RESEARCH ARTICLE

Editorial Process: Submission:09/25/2022 Acceptance:03/10/2023

Association between Mortality Due to Nasopharyngeal Carcinoma and Race in the United States from 2007 to 2016

Shahm Raslan[1]*, Edwin Rodriguez[1], Chengcheng Zheng[1], Juan Lozano[1], Noël C Barengo[1,2,3], Zoukaa Sargi[4]

Abstract

Background: Asians and Pacific Islanders (API) exhibit increased incidence of nasopharyngeal carcinoma (NPC). However, they are often excluded when the disease is studied. Risk-factors and incidence are well-researched while cancer-specific mortality trends remain unclear. We aimed to determine whether insurance status modifies the association between race and cancer-specific mortality in NPC patients. **Methods:** This retrospective cohort study used secondary data analysis from the Surveillance, Epidemiology, and End Results Program database. Patients ≥18 years with histologically confirmed primary NPC from 2007 - 2016 were included. The main outcome assessed was 5-year survival and the main exposure variable was race (API, white, black). Insurance status was classified into uninsured, any Medicaid, and insured (with any insurance). Potential confounders included age, sex, marital status, stage at diagnosis, and surgical treatment. Adjusted Cox regression analysis was used to calculate hazard ratios (HR) and corresponding 95% confidence intervals (CI). **Results:** 1610 patients were included (72.98% male, 27.02% female). 49.8% were API, 40.5% were Whites, and 9.8% Blacks. Maximum follow-up was 5-years. The adjusted hazards of 5-year cancer-specific death for API and Blacks compared with Whites were 0.77 (95% CI 0.62 – 0.96) and 0.92 (95% CI 0.65 – 1.31), respectively. Cases decreased with age in API and Blacks. 8.2% of cases had localized disease, 45.3% had local spread, and 44.6% had distant metastasis. Insurance status did not modify the association between race and mortality. **Conclusion:** Race is an important prognostic factor to account for in NPC patients. Investigating risk-factors and subtypes stratified by race may explain our findings.

Keywords: Nasopharyngeal carcinoma- asians and pacific islanders- insurance status- effect modifier- survival

Asian Pac J Cancer Prev, **24 (3)**, 915-921

Introduction

Nasopharyngeal carcinoma (NPC) is a unique subset of head and neck cancers. 86,000 cases of NPC present annually with distinct ethnic and geographic predilections (Chua et al., 2016; Ferlay et al., 2015). It is most prevalent in Southern China with 25 cases per 100,000 people annually. High-risk groups exhibit peak incidence at 50-59 years of age. Low-risk groups exhibit a steady increase of incidence with age. In the US, incidence increases with age, despite a minor peak in adolescents and young adults. Men are 2-3 times more likely to be affected than women. Increased risk due to immigration from endemic areas decreases with each passing generation (Mousavi et al., 2010; Chen et al., 2019, Chang et al., 2021). Immigrants from China in the US have the highest incidence of NPC and are 108 times more likely to be affected than non-immigrant Whites (Dickson and Flores, 1985; Mousavi et al., 2010; Lee et al., 2019). Chinese Americans overall maintain a 10-20 times higher incidence of NPC compared to White or Black Americans (Chang et al., 2021). Incidence in the US has decreased steadily while prognosis and outcomes have improved (Lee and Ko, 2005; Chen et al., 2019).

Surveillance, Epidemiology, and End Results Program (SEER) combines data from diverse population groups including Chinese immigrants and Pacific Islanders into a single Asians and Pacific Islanders group (API). Despite increased incidence, the current literature on cancer-specific mortality in API is inconsistent. Some studies suggest Asians have lower cancer-specific mortality compared with Whites and Blacks (Sun et al., 2007; Ou et al., 2007; Trinh et al., 2015; Chang et al., 2021). Other studies report no significant differences (Dickson and Flores, 1985; Bhattacharyya, 2004). There are reports of increased cancer-specific mortality among API up to

*[1]Department of Translational Research, Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, United States. [2]Faculty of Medicine, Riga Stradins University, Riga, Latvia, United States. [3]Department of Public Health, Faculty of Medicine, Riga Stradins University, Riga, Latvia, United States. [4]Department of Otolaryngology, University of Miami Miller School of Medicine, Miami, Florida, United States. *For Correspondence: srasl001@fiu.edu. Shahm Raslan, Edwin Rodriguez and Chengcheng Zheng have equal contribution in this study.*

10 times versus other races (Huang et al., 2013; Miller et al., 2008; Levine et al., 1987). Breaking down the API population into ethnicities and countries of origin suggested that the increased incidence and mortality burdens in NPC are not equally distributed among various API groups. Chinese, Filipinos, and Vietnamese may show particularly high cancer-specific mortality among API (Levine et al., 1987; Miller et al., 2008; Trinh et al., 2015). Blacks below 30 years of age have been shown to have an increased incidence of NPC. However, Black race is not associated with cancer-specific mortality when controlled for covariates (Lee and Ko, 2005; Cannon et al., 2006; Richey et al., 2006; Ferrari et al., 2012).

