Propensity-score Matching Analysis for Marital Status and Survival of Oral and Oropharyngeal Squamous Cell Carcinoma Based on SEER Database

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Abstract

Object

Marital status plays different roles as a risk factor on survival in various cancers. The study is aimed to analyze the impact of marital status on survival of oral and oropharyngeal squamous cell carcinoma (OPSCC) at population level based on SEER database using propensity-score matching method (PSM).

Methods

37,023 eligible patients were extracted from the Surveillance, Epidemiology, and End Results (SEER) database, and analyzed the impact of various marital status on cancer-specific survival (CSS) of OPSCC by Kaplan-Meier method and Cox regression model. Then we used propensity-score matching analysis to balance baseline characteristics between married, single, divorced and widowed patients. The impact of various marital status after pairwise matching using p-value adjusted and PSM on CSS was re-analyzed by Kaplan-Meier method.

Results

The age, sex, race, tumor location, pathologic grades, SEER stages, treatments, composite socioeconomic status (C-SES), insurance, and marital status were identified as independent prognostic factors for CSS of OPSCC. Widowed patients presented the worst CSS, compared with married, single, and divorced patients (P<0.001). Subgroup analysis indicated that widowed patients always presented with the significantly decreasing risk of CSS compared with other marital status in different SEER stages (P<0.001), and different C-SES (P<0.001). After propensity-score matching, widowed patients were still found to be associated with significantly decreased CSS compared with other marital groups (P<0.001).

Conclusion

Marital status was first analyzed after using PSM to balance clinicopathological and socioeconomic confounding factors and identified as an independent prognostic factor for CSS of OPSCC. Widowed patients was significantly associated with a decreasing CSS, which indicated that absence of spousal support and optimal psychosocial coping strategies may explain the phenomena.

Introduction

Oral and oropharyngeal squamous cell carcinoma (OPSCC) was one of the common malignant tumor in head neck. The incidence of OPSCC continued to increase, due to excessive tobacco, alcohol consumption and HPV infection [1,2]. Furthermore, mortality rates were relentlessly increasing overall by 0.5% per year from 2009 to 2018, although optimized multidisciplinary treatments improved local control [3,4].

As we know that the anatomy of oral and oropharynx is not deeply hidden, primary tumor should been easier to be examined in early stage, and have more opportunities to be cure and better survival. However, the reality of survival of OPSCC was opposite. Therefore, we need to further analyze the predictive factors to establish comprehensive treatment strategies and improve survival of patients with OPSCC.

Prior studies suggested that the confounding risk factors, including age, sex, race, tumor site, pathologic grade, treatment, socioeconomic status, alcohol and tobacco consumption, HPV infection and marital status, played controversial roles in survival of patients with OPSCC [5-10]. Many studies also indicated that unmarried status was an increasing risk of mortality in oral cavity or oropharyngeal cancer, compared with married status based on a population studies [11-14]. However, the impact of more detailed unmarried status on survival has not been previously reported. The effect of socioeconomic and marital status on survival of OPSCC had been reported in seldom. Therefore, it is important to explore the effect of different marital status on survival of OPSCC patients and formulate more reasonable strategies.
In the present study, we extracted data from the Surveillance, Epidemiology, and End Results cancer registry database to assess and compare the effects of married, single, divorced and widowed status on cancer-specific survival using PSM and explored the possible mechanisms.

**Materials And Methods**

**Patient population**

All eligible patients with OPSCC diagnosed from 1975 to 2016 were identified in the SEER database (version 8.3.9,updated at Sep 20th, 2021). The current database we used was Incidence-SEER 18 Regs Custom Data (with additional treatment fields), Nov 2018 Sub (1975-2016 varying). Patients over the age of 20-year old and who received a pathological diagnosis of OPSCC (ICD-O-3 histology code: 8052, 8053, 8070, 8071, 8072, 8073, 8074, 8075, 8076, 8078, 8083, 8084) were included in our studies. The criteria of tumor stage was based on SEER combined summary stage 2000. Patients with more than one primary tumor, incomplete follow-up information, and incomplete clinicopathological characteristics (age, sex, race, pathologic grade, SEER stages, treatments) and socioeconomic characteristics (insurance, composite SES, marital status) were excluded.

