Introduction
Pancreatic neuroendocrine tumors (pancreatic NETs) are rare pancreatic neoplasms with an annual incidence of 1 per 100,000 individuals. The incidence has been rising in the United States and elsewhere over the last two decades, which is due to recent improvements in detecting pancreatic NETs [1–3]. The tumors are categorized as functional or nonfunctional, and approximately 10–30% of pancreatic NETs are functional [4]. They account for 3–5% of pancreatic malignancies and overall have a better prognosis than pancreatic exocrine tumors [5]. The overall 5-year relative survival rate of pancreatic NETs is approximately 42% [5]. There are some prognostic factors of pancreatic NETs being reported in studies, including tumor-size, histologic grade, TNM stage, treatment strategy, and marital status [6, 7]. Studies about the impact of race and ethnicity on tumors have published widely in recent years [8–10]. Black patients or African American patients are associated with the poor overall survival in a variety of tumors. However, no study has rigorously explored the impact of ethnic disparity on survival of pancreatic NETs.

Abstract
Pancreatic neuroendocrine tumor (pancreatic NETs), is an important cause of cancer-related death worldwide. No study has rigorously explored the impact of ethnicity on pancreatic NETs. We aimed to demonstrate the relationship between ethnicity and the survival of patients with pancreatic NETs. We used the SEER database to identify patients with pancreatic NETs from 2004 to 2013. Kaplan–Meier methods and Cox proportional hazard models were used to evaluate the impact of race on survival in pancreatic NETs patients. A total of 3850 patients were included: 3357 Non-Blacks, 493 Blacks. We stratified races as “Black” and “White/Other.” Blacks were more likely to be diagnosed with later stages of tumors ($P = 0.021$). As for the treatment, the access to surgery seemed to be more limited in Blacks than non-Black patients ($P = 0.012$). Compared with non-Black patients, Black patients have worse overall survival (OS) (HR = 1.17, 95% CI: 1.00–1.37, $P = 0.046$) and pancreatic neuroendocrine tumors specific survival (PNSS) (HR = 1.22, 95% CI: 1.01–1.48, $P = 0.044$). Multivariate Cox analysis identified that disease extension at the time of diagnosis and surgical status contributed to the ethnical survival disparity. Black patients whose stages at diagnosis were localized had significantly worse OS (HR = 2.09, 95% CI: 1.18–3.71, $P = 0.011$) and PNSS (HR = 3.79, 95% CI: 1.62–8.82, $P = 0.002$). As for the patients who did not receive surgery, Blacks also have a worse OS (HR = 1.18, 95% CI: 1.00–1.41, $P = 0.045$). The Black patients had both worse OS and PNSS compared to non-Black patients. The restricted utilization of surgery, and the advanced disease extension at the time of diagnosis are the possible contributors to poorer survival of Blacks with pancreatic NETs.
patients with pancreatic NETs. Our study aimed to demonstrate the relationship between ethnic disparity and survival in pancreatic NETs patients using the Surveillance, Epidemiology, and End Results (SEER) database.

Materials and Methods

Patients selection

The SEER*Stat software version 8.3.2 (accession number: 13693-Nov2015) was used to extract data from the SEER database [11, 12]. We identified patients diagnosed with pancreatic NETs that were reported to the SEER database from 2004 to 2013. ICD-O-3 (International Classification of Diseases for Oncology, 3rd edition) morphology codes 8150, 8151, 8152, 8153, 8155, 8156, 8157, 8240, 8241, 8242, 8243, 8246, and 8249 were used to identify pancreatic NETs. All pancreatic anatomical sites (C25.0—C25.9) were included in the study [13].

The exclusion criteria were as follows: (1) who had more than one primary cancer and the pancreatic NETs was not the first; (2) incomplete follow-up information or unknown survival length; (3) and who had an unknown cause of death; (4) and who had incomplete county-level socioeconomic data [14].

Variable definition

We included variabilities as sex, age, marital status, education, income, tumor location, tumor size, metastatic status, histologic type, pathology grade, extent of disease, TNM stage, surgery, and race. We grouped races as “Black” and “White/Other” (non-Black). Marital status was divided as married, unmarried, and unknown. We included socioeconomic status (SES, an economic, and sociological combined total measure) related variables as following: education (the percentage of adults aged ≥25 years who <12 years of education), poverty (the percentage of individuals living below the poverty line), and income (median annual household income). These variables were used as continuous variables in this study. According to the definitions of Country Attributes in SEER data, the higher the values of variables of education and poverty are, the lower the values of SES are. SEER staging was used to define disease extension: localized, regional and distant [15]. CS Mets at Dx(metastatic status) identifies whether there is metastatic involvement of distant site(s) at the time of diagnosis. CS Mets at Dx is part of the Collaborative Stage Data Collection System (CS), and was first introduced in 2004. It is used to derive some American Joint Committee on Cancer TNM Staging System (AJCC) M values and SEER Summary Stage codes [16]. The CS Mets at Dx was introduced into yes, no and unknown. We set 2 and 4 cm as the cutoff points of tumor size according to The European Neuroendocrine Tumor Society Staging Classification (ENETS) [17].

