The Influence of Marital Status on Survival in Patients with Nasopharyngeal Carcinoma: A Surveillance, Epidemiology, and End Results (SEER) Database Analysis

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Abstract

Purpose: To assess the influence of marital status on survival in patients with nasopharyngeal carcinoma (NPC).

Methods: We used the Surveillance, Epidemiology, and End Results (SEER) database to analyze 5477 patients who were diagnosed with NPC from 2004 to 2016. Kaplan–Meier survival analysis and Cox proportional hazard regression were used to analyze the influences of marital status on cause-specific survival (CSS) and overall survival (OS). Subgroup analyses was used to assess the influences of marital status on CSS based on different factors.

Results: The 5477 patients were divided into three groups, with 61.5%, 22.4%, and 16.1% of patients being married, single/unmarried, and separated/widowed/divorced, respectively. The separated/widowed/divorced group were more likely to be female ($P < 0.001$); had the highest proportion of elderly subjects ($P < 0.001$); were mostly Caucasian ($P < 0.001$); had pathological grading I/II ($P < 0.001$); were likely to receive surgery ($P = 0.032$); and were registered at the northeast, north central, and south ($P < 0.001$) regions. The 5-year CSS was 92.6%, 92.4%, and 85.1% in the married, single/unmarried, and separated/widowed/divorced groups, respectively ($P < 0.001$); and respective 5-year OS was 60.7%, 54.6%, and 40.1% ($P < 0.001$). Marital status was the independent prognostic factor for NPC. Compared with married patients, separated/widowed/divorced patients had a significantly increased risk of NPC-related death (hazard ratio [HR]=2.180, 95% confidence interval [CI] 1.721–2.757, $P < 0.001$). The single/unmarried ($P = 0.355$) group had a similar CSS as that of the group.

Conclusion: Marital status is an independent prognostic factor for survival of NCP patients. Separated/widowed/divorced status increases the risk of NPC mortality; hence, more social and psychosocial support should be given to patients who are separated, widowed, or divorced.

Introduction

Nasopharyngeal carcinoma (NPC) is a rare and malignant cancer with the highest incidences in South-Eastern Asia, Eastern Asia, Eastern Africa, and Middle Africa[1]. Radiotherapy and chemotherapy remain the most effective treatment options. However, owing to drug-induced toxicity and radiation-related sequelae, patients often experience severe side effects that significantly affect their quality of life and survival[2–4]. Social support plays a very important role in the lives of patients with cancer, especially marital status, which has been confirmed to affect the survival rate in different tumors[5–8]. Understandably, marital status is of significance even for patients with NPC.

A recent study analyzed the 10 leading causes of tumor-related deaths; the results showed a generally significant survival benefit for married patients as compared to unmarried patients. Moreover, the former group had lower risk of early tumor-related death than the latter[5]. Osazuwa–Peters’ study of head and neck cancer (HNC) found that being married conferred a survival advantage among HNC survivors, but the study only classified patients as married or unmarried[8]. One Surveillance, Epidemiology, and End

Results (SEER) database-based study on marital status found that being married had a protective effect on cause-specific survival (CSS) and overall survival (OS) compared to unmarried status. Nevertheless, this study did not compare married patients with specific subgroups of unmarried patients such as single/unmarried and separated/divorced/widowed[9]. The other SEER-based marital status study showed that widowed patients were associated with higher risk of mortality in NPC than married, divorced, or single patients, but the sample size was small. Furthermore, some essential medical data were lacking, which may have had significant effects on patient outcomes with NPC. In addition, it only recorded data from 2004 to 2013 from the SEER database[10]. However, the SEER database has been updated until 2016, and there are few studies on the impact of different marital status on NPC. Therefore, we used patient data of those diagnosed between 2004 and 2016 included in the SEER Cancer Registry to explore in detail the relationship between different marital status and patient survival of patients.

Material And Methods

Patients

We extracted data from the SEER database released in April 2016 as the data source for this study. The SEER program is sponsored by the National Cancer Institute and consists of 17 population-based cancer registries that represents approximately 28% of the US population[11]. The SEER program provides accurate and continuous information on cancer incidence, survival, prevalence, and patient demographics. With the help of the National Cancer Institute's SEER * Stat software (Version 8.3.5; www.seer.cancer.gov/seerstat), patients diagnosed with NPC from 2004 and 2016 were included. The excluded criteria were as follows: (1) age at diagnosis was less than 18 years; (2) unknown survival month; (3) unknown marital status; (4) a prior diagnosis of malignancy; (5) more than one primary site.