**Study variables**

Variables about clinicopathological and composite socioeconomic characteristics were shown in Table 1. The tumor location was divided into tongue(anterior and basal), oropharynx(tonsils) and others(mucous of buccal, mouth floor, lip, palate and others). Pathological grades were divided into 2 categories: low grade (well and moderately differentiated) and high grade (poorly and undifferentiated). In our study, we merged separated and divorced patients into divorced group.

Three standard 2000 US Census variables from SEER database, including median family income, the percentage of persons who have less than high school education, and the percentage of persons with income below the poverty level, were extracted. A composite SES variable was set up according to the three SES variables as described in previous studies [15-17]. The composite SES variables was further classified as low C-SES (C-SES score <5) and high C-SES (C-SES score ≥5)[18].

**Propensity-score matching:**

Marital status was divided into married, single, divorced, and widowed groups from SEER database. To precisely assess the roles of marital status in prognosis of OPSCC patients, propensity-score matching method was performed to balance clinicopathological and socioeconomic characteristics between different marital pairwise groups. After p-value adjusted and pairwise matching, the prognostic importance of marital status on CSS were re-analyzed within the matching pair of groups.

**Statistical analysis**

Pearson's Chi-squared test was performed to analyze relationship of different clinicopathological and socioeconomic characteristics between various marital groups. CSS was estimated by Kaplan–Meier methods. Log rank test was performed to evaluate the statistical significance of differences between survival curves of various marital groups. Multivariable Cox proportional-hazards regression model was performed to analyze the hazard ratios of risk factors. All statistical tests were two-tailed. Statistical significance was identified as p value less than 0.05. The statistical analysis was conducted using SPSS(version 20.0) and R(version4.1.1).

**Results**

**Baseline clinicopathological and socioeconomic characteristics**

A total of 37,023 eligible patients (27,776 males and 9,247 females) were included in our studies from the SEER database. Of these patients, there were 21,049(56.9%) married patients, 7,554(20.4%) single, 5,428(14.7%) divorced and 2,992(8.1%) widowed patients. Detailed clinicopathological and composite socioeconomic characteristics were shown in Table 1. Statistically significant differences were identified in age, sex, race, tumor location, pathological grades, SEER stages,
treatments, insurance, C-SES between different marital groups (P<0.001). Among the comparisons of risk factors, widowed patients had twice or three times higher proportion in the group of age ≥ 60-year old (87.9%), and female (62.6%), than that of other corresponding marital groups.

The roles of marital status on CSS of OPSCC

The detailed univariate and Cox-regression multivariate analysis were shown in Table 2. The groups of age ≥ 60-year old, female, black race, other tumor location, low pathological grade group, the distant SEER stage, low C-SES, non-insurance, and non-treatment had significant worse 5-year CSS (P<0.001). Furthermore, these variables were also determined as independent risk factors for CSS of OPSCC by multivariate analysis. Forest plot was showed in Figure 1 according to multivariate Cox-proportional hazard analysis.

Univariate analysis by Kaplan-Meier method showed that significant differences were observed in CSS among different marital groups. In a crude survival analysis, the widowed group was associated with a significant decreasing risk of CSS (P>0.001), as shown in Figure 2A. The 5-year CSS of widowed group was significantly worse than that of married, single and divorced groups. Furthermore, the widowed patients had a significant lower risk of cancer-specific survival compared with married, single and divorced patients after controlling for the confounding risk factors (P<0.001), as showed in Figure 2B.

Subgroup analysis of the roles of marital status by SEER stage

The effects of marital status on CSS were evaluated regarding the SEER stage, as shown in Table 3. We found that widowed patients invariably had the worse 5-year CSS compared with married, single and divorced patients in the localized, regional and distant groups (Figure 3). In the subgroup of different SEER stages, multivariate Cox-regression analysis indicated that widowhood was invariably significant decreasing risk of CSS compared with married patients (local, HR 1.607, 95%CI: 1.372-1.882, P<0.001; region, HR 1.887, 95%CI: 1.703-2.090, P<0.001; distant, HR 1.499, 95%CI: 1.307-1.719, P<0.001).