Outcomes

The primary outcomes of this study were overall survival and pancreatic neuroendocrine tumors specific survival. OS was defined as the time from diagnosis to date of any death. pancreatic neuroendocrine tumors specific survival (PNSS) was derived from the time of diagnosis to date of pancreatic NETs cancer-specific death. Death attributed to pancreatic NETs was regarded as an event. Patients who died from other causes or were still alive at the follow-up cutoff date were treated as censored observations [14]. The follow-up cutoff date was December 31, 2013.

Statistical analyses

The baseline patients’ demographic characteristics, tumor characteristics, and treatments were compared by Mann–Whitney U test (continuous variables) or Pearson chi-squared test (categorical variables). Kaplan–Meier curve was used to describe the overall survival, pancreatic neuroendocrine tumors specific survival and the differences between groups were tested by log-rank method. Factors significantly relating to outcomes in the univariate analysis were selected for the Cox proportional hazard model for recognizing confounding factors. Thus, we would see whether race impacted the survival time of pancreatic NETs. We also stratified each ethnic group into different SEER stages at diagnosis and different surgical status, so that subgroup analysis was carried out. Statistical significance was set at two-sided $P < 0.05$. All statistical analyses were performed using R 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org).

Results

Population characteristics

Based on selection criteria, this retrospective cohort study included a total of 3852 patients who were diagnosed with pancreatic NETs from 2004 to 2013. The population characteristics are summarized in Table 1. Among them, 3357 (87%) were non-Black patients, 493 (13%) were Blacks ($P < 0.001$). The Black patients had a lower percentage of males, younger average age and a lower marriage rate ($P < 0.001$). The socioeconomic status of Blacks was significantly unfavorable than non-Black patients’ condition, including education ($P = 0.051$), higher poverty rate ($P < 0.001$) and lower annual income ($P < 0.001$). Blacks were more likely to be diagnosed with later stages.
of tumors ($P = 0.021$). As for the treatment, the access to surgery seemed to be more limited in Blacks than non-Black patients ($P = 0.012$). We found no statistically significant differences between the ethnicities in other characteristics including tumor size, histology type, pathology grade and AJCC groups ($P > 0.05$).

**Table 1.** Baseline demographic and tumor characteristics of patients in Surveillance, Epidemiology, and End Results (SEER) database.