Study variables and endpoints

The following variables were identified from the SEER database: age, sex, ethnicity, pathology grade, primary site, insurance, registry site, year of diagnosis, surgery, and radiotherapy. We divided patients into three categories: "married", "single/unmarried," and "separated/widowed/divorced." The pathology grade was also divided into three groups: well differentiated, grade I and moderately differentiated, grade II; poorly differentiated, grade III and undifferentiated, anaplastic, grade IV; and unknown group. The TNM stage group was derived by the American Joint Committee on Cancer, Cancer Staging Manual (7th edition, 2010), T-stage (T1, T2, T3, T4, or unknown); N-stage (N0, N1, N2, N3, or unknown); M-stage (M0, M1, or unknown).

According to the classification principles of the US Census Bureau, 18 cancer registries were categorized into four regions, namely West, Northeast, North central, and South[12]. The primary sites included six groups, namely superior wall of the nasopharynx, posterior wall of the nasopharynx, lateral wall of the nasopharynx, anterior wall of the nasopharynx, overlapping lesion of the nasopharynx, and nasopharynx.

Patients were also categorized based on whether they underwent surgery and radiotherapy. The endpoints in this study were the 5-year cause-specific survival (CSS) that was calculated from diagnosis until death due to NPC or last known date alive and the 5-year overall survival (OS) that was calculated as death from any cause.

Statistical analysis

Patients' baseline characteristics were compared by using the chi-squared (χ^2) test. We used the Kaplan–Meier method to estimate the CSS and OS, and the survival differences were calculated by the log-rank test. The binary Cox regression model was calculated using the hazard ratio (HR) for relationships between each variable and mortality. Every variable for which $P < 0.05$ in the univariate analyses was initially included in multivariate analyses. Notably, we still included some necessary variables for the Cox proportional hazards regression despite $P > 0.05$ in their respective univariate analyses, because they were common confounders of NPC such as T-stage and N-stage. All confidence intervals (CIs) were stated at the 95% confidence level. Statistical analysis was conducted using SPSS software version 22.0 (IBM Corporation, Armonk, USA). P value < 0.05 indicated statistical significance.

Results

Patient baseline characteristics

Initially, 7380 patient records were extracted between 2004 and 2016 from the SEER database. Based on the inclusion and exclusion criteria, 5477 eligible patients (3886 men and 1591 women) were identified during the 12-year study period. A flow diagram of the study selection is presented in Figure 1. Among these patients, 3370 (61.5%) were married, 1226 (22.4%) were single/unmarried, and 881 (16.1%) were separated/widowed/divorced. Significant differences were noticed in all the comparisons. With respect to sex, men were more likely to be married (74.4%), while female patients were more likely to be separated/widowed/divorced (44.0%). The separated/widowed/divorced group were more likely to be female ($P < 0.001$); had the highest proportion of elderly subjects (> 50 years, $P < 0.001$); were mostly Caucasian ($P < 0.001$); had pathological grading I/II ($P < 0.001$); were likely to receive surgery ($P = 0.032$); and were registered at the northeast, north central, and south ($P < 0.001$) sites. Compared with the other groups, married patients were more likely to be in the West registry site, have grade III/IV NPC, and the highest proportion of radiation and chemotherapy history. However, there was no significant difference in primary site cancer among the three study groups. The demographic and clinical characteristics of NPC and treatment types are summarized in Table 1.

Effect of marital status on CSS in the SEER database

The univariate log-rank test was used to evaluate the 5-year CSS, which was 92.6%, 92.4%, and 85.1% in the married, single/unmarried, and separated/widowed/divorced, respectively ($P < 0.001$). In the

