



Racial differences in nasopharyngeal carcinoma in the United States

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ABSTRACT

Background: Nasopharyngeal carcinoma (NPC) is a malignant neoplasm arising from the mucosal epithelium of the nasopharynx. Different races can have different etiology, presentation, and progression patterns. **Methods:** Data were analyzed on NPC patients in the United States reported to the SEER (Surveillance, Epidemiology, and End Results) database between 1973 and 2009. Racial groups studied included non-Hispanic whites, Hispanic whites, blacks, Asians, and others. Patient characteristics, age-adjusted incidence and mortality rates, treatment, and five-year relative survival rates were compared across races. Stratification by stage at diagnosis and histologic type was considered. Multivariate regression was conducted to evaluate the significance of racial differences. **Results:** Patient characteristics that were significantly different across races included age at diagnosis, histologic type, in situ/malignant tumors in lifetime, stage, grade, and regional nodes positive. Incidence and mortality rates were significantly different across races, with Asians having the highest rates overall and stratified by age and/or histologic type. Asians also had the highest rate of receiving radiation only. The racial differences in treatment were significant in the multivariate stratified analysis. When stratified by stage and histologic type, Asians had the best five-year survival rates. The survival experience of other races depended on stage and type. In the multivariate analysis, the racial differences were significant. **Conclusions:** Analysis of the SEER data shows that racial differences exist among NPC patients in the U.S. This result can be informative to cancer epidemiologists and clinicians.

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1. Introduction

Nasopharyngeal carcinoma (NPC) is a malignant neoplasm arising from the mucosal epithelium of the nasopharynx. It differs from other head and neck cancers in occurrence, causes, clinical behaviors, and treatment. It is uncommon in the U.S. and most other nations, representing less than 1 case per 100,000 in most populations [1]; it is much more common in the southern regions of China. In the Guangdong province of China, NPC occurs in about 25 cases per 100,000 people. Additionally, NPC is more common in males. While it is seen primarily in middle-aged people in Asia, a high proportion of African cases appear in children. Multiple risk factors have been suggested as associated with the risk of developing NPC, including tobacco use, alcohol consumption, geography, ancestry, Epstein–Barr virus (EBV), gender, age, diet, occupational exposures, and environmental exposures.

In 1978, the World Health Organization (WHO) classified NPC into three major histologic types. Type 1 was keratinizing squamous cell carcinoma, Type 2 was non-keratinizing carcinoma, and Type 3 was undifferentiated carcinoma. The 1991 WHO classification retained the keratinizing squamous cell carcinoma type and combined the 1978 WHO Type 2 and 3 into “non-keratinizing carcinoma”. Non-keratinizing carcinoma was then further classified as “differentiated” and “undifferentiated”. The differentiated type constituted the 1978 WHO Type 2, and the undifferentiated type constituted the 1978 WHO Type 3. The 2005 WHO classification was the same as that developed in 1991, with the exception that “basaloid squamous cell carcinoma” was added. Among U.S.-born Chinese and white individuals, keratinizing squamous cell carcinomas are more common, whereas among Chinese who reside in HongKong, Taiwan, and Macao, differentiated non-keratinizing carcinomas dominate.

Treatment of NPC depends on multiple factors, such as the stage of the cancer and the overall health condition of a patient. Commonly adopted treatments include surgery, radiation therapy, chemotherapy, targeted therapy, and others. Depending upon the stage of the cancer, some of these treatments may be combined. For many patients, a combination of radiation therapy and chemotherapy is used.

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Prognosis depends on stage. According to the American Cancer Society [2], for stage 0 patients, the five-year survival rate is almost 100%. The rate drops to 80% for stage I patients and 60% for stage II patients. For patients at stage III, IVc, and IVb, the five-year survival rate is between 30% and 40%. Stage IVc patients with distant metastasis have a five-year survival rate of less than 10%. In addition, epidemiologic studies in the U.S. have identified histologic type as an independent prognostic factor [3,4]. Non-keratinizing carcinomas are generally associated with EBV positivity, which has been associated with improved NPC survival [5]. In addition, non-keratinizing carcinomas are often better controlled by ionizing radiation than keratinizing ones, and as a result, the five-year survival rate is significantly better for non-keratinizing carcinoma than keratinizing squamous cell carcinoma (51% vs. 6%) [6]. Other factors that may influence prognosis include patient age and gender, lymph node metastasis, molecular risk factors, and treatment regimens.

The goal of this study is to provide a comprehensive description of racial differences among NPC patients in the U.S. in terms of patients' characteristics, clinical-pathologic features, incidence, treatment strategy, and survival rates by analyzing the SEER database. Racial differences among cancer patients have attracted extensive attention [7,8]. However, research on NPC remains scarce. The available NPC studies may have limitations by either focusing on specific racial groups (i.e., Bhattacharyya [9] compared Chinese and whites) or specific outcomes (i.e., Ou and others [10] analyzed survival only).