| Characteristics          | Total       | White/Other | Black       | $P$ value |
|--------------------------|-------------|-------------|-------------|-----------|
|                         | 3850 (100)  | 3357 (87.19)| 493 (12.80) |           |
| Sex                      |             |             |             |           |
| Male                     | 2118 (55.0) | 1894 (56.4) | 224 (45.4)  | <0.001    |
| Female                   | 1732 (45.0) | 1463 (43.6) | 269 (54.6)  |           |
| Age at diagnosis (mean [SD]) | 59.36 (13.98) | 59.78 (13.96) | 56.54 (13.82) | <0.001    |
| Marital status           |             |             |             | <0.001    |
| Married                  | 2402 (62.4) | 2201 (65.6) | 201 (40.8)  |           |
| Unknown                  | 181 (4.7)   | 153 (4.6)   | 28 (5.7)    |           |
| Unmarried                | 1267 (32.9) | 1003 (29.9) | 264 (53.5)  |           |
| Education (mean [SD])    | 14.98 (6.16) | 14.91 (6.29) | 15.49 (5.18) | 0.051     |
| Poverty (mean [SD])      | 14.23 (5.13) | 13.90 (5.03) | 16.50 (5.24) | <0.001    |
| Income (mean [SD])¹      | 6078.42 (1479.09) | 6161.98 (1489.22) | 5509.43 (1270.79) | <0.001    |
| Primary Site             |             |             |             | <0.001    |
| Body                     | 478 (12.4)  | 412 (12.3)  | 66 (13.4)   |           |
| Head                     | 1180 (30.6) | 1012 (30.1) | 168 (34.1)  |           |
| Others                   | 1046 (27.2) | 894 (26.6)  | 152 (30.8)  |           |
| Tail                     | 1146 (29.8) | 1039 (31.0) | 107 (21.7)  |           |
| Metastatic status        |             |             |             | 0.322     |
| No                       | 1975 (51.3) | 1733 (51.6) | 242 (49.1)  |           |
| Unknown                  | 101 (2.6)   | 91 (2.7)    | 10 (2.0)    |           |
| Yes                      | 1774 (46.1) | 1533 (45.7) | 241 (48.9)  |           |
| Tumor size               |             |             |             | 0.111     |
| <2 cm                    | 674 (17.5)  | 599 (17.8)  | 75 (15.2)   |           |
| >4 cm                    | 1359 (35.3) | 1175 (35.0) | 184 (37.3)  |           |
| 2–4 cm                   | 1210 (31.4) | 1067 (31.8) | 143 (29.0)  |           |
| Unknown                  | 607 (15.8)  | 516 (15.4)  | 91 (18.5)   |           |
| Histology                |             |             |             | 0.108     |
| Functional               | 100 (2.6)   | 93 (2.8)    | 7 (1.4)     |           |
| Nonfunctional            | 3750 (97.4) | 3264 (97.2) | 486 (98.6)  |           |
| Grade                    |             |             |             | 0.179     |
| Grade I                  | 1435 (37.3) | 1265 (37.7) | 170 (34.5)  |           |
| Grade II                 | 371 (9.6)   | 325 (9.7)   | 46 (9.3)    |           |
| Grade III                | 258 (6.7)   | 219 (6.5)   | 39 (7.9)    |           |
| Grade IV                 | 67 (1.7)    | 63 (1.9)    | 4 (0.8)     |           |
| Unknown                  | 1719 (44.6) | 1485 (44.2) | 234 (47.5)  |           |
| Disease extension (%)    |             |             |             | 0.021     |
| Distant                  | 1875 (48.7) | 1623 (48.3) | 252 (51.1)  |           |
| Localized                | 1102 (28.6) | 988 (29.4)  | 114 (23.1)  |           |
| Regional                 | 780 (20.3)  | 669 (19.9)  | 111 (22.5)  |           |
| Unknown                  | 93 (2.4)    | 77 (2.3)    | 16 (3.2)    |           |
| AJCC groups (%)          |             |             |             | 0.232     |
| VII                      | 1144 (29.7) | 1009 (30.1) | 135 (27.4)  |           |
| III/IV                   | 1562 (40.6) | 1345 (40.1) | 217 (44.0)  |           |
| Unknown                  | 1144 (29.7) | 1003 (29.9) | 141 (28.6)  |           |
| Surgery (%)              |             |             |             | 0.012     |
| Yes                      | 1887 (49.0) | 1676 (49.9) | 211 (42.8)  |           |
| No                       | 1951 (50.7) | 1671 (49.8) | 280 (56.8)  |           |
| Unknown                  | 12 (0.3)    | 10 (0.3)    | 2 (0.4)     |           |

¹Income is displayed as dollars in tens in SEER database (e.g., 6688 represents $66,880).

Ethnic disparity in OS in overall pancreatic NETs population

As the OS Kaplan–Meier curve shown in Figure 1A, there was a significant survival difference according to race (log rank test $P = 0.008$). Compared with other racial groups,
Black patients have worse OS. The 5-year OS was 45.0% in Black patients, 50.3% in other racial groups. Similarly, the median OS of Black patients (43 months) was lower than the others (61 months). According to univariate log-rank test, several variables were closely associated with OS, including sex, age, marital status, education, poverty, income, primary site, tumor size, metastatic status, histologic type, pathology grade, extension of disease, AJCC stage, and surgical status. Race was still an independent prognostic factor after adjusting for aforementioned variables in the Cox proportional hazard regression model, and Black patients have worse OS than non-Black patients (hazard ratio [HR] = 1.17, confidence interval [95% CI]: 1.00–1.37, \( P = 0.046 \)) (Table 2).

### Ethnic disparity in OS and PNSS in patients stratified by SEER stage

We also explored the survival patterns among ethnicities in subgroups stratified by SEER stage at diagnosis: localized (28.6%), regional (20.2%), and distant (48.7%) (\( P = 0.003 \)). We excluded the unstaged patients and patients whose stages at diagnosis were unknown, which only added up to 2.4% of the total. The patients whose stages at diagnosis were localized accounted for 28.6% of the total patients: 23.1% of Blacks (\( n = 114 \)), 29.4% of non-Blacks (\( n = 988 \)). The patients whose stages at diagnosis were regional accounted for 20.2% of the total patients: 22.5% of Blacks (\( n = 111 \)), 19.9% of non-Blacks (\( n = 669 \)). The patients whose stages at diagnosis were distant accounted for 48.7% of the total patients: 51.1% of Blacks (\( n = 252 \)), 48.3% of non-Blacks (\( n = 1623 \)).