Most of the previous scientific studies of race and NPC do not account for presentation, viral status, or histologic subtypes. Substantial research has been done on East Asian populations due to the region's high prevalence while American populations are less examined (Ferlay et al., 2015; Wang et al., 2013). Epidemiological studies on NPC in the United States often exclude API (Ferlay et al., 2015; Sun et al., 2007; Ou et al., 2007; Bhattacharyya, 2004; Cannon et al., 2006; Wang et al., 2013). Even in studies focusing on API, small sample sizes prevent researchers from examining the mortality of the individual ethnicities and respective countries of origin within the API population with enough power (Miller et al., 2008). Most similar studies have relatively small sample sizes (Ferlay et al., 2015; Sun et al., 2007; Ou et al., 2007; Bhattacharyya, 2004; Cannon et al., 2006; Chan et al., 2017). Population-based cancer registries offer pooled data and provide another opportunity to study this rare disease (Bhattacharyya, 2004; Richey et al., 2006; Ou et al., 2007; Sun et al., 2007; Ferlay et al., 2015; Raghupathy et al., 2014; Chan et al., 2017; Chang et al., 2021). However, such registries over-represent select urban areas and developed countries and include just 21% of the global population (Raghupathy et al., 2014). Important prognostic elements such as histologic subtype, treatment modality, and viral status in NPC are not well-researched on a large scale (Geara et al., 1997; Lo et al., 1999; Chan and Lo, 2002; Lin et al., 2004; Le et al., 2005; Stevens et al., 2005; Leung et al., 2006; Sun et al., 2007; Ou et al., 2007; Chan et al., 2013; Raghupathy et al., 2014; Chan et al., 2017). Furthermore, insurance status is an important social determinant of health that may modify the association between race and mortality in patients with NPC. However, its role in the association between race and cancer-specific mortality in NPC patients has not been investigated. Current mortality rates and relevant factors must be determined for providers to deliver fully comprehensive care to API patients.

The objective of our study was to determine the prognostic relation of race and cancer-specific mortality in patients with NPC, and to check whether insurance status modifies this association.

Materials and Methods

Study design and population

This was a retrospective cohort study and secondary data analysis of the SEER database. SEER is a program of the National Cancer Institute (NCI) focused on cancer surveillance. Mortality data reported by SEER are provided by the National Center for Health Statistics, and population data is taken from the Census Bureau (SEER 2019). SEER collects survival and incidence data on cancer in 34.6 percent of the American population. Insurance status was reported to SEER from 2007 – 2016. The inclusion criteria of our study were patients with a histologically-confirmed diagnosis of a primary NPC (C110-C113, C118-C119 sites and 8000 – 9975 /3 histology) recorded between 2007 and 2016 who were 18 years or older and whose race was recorded in SEER. Exclusion criteria were patients who died of an unknown cause, patients missing follow-up data, and patients who were American Indian/Alaskan Natives (AI/AN) or of unknown race.

Variables

Variables on SEER database include gender, age, ethnicity, histological type, marital status, tumor size, surgery history, disease stage, cause of death, and survival time. Race was classified as White, Black, and API. The primary outcome was 5-year mortality calculated from the date of diagnosis to the date of cancer-specific death. Maximum follow-up time was five years. Ethnicity was grouped as Hispanic or Non-Hispanic. Insurance status was classified as uninsured, on Medicaid, and insured (including any Non-Medicaid insurance). Age, sex, marital status, stage of diagnosis, and surgical treatment at the primary site were included as covariates. Age was categorized as less than 50, 50-59, 60-69, 70-79, and 80 years or older. Sex was grouped as male and female. Marital status was classified as partnered and unpartnered. Surgical intervention was classified into any intervention and none. Disease stage at diagnosis was classified as localized disease (disease confined to the nasopharynx), regional disease (regional lymph node invasion), and metastatic disease.

