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Racial and Ethnic Disparities in a National Cohort of Ampullary Cancer Patients

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Abstract

Background and Objectives—Racial and ethnic variations have been described in different malignancies, but no such data exists for ampullary cancer. The aims of this study were to present an updated report on the epidemiology, treatment patterns, and survival of a national cohort of ampullary cancer patients.

Methods—Patients diagnosed with ampullary cancer between 2004 and 2014 were identified in the National Cancer Database. Overall survival was estimated and compared between racial/ethnic groups using the log-rank test.

Results—A total of 14,879 patients were identified; 78% of the patients were White, 9% Hispanic, 8% Black, and 5% Asian. We noted significant differences in disease presentation, socioeconomic status, and outcomes. Blacks had the lowest median overall survival at 18.9 months followed by Whites at 23.9 months, Hispanics at 32.7 months, and Asians at 37.4 months. On a multivariate Cox proportional-hazards model, being Black was associated with worse survival compared to being White while being Asian and Hispanic were associated with better survival.

Conclusions—Overall survival of ampullary cancer patients was independently associated with race and ethnicity. Further studies are needed to clarify whether these disparities are primarily due to socioeconomic status or biologic factors.

Keywords

Ampullary cancer; race; ethnicity; disparity; ampullary carcinoma

INTRODUCTION

Racial and ethnic disparities in outcomes have been described in a variety of cancers such as gastric, colorectal, and breast.^(1–3) Socioeconomic status and environmental factors, such as adherence to screening guidelines, access to care, high-risk behavior, and obesity, all likely contribute to disparities in cancer-related incidence and mortality of racial and ethnic minorities. However, recent studies have also suggested that there may be underlying

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biologic distinctions between patients of different races and ethnicities that account for variation in outcomes.(1,4–7) Whether these differences are driven primarily by socioeconomic status or underlying disease biology require further studies and has important implications in allocating resources to improve cancer survival.

Ampullary cancer is a rare disease with an incidence of 4 to 6 cases per million persons and accounts for 0.2% of all gastrointestinal malignancies.(8–11) There are no guidelines from the National Comprehensive Cancer Network for the management of ampullary cancer. Patients who have resectable tumors usually undergo pancreaticoduodenectomy, with some centers advocating for adjuvant therapy.(12,13) The natural history and epidemiology of this disease have been described only in small single-institution studies and older population-level reports performed more than a decade ago.(8,9,11,14–19) In addition, little information exists about the racial and ethnic variation in the clinical presentation, treatment, and outcomes of this malignancy.(8)

In this study, we used information from the National Cancer Database (NCDB) to compare the presentation, treatment patterns, and survival between White, Black, Asian, and Hispanic patients with ampullary cancer treated from 2004 to 2014.

MATERIALS AND METHODS

Study Design

This was a retrospective study of records in the NCDB of ampullary cancer patients diagnosed between 2004 to 2014. The NCDB is sponsored by the American College of Surgeons and the American Cancer Society and collects clinical data from 1,500 Commission on Cancer-accredited facilities and encompasses more than 70% of new cancer diagnoses in the United States.(20) It is used to describe and analyze the presentation, treatment, and outcomes of a wide variety of malignancies. The study was approved by the University of Texas Southwestern Medical Center institutional review board.

Patient Selection

We identified patients with ampullary cancer using the International Classification of Diseases for Oncology, 3rd edition, ICD-O-3 code C24.1. We then selected patients with a diagnosis of carcinoma or adenocarcinoma based on the ICD-O-3 Surveillance, Epidemiology, and End Results Program (SEER) histology validation list and excluded patients with other histological types. The patients were divided into four racial and ethnic groups: Whites, Blacks, Asians, and Hispanics. Hispanic ethnicity was defined as being Mexican, Puerto Rican, Cuban, South or Central American (except Brazilian), Dominican, having another specified Spanish origin, Spanish—not otherwise specified, or having a Spanish surname only. Asian was defined as being Chinese, Japanese, Filipino, Korean, Vietnamese, Laotian, Hmong, Kampuchean, Thai, Asian Indian, Pakistani, and other Asian.

Variables and Outcomes

We abstracted data on gender, age, Charlson/Deyo score, insurance status, median household income of each patient's area of residence, tumor differentiation, tumor histology, and stage.

In addition, we included data on facility type, type of resection, margin status, receipt of regional lymphadenectomy, number of positive lymph nodes, 30-day readmission, 90-day mortality, and vital status. Treatment utilization was defined as the receipt of surgery, chemotherapy, radiation therapy, or any combination of the three.