As is shown in Figure 2C, for the patients whose stages at diagnosis were localized, of interest, Blacks (HR = 2.09, 95% CI: 1.18–3.71, \( P = 0.011 \)) had an extremely worse OS compared to non-Black patients. And the PNSS for Blacks (HR = 3.79, 95% CI: 1.62–8.82, \( P = 0.002 \), shown in Figure 2D, was extraordinarily worse compared to non-Black patients. As for the patients whose stages at diagnosis were regional and distant, the survival disparity of Blacks and non-Blacks was not significant (Fig. 2 A, B, E and F, Table 4).

### Ethnic disparity in OS and PNSS in patients stratified by surgical status

We also explored the survival patterns among ethnicities in subgroups stratified by surgical status: surgery performed (50.7%), and no surgery performed (49.0%) (\( P = 0.012 \)).
We excluded the patients with unknown surgical status (0.3%). The patients who received surgery accounted for 50.7% of the total, 42.8% of Blacks (n = 211), and 49.9% of non-Blacks (n = 1676). The patients who did not receive surgery accounted for 49.0% of the total, 56.8% of Blacks (n = 280), and 49.8% of non-Blacks (n = 1671). As for the patients who did not receive surgery, Blacks (HR = 1.18, 95% CI: 1.00–1.41, P = 0.045) have a
Table 3. Univariate and Multivariate survival analysis of PNSS in pancreatic endocrine tumor patients. Surveillance, Epidemiology, and End Results 2004–2013 (n = 3850).

| Characteristic                      | Univariate analysis | Multivariate analysis |
|-------------------------------------|---------------------|-----------------------|
|                                     | Log-rank $\chi^2$   | $P$ value              | HR        | 95% CI    | $P$ value   |
| Sex                                 | 9.86                | 0.002                 | Reference |          |            |
| Male                                |                     |                       | 1.18      | 1.03–1.35 | 0.020      |
| Female                              |                     |                       | 1.03      | 1.02–1.03 | <0.001     |
| Age at diagnosis                    | 144.28              | <0.001                |           |           |            |
| Marital status                      | 16.50               | <0.001                |           |           |            |
| Married                             |                     |                       | 0.88      | 0.62–1.26 | 0.490      |
| Unknown                             |                     |                       | 1.20      | 1.04–1.38 | 0.014      |
| Education                           | 1.74                | 0.187                 |           |           |            |
| Poverty                             | 4.07                | 0.044                 |           |           |            |
| Income                              | 6.78                | 0.009                 |           |           |            |
| Primary site                        | 43.48               | <0.001                |           |           |            |
| Body                                |                     |                       |           |           |            |
| Head                                | 1.22                |                       |           |           |            |
| Tail                                | 1.00                | 0.78–1.29             |           |           |            |
| Others                              | 1.12                | 0.87–1.43             |           |           | 0.379      |
| Metastatic status                   | 563.69              | <0.001                |           |           |            |
| No                                  |                     |                       |           |           |            |
| Unknown                             | 1.81                | 1.13–2.90             | 0.014     |           |            |
| Yes                                 | 1.12                | 0.79–1.60             | 0.529     |           |            |
| Tumor size                          | 179.55              | <0.001                |           |           |            |
| <2 cm                               |                     |                       |           |           |            |
| >4 cm                               | 1.14                | 0.83–1.56             | 0.407     |           |            |
| 2–4 cm                              | 1.21                | 0.88–1.66             | 0.239     |           |            |
| Unknown                             | 1.11                | 0.80–1.54             | 0.545     |           |            |
| Histology                           | 16.04               | <0.001                |           |           |            |
| Functional                          |                     |                       |           |           |            |
| Nonfunctional                       | 1.73                | 0.91–3.29             | 0.096     |           |            |
| Grade                               | 553.52              | <0.001                |           |           |            |
| Grade II                            |                     |                       |           |           |            |
| Grade I                             | 0.77                | 0.56–1.05             | 0.101     |           |            |
| Grade III                           | 3.47                | 2.55–4.73             | <0.001    |           |            |
| Grade IV                            | 3.97                | 2.61–6.06             | <0.001    |           |            |
| Unknown                             | 1.45                | 1.10–1.90             | 0.007     |           |            |
| Disease extension                   | 587.99              | <0.001                |           |           |            |
| Distant                             |                     |                       |           |           |            |
| Localized                           | 0.24                | 0.15–0.39             | <0.001    |           |            |
| Regional                            | 0.82                | 0.55–1.22             | 0.336     |           |            |
| Unknown                             | 0.41                | 0.22–0.75             | 0.004     |           |            |
| AJCC groups                         | 558.94              | <0.001                |           |           |            |
| I/II                                |                     |                       |           |           |            |
| II/IV                               | 1.64                | 1.17–2.29             | 0.004     |           |            |
| Unknown                             | 1.16                | 0.86–1.59             | 0.333     |           |            |
| Surgery                             | 682.66              | <0.001                |           |           |            |
| No                                  |                     |                       |           |           |            |
| Yes                                 | 0.37                | 0.30–0.45             | <0.001    |           |            |
| Unknown                             | 1.16                | 0.43–3.13             | 0.772     |           |            |
| Race                                | 6.11                | 0.014                 |           |           |            |
| White/Other                         |                     |                       |           |           |            |
| Black                               | 1.22                | 1.01–1.48             | 0.044     |           |            |