Statistical Analysis

STATA was used to perform statistical analyses. Percentages were used to analyze nominal variables. Chi-squared tests were used to compare distributions of possible confounders by race. Kaplan-Meier survival curves were constructed to visually measure the survival rates of NPC patient according to race over the course of 5 years. The log-rank test was used to assess for differences in survival between each race. Unadjusted and adjusted Cox regression models were used to test for the associations between race and survival. Adjusted hazard ratios (aHR) and their corresponding 95% confidence intervals (CI) were calculated to interpret the differences in risk of death of API and Blacks as compared to Whites. Interaction was tested by adding an interaction term race*insurance status to the statistical model. The proportional hazard assumptions were tested graphically. Alpha of 0.05 was used for all statistical tests. All tests measuring p-value and Cis are two-sided. P-values less than or equal to alpha are assumed statistically significant. All Cis which do not include 1 are assumed to have adequate power.

Results

Between 2007 and 2016, there were 1729 adult patients with primary histologically confirmed NPC with active follow-up reported in SEER. Exclusions were made for unknown or AI/AN race (n=32), unknown insurance status (n=68), and causes of death unrelated to NPC or unknown (n=28). Our final cohort included 1,610 patients. Table 1 describes baseline characteristics based on race. API constituted 49.8% of our population. Whites and Blacks constituted 40.5% and 9.8% respectively. Ethnicity was not included in the statistical model as only 88 patients

Table 1. Baseline Characteristics of Our Cohort of Nasopharyngeal Carcinoma Patients by Race Reported to the SEER Database from 2007-2016

Characteristics	Race						p-value
	White n= 652		Black n= 157		Asian Pacific Islanders n= 801		
	N	%	N	%	N	%	
Age							<0.001
18-49	150	23.01	57	36.31	318	39.7	
50-59	202	30.98	50	31.85	237	29.59	
60-69	188	28.83	27	17.20	149	18.6	
70-79	78	11.96	21	13.38	65	8.11	
80+	34	5.21	2	1.27	32	4	
SEER Registry							<0.001
San Francisco-Oakland	79	12.12	22	14.01	471	58.8	
Connecticut	91	13.96	12	7.64	13	1.62	
Metropolitan Detroit	139	21.32	48	30.57	16	2	
Hawaii	13	1.99	0	0.00	138	17.23	
Iowa	96	14.72	5	3.18	8	1	
New Mexico	53	8.13	1	0.64	1	0.12	
Seattle	87	13.34	11	7.01	104	12.98	
Utah	43	6.6	2	1.27	15	1.87	
Metropolitan Atlanta	51	7.82	56	35.67	35	4.37	
Insurance Status							<0.001
Uninsured	30	4.6	12	7.64	16	2	
Medicaid	92	14.11	44	28.03	181	22.6	
Insured	530	81.29	101	64.33	604	75.41	
Marital Status							<0.001
Partnered	364	58.24	49	33.33	581	75.36	
Unpartnered	261	41.76	98	66.67	190	24.64	
Sex							0.175
Male	490	75.15	117	74.52	568	70.91	
Female	162	24.85	40	25.48	233	29.09	
Tumor Size (cm)							0.135
None Found	4	0.61	2	1.27	7	0.87	
<1	7	1.07	1	0.64	8	1	
1-1.9	25	3.83	8	5.10	51	6.37	
2-2.9	63	9.66	12	7.64	101	12.61	
3-3.9	72	11.04	18	11.46	103	12.86	
4+	159	24.39	47	29.94	171	21.35	
Unknown	322	49.39	69	43.95	360	44.94	
Tumor Stage							0.55
Localized	57	8.92	12	7.74	63	8.02	
Regional	297	46.48	63	40.65	370	47.07	
Distant	285	44.6	80	51.61	353	44.91	
Surgery							<0.001
None	546	83.74	143	91.08	762	95.25	
Any	106	16.26	14	8.92	38	4.75	