Statistical Analysis

We used SPSS (version 21.0) to perform all statistical analysis. Continuous variables were presented as medians with interquartile ranges and categorical variables as counts with percentages. We used the chi-squared test to compare categorical variables and the Mann-Whitney U test to compare continuous variables. A multivariate logistic regression model was used to determine the predictors of treatment utilization. Overall and stage-specific median survival rates were determined using the Kaplan-Meier method. The log-rank test was used to compare the groups. We estimated the 1-, 3-, and 5-year survival. A multivariate Cox proportional-hazards model was used to determine the independent predictors of survival. Results were based on two-sided tests with a significance level of .05.

RESULTS

Patient Characteristics

Patient- and tumor-related characteristics are summarized in Table 1. We excluded 1,228 patients who did not have race/ethnicity information or were classified as “other” and 892 patients for non-carcinoma histology. In all, 14,879 patients with ampullary cancer diagnosed between 2004 and 2014 were included in this study; 78% were White, 9% Hispanic, 8% Black, and 5% Asian. The number of patients annually diagnosed with ampullary cancer increased from 1,186 patients in 2004 to 1,583 in 2014 (Supplementary Table 1). The proportion of White patients decreased from 81% in 2004 to 74% in 2014, while Blacks increased from 7% to 10%, Asians from 4% to 6%, and Hispanics from 8% to 10% during the same period.

Whites presented at an older median age (72 years) than the other groups (Asians at 67 years, Blacks and Hispanics at 65 years; $P < .01$) but Blacks tended to have more comorbidities on presentation ($P < .01$) and were diagnosed more often with metastatic disease (13%) than Whites (10%), Hispanics (9%), and Asians (9%, $P < .01$). Whites were less likely to be uninsured (2%, $P < .01$) compared to Asians, Blacks (5% for both), and Hispanics (14%). Blacks lived in areas with lowest median household income, with 43% residing in areas where median income was less than \$38,000 annually compared to 27% for Hispanics, 14% for Whites, and 12% for Asians ($P < .01$).

Treatment Utilization

There was a significant difference in treatment utilization with Blacks having the highest rate of non-treatment (26%), followed by Whites (24%), Hispanics (21%), and Asians (18%, $P < .01$). Significantly, Blacks were least likely to have a surgical intervention overall (61%) as compared to Whites (66%), Hispanics (71%), and Asians (73%, $P < .01$). There were no differences in 30-day readmission or 90-day mortality between the four groups.

To determine if there were any stage-specific differences in treatment use, we evaluated treatment patterns in a stage-specific manner and summarized the results in Supplementary Table 2. We found that Blacks were more likely to have no treatment for stage I disease (27%) compared to Whites (23%), Hispanics (20%), and Asians (17%). When adjusted for stage, predictors of treatment utilization were male gender, lower Charlson comorbidity index, private insurance, and living in areas with higher median household income (Table 2). After adjusting for all these factors, Black patients still had less treatment utilization than Whites (odds ratio, 0.76; 95% CI, 0.64–0.90).

Survival Analysis

Short- to long-term survival data are presented in Figure 1. Blacks had the lowest median overall survival at 18.9 months (95% CI, 16.8–21.0 months) followed by Whites at 23.9 months (95% CI, 23.0–24.8), Hispanics at 32.7 months (95% CI, 28.8–36.7), and Asians at 37.4 months (95% CI, 30.8–44.0). The 5-year overall survival was 24% for Blacks, 30% for Whites, and 38% for Asians and Hispanics. This pattern of differential survival was consistent when we evaluated outcomes based on stage (Figure 2) and was especially striking in early stage disease (Table 3). Median survival for Black patients with stage I disease was only 38.5 months compared to 82.8 months for Asians, 66.6 months for Hispanics, and 53.0 months for Whites. For stage II patients, median survival was 27.3 months for Blacks, 31.0 months for Whites, 37.0 months for Asians, and 40.9 months for Hispanics.

Based on a Cox proportional-hazards regression model (Table 4), the predictors of worse survival after adjusting for stage and having undergone treatment were male gender, increasing age, increased Charlson comorbidity index, Medicaid insurance in comparison to no insurance, living in areas with lower median household income, and poorly/undifferentiated histology. After adjusting for all these factors, Black race was independently associated with worse survival (hazard ratio [HR], 1.17; 95% CI, 1.07–1.27) compared to Whites. In contrast, Asians (HR, 0.81; 95% CI, 0.72–0.91) and Hispanics (HR, 0.79; 95% CI, 0.72–0.86) experienced better survival compared to Whites. To rule out stage migration as a cause of differential outcomes, we examined the subset of patients who underwent surgery and found that regional lymphadenectomy was performed at a similar rate with an equivalent lymph node yield (Table 1).