Figure 2. Survival curves in different Surveillance, Epidemiology, and End Results (SEER) stage subgroup patients with pancreatic neuroendocrine tumors according to race. (A). Distant, Overall survival (OS): $\chi^2 = 4.32$, $P = 0.037$; (B). Distant, Pancreatic neuroendocrine tumors cause specific survival (PNSS): $\chi^2 = 3.19$, $P = 0.073$; (C). Localized, OS: $\chi^2 = 3.31$, $P = 0.068$; (D). Localized, PNSS: $\chi^2 = 8.76$, $P = 0.003$; (E). Regional, OS: $\chi^2 = 0.19$, $P = 0.666$; (F). Regional, PNSS: $\chi^2 = 0.53$, $P = 0.465$. 

© 2017 The Authors. *Cancer Medicine* published by John Wiley & Sons Ltd.
significantly worse OS than non-Black patients (Fig. 3C). The PNSS for Blacks (HR = 1.21, 95% CI: 0.98–1.50, \( P = 0.071 \)) has no significant disparity (Fig. 3D).

For the patients who received surgery, both the OS (HR = 1.07, 95% CI: 0.71–1.61, \( P = 0.74 \)) and PNSS (HR = 1.20, 95% CI: 0.71–2.02, \( P = 0.50 \)) for Blacks display no significant disparity (Fig. 3A, B, Table 5).

**Discussion**

Our study shows the racial disparities among pancreatic NETs patients. As shown in the univariable and multivariable analysis, the Black patients have worse OS and PNSS than other racial groups, even after adjusting for sex, age, marital status, presence of distant metastasis, tumor size, histology, grade, AJCC stage, disease extension, and therapies. Actually, Yao and Dasari have reported the same worse overall survival for African American patients with pancreatic NETs, but without in-depth exploration about factors influencing outcome [18, 19]. We want to explore the reasons behind the phenomenon to have a better understanding of its contributors, which will provide useful inventions to reduce the disparity. Several factors have previously been studied in articles about ethnic disparity in survival for other tumors, such as marital status, SES, advanced stage and treatment [8–10].

According to the demographics of SEER patients, Blacks had a more advanced tumor stage at the moment of diagnosis comparing to non-Black patients. Several studies supported the reason for delayed diagnosis may be due to Blacks’ low marriage rate and unfavorable SES [20–22]. Previous studies demonstrated that marriage is associated with earlier stage at diagnosis and more favorable survival for various cancer types [22–26]. It is also the case in pancreatic NETs. Our previous study revealed that being married contributes to a better survival in pancreatic NETs patients [14]. Also, SES could be the potential contributor to ethnic survival disparity as it can affect the usage of medical resources of pancreatic NETs patients. Julien et al. found that SES are associated with treatment choice in pancreatic NETs [27]. Blacks are more likely to be in disadvantaged SES, and tend to cluster in low quality hospital [28, 29].

Of interest, our subgroup analysis demonstrates that Blacks whose stage at diagnosis were localized had significantly worse OS and PNSS compared with non-Black patients. However, we found no special disparity in distant and regional patients, that means race was an independent prognostic factor for OS and PNSS in localized disease, but not in regional disease or distant stage disease. We speculated that the reason may be that effective health care was not available to Blacks in the early stage.