a, Hazard Ratio; b, Confidence Interval; c, Reference Category

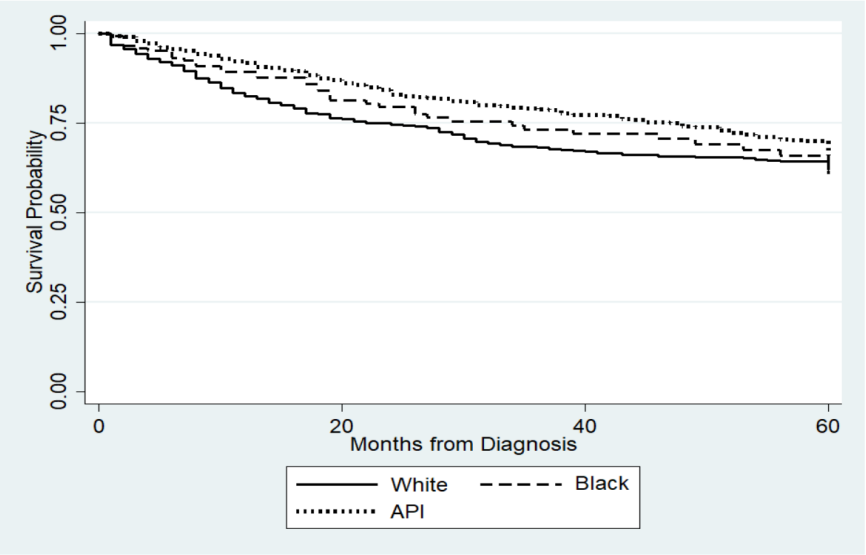

Figure 1. Survival Estimates Based on a log-rank Test. The survival curves differed according to race. API had a statistically significant higher 5-year survival rate compared to Whites (p-value = 0.008).

Table 2. Unadjusted and Adjusted Hazard Ratios between Race and 5-Year Cancer-Specific Survival in Our Cohort of 1610 Nasopharyngeal Carcinoma Patients in the US from 2007-2016

Characteristics	Unadjusted HR[a] (95% CI[b])	Adjusted HR (95% CI)
Race		
White	1 (Refc)	1 (Ref)
Black	0.84 (0.59, 1.20)	0.92 (0.65, 1.31)
API	0.70 (0.57, 0.86)	0.77 (0.62, 0.96)
Insurance (v Insured)		
Insured	1 (Ref)	1 (Ref)
Uninsured	2.26 (1.50, 3.40)	2.25 (1.45, 3.47)
Medicaid	1.40 (1.12, 1.76)	1.32 (1.04, 1.69)
Stage (v Localized)		
Localized	1 (Ref)	1 (Ref)
Regional	1.76 (1.02, 3.07)	1.92 (1.11, 3.30)
Distant	4.37 (2.55, 7.48)	4.53 (2.66, 7.72)
Age (years)		
18-49	1 (Ref)	1 (Ref)
50-59	1.55 (1.18, 2.04)	1.43 (1.09, 1.87)
60-69	2.09 (1.57, 2.76)	2.14 (1.60, 2.86)
70-79	2.32 (1.64, 3.29)	2.71 (1.90, 3.87)
80+	6.81 (4.63, 10.01)	7.65 (5.11, 11.46)
Gender		
Male	1 (Ref)	1 (Ref)
Female	0.76 (0.60, 0.96)	0.81 (0.64, 1.03)
Marital Status		
Partnered	1 (Ref)	1 (Ref)
Unpartnered	1.37 (1.12, 1.67)	1.26 (1.02, 1.57)
Surgery		
No Surgery	1 (Ref)	1 (Ref)
Any Surgery	0.58 (0.39, 0.86)	0.73 (0.49, 1.09)

a, Hazard Ratio; b, Confidence Interval; c, Reference Category

reported Hispanic ethnicity. Total average age was 54.94 years, 57.52 for Whites, 53.08 for Blacks, and 53.20 for API. In Blacks and API, frequency of cases decreased with increasing age. In Whites, cases peaked in the 50-59-year age range (p-value < 0.001). Most cases of White patients were reported in Detroit, most Black patients in Atlanta, and most API patients in the San Francisco – Oakland area (p-value < 0.001). Most patients had private insurance, followed by Medicaid then by no insurance. 64% of Blacks and 75% of API had private insurance compared to 81% of Whites. 8% of Blacks and 2% of API were uninsured compared to 5% of Whites (p-value < 0.001). 33.33% of Blacks, 75.36% of API and 58.24% of Whites were partnered (p-value < 0.001). Marital status was unavailable for 27 Whites, 10 Blacks, and 30 API. Patient sex did not significantly differ among the races (p-value = 0.175). Twenty-nine histological subtypes were reported in our cohort. The seven most frequent were large cell squamous cell carcinoma (SCC) non-keratinizing (25.44%), SCC not otherwise specified (NOS, 23.88%), carcinoma NOS (19.78%), carcinoma undifferentiated type, NOS (14.99%), keratinizing SCC NOS (4.35%), lymphoepithelial carcinoma (4.17%), and adenoid cystic carcinoma (1.55%). The remaining 22 subtypes individually represented 5.85% in total and individually less than 1%. Due to limited sample sizes and reliability within SEER, histological subtypes were excluded from our statistical model. Tumor size was not reported in more than 43% of all cases and did not statistically significantly change according to race (p-value = 0.135). Stage at diagnosis also did not significantly change according to race (p-value = 0.550). At diagnosis, most White and API patients had regional disease (which includes regional lymph node invasion) whereas most Black patients had distant metastases. Localized tumor was seen in less than 9% of all cases. Staging data was unavailable for 13 Whites, 2 Blacks, and 15 API. More White patients underwent surgery at the primary site (16%) compared to Blacks (9%) and API (5%) (p-value < 0.001). Surgical