multivariate analysis, the HR of the single/unmarried group was lower than that of the married group (HR = 0.811, 95% CI = 0.675–1.152, $P = 0.355$), and the HR of separated/widowed/divorced group was higher than that of the married group (HR = 2.180, 95% CI = 1.727–2.751, $P < 0.001$). The CSS of NPC patients were calculated by Kaplan–Meier curve (Figure 2). In univariate analyses, age ($P < 0.001$), ethnicity ($P < 0.001$), registry site ($P = 0.005$), grade ($P = 0.001$), pathologic T stage ($P = 0.001$), pathologic N stage ($P < 0.001$), pathologic M stage ($P = 0.003$), radiotherapy ($P < 0.001$) and chemotherapy ($P < 0.001$) were regarded as significant risk factors for CSS in NPC patients (Table 2). The multivariate analysis was performed by Cox regression, and variables that were validated as independent prognostic factors included age (>50 years, [HR = 3.878, 95% CI = 3.025–4.971, $P < 0.001$]); other ethnicities (HR = 0.560, 95% CI = 0.451–0.695, $P < 0.001$); southern registry site (HR = 1.531, 95% CI = 1.207–1.941, $P < 0.001$); pathological grading III/IV (HR = 0.599, 95% CI = 0.441–0.812, $P = 0.001$); pathologic N2 stage (HR = 0.623, 95% CI = 0.463–0.837, $P = 0.002$); pathologic N unknown stage, (HR = 1.514, 95% CI = 1.096–2.091, $P = 0.012$); pathologic M1 stage (HR = 1.457, 95% CI = 1.004–2.114, $P = 0.048$); pathologic M unknown stage (HR = 1.550, 95% CI = 1.160–2.072, $P = 0.003$); no radiotherapy (HR = 2.460, 95% CI = 1.961–3.086, $P < 0.001$); and no chemotherapy (HR = 2.180, 95% CI = 1.778–2.674, $P < 0.001$) (Table 2).

Effect of marital status on OS in the SEER database

We used univariate log-rank test to evaluate the 5-year OS of NPC patients. Patients in the married group had a better 5-year OS (60.7%) than those who were single/unmarried (54.6%) and separated/widowed/divorced (40.1%). The Kaplan–Meier curve was used to calculate the OS of NPC patients (Figure 3). All the differences were significant independent factors for OS among NPC patients according to the univariate log-rank test ($P < 0.001$), including age ($P < 0.001$), ethnicity ($P < 0.001$), sex ($P < 0.001$), registry site ($P < 0.001$), grade ($P < 0.001$), primary site ($P < 0.001$), pathologic T stage ($P < 0.001$), pathologic N stage ($P < 0.001$), pathologic M stage ($P < 0.001$), surgery performed ($P < 0.001$), insurance ($P < 0.001$), radiotherapy ($P < 0.001$), chemotherapy ($P < 0.001$), and marital status ($P < 0.001$) (Table 3). The variables that were significant in the univariate log-rank test were validated as independent risk factors by multivariate modeling analysis using Cox regression (Table 3). The single/unmarried and separated/widowed/divorced patients had higher HRs (HR = 1.219, 95% CI = 1.100–1.351, $P < 0.001$ vs. HR = 1.977, 95% CI = 1.784–2.191, $P < 0.001$, respectively) than married patients.

Subgroup analysis by age, gender, grade, insurance, surgery, radiation, and chemotherapy

We analyzed the effects of marital status on CSS according to age, sex, grade, surgery, radiation, and chemotherapy. Interestingly, univariate analysis showed that only married patients of both age groups (i.e., ≤ 50 years or >50 years) had better 5-year CSS than other patients ($P < 0.001$), although the HRs among unmarried male patients were all higher than those of their female counterparts. Further, patients in the separated/widowed/divorced group had the lowest 5-year survival rate except those that had

grade I/II stage NPC. Patients in the single/unmarried group had the highest number of surgery-naïve female patients, with unknown grade, and who had not undergone radiotherapy and chemotherapy. Moreover, multivariate analysis showed that the separated/windowed/divorced group had significant differences with respect to all parameters except for the grade I/II staging and being uninsured, when compared with the married group ($P<0.05$). The single/divorced group had no significant differences as compared to the married group, except for those that did not receive chemotherapy. The married group and single/unmarried group seemed to have a similar 5-year survival rate in with respect to sex, NPC grade, and history of radiotherapy.

Discussion

Herein, we evaluated the influence of marital status on survival outcome in patients diagnosed with NPC between 2004 and 2016 based on a SEER-database cohort study; the SEER data was well-matched and had long-term follow-up. Our results showed that married patients have a highest CSS and OS, and the lowest mortality among the study groups. The beneficial influence of married status persisted despite adjusting for age, ethnicity, sex, registry site, grade, primary site, pathologic TNM stage, insurance, surgery, radiotherapy, and chemotherapy. Furthermore, separated/windowed/divorced patients were more likely to have poor survival than other patients. Additionally, subsequent subgroup analysis according to age, sex, grade, surgery, radiation, and chemotherapy based on the SEER stage, validated the prognostic value of marital status in NCP. Hence, being married was suggested to have a protective effect on survival as compared to other marital status; these results were consistent with Huang et al's study[13].