DISCUSSION

This is a contemporary hospital-based analysis of ampullary cancer outcomes. We found significant differences in presentation, treatment utilization, and outcomes across different races and ethnicities. Most strikingly, we found that after controlling for other prognostic factors, Blacks had the worst overall survival, while Asians and Hispanics had the longest survival. Our findings confirmed that race and ethnicity are associated with differential outcomes in ampullary cancer patients. Furthermore, this study provides a comprehensive updated survival analysis stratified by stage, race, and ethnicity, which can be used when counseling patients with this rare disease.

Cancer outcomes disparity due to race and ethnicity have been attributed to interrelated effects of socioeconomic status, access to care, and inherent tumor biology.(1,6,7) It is unclear to what magnitude race and ethnicity are surrogate markers for socioeconomic factors, such as education, insurance, occupation, living conditions, and behavioral risk factors (smoking, obesity, etc.) or whether there are inherent biologic differences between patients of different races and ethnicities. While some authors have concluded that non-cancer deaths, presentation, and treatment drive the differential outcomes seen in cancer patients of different races and ethnicities,(21) other studies have shown that race and ethnicity are associated with biological differences, such as chemotherapy response rate. (4,5) In this study, we found that Blacks tended to have lower socioeconomic status and lower treatment utilization that may partially explain the poor outcomes and higher rate of metastasis on presentation. Thus, improving access to care for Black patients may decrease the gap in outcomes. However, we also found that after adjusting for treatment utilization, being Black was still associated with worse survival, which indicates that other factors such as biology may be responsible for the difference.

Another striking finding in our study is that Asian and Hispanic patients had better overall survival. Asians and Hispanics have been found previously to have improved outcomes in cancers such as gastric, lung, colorectal, and prostate.(3,22) One explanation would be a difference in disease biology between Asians and Hispanics in comparison to Whites and Blacks. In fact, after adjusting for patient-, tumor-, and treatment-related factors, being Asian or Hispanic independently predicted improved survival when compared to Whites, which would be consistent with the concept that distinctions in disease biology in different races/ethnicities contribute to survival differences. It was also notable to find that Hispanics demonstrated improved outcomes compared to Whites, despite Hispanics having a higher uninsured rate and living in areas with lower median household income.(3) This result is consistent with the “Hispanic paradox” where Hispanics have unexpectedly improved health outcomes despite lower socioeconomic status.(23)

This retrospective study is likely limited by selection and information biases. In addition, data on only superficial markers of socioeconomic status were available, and more granular information, such as information on diet or detailed education history that may also explain the disparity in outcomes, are missing in the NCDB. The NCDB also did not have information about treatment completion rates, the type of chemotherapy agents used, and recurrence data, which are important for developing a complete understanding of the disease course. Another limitation of this analysis is that Blacks have shorter life expectancy than other groups. (24) This confounder may be especially relevant when examining patients with stage I disease, which demonstrated the largest survival gap between the groups, but likely cannot completely explain the large disparity in overall survival between the different races and ethnicities. For instance, the life expectancy of Blacks at 65 years of age is about 1.5 years shorter than Whites during the study timeframe and this difference is smaller than the overall survival disparities between both races across all stages. (24) Future studies with detailed disease specific survival will be necessary to further clarify this point. We also could not determine the incidence of ampullary by race and ethnicity as we could not ascertain the total number of patients studied. Finally, the NCDB lacked disease-specific variables, such as intestinal or pancreaticobiliary histology, which have been shown to be

prognostic in ampullary cancer.(25–30) However, a previous study by Carter et al. showed that there was no association between race/ethnicity and histology type. (29)

Despite these limitations, this study highlights differences in survival between White, Black, Asian, and Hispanic patients with ampullary cancer. It showed that Black patients had the worst survival, while Asians and Hispanics had the best outcomes even after adjusting for stage, treatment utilization, and socioeconomic status. There is an urgent need to understand the extent that socioeconomic factors versus inherent tumor biology determine cancer outcome disparities associated with race and ethnicity. Identifying the principal drivers of these differences in survival will define the most effective strategies for reducing the survival gap between different racial and ethnic groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Synopsis

In a national cohort of ampullary cancer patients, overall survival and treatment utilization were independently associated with race and ethnicity. Compared to White patients, Blacks received less treatment and had worse survival while Hispanics and Asians had longer survival.