intervention data was not available for 1 API.

Figure 1 represents survival estimates based on a log-rank test. The survival curves differed according to race. API had a statistically significant increased 5-year survival rate compared to Whites (p-value = 0.008).

Interaction testing revealed no interaction between race and insurance status on survival. API had a lower aHR of 5-year cancer-specific mortality compared to Whites (aHR 0.77; 95% CI 0.62 – 0.96) (Table 2). The aHRs did not show a significant difference in cancer-specific mortality between Whites and Blacks (aHR 0.92; 95% CI 0.65 – 1.31). Uninsured patients had 125% increased aHRs (aHR 2.25; 95% CI 1.45 – 3.47) and Medicaid patients had 132% increased aHRs for 5-year cancer-specific mortality (aHR 1.32; 95% CI 1.04 – 1.69) compared with insured patients. Regional metastases and distant metastases were associated with increased cancer-specific mortality compared with localized disease (aHR 1.92; CI 1.11 – 3.30 and aHR 4.53; CI 2.66 – 7.72 respectively). Older patients had increased cancer-specific mortality compared with 18-49-year-old patients. Unpartnered patients had significantly increased aHRs compared to partnered patients (aHR 1.26; CI 1.02 – 1.57). Female sex showed no significant difference in cancer-specific mortality compared to males (CI 0.64 – 1.03). Surgical intervention showed no benefit in aHR compared with no surgical intervention (CI 0.49 – 1.09).

Discussion

Our data revealed that API had higher 5-year cancer-specific survival than Whites. No difference in cancer-specific mortality was found between Blacks and Whites. Patients without insurance and patients with Medicaid had increased cancer-specific mortality compared to patients with insurance. There was no evidence that insurance status modified the association between race and survival. Age, tumor stage, and marital status predicted cancer-specific mortality, while surgical history and sex were not associated with survival.

There is no consensus within the scientific literature regarding the association between race and cancer-specific mortality in NPC patients. However, current evidence has revealed associations between Asian race and the incidence of NPC (Dickson and Flores, 1985; Chang et al., 2021). In agreement with our findings, some studies have found that Asian NPC patients had greater survival rates compared to other racial groups in the US (Ou et al., 2007; Ferlay et al., 2015; Chan et al., 2017). Other studies did not find a significant difference in cancer-specific mortality among races in the US (Bhattacharyya, 2004; Richey et al., 2006; Sun et al., 2007). One study found that overall survival was higher in Asians while cancer-specific survival was not (Sun et al., 2007). This suggests that increased overall survival in Asians may confound the reports in which Asians exhibit lower cancer-specific mortality. Another study reported that Black, White, and Asian NPC patients under 30 shared similar cancer-specific survival possibly due to an overall lack of insurance and comorbidities within the age group (Richey et al., 2006). A third study initially found better cancer-specific mortality in Asians compared to Whites, but after matching Asian and White patients according to epidemiological factors, including disease subtype and staging, the study found no significant difference in cancer-specific death (Bhattacharyya, 2004). This may indicate that Asians are more likely to present early and with more favorable subtypes of NPC. Other studies support this conclusion and show that Asians are more likely to present with Type 2b non-keratinizing undifferentiated carcinoma (or World Health Organization [WHO] subtype III) NPC, which is more sensitive to treatment (Arnold et al., 2013; Ferlay et al., 2015). WHO subtypes II and III are associated with positive Epstein-Barr virus (EBV) status. Literature shows EBV+ NPC exhibits better outcomes compared to NPC with other viral statuses (Pathmanathan et al., 1995; Raghupathy et al., 2014; Le et al., 2005; Chen et al., 2019; Lee et al., 2019; Chang et al., 2021). EBV+ status, Chinese ethnicity, and male gender are the most significant predictors of NPC incidence globally (Yu and Yuan, 2002; Raghupathy et al., 2014; Chen et al., 2019; Lee et al., 2019; Chang et al., 2021). These findings are paralleled in the US API population (Sun et al., 2007). This combination of findings provides a likely explanation for the lower cancer-specific mortality of API observed in our study. With EBV and NPC endemic in China, it is appropriate that API race in the US is associated with increased incidence of viral NPC and histomolecular subtypes purporting better prognoses. Possible explanations for the racial disparities in NPC incidence may include variable exposures to life-style related risk factors such as diet, smoking, pollution, ethanol use, and viral status. Nonracial factors associated with worse cancer-specific mortality in NPC may include age, substance abuse, and low socioeconomic status (Richey et al., 2006; Chen et al., 2019; Lee et al., 2019).

