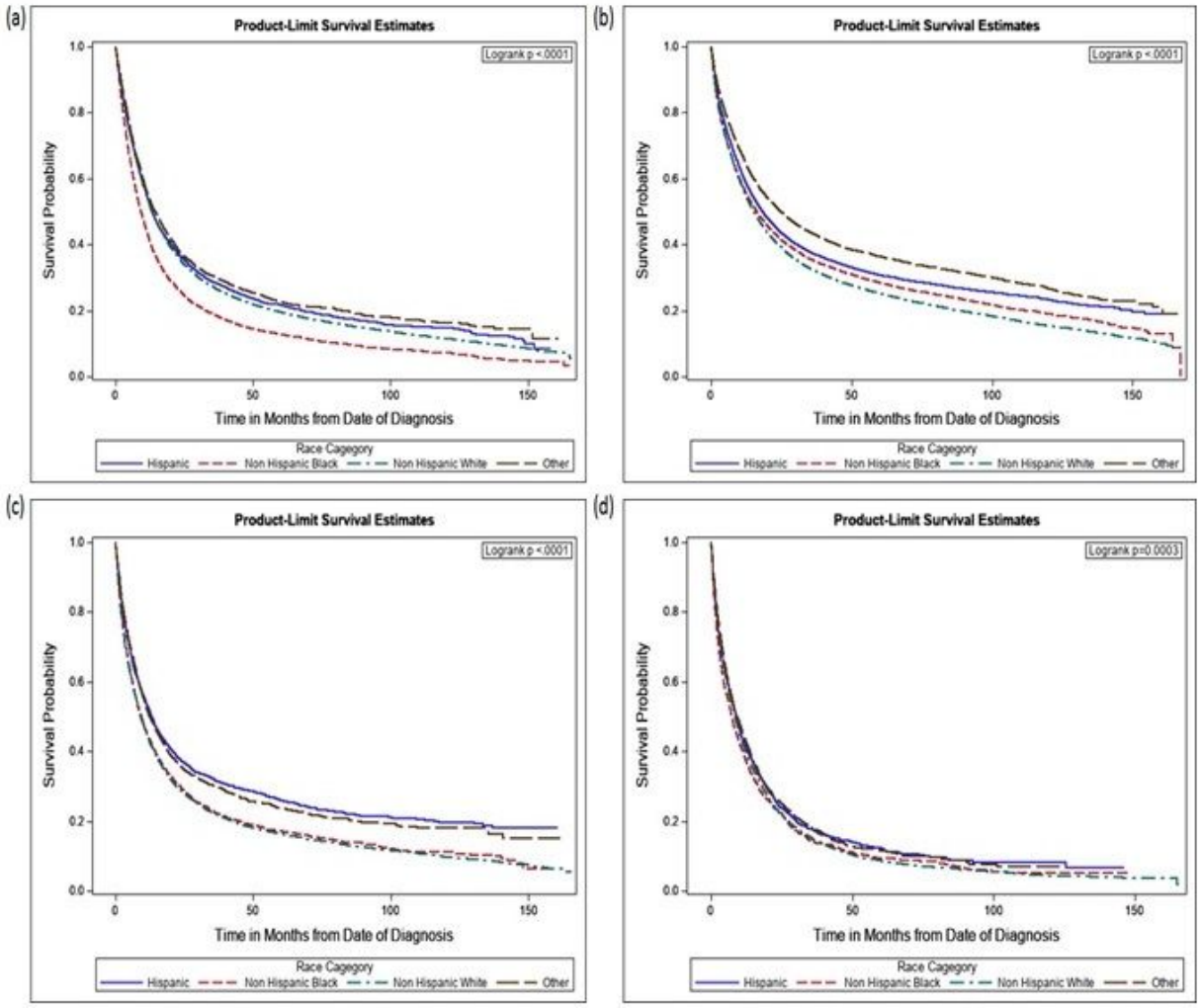

Figure 5:.Survival probability for (a) Esophagus (b) Stomach (c) Gallbladder and (d) Intrahepatic bile cancers.

Figure 5

(caption in Figure)