Our analysis showed that access to effective options of treatment may be a reason for the poor survival of Blacks. The only curative treatment of pancreatic NETs is radical surgery. The majority of studies have demonstrated that Black patients with pancreatic cancer are less likely to undergo

---

**Table 4.** Univariate and Multivariate survival analysis of pancreatic endocrine tumor survival based on different extension. Surveillance, Epidemiology, and End Results 2004–2013 (n = 3850).

| Characteristic                  | Univariate analysis |          | Multivariate analysis |          |
|--------------------------------|---------------------|----------|-----------------------|----------|
|                                | Log-rank \( \chi^2 \) | \( P \)   | HR 95% CI             | \( P \)   |
| Overall survival               |                      |          |                       |          |
| Localized                      | 3.31                | 0.068    | Reference 2.09        | 1.18–3.71 | 0.011    |
| White/Other                    | Reference 1.17      | 0.98–1.39| 0.086                 |          |
| Black                          | Reference 1.06      | 0.68–1.66| 0.797                 |          |
| Distant                        | 4.32                | 0.037    |                       |          |
| White/Other                    | 0.19                | 0.666    |                       |          |
| Black                          | 1.06                | 0.68–1.66| 0.797                 |          |
| Regional                       |                      |          |                       |          |
| White/Other                    | 8.76                | 0.003    | Reference 3.79        | 1.62–8.82| 0.002    |
| Black                          | Reference 1.22      | 0.98–1.52| 0.072                 |          |
| PNET cause-specific survival   |                      |          |                       |          |
| Localized                      | 3.19                | 0.073    |                       |          |
| White/Other                    | 0.53                | 0.465    |                       |          |
| Black                          | 1.16                | 0.68–1.98| 0.584                 |          |

PNET, pancreatic neuroendocrine tumor (pancreatic NETs).
resection and have worse outcomes compared with white patients [8, 13, 16]. Our study agreed with the above: Blacks had less surgical treatment compared to Whites and Others (42.8% vs. 49.9%, \( P = 0.012 \)). As for those patients underwent surgery, the OS and PNSS display no significant racial disparity. However, contrary to our study, a pancreatic NETs research based on National Cancer Database reported that race was not associated with treatment choice or survival in pancreatic NETs [27]. The possible reason may be different select criteria, and what they focused on were patients with non-metastatic. Our results suggested that surgery may be underused for Blacks due to unfavorable SES. And maximizing surgery rates appropriately may be good for reducing racial disparities for pancreatic NETs.

Though those factors above may partly contribute to the poor survival of Blacks, in our multivariate analysis, we could still observe the influence on pancreatic NETs’ survival by race itself. We made a hypothesis that genetic differences between races and ethnicities may be a significant reason to pancreatic NETs survival disparity. Previous studies on racial disparities in cancer attribute some of the difference in survival to tumor biology and genetic variation, especially in prostate cancer and breast cancer [30–32]. For instance, a study showed that miR-24 expression was linked to a racial difference between African-American and Caucasian–American, which could contribute to race-related tumorigenesis in prostate cancer [30]. Also, for multiple myeloma, African American’s higher

![Survival curves in different surgical status subgroup patients with pancreatic neuroendocrine tumors according to race.](image-url)

**Figure 3.** Survival curves in different surgical status subgroup patients with pancreatic neuroendocrine tumors according to race. (A). Received Surgery, Overall survival (OS): \( \chi^2 = 0.01, P = 0.937 \); (B). Received Surgery, Pancreatic neuroendocrine tumors cause specific survival (PNSS): \( \chi^2 = 0.04, P = 0.850 \); (C). Not Received Surgery, OS: \( \chi^2 = 1.94, P = 0.164 \); (D). Not Received Surgery, PNSS: \( \chi^2 = 1.56, P = 0.212 \).
levels of phenotypic heterogeneity and monoclonal immunoglobulin levels caused the unfavorable survival, compared with their white counterparts [33]. Compared with Whites, African Americans have also been proved to have worse survival in other tumors due to racial genetic differences, including head and neck squamous cell carcinoma, kidney cancer [34, 35]. However, no study has specifically explored pancreatic NETs-related genetic differences in races and ethnicities and their contribution to pancreatic NETs survival disparity. Based on these findings above, we speculated that genetic differences may contribute to race disparity in pancreatic NETs survival. Further studies are required.

Our study also had limitations. First, as pancreatic NETs is a rare disease, the sample size is relatively small. Second, the SEER database does not provide patient-level socioeconomic information, and the county-level information cannot reflect the socioeconomic condition of individual patients, which may have a significant impact on patients’ access to medical care and their survival. Third, the clinical details are not available from SEER database, which may affect the use of therapies and the survival. Fourth, the recurrence information is unavailable, so the differences in recurrence rates could not be examined. Finally, for lack of evidence, we were unable to know how ethnic disparity affected on survival due to our research design. Further studies are required to gain more evidence to confirm the findings.