Subgroup analysis the role of marital status by C-SES

The effects of marital status on CSS at different C-SES were assessed, as shown Table 4. Subgroup analysis showed that marital status was invariably determined to be an independent risk factors of CSS among OPSCC patients with low and high C-SES according to the log-rank tests and Cox-regression multivariate analysis (Figure 4, P<0.001). In low and high C-SES group, widowed patients invariably had the worse CSS, compared with married patients (HR 1.685, 95%CI: 1.446-1.963, P<0.001; HR 1.762, 95%CI: 1.623-1.914, P<0.001).

Propensity-score matching for different pairwise marital groups

P-values adjusted method (BH) was used to test the statistically differences between pairwise marital groups. Then we found that there were significant differences between widowed and other marital groups (P<0.001), between married and other marital groups (P<0.001) respectively. Since the several baseline characteristics among different marital groups were significantly different, we performed propensity-score matching analysis to balance the confounding factors. If there was statistically significant differences of survival analysis between different marital status using Kaplan-mier methods, each group was matched a 1:1 ratio. The detailed variables after propensity-score matching were shown in Table 5.

Survival analysis after propensity-score matching

Figure 5A and 5B showed that before and after PSM, CSS of widowed patients was always significantly worse than that of married patients (P<0.001). After adjusting for confounding factors (age, sex, race, pathological grade, tumor location, treatments, insurance, C-SES), widowhood was still statistically significant increasing risk of mortality (HR 1.366, 95%CI: 1.246-1.497, P<0.001).

Figure 5C and 5D showed before and after PSM of widowed and divorced patients, CSS of widowed patients was also significantly worse than that of divorced patients (P<0.001). After adjusting for confounding factors, widowed status was
statistically significant risk factor of CSS (HR 1.255, 95%CI:1.145-1.376, P<0.001).

Pairwise comparison of different marital status effect on CSS before and after PSM, as such married and divorced (HR 1.348, 95%CI:1.255-1.449, P<0.001), single and widowed(HR 1.291, 95%CI:1.174-1.419, P<0.001), married and single patients(HR 1.384, 95%CI:1.301-1.473, P<0.001), were shown in from Figure 5E to Figure 5J. After balancing the confounding prognostic factors, marital status was statistically significant risk factor for CSS of OPSCC patients.

Discussion

The effect of marital status on prognostic of various diseases was inconsistent. Some studies indicated married status had a better life expectancy and quality in cardiovascular disease and carcinomas[19,20,21], while no significant effects on survival of cancer patients were suggested in other studies[22,23]. Prior studies on marital status on survival of oral or oropharyngeal squamous cell carcinoma showed that marital status was an independent prognostic factor, and marriage had an protective effect on survival for for oral or oropharyngeal cancer[11,24]. However, these studies had not been combined clinicalpathological characteristics with socioeconomic characteristics of OPSCC, and analyzed survival of the pairwise marital patients after using propensity-score matching without p adjusted method. Therefore, it is necessary to clarity the holistic impact of marital status on survival.

Based on clinicopathological and socioeconomic characteristics of OPSCC, marital status is definitely identified as an independent prognostic risk factor for CSS after balancing age, sex, race,pathologic grade, SEER stage, tumor location, treatment modalities, insurance, C-SES using PSM and p-values adjusted method. Furthermore, we found that in both in multivariate survival analysis and pairwise matching survival after p-value adjusted method and propensity-scores matching, widowed patients invariably had the worst cancer-specific survival compared with married, single and divorced patients. Our studies also indicated that prognostic factors of non-insurance and low composite socioeconomic status were determined to be decreasing risk factors of survival. Therefore, evaluating the socioeconomic status was necessary for the prognosis of OPSCC patients.

Marital status has been indicated to be associated with the prognosis in various malignant tumors. Prior studies have demonstrated that marriage had an independent protective effects on survival, and married patients had lower risk for metastatic caners, and were more inclined to receive definite treatment. Perhaps, there were the strong social support and insurance coverage, better living habits and psychology state in the married populations[11,23,25,26,27]. Our findings also confirmed the protective roles of marriage in OPSCC. Furthermore, the detailed classification of marital status indicated that widowed patients had the worst CSS compared with married, single and divorced patients.