Numbers at risk						
White	10,367	6637	4436	2990	2173	1564
Black	1049	613	379	248	163	114
Asian	644	473	331	222	160	99
Hispanic	1232	825	567	378	280	198

Race/Ethnicity	Median in Months (95% Confidence Interval)	1-Year (%)	3-Year (%)	5-Year (%)
White	23.9 (23.0-24.8)	68	40	30
Black	18.9 (16.8-21.0)	62	33	24
Asian	37.4 (30.8-44.0)	79	51	38
Hispanic	32.7 (28.8-36.7)	74	47	38

Figure 1.
Overall survival by race and ethnicity

Figure 2.
Overall survival stratified by stage, race, and ethnicity

Table 1

Patient-, Tumor-, and Treatment-Related Characteristics

	White	Black	Asian	Hispanic	P Value
	n (%)				
All patients *	11,543 (78)	1212 (8)	733 (5)	1391 (9)	
Gender					<.01
Male	6570 (57)	562 (46)	350 (48)	793 (57)	
Female	4973 (43)	650 (54)	383 (52)	598 (43)	
Age median [IQ range]					<.01
>65 years	72 [62–80] 7740 (67)	65 [56–75] 605 (50)	67 [57–75] 398 (54)	65 [55–75] 657 (47)	<.01
Charlson comorbidity index					<.01
0	8075 (70)	777 (64)	563 (77)	1018 (73)	
1	2595 (23)	318 (26)	133 (18)	286 (21)	
2	873 (8)	117 (10)	37 (5)	87 (6)	
Stage					<.01
I	3083 (27)	251 (21)	204 (29)	368 (27)	
II	3519 (31)	383 (32)	249 (35)	449 (33)	
III	1929 (17)	225 (19)	119 (17)	252 (19)	
IV	1084 (10)	158 (13)	64 (9)	122 (9)	
Unknown	1618 (14)	175 (15)	81 (11)	172 (13)	
Differentiation					<.01
Well-differentiated	1115 (10)	177 (10)	71 (10)	137 (10)	
Moderately	4585 (40)	484 (40)	316 (43)	588 (42)	
Poorly/undifferentiated	3294 (28)	302 (25)	201 (27)	401 (29)	
Unknown	2594 (23)	309 (26)	145 (20)	265 (19)	
Facility type					<.01
Community CP	698 (6)	72 (6)	38 (5)	80 (6)	

	White	Black	Asian	Hispanic	P Value
Comprehensive community CP	3933 (34)	339 (29)	232 (32)	415 (30)	
Academic/research program	5561 (49)	610 (51)	392 (55)	662 (49)	
Integrated network CP	1225 (11)	165 (14)	53 (7)	186 (14)	
Insurance					<.01
Private	3491 (31)	379 (32)	281 (40)	370 (28)	
Medicare	7184 (64)	609 (52)	294 (42)	536 (41)	
Medicaid	296 (3)	129 (11)	97 (14)	227 (17)	
No insurance	218 (2)	57 (5)	37 (5)	185 (14)	
Median household income for each patient's area of residence					<.01
<\$38,000	1609 (14)	511 (43)	83 (12)	368 (27)	
\$38,000–\$47,999	2695 (24)	287 (24)	100 (14)	360 (26)	
\$48,000–\$62,999	3170 (28)	221 (19)	200 (28)	362 (26)	
\$63,000+	3827 (34)	174 (15)	339 (47)	281 (21)	
Had surgical resection	7609 (66)	739 (61)	534 (73)	978 (71)	<.01
Regional lymphadenectomy	7045 (94)	688 (94)	505 (96)	904 (94)	.42
Lymph node resected median [IQ range]	12 [7–18]	13 [7–20]	13 [7–19]	13 [7–19]	.16
Margin					.33
Negative	6821 (94)	653 (93)	492 (95)	878 (95)	
Residual tumor, NOS	184 (3)	21 (3)	6 (1)	24 (3)	
Microscopic residual tumor	255 (4)	25 (4)	17 (3)	20 (2)	
Macroscopic residual tumor	30 (0.4)	3 (0.4)	1 (0.2)	5 (1)	
Treatment					<.01
No treatment	2619 (24)	293 (26)	125 (18)	273 (21)	
Surgery alone	4001 (37)	346 (30)	274 (40)	493 (38)	
Surgery + chemotherapy	1432 (13)	159 (14)	125 (18)	204 (16)	
Surgery + radiation	66 (0.6)	12 (1)	7 (1)	13 (1)	
Surgery + chemo + radiation	1670 (15)	177 (16)	96 (14)	203 (16)	
Chemo alone	644 (6)	96 (8)	43 (6)	73 (6)	

	White	Black	Asian	Hispanic	P Value
Radiation alone	129 (1)	15 (1)	8 (1)	7 (0.5)	
Chemo + radiation	326 (3)	44 (4)	13 (2)	26 (2)	
30-day readmission	629 (8.7)	73 (10.6)	35 (7.0)	68 (7.4)	.07
90-day mortality	444 (6.6)	33 (5.3)	20 (4.5)	44 (5.4)	.11

Abbreviations: CP, cancer program; IQ, interquartile; NOS, not otherwise specified

* Percentages add up across row. Otherwise percentages add up by column.

Table 2

Multivariate Logistic Regression to Determine the Predictors of Treatment Utilization, Adjusted for Stage

	Odds Ratio	P Value	95% CI
Sex			
Male	Ref		
Female	0.79	<.01	0.72–0.87
Age			
65 years	Ref		
> 65 years	0.35	<.01	0.30–0.40
Ethnicity			
White	Ref		
Black	0.76	<.01	0.64–0.90
Asian	1.10	.42	0.87–1.40
Hispanic	0.96	.65	0.81–1.14
Charlson comorbidity index			
0	Ref		
1	0.86	<.01	0.77–0.96
2	0.59	<.01	0.50–0.70
Insurance			
No insurance	Ref		
Private	1.77	<.01	1.31–2.37
Medicaid	1.31	.14	0.91–1.87
Medicare	1.34	.05	1.00–1.81
Median household income for each patient's area of residence			
<\$38,000	Ref		
\$38,000–\$47,999	1.09	.23	0.95–1.27
\$48,000–\$62,999	1.22	<.01	1.05–1.41
\$63,000+	1.17	.03	1.02–1.35
Facility type			
Community CP	Ref		
Comprehensive community CP	1.12	.23	0.93–1.34
Academic/research program	2.41	<.01	2.01–2.90
Integrated network CP	1.49	<.01	1.19–1.85

Abbreviations: CI, confidence interval; CP, cancer program

Table 3

Median and 1-, 3-, and 5-Year Overall Survival by Stage, Race, and Ethnicity

Stage	Race/Ethnicity	Median (Months)	1-Year (%)	3-Year (%)	5-Year (%)
I	White	53.0	76	56	47
	Black	38.5	72	52	43
	Asian	82.8	89	71	59
II	Hispanic	66.6	79	60	53
	White	31.0	78	45	34
	Black	27.3	78	41	29
	Asian	37.0	85	53	36
	Hispanic	40.9	85	54	43
III	White	19.8	68	30	19
	Black	17.8	60	25	13
	Asian	20.9	72	35	21
	Hispanic	27.7	73	41	28
IV	White	7.5	35	9	4
	Black	6.0	28	6	2
	Asian	10.0	47	18	14
	Hispanic	9.7	46	15	13

Table 4

Cox Regression Model to Determine the Predictors of Overall Survival

	Hazard Ratio	P Value	95% CI
Year of diagnosis *	0.99	<.01	0.98–0.997
Sex			
Male	Ref		
Female	0.93	<.01	0.89–0.97
Age 65 years	Ref		
> 65 years	1.43	<.01	1.33–1.52
Ethnicity			
White	Ref		
Black	1.17	<.01	1.07–1.27
Asian	0.81	<.01	0.72–0.91
Hispanic	0.79	<.01	0.72–0.86
Charlson comorbidity index			
0	Ref		
1	1.21	<.01	1.14–1.27
2	1.57	<.01	1.44–1.70
Insurance			
No insurance	Ref		
Private	0.93	.30	0.80–1.07
Medicaid	1.21	.04	0.97–1.31
Medicare	1.13	.11	0.97–1.31
Median household income for each patient's area of residence			
<\$38,000	Ref		
\$38,000–\$47,999	0.94	.07	0.88–1.00
\$48,000–\$62,999	0.88	<.01	0.82–0.95
\$63,000+	0.83	<.01	0.77–0.88
Facility type			
Community CP	Ref		
Comprehensive community CP	0.91	.04	0.83–0.99
Academic/research program	0.83	<.01	0.75–0.90
Integrated network CP	0.93	.22	0.84–1.04
Stage			
I	Ref		
II	1.43	<.01	1.34–1.52
III	2.07	<.01	1.93–2.23
IV	3.51	<.01	3.24–3.81

	Hazard Ratio	P Value	95% CI
Unknown	1.44	<.01	1.33–1.52
Differentiation			
Well-differentiated	Ref		
Moderately	1.19	<.01	1.09–1.30
Poorly/undifferentiated	1.62	<.01	1.48–1.77
Unknown	1.38	<.01	1.25–1.51
Treatment			
No treatment	Ref		
Any treatment	0.32	<.01	0.30–0.34

Abbreviations: CI, confidence interval, CP, cancer program.

* Continuous variable