**Conclusion**

In conclusion, our study has found that Blacks had unfavorable OS and PNSS compared with non-Black patients. Poor prognosis of Black patients may be associated with advanced disease extension at diagnosis, limited utilization of surgery. Also, we speculated that the ethnicity-related genetic differences may contribute to the survival disparity of pancreatic NETs patients. Further studies are required on our findings.

**Acknowledgments**

The authors acknowledge the efforts of the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in providing high quality open resources for researchers.

**Conflicts of Interest**

All of the authors have no conflicts of interest to declare.

**References**

1. Kloppel, G., A. Perren, and P. U. Heitz. 2004. The gastroenteropancreatic neuroendocrine cell system and its tumors: the WHO classification. Ann. N. Y. Acad. Sci. 1014:13–27.
2. Klimstra, D. S. 2007. Nonductal neoplasms of the pancreas. Mod. Pathol. 20(Suppl 1):S94–S112.
3. Hallet, J., C. H. Law, M. Cukier, R. Saskin, N. Liu, and S. Singh. 2015. Exploring the rising incidence of neuroendocrine tumors: a population-based analysis of epidemiology, metastatic presentation, and outcomes. Cancer 121:589–597.
4. Liakakos, T., and D. H. Roukos. 2011. Everolimus and sunitinib: from mouse models to treatment of pancreatic neuroendocrine tumors. Future Oncol. 7:1025–1029.
5. Ries, L. A. G., J. L. Young, G. E. Keel, M. P. Eisner, Y. D. Lin, and M. Horner, eds. 2007. SEER survival monograph: cancer survival among adults: U.S. SEER program, 1988–2001, patient and tumor characteristics. National Cancer Institute, SEER Program. NIH Pub. No. 076215.

6. Han, X., X. Xu, D. Jin, D. Wang, Y. Ji, and W. Lou. 2014. Clinicopathological characteristics and prognosis-related factors of resectable pancreatic neuroendocrine tumors: a retrospective study of 104 cases in a single Chinese center. Pancreas 43:526–531.

7. Yang, M., B. L. Tian, Y. Zhang, A. P. Su, P. J. Yue, S. Xu, et al. 2014. Evaluation of the World Health Organization 2010 grading system in surgical outcome and prognosis of pancreatic neuroendocrine tumors. Pancreas 43:1003–1008.

8. Clegg, L. X., F. P. Li, B. G. Hankey, K. Chu, and B. K. Edwards. 2002. Cancer survival among US whites and minorities - A SEER (Surveillance, Epidemiology, and End Results) program population-based study. Arch. Intern. Med. 162:1985–1993.

9. Farmer, M. M., and K. F. Ferraro. 2005. Are racial disparities in health conditional on socioeconomic status? Soc. Sci. Med. 60:191–204.

10. Mathur, A. K., N. H. Osborne, R. J. Lynch, A. A. Ghaferi, J. B. Dimick, and C. J. Sonnenday. 2010. Racial/ethnic disparities in access to care and survival for patients with early-stage hepatocellular carcinoma. Arch. Surg. 145:1158–1163.

11. Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.3.2.

12. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2015 Sub (1973-2013 varying) - Linked To County Attributes - Total U.S., 1969–2014 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2016, based on the November 2015 submission.

13. Luo, G., A. Javed, J. R. Strosberg, K. Jin, Y. Zhang, C. Liu, et al. 2017. Modified staging classification for pancreatic neuroendocrine tumors on the basis of the American Joint Committee on Cancer and European Neuroendocrine Tumor Society Systems. J. Clin. Oncol. 35:274–280.

14. Zhou, H. Q., Y. Z. Zhang, Y. Y. Song, W. L. Tan, and Z. T. Qiu. 2017. Marital status is an independent prognostic factor for pancreatic neuroendocrine tumors patients: an analysis of the surveillance, epidemiology, and end results (SEER) database. Clin. Res. Hepatol. Gastroenterol. 41:476–486.

15. Li, J., B. E. Hansen, M. P. Peppelenbosch, R. A. De Man, Q. W. Pan, and D. Sprengers. 2017. Factors associated with ethnic disparity in overall survival for patients with hepatocellular carcinoma. Oncotarget 8:15193–15204.

16. Bilimoria, K. Y., A. K. Stewart, D. P. Winchester, and C. Y. Ko. 2008. The National Cancer Data Base: a powerful initiative to improve cancer care in the United States. Ann. Surg. Oncol. 15:683–690.

17. Kloppel, G., G. Rindi, A. Perren, P. Komminoth, and D. S. Klimstra. 2010. The ENETS and AJCC/UICC TNM classifications of the neuroendocrine tumors of the gastrointestinal tract and the pancreas: a statement. Virchows Arch. 456:595–597.