Some studies found that the worse prognosis in widowed patients was due to delayed diagnosis and insufficient treatments. Lack of spousal support and financial assistance were mainly disadvantages in widowed patients[28,29,30]. Our studies also showed that the higher percentage of low composite socioeconomic status was in widowed patients, compared with married and divorced patients. Moreover, subgroup analysis in low and high C-SES indicated that widowed patients always had the worst CSS, compared with other marital status. Even if balancing the confounding factors using PSM, widowed patients still had the worst CSS, compared with others. The association between widowhood and poor survival may be attributed to the psychosocial factors[31]. The spousal death and the need of adaption to new social roles were very depressed and stressful for the surviving companion. Psychological depression could lead to poor medical compliance, and increasing the mortality risk of malignant tumor[32].

Marriage had protective roles for survival of oral cancer. However, widowed status was faced by almost everyone in the course of life. To explore the disadvantaged prognostic factors for survival seemed to be more pressing. Our studies also indicated that the importance of marital status in survival of OPSCC patients. Marriage had an advantage on cancer prognosis, and more compliant to proper treatments under their spousal support and encouragements. However, widowed patients seemed to be particularly prone to depression[33], and widowhood had a negative impact on immune status and hormone level.
However, a few researchers suggested that there were no significant differences in prognosis between malignant tumor and marital status. These authors suggested that the phenomena may be originated from the limitations of the database, including the number of confounding prognostic factors, different clinicopathological and socioeconomic characteristics, and study design type[23,29]. In our studies, we extracted 3 standard 2000 US Census variables to set up a composite socioeconomic status variable, and explored the association between marital status and CSS after controlling socioeconomic and clinicopathologic variables using propensity-score matching method.

There are some limitations in our studies. First, the information of marital status in SEER database was acquired only at the time of tumor diagnosis, and there were no changes during the course of therapy, even till death. Second, psychosocial factors, tobacco and alcohol consumption, and HPV infection were not including in SEER database, the association of psychosocial and survival should be further performed and validated. Third, although we utilized the PSM methods to reduce the bias, there were inherent bias of retrospective research. The evaluation of life quality was also an important goal missing from the SEER database.

**Conclusion**

Based on population level of SEER database, widowed patients with oral and oropharyngeal carcinoma were first identified to have the worst cancer-specific survival compared with married, single and divorced patients, and marital status was shown as an independent prognostic risk factor for survival after balancing the confounding prognostic factors using p-value adjusted method and propensity-score matching method. Psychosocial depression and loss of spousal support leading to the negative effects on the widowed patients should be further studied in multicenter, large samples, randomized control study.

**Declarations**

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**Availability data and materials**

The datasets used and/or analyzed during the current study are available from the Surveillance, Epidemiology, and End Results (SEER) database.

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**Contributions**

All persons designated as the authors have participated sufficiently in the work to take public responsibility for the content of the manuscript.

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Ethics declarations

Ethics approval and consent to participate

The study was approved by the Renmin hospital of Wuhan University Ethics Committee and conducted in accordance with the ethical standards of the declaration of Helsinki. Based on the public data of SEER programs, signing an informed consent was not required.

Consent for publication

Not applicable

Competing interests

The authors declare that there is no conflict of interest.

References

1. Warnakulasuriya S (2009) Global epidemiology of oral and oropharyngeal cancer. Oral Oncol 45:309-16. 
   https://doi.org/10.1016/j.oraloncology.2008.06.002.

2. Bundgaard T, Wildt J, Frydenberg M, et al (1995) Case-control study of squamous cell cancer of the oral cavity in Denmark. 
   Cancer Causes Control 6:57-67. https://10.1007/BF00051681.

3. Siegel RL, Miller KD, Fuchs HE, et al (2021) Cancer Statistics, 2021. CA Cancer J Clin 71:7-33. 
   https://doi.org/10.3322/caac.21654.

4. Monsjou HSV, Schaapveld M, Hamming-Vrieze O, et al (2016) Cause-specific excess mortality in patients treated for cancer 
   of the oral cavity and oropharynx: A population-based study. Oral Oncol 52:37-44. 
   https://doi.org/10.1016/j.oraloncology.2015.10.013.