Here, we report several new findings. First, risk of death in the 5-year OS among uninsured patients was obviously higher than insured patients and those on Medicaid ($P<0.001$) and was not reported in previous studies[9, 10]. Second, the risk of death in 5-year CSS and OS among primary site tumor in the anterior wall of the nasopharynx was the higher. Third, patients with pathological grading III/IV were more likely to have higher survival rate than pathological grading I/II and unknown grading in CSS and OS. Taken together, these factors may play an important role in NPC patients, especially with regard to insurance. Some studies indicated that insurance status offers protection for cancer patients[14, 15], while others implied that the health insurance status is related to the mortality and presentation stage of cancer patients[16, 17]. Insurance is a socioeconomic factor and understanding how populations of cancer patients are influenced by it will better clarify how to mitigate disparities in care and outcomes[15]. In our subgroup multivariate analysis, single/unmarried patients had lower HRs than married patients, with respect to their insurance plans, while separated/windowed/divorced patients showed contrary results, because in addition to the obvious psychological stress of an unfavorable diagnosis, the lack of a spouse may also reduce their ability to pay for treatment[18]. Besides, cancer diagnosis can lead to psychological disorders (e.g., despair, loss, worry, fear, anxiety), and if patients are older and without a spouse, this will lead to poorer CSS[19] (Table 4).

Cancer treatment mainly involves surgery, radiotherapy, and chemotherapy. Previous studies based on SEER data have shown that different categories of cancer patients can benefit from different treatment

options, and the survival rates of patients who are treated is not necessarily high[20–22]. In our study, separated/widowed/divorced patients had the lowest 5-year CSS in those that underwent surgery, radiotherapy, and/or chemotherapy, and the HRs of single/unmarried patients who received radiotherapy were even lower than married patients. The 5-year CSS was similar. Interestingly, single/unmarried surgery-naïve patients had highest 5-year CSS when surgery was performed, and the HRs of single/unmarried patients were lower than patients who received surgery and chemotherapy. The 5-year CSS of single/unmarried patients who accepted chemotherapy was similar to those that did not accept chemotherapy. These results suggest that surgery and chemotherapy are not especially important for single/unmarried patients.

Another previous SEER study by Wu et al. [10] evaluated the influence of marital status in NPC between 2004 and 2013, and the results indicated that widowed patients were associated with an increased risk of cancer mortality in NPC. However, the influence of marital status—married, unmarried, single, separated, divorced, and widowed—were not further compared in the subgroup multivariate analysis by age, sex, grade, insurance, surgery, radiation, and chemotherapy. In addition, we grouped different marital status rather than grouping them separately and included unmarried and separated patients. Our results showed that separated/widowed/divorced patients had poorer CSS than married, single/unmarried patients. However, the married and single/unmarried groups had their own advantages under different influencing factors, and there was no significant difference except with respect to no chemotherapy. Thus, our results are consistent with those from previous studies of various cancer sites showing that separated/widowed/divorced patients were more likely to increase risk of cancer mortality[23–25].

Our study has several limitations. First, the SEER program only records the marital status at the time of diagnosis, and the details of patients' marital status were not reported or tracked during treatment, which might affect the outcomes of NPC patients. Second, the classification of patient ethnicity in the SEER program is not very distinct and detailed (e.g., American Indian, AK Native, and Asian/Pacific Islanders), which may have led to an underestimation of the true impact of ethnicity on survival outcomes. Third, the SEER program lacks sufficient information about subsequent therapy, comorbidities, disease recurrence, and adjuvant therapy, and it also does not record important demographic factors such as education and income. Finally, our research is based on the US population, and the results therefore represent only 28% of all Americans, and are not a true representation of the global population.

Conclusion

Our results suggest that being separated/widowed/divorced increases the risk of NPC mortality when compared to patients who are married or single/unmarried patients. In the subgroup analysis, separated/widowed/divorced patients were regarded as a high-risk group with poor prognosis. Therefore, more social and psychosocial support should be given to cancer patients who are separated, widowed, or divorced. Furthermore, clinicians should pay more attention to patients' marital status in case of an NPC diagnosis, and provide them with an individualized care and treatment plan.