Several mechanisms have been proposed to explain the higher survival in API patients. The trends in NPC incidence and survival in API are related to the prevalence of EBV in Asian-Americans. EBV infection leads to genetic alterations that promote tumorigenesis (El-Naggar et al., 2017). Diets high in volatile nitrosamines and salt-cured fish are associated with either latent EBV activation or other carcinogenic effects (Guo et al., 2009; Chua et al., 2016; Lee et al., 2019). These exposures are more frequent in developing countries, many in East Asia. Familial, molecular, and chromosomal models for pathogenesis reportedly also contribute to carcinogenesis (Chan and Lo, 2002; Chen et al., 2019). It is proposed that dietary elements lead to a loss of heterozygosity that causes premalignant and low-grade lesions to develop. Further mutations make these lesions susceptible to EBV infection that provides cells with proliferative and survival advantages and mutagenicity with latent viral genes (Rohlfing et al., 2017).

Our data revealed differences in cancer-specific survival according to health insurance status. This agrees with current scientific literature. Insured patients exhibit earlier presentation, better survival, fewer surgical complications, shorter lengths of stay, and fewer comorbidities compared to Medicaid or uninsured patients (Rohlfing et al., 2017; Amini et al., 2018; Obeng-Gyasi et al., 2018). Adjusting for possible confounders, our

data showed that having Medicaid or no insurance was associated with higher cancer-specific mortality compared with having insurance.

We recognize some limitations of this study. Hispanic ethnicity was not included in our statistical model due to small sample size. Ethnicity is a social determinant of health in the US, and its inclusion would have provided relevant data. API was assessed as a single group as coded in SEER which excludes important variations of risk between API subgroups. SEER does not include NPC tumorigenesis and progression so we did not assess relevant carcinogenic exposures. Possibly confounding comorbidities were not reported to SEER. We excluded all radiation and chemotherapy history from study due to unreliable coding and reporting within SEER. Positive and negative margins for tumor resections as well as types of surgeries are valuable prognostic factors that unfortunately were unavailable. We were only able to dichotomize surgical history into yes or no. We also excluded histological classifications of NPC from study due to limited sample sizes, outdated classifications, and limited reliability of histology within SEER. This meant excluding histological subtypes differing among racial lines which significantly affect prognosis (Yu et al., 2009; Arnold et al., 2013). SEER does not have information on viral status. EBV is a well-established prognostic factor in NPC while Human Papilloma Virus is likely implicated as well (Le et al., 2005; Guo et al., 2009; El-Naggar et al., 2017).

Our study shows that race plays a significant role in predicting survival rates among patients with NPC. Particularly, API showed decreased cancer-specific mortality risk compared to Whites. Understanding racial and ethnic trends in mortality due to cancer are useful in guiding screening and early detection. Early detection of NPC and awareness of risk-factor exposure are effective preventative measures. Further study is of racial influences on the progression of NPC may be fruitful. There are many differences in genetics and risk-exposures between the various groups within API and we suggest conducting separate sub-group analyses in future studies. Ethnicity is associated with differences in care and must be assessed in the future as well. Analyses of mortality differences between histological subtypes and virally associated disease are also warranted. Furthermore, time to treatment and time to diagnosis are critical prognostic factors in cancer care and epidemiology that could not be addressed in this study. These factors differ along racial lines and addressing them is suggested for future studies. Rather than assessing insurance status alone, it would be valuable to assess mortality rates according to multiple socioeconomic metrics.