5. Jemal A, Simard EP, Dorell C, et al (2013) Annual Report to the Nation on the Status of Cancer, 1975-2009, featuring the 
   burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. J Natl Cancer Inst 
   105:175-201. https://doi.org/10.1093/jnci/djs491.

6. Brouwer AF, Eisenberg MC, Meza R (2016) Age Effects and temporal trends in HPV related and HPV-unrelated oral cancer in 
   the United States: a multistage carcinogenesis modeling analysis. PLoS One 11:e0151098. 
   https://doi.org/10.1371/journal.pone.0151098.

7. Elwood JM, Youlden DR, Chelimo C, et al (2014) Comparison of oropharyngeal and oral cavity squamous cell cancer 
   incidence and trends in New Zealand and Queensland, Australia. Cancer Epidemiol 38:16–21. 
   https://doi.org/10.1016/j.canep.2013.12.004.

8. Chaturvedi AK, Anderson WF, Lortet-Tieulent J, et al (2013) Worldwide trends in incidence rates for oral cavity and 
   oropharyngeal cancers. J Clin Oncol 31:4550–4559. https://doi: 10.1200/JCO.2013.50.3870.

9. Moro JDS, Maroneze MC, Ardenghi TM, et al (2018) Oral and oropharyngeal cancer: epidemiology and survival analysis. 
   Einstein(Sao Paulo) 16:eA04248. https://doi.org/10.1590/S1679-45082018A04248.

10. Schneider IIJ, Flores ME, Nickel DA, et al (2014) Survival rates of patients with cancer of the lip, mouth and pharynx: a 
    cohort study of 10 years. Rev Bras Epidemiol 17:680-91. https://doi.org/10.1590/1809-4503201400030009.
11. Shi X, Zhang T, Hu W, et al (2017) Marital status and survival of patients with oral cavity squamous cell carcinoma: a population-based study. Oncotarget 8:28526-543. [https://doi.org/10.18632/oncotarget.16095]

12. Osazuwa-Peters N, Christopher KM, Cass LM, et al (2019) What’s Love Got to do with it Marital status and survival of head and neck cancer. Eur J Cancer Care(Engl) 28:e13022. [https://doi.org/10.1111/ecc.13022]

13. Monsjou HSV, Schaapveld, M, Hamming-Vrieze O, et al (2016) Cause-specific excess mortality in patients treated for cancer of the oral cavity and oropharynx. Oral Oncol 52:37-44. [https://doi.org/10.1016/j.oraloncology.2015.10.013]

14. Jensen JS, Jensen DH, Grønhøj C, et al (2018) Incidence and survival of oropharyngeal cancer in Denmark a nation wide population based study from 1980 to 2014. Acta Oncol 57:269-75. [https://doi.org/10.1080/0284186X.2017.1390251]

15. Robert SA, Strombom I, Trentham-Dietz A et al (2004) Socioeconomic risk factors for breast cancer: Distinguishing individual- and community-level effects. Epidemiology 15: 442–50. [https://doi.org/10.1097/01.ede.0000129512.61698.03]

16. Du XL, Fang S, Coker AL et al (2006) Racial disparity and socioeconomic status in association with survival in older men with local/regional stage prostate carcinoma: Findings from a large community-based cohort. Cancer 106: 1276–85. [https://doi.org/10.1002/cncr.21732]

17. Sun M, Abdollah F, Liberman D et al (2011) Racial disparities and socioeconomic status in men diagnosed with testicular germ cell tumors: A survival analysis. Cancer 117: 4277–85. [https://doi.org/10.1002/cncr.25969]

18. Gao ZY, Ren FG, Song H, et al (2018) Marital Status and Survival of Patients with Chondrosarcoma: A Population-Based Analysis. Med Sci Monit 24:6638-6648. [https://doi.org/10.12659/MSM.911673]

19. Chen Z, Yin K, Zheng D, et al (2020) Marital status independently predicts non-small cell lung cancer survival: a propensity-adjusted SEER database analysis. J Cancer Res Clin Oncol 146:67-74. [https://doi.org/10.1007/s00432-019-03084-x]

20. Shi RL, Qu N, Lu ZW et al