18. Yao, J. C., M. Hassan, A. Phan, C. Doghoy, C. Leary, J. E. Mares, et al. 2008. One hundred years after “carcinoid”: epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J. Clin. Oncol. 26:3063–3072.

19. Dasari, A., C. Shen, D. Halperin, B. Zhao, S. Zhou, Y. Xu, T. Shih, et al. 2017. Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. JAMA Oncol. https://doi.org/10.1001/jamaoncol.2017.0589 [Epub ahead of print].

20. Rendall, M. S., M. M. Weden, M. M. Favreault, and H. Waldron. 2011. The protective effect of marriage for survival: a review and update. Demography 48:481–506.

21. DeSantis, C. E., R. L. Siegel, K. D. Miller, S. A. Fedewa, K. I. Alcaraz, et al. 2016. Cancer statistics for African Americans, 2016: progress and opportunities in reducing racial disparities. CA Cancer J. Clin. 66:290–308.

22. Schaefer, E. W., M. Z. Wilson, D. Goldenberg, H. Mackley, W. Koch, and C. S. Hollenbeak. 2015. Effect of marriage on outcomes for elderly patients with head and neck cancer. Head Neck 37:735–742.

23. Wang, L., S. E. Wilson, D. B. Stewart, and C. S. Hollenbeak. 2011. Marital status and colon cancer outcomes in US surveillance, epidemiology and end results registries: does marriage affect cancer survival by gender and stage? Cancer Epidemiol. 35:417–422.

24. Martinez, M. E., K. Anderson, J. D. Murphy, S. Hurley S, A. J. Canchola, T. H. Keegan, et al. 2016. Differences in marital status and mortality by race/ethnicity and nativity among California cancer patients. Cancer 122:1570–1578.

25. Gomez, S. L., S. Hurley, A. J. Canchola, T. H. Keegan, I. Cheng, J. D. Murphy, et al. 2016. Effects of marital status and economic resources on survival after cancer: a population-based study. Cancer 122:1618–1625.

26. Wang, X. D., J. J. Qian, D. S. Bai, Z. N. Li, G. Q. Jiang, and J. Yao. 2016. Marital status independently predicts pancreatic cancer survival in patients treated
with surgical resection: an analysis of the SEER database. Oncotarget 7:24880–24887.

27. Jamii St. Julien, J. H., and T. Ya-Chen 2016. Impact of race on surgical management of pancreatic neuroendocrine tumors. J. Clin. Oncol. 34(Suppl 15):e18081.

28. Liu, J. H., D. S. Zingmond, M. L. McGory, N. F. SooHoo, S. L. Ettner, R. H. Brook, et al. 2006. Disparities in the utilization of high-volume hospitals for complex surgery. JAMA 296:1973–1980.

29. Williams, D. R., S. A. Mohammed, J. Leavell, and C. Collins. 2010. Race, socioeconomic status, and health: complexities, ongoing challenges, and research opportunities. Ann. N. Y. Acad. Sci. 1186:69–101.

30. Hashimoto, Y., M. Shiina, T. Kato, S. Yamamura, Y. Tanaka, S. Majid, et al. 2017. The role of miR-24 as a race related genetic factor in prostate cancer. Oncotarget 8:16581–16593.

31. Thompson, I., C. Tangen, A. Tolcher, E. Crawford, M. Eisenberger, and C. Moinpour. 2001. Association of African–American ethnic background with survival in men with metastatic prostate cancer. J. Natl Cancer Inst. 93:219–225.

32. D’Arcy, M., J. Fleming, W. R. Robinson, E. L. Kirk, C. M. Perou, and M. A. Troester. 2015. Race-associated biological differences among Luminal A breast tumors. Breast Cancer Res. Treat. 152:437–448.

33. Manojlovic, Z. Comprehensive molecular studies of multiple myeloma in African Americans. 2016 AACR Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved. Presented –September 26, 2016.

34. Krishnan, B., T. L. Rose, J. Kardos, M. I. Milowsky, and W. Y. Kim. 2016. Intrinsic genomic differences between African American and white patients with clear cell renal cell carcinoma. JAMA Oncol. 2:664–667.

35. Ramakodi, M. P., K. Devarajan, E. Blackman, D. Gibbs, D. Luce D, J. Deloumeaux, et al. 2017. Integrative genomic analysis identifies ancestry-related expression quantitative trait loci on DNA polymerase beta and supports the association of genetic ancestry with survival disparities in head and neck squamous cell carcinoma. Cancer 123:849–860.