Author Contribution Statement

Conceptualization CZ, ER, SR, NB; Methodology: NB; Validation: CZ, ER, SR, JL, NB, ZS; Investigation: CZ, ER, SR; Writing - Original Draft: CZ, ER, SR; Writing - Review & Editing: CZ, ER, SR, JL, NB, ZS; Visualization: NB, ZS; Supervision: JL, NB, ZS.

Acknowledgements

No funding was procured for the completion of this study. The authors have no competing interests to declare. Our study was exempt from full ethical board review and approval because the dataset was already deidentified. The FIU IRB declared this study as non-human subject research and their approval, thus, was not necessary. SEER organizes data without any form of protected health information. All identifiable data are removed.

References

Amini A, Yeh N, Jones BL, et al (2018) Perioperative Mortality in Nonelderly Adult Patients With Cancer: A Population-based Study Evaluating Health Care Disparities in the United States According to Insurance Status. *Am J Clin Oncol*, **41**, 476–84.

Allen CK, Hung ECW, Woo JKS, et al (2013) Early detection of nasopharyngeal carcinoma by plasma Epstein-Barr virus DNA analysis in a surveillance program. *Cancer*, **119**, 1838–44.

Arnold M, Wildeman MA, Visser O, et al (2013). Lower mortality from nasopharyngeal cancer in The Netherlands since 1970 with differential incidence trends in histopathology. *Oral Oncol*, **49**, 237–43.

Bhattacharyya N (2004) The impact of race on survival in nasopharyngeal carcinoma: a matched analysis. *Am J Otolaryngol*, **25**, 94–7.

Cannon T, Zanation AM, Lai V, Weissler MC (2006). Nasopharyngeal carcinoma in young patients: a systematic review of racial demographics. *Laryngoscope*, **116**, 1021–6.

Chan KCA, Lo YMD, (2002). Circulating EBV DNA as a tumor marker for nasopharyngeal carcinoma. *Semin Cancer Biol*, **12**, 489–96.

Chan KCA, Woo JKS, King A, et al (2017). Analysis of Plasma Epstein–Barr Virus DNA to Screen for Nasopharyngeal Cancer. *N Engl J Med*, **377**, 513–22.

Chang ET, Ye W, Zeng YX, Adami HO (2021). The Evolving Epidemiology of Nasopharyngeal Carcinoma. *Cancer Epidemiol Biomarkers Prev*, **30**, 1035-47.

Chen YP, Chan AT, Le QT et al. (2019) Nasopharyngeal carcinoma. *Lancet*, **394**. 64–80.

Chua MLK, Wee JTS, Hui EP, Chan ATC (2016). Nasopharyngeal carcinoma. *Lancet*, **387**, 1012–24.

Dickson RI, Flores AD (1985). Nasopharyngeal carcinoma: an evaluation of 134 patients treated between 1971-1980. *Laryngoscope*, **95**, 276–83.

El-Naggar AK, Chan JKC, Takashi T, Grandis JR, Slootweg PJ (eds) (2017). WHO classification of head and neck tumours, 4th edition. International Agency for Research on Cancer, Lyon.

Ferlay J, Soerjomataram I, Dikshit R, et al (2015). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*, **136**, 359-86.

Ferrari D, Codecà C, Bertuzzi C, et al (2012). Role of plasma EBV DNA levels in predicting recurrence of nasopharyngeal carcinoma in a Western population. *BMC Cancer*, **12**, 208.

Geara FB, Sanguineti G, Tucker SL, et al (1997). Carcinoma of the nasopharynx treated by radiotherapy alone: determinants of distant metastasis and survival. *Radiother Oncol*, **43**, 53–61.

Guo X, Johnson RC, Deng H, et al (2009). Evaluation of nonviral risk factors for nasopharyngeal carcinoma in a high-risk population of Southern China. *Int J Cancer*, **124**, 2942–7.