Abbreviations

SEER: Surveillance, Epidemiology, and End Results

NPC: nasopharyngeal carcinoma;

CSS: cause-specific survival;

OS: overall survival;

HR: hazard ratio;

HNC: head and neck cancer;

CI: confidence intervals;

TNM: tumor node metastasis

Declarations

Ethics approval and consent to participate

We got approval from the National Cancer Institute to use data of patient from SEER database. Participant consent was not necessary as this study involved the use of a previously-published de-identified database according to SEER database.

Consent for publication

Not applicable.

Availability of data and material

The datasets generated and/or analysed during the current study are available in the SEER database, <https://seer.cancer.gov/data/>.

Competing interests

The authors declare no conflicts of interest.

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Authors' contributions

Bin Yu and Fei Lin contributed equally to this work. Bin Yu, Fei Lin, and Shan Xu conceived and designed the study. Li Qin and Hong Ning searched the databases and collected the data. Bin-wei Lin, Fei Lin, and Shan Xu analyzed and interpreted the data. Bin Yu wrote the manuscript. and Li Qin reviewed the final manuscript

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Tables

Table 1. Baseline demographic and tumor characteristics of patients with nasopharyngeal carcinoma according to marital status in SEER database

Characteristic	Total (n=5477) N (%)	Married (n=3370) N (%)	Single/unmarried (n=1226) N (%)	Separated/widowed/divorced (n=881) N (%)	<i>P</i> value
Gender					<0.001
Male	3886(71.0)	2506(74.4)	887(72.3)	493(56.0)	
Female	1591(29.0)	864(25.6)	339(27.7)	388(44.0)	<0.001
Age					
≤50	2121(38.7)	1242(36.9)	697(56.9)	182(20.7)	
>50	3356(61.3)	2128(63.1)	529(43.1)	699(79.3)	<0.001
Race					
White	2529(46.2)	1445(42.9)	538(43.9)	546(62.0)	
Black	627(11.4)	224(6.6)	289(23.6)	114(12.9)	
Other ¹	2274(41.5)	1671(49.6)	387(31.6)	216(24.5)	
Unknown ²	47(0.9)	30(0.9)	12(1.0)	5(0.6)	<0.001
Registry Region ²					
West	3473(63.4)	2269(67.3)	732(59.7)	472(53.6)	
Northeast	626(11.4)	365(10.8)	145(11.8)	116(13.2)	
North Central	351(6.4)	183(5.4)	95(7.7)	73(8.3)	
South	1027(18.8)	553(16.4)	254(20.7)	220(25.0)	<0.001
Grade					
I/II	545(10.0)	299(8.9)	121(9.9)	125(14.2)	
III/IV	3108(56.7)	1986(58.9)	686(56.0)	436(49.5)	
Unknown	1824(33.3)	1085(32.2)	419(34.2)	320(36.3)	0.066
Primary Site					
Superior wall of nasopharynx	62(1.1)	41(1.2)	15(1.2)	6(0.7)	
Posterior wall of nasopharynx	564(10.3)	358(10.6)	107(8.7)	99(11.2)	
Lateral wall of nasopharynx	461(8.4)	306(9.1)	83(6.8)	72(8.2)	
Anterior wall of nasopharynx					
Overlapping lesion of nasopharynx	56(1.0)	32(0.9)	13(1.1)	11(1.2)	
nasopharynx	203(3.7)	132(3.9)	37(3.0)	34(3.9)	