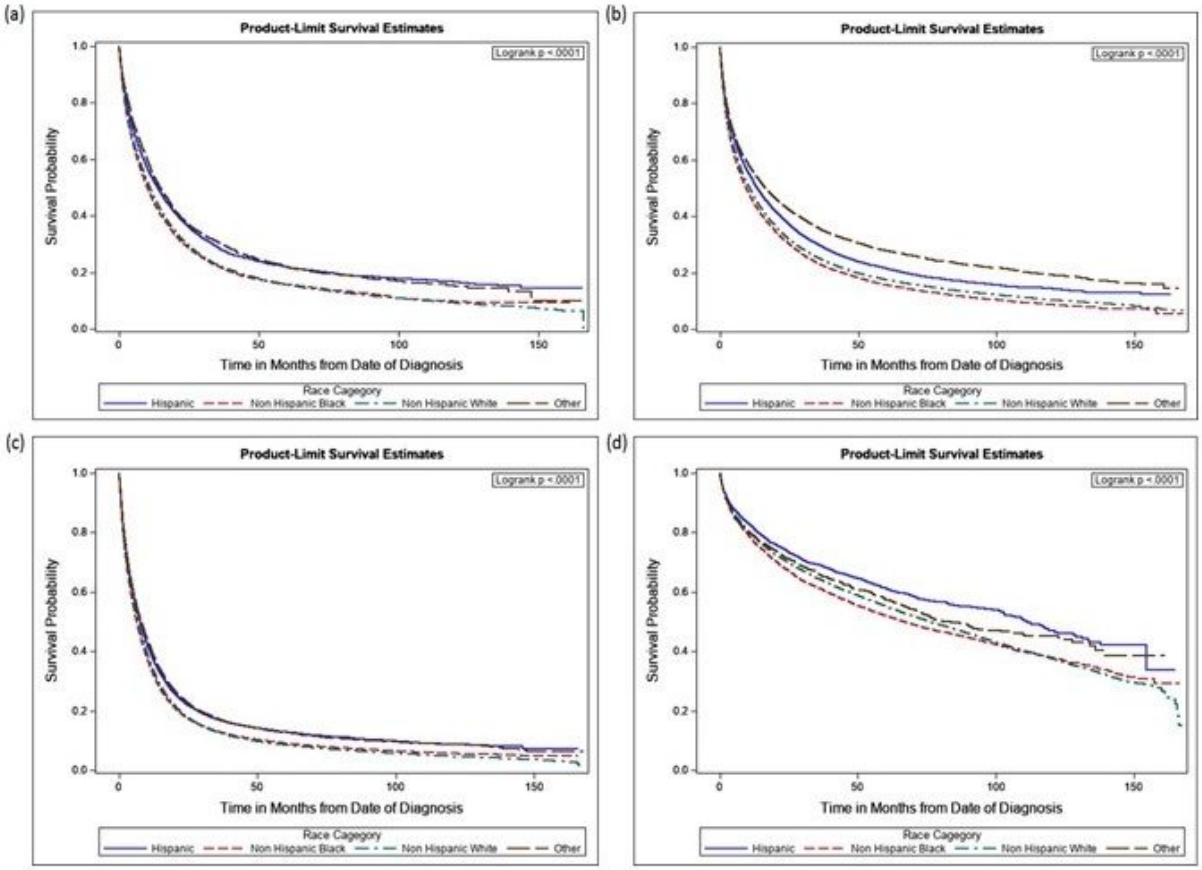

Figure 6. Survival probability for (a) Extrahepatic bile duct (b) Liver (c) Pancreas and (d) Small intestine cancers.

Figure 6

(caption in Figure)

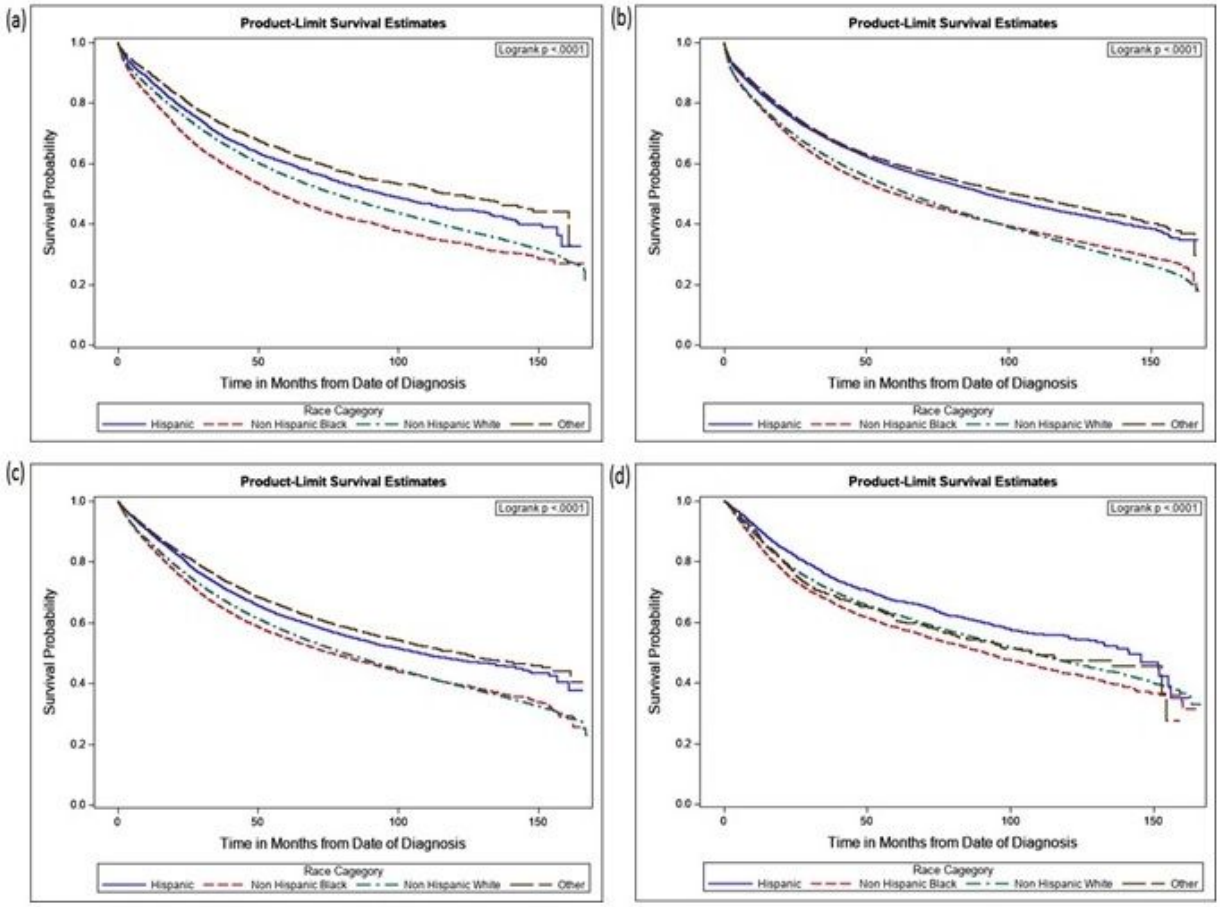

Figure 7: Survival probability for (a) Colon (b) Rectosigmoid (c) Rectum and (d) Anal cancers.

Figure 7

(caption in Figure)