2. Methods

2.1. Source population

The population-based sample was obtained from the SEER database, which contains data from 18 population-based regional and state cancer registries in the U.S. All SEER registries were included in the analysis, although not all contributed cases throughout the entire study period. NPC patients were identified from 1973 to 2009, using data published in 2011. Tumor site and histology were coded according to criteria specified by the WHO in the *International Classification of Diseases for Oncology* (ICD-O-3) [11]. NPC cases were identified using ICD-O-3 site code C110–C119. Histologic types were grouped using the ICD-O-3 code. Since there were very few basaloid squamous cell carcinomas, NPC patients were classified as keratinizing squamous cell carcinoma, differentiated non-keratinizing squamous cell carcinoma, undifferentiated non-keratinizing squamous cell carcinoma, and others. Squamous cell carcinoma (ICD-O codes 8070 and 8071) formed the keratinizing squamous cell carcinoma group. Large- and small-cell non-keratinizing carcinoma (ICD-O codes 8072 and 8073) formed the differentiated non-keratinizing carcinoma group. Undifferentiated, anaplastic, and lymphoepithelial carcinoma (ICD-O codes 8020, 8021, and 8082) formed the undifferentiated non-keratinizing carcinoma group. The rest were in the “others” group.

For the analysis of patients' characteristics and clinical-pathologic features, SEER 9 has data for cancers diagnosed between 1973 and 2009. Among the 5868 patients, there are 2901 non-Hispanic whites; 212 Hispanic whites; 527 blacks; 1945 Asians; and 232 other races. The “other” category includes American Indians, Alaska natives, others unspecified, and unknown. Features available for analysis include gender, age at diagnosis, histologic type, in situ/malignant tumors in lifetime (one primary only in lifetime, first of two or more primaries, second of two or more, third of three or more, fourth of four or more), stage (in situ, localized, regional, and distant), grade (I, II, III, and IV), tumor size, and presence of regional nodes positive. Outcome

variables include incidence, treatment strategy (no treatment, surgery, radiation, radiation and surgery), mortality, and survival. For incidence, SEER 13 data, which include detailed race and incidence information for cancers diagnosed between 1992 and 2009, is analyzed. For mortality, SEER has data available from 1990 to 2009. For treatment strategy, SEER 9 has data for cancers diagnosed between 1973 and 2009. And for survival, SEER 18 has data for cancers diagnosed between 1973 and 2004 and followed up to 12/31/2009.

2.2. Statistical analysis

In the comparison of patient characteristics and clinical-pathologic features across racial groups, Chi-squared tests and ANOVA were used, and *P*-values were computed. The analysis was conducted using SAS version 9.2. Age-adjusted incidence and mortality rates were calculated using SEER*Stat and U.S. 2000 Census data for age-standardization. In the analysis of treatment strategy, multivariate logistic regressions were conducted, adjusting for age and gender and stratified by stage at diagnosis and histologic type. Five-year relative survival rates were calculated using SEER*Stat with an actuarial method [12]. Multivariate Cox regressions were then conducted, adjusting for age at diagnosis, gender, and treatment and stratified by stage at diagnosis and histologic type.

3. Results

3.1. Patients' characteristics and clinical-pathologic features

Main results are shown in Table 1, and a more detailed age distribution of NPC patients is shown in Table 5 (Appendix A). There are more male patients. The gender distributions are borderline different across races ($P = 0.081$), with the “other” race category having the most male patients (75%) and the Hispanic white category having the least (66.5%). The age at diagnosis is significantly different across races. For blacks, the mean age at diagnosis is 48.3 years, compared to 58.1 years for non-Hispanic whites. The distributions of histologic types are also significantly different across races. Compared with whites and blacks, much fewer Asians and other races were diagnosed with keratinizing squamous cell carcinoma. Distributions of in situ/malignant tumors in the lifetime are also significantly different. The majority of observations are “one primary only in lifetime”, with Asians having the most (88.9%) and non-Hispanic white having the least (77.7%). Further, the stage distributions are significantly different. Non-Hispanic whites have the most localized tumors (18.3%), Asians have the most regional (72.2%), and other races have the most distant (24.9%). For the whole sample, there are 3.8%, 14.0%, 52.4%, and 29.8% grade I–IV patients, respectively. Non-Hispanic whites have more grade II (20.1%) and grade III (53.3%) patients, whereas Asians (40.9%) and other races (42.6%) have more grade IV patients. For all patients, the average tumor size is 38.1 mm, and the difference is not significant across races. Asians (27.8%) and other races (23.2%) have the lowest rates of all nodes negative, non-Hispanic whites have the highest (40.0%), and the racial difference is significant. Different races also have different treatment strategies. Blacks have the highest rate of no treatment (8.2%), non-Hispanic whites have the highest rate of surgery (7.8%), Asians have the highest rate of radiation (81.1%), and Hispanic whites have the highest rate of radiation and surgery (23.8%). On average, Asians have the longest survival time, with a mean of 163.9 months, and non-Hispanic whites have the shortest survival time, with a mean of 100.4 months.

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