T stage (AJCC6)	4131(75.4)	2501(74.1)	971(79.2)	659(74.8)	<0.001
T0	43(0.8)	30(0.9)	6(0.5)	7(0.8)	
T1	1361(24.9)	925(27.4)	250(20.4)	188(21.3)	
T2	1064(19.4)	668(19.8)	227(18.5)	169(19.2)	
T3	952(17.4)	546(16.2)	233(19.0)	173(19.6)	
T4	1030(18.8)	577(17.1)	291(23.7)	162(18.4)	
Unknown	1025(18.7)	624(18.5)	219(17.9)	182(20.7)	
N stage (AJCC6)					<0.001
N0	1103(20.1)	681(20.2)	231(18.8)	191(21.7)	
N1	1594(29.1)	1030(30.6)	311(25.4)	253(28.7)	
N2	1292(23.6)	783(23.2)	336(27.4)	173(19.6)	
N3	611(11.2)	342(10.1)	167(13.6)	102(11.6)	
Unknown	877(16.0)	534(15.8)	181(14.8)	162(18.4)	
M stage (AJCC6)					0.005
M0	4054(74.0)	2537(75.3)	876(71.5)	641(72.8)	
M1	536(9.8)	305(9.1)	151(12.3)	80(9.1)	
Unknown	887(16.2)	528(12.7)	199(16.2)	160(18.2)	
Surgery performed					0.032
Yes	618(11.3)	397(11.8)	114(9.3)	107(12.1)	
NO	4859(88.7)	2973(88.2)	1112(90.7)	774(87.9)	
Radiation					<0.001
Yes	4434(81)	2825(83.8)	943(76.9)	666(75.6)	
No	1043(19)	545(16.2)	283(23.1)	215(24.4)	
Chemotherapy					<0.001
Yes	4178(76.4)	2640(78.3)	944(77.0)	603(68.4)	
No	1290(23.6)	730(21.7)	282(23.0)	278(31.6)	

¹“Other” includes American Indian, AK Native, and Asian/Pacific Islander.

²“West” includes Hawaii, Greater California, Utah, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, San Jose-Monterey, Los Angeles, and Alaska. “Northeast” includes New Jersey, and Connecticut. “North central” includes Detroit and Iowa. “South” includes Greater Georgia, Rural Georgia, Atlanta, Louisiana, and Kentucky.

³“Unknownr” includes TX, NA, and Blanks.

⁴“Unknown” includes NX, NA, and Blanks

⁵“Unknown” includes NA and Blanks

Table 2. Univariate and multivariate survival analysis for evaluating the influence of marital status on nasopharyngeal carcinoma CSS in SEER database.

Variable	5-year CSS (%)	Univariate analysis		Multivariate analysis		
		Log Rank χ^2 test	<i>P</i> value	Hazard ratio	95% Confidence interval	<i>P</i> value
Age		132.712	<0.001			
≤50	96.4			Reference		
>50	87.8			3.878	3.025-4.971	<0.001
Race		32.944	<0.001			
White	90.4			Reference		
Black	87.7			1.081	0.810-1.443	0.596
Other	93.6			0.560	0.451-0.695	<0.001
Unknown	93.7			0.643	0.206-2.010	0.448
Gender		3.051	0.081			
Male	91.2			Reference		
Female	92.3			0.823	0.661-1.025	0.081
Registry Region		12.944	0.005			
West	92.6			Reference		
Northeast	89.1			1.243	0.919-1.681	0.158
North central	92.2			1.121	0.748-1.679	0.581
South	89.0			1.531	1.207-1.941	<0.001
Grade		14.968	0.001			
I/II	89.4			Reference		
III/IV	92.7			0.599	0.441-0.812	0.001
Unknown	90.0			0.809	0.588-1.113	0.193
Primary Site		2.321	0.803			
Superior wall of nasopharynx	93.9			Reference		
Posterior wall of nasopharynx	92.5			1.012	0.401-2.554	0.980
Lateral wall of nasopharynx	92.6			0.885	0.345-2.270	0.799
Anterior wall of nasopharynx	88.9			1.563	0.452-5.403	0.480
Overlapping wall of nasopharynx	94.1			0.953	0.340-2.673	0.927
	91.2			1.090	0.451-2.637	0.848
Nasopharynx T stage (AJCC6)		20.224	0.001			
T0	92.0			Reference		
T1	93.1			1.118	0.355-3.528	0.849
T2	92.4			1.344	0.425-4.249	0.615

T3	89.4			1.755	0.554-5.559	0.339
T4	92.3			1.852	0.585-5.866	0.295
Unknown N stage (AJCC6)	88.1	28.706	<0.001	1.969	0.618-6.278	0.252
N0	90.0			Reference		
N1	92.1			0.822	0.637-1.062	0.134
N2	94.8			0.623	0.463-0.837	0.002
N3	91.1			0.915	0.639-1.309	0.626
Unknown M stage (AJCC6)	83.7	11.611	0.003	1.514	1.096-2.091	0.012
M0	92.2			Reference		
M1	88.3			1.457	1.004-2.114	0.048
Unknown Insurance	86.9	2.172	0.338	1.550	1.160-2.072	0.003
Insured/medicaid	92.3			Reference		
Uninsured	92.8			1.257	0.733-2.155	0.406
Unknown Surgery performed	89.8	1.022	0.312	1.156	0.930-1.435	0.191
Yes	90.7			Reference		
NO Radiation	91.7	64.744	<0.001	1.168	0.864-1.578	0.313
Yes	92.8			Reference		
No Chemotherapy	83.8	59.195	<0.001	2.460	1.961-3.086	<0.001
Yes	93.5			Reference		
No Marital status	83.9	53.198	<0.001	2.180	1.778-2.674	<0.001
Married	92.6			Reference		
Single/unmarried	92.4			0.811	0.675-1.152	0.355
Separated/windowed/divorced	85.1			2.180	1.727-2.751	<0.001

Table 3. Univariate and multivariate survival analysis for evaluating the influence of marital status on nasopharyngeal carcinoma OS in SEER database.

Variable	5-year CSS (%)	Univariate analysis		Multivariate analysis		
		Log Rank χ^2 test	P value	Hazard ratio	95% Confidence interval	P value
Age		255.358	<0.001			
≤50	68.1			Reference		
>50	48.0			2.057	1.878-2.253	<0.001
Race		129.633	<0.001			
White	51.6			Reference		
Black	46.3			1.060	0.935-1.201	0.364
Other	63.1			0.628	0.574-0.688	<0.001
Unknown	83.0			0.291	0.139-0.612	0.001
Gender		14.878	<0.001			
Male	54.0			Reference		
Female	60.7			0.834	0.760-0.915	<0.001
Registry Region		35.353	<0.001			
West	58.2			Reference		
Northeast	53.3			1.116	0.979-1.272	0.100
North central	58.5			1.015	0.850-1.211	0.870
South	49.0			1.355	1.223-1.501	<0.001
Grade		99.775	<0.001			
I/II	43.5			Reference		
III/IV	60.5			0.565	0.498-0.642	<0.001
Unknown	51.9			0.769	0.674-0.878	<0.001
Primary Site		38.424	<0.001			
Superior wall of nasopharynx	68.8			Reference		
Posterior wall of nasopharynx	63.5			1.271	0.794-2.033	0.317
Lateral wall of nasopharynx	66.6			1.073	0.665-1.730	0.773
Anterior wall of nasopharynx	43.3			1.986	1.104-3.572	0.022
Overlapping wall of nasopharynx	53.0			1.609	0.979-2.645	0.061
	53.8			1.625	1.034-2.554	0.035
Nasopharynx T stage (AJCC6)		297.469	<0.001			
T0	73.0			Reference		
T1	69.3			0.984	0.578-1.675	0.952
T2	64.0			1.216	0.714-2.072	0.472

T3	49.4			1.939	1.139-3.299	0.015
T4	43.7			2.379	1.400-4.044	0.001
Unknown N stage (AJCC6)	42.2	110.256	<0.001	2.269	1.331-3.869	0.003
N0	58.2			Reference		
N1	62.3			0.887	0.788-0.998	0.046
N2	57.7			0.968	0.856-1.094	0.602
N3	44.4			1.413	1.227-1.628	<0.001
Unknown M stage (AJCC6)	40.3	613.753	<0.001	1.624	1.406-1.877	<0.001
M0	62.5			Reference		
M1	18.2			3.556	3.189-3.964	<0.001
Unknown Insurance	43.7	33.728	<0.001	1.752	1.547-1.985	<0.001
Insured/medicaid	59.0			Reference		
Uninsured	40.9			1.610	1.331-1.949	<0.001
Unknown Surgery performed	50.9	20.836	<0.001	1.188	1.084-1.303	<0.001
Yes	63.5			Reference		
NO Radiation	55.0	652.423	<0.001	1.375	1.198-1.579	<0.001
Yes	62.4			Reference		
No Chemotherapy	28.2	184.535	<0.001	3.035	2.274-3.322	<0.001
Yes	59.9			Reference		
No Marital status	42.9	176.318	<0.001	1.831	1.675-2.002	<0.001
Married	60.7			Reference		
Single/unmarried	54.6			1.219	1.100-1.351	<0.001
Separated/windowed/divorced	40.1			1.977	1.784-2.191	<0.001

Table 4. Univariate and multivariate analysis of marital status on nasopharyngeal carcinoma CSS according to different cancer stage.

Variable	5-year CSS (%)	Univariate analysis		Multivariate analysis		
		Log Rank χ^2 test	<i>P</i> value	Hazard ratio	95% Confidence interval	<i>P</i> value
Age		15.474	<0.001			
≤50						
Married	97.1			Reference		
Single/unmarried	95.8			1.499	0.907-2.477	0.114
Separated/windowed/divorced	93.2			3.251	1.756-6.020	<0.001
>50		18.399	<0.001			
Married	89.4			Reference		
Single/unmarried	86.5			1.055	0.759-1.467	0.748
Separated/windowed/divorced	82.4			1.710	1.330-2.198	<0.001
Gender		40.422	<0.001			
Male						
Married	92.3			Reference		
Single/unmarried	91.5			0.932	0.690-1.259	0.646
Separated/windowed/divorced	84.0			2.352	1.766-3.134	<0.001
Female		19.444	<0.001			
Married	93.4			Reference		
Single/unmarried	94.6			0.737	0.410-1.325	0.308
Separated/windowed/divorced	86.6			2.174	1.438-3.285	<0.001
Grade		0.572	0.571			
I/II						
Married	89.2			Reference		
Single/unmarried	89.4			0.744	0.329-1.684	0.479
Separated/windowed/divorced	89.9			0.865	0.414-1.806	0.699
III/IV		34.830	<0.001			
Married	93.8			Reference		
Single/unmarried	93.0			0.941	0.655-1.352	0.742
Separated/windowed/divorced	86.1			2.443	1.768-3.376	<0.001

Separated/windowed/divorced		25.004	<0.001			
Unknown	91.2			Reference		
Married	92.0			0.856	0.542-1.352	0.506
Single/unmarried	81.6			2.356	1.610-3.449	<0.001
Separated/windowed/divorced Insurance		28.627	<0.001			
Insured/medicaid						
Married	93.0			Reference		
Single/unmarried	92.8			0.910	0.649-1.276	0.584
Separated/windowed/divorced		87.8		2.136	1.573-2.902	<0.001
Uninsured		0.592	0.744			
Married	91.9			Reference		
Single/unmarried	94.0			0.908	0.277-2.976	0.873
Separated/windowed/divorced		93.2		1.556	0.388-2.246	0.533
Separated/windowed/divorced		24.538	<0.001			
Unknown	91.8			Reference		
Married	90.9			0.801	0.494-1.297	0.367
Single/unmarried	79.3			2.293	1.582-3.325	<0.001
Separated/windowed/divorced Surgery performed		9.210	0.01			
Yes						
Married	92.5			Reference		
Single/unmarried	89.9			1.592	0.758-3.345	0.220
Separated/windowed/divorced		84.3	46.992	<0.001	2.642	1.378-5.066
NO		92.6			Reference	
Married	92.7			0.812	0.609-1.082	0.155
Single/unmarried	85.6			2.142	1.667-2.751	<0.001
Separated/windowed/divorced Radiation		43.806	<0.001			

Yes					
Married	93.8		Reference		
Single/unmarried	93.6		0.884	0.647-1.209	0.441
Separated/windowed/divorced	86.4		2.254	1.727-2.942	<0.001
		8.950	0.011		
No					
Married	83.7		Reference		
Single/unmarried	86.5		0.717	0.427-1.206	0.210
Separated/windowed/divorced	78.5		1.719	1.061-2.785	0.028
Chemotherapy		29.076	<0.001		
Yes					
Married	94.8		Reference		
Single/unmarried	92.5		1.122	0.827-1.524	0.460
Separated/windowed/divorced	88.7		2.192	1.632-2.945	<0.001
		25.093	<0.001		
No					
Married	84.0.		Reference		
Single/unmarried	92.0		0.461	0.258-0.826	0.009
Separated/windowed/divorced	72.9		1.946	1.329-2.850	0.001

Figures

Figure 1

Flow diagram depicting the inclusion and exclusion criteria for patients

Figure 2

Survival curves for cause-specific survival (CSS) in patients with nasopharyngeal carcinoma according to marital status ($\chi^2 = 53.198$, $P < 0.001$).

Figure 3

Survival curves for overall survival (OS) in patients with nasopharyngeal carcinoma according to marital status ($\chi^2 = 153.856$, $P < 0.001$).