Huang V, Li W, Tsai J, Begier E (2013). Cancer Mortality among

Asians and Pacific Islanders in New York City, 2001-2010. *J Cancer Epidemiol*, **2013**, 986408.
Le QT, Jones CD, Yau TK, et al (2005). A comparison study of different PCR assays in measuring circulating plasma epstein-barr virus DNA levels in patients with nasopharyngeal carcinoma. *Clin Cancer Res*, **11**, 5700–7.
Lee JT, Ko CY (2005). Has survival improved for nasopharyngeal carcinoma in the United States?. *Otolaryngol Head Neck Surg*, **132**, 303–8.
Lee HM, Okuda KS, González FE, Patel V (2019). Current Perspectives on Nasopharyngeal Carcinoma. In "Human Cell Transformation. Advances in Experimental Medicine and Biology", Eds Rhim JS., Dritschilo A, Kremer R. Springer, Cham, pp 11-34. doi:10.1007/978-3-030-22254-3.
Leung S, Zee B, Ma BB, et al (2006). Plasma Epstein-Barr viral deoxyribonucleic acid quantitation complements tumor-node-metastasis staging prognostication in nasopharyngeal carcinoma. *J Clin Oncol*, **24**, 5414–8.
Levine PH, McKay FW, Connelly RR (1987). Patterns of nasopharyngeal cancer mortality in the United States. *Int J Cancer*, **39**, 133–7.
Lin J-C, Wang W-Y, Chen KY, et al (2004). Quantification of plasma Epstein-Barr virus DNA in patients with advanced nasopharyngeal carcinoma. *N Engl J Med*, **350**, 2461–70.
Lo YM, Chan LY, Lo KW, et al (1999). Quantitative analysis of cell-free Epstein-Barr virus DNA in plasma of patients with nasopharyngeal carcinoma. *Cancer Res*, **59**, 1188–91.
Miller BA, Chu KC, Hankey BF, Ries LAG (2008). Cancer incidence and mortality patterns among specific Asian and Pacific Islander populations in the U.S. *Cancer Causes Control*, **19**, 227–56.
Mousavi SM, Sundquist J, Hemminki K et al (2010). Nasopharyngeal and hypopharyngeal carcinoma risk among immigrants in Sweden. *Int J Cancer*, **127**, 2888–92.
Obeng-Gyasi S, Timsina L, Miller KD, et al (2018). The implications of insurance status on presentation, surgical management, and mortality among nonmetastatic breast cancer patients in Indiana. *Surgery*, **164**, 1366–71.
Ou S-HI, Zell JA, Ziogas A, Anton-Culver H (2007). Epidemiology of nasopharyngeal carcinoma in the United States: improved survival of Chinese patients within the keratinizing squamous cell carcinoma histology. *Ann Oncol*, **18**, 29–35.
Pathmanathan R, Prasad U, Chandrika G, et al (1995). Undifferentiated, nonkeratinizing, and squamous cell carcinoma of the nasopharynx. Variants of Epstein-Barr virus-infected neoplasia. *Am J Pathol*, **146**, 1355–67.
Raghupathy R, Hui EP, Chan ATC (2014). Epstein-Barr virus as a paradigm in nasopharyngeal cancer: from lab to clinic. *Am Soc Clin Oncol Educ Book*, **2014**, 149–53.
Richey LM, Olshan AF, George J, et al (2006). Incidence and survival rates for young blacks with nasopharyngeal carcinoma in the United States. *Arch Otolaryngol Head Neck Surg*, **132**, 1035–40.
Rohlfing ML, Mays AC, Isom S, Waltonen JD (2017). Insurance status as a predictor of mortality in patients undergoing head and neck cancer surgery. *Laryngoscope*, **127**, 2784–9.
SEER (2019) Overview of the SEER Program. https://seer.cancer.gov/about/overview.html.
Stevens SJC, Verkuijlen SAWM, Hariwiyanto B, et al (2005). Diagnostic value of measuring Epstein-Barr virus (EBV) DNA load and carcinoma-specific viral mRNA in relation to anti-EBV immunoglobulin A (IgA) and IgG antibody levels in blood of nasopharyngeal carcinoma patients from Indonesia. *J Clin Microbiol*, **43**, 3066–73.
Sun L-M, Li CI, Huang E-Y, Vaughan TL (2007). Survival differences by race in nasopharyngeal carcinoma. *Am J Epidemiol,* **165**, 271–8.
Trinh QD, Nguyen PL, Leow JJ, et al (2015). Cancer-specific mortality of Asian Americans diagnosed with cancer: a nationwide population-based assessment. *J Natl Cancer Inst*, **107**, pp djv054.
Wang Y, Zhang Y, Ma S (2013). Racial differences in nasopharyngeal carcinoma in the United States. Cancer Epidemiol, 37, 793–802.
Yu JB, Gross CP, Wilson LD, Smith BD (2009). NCI SEER public-use data: applications and limitations in oncology research. *Oncology (Williston Park)*, **23**, 288–95.
Yu MC, Yuan J-M (2002). Epidemiology of nasopharyngeal carcinoma. *Semin Cancer Biol*, **12**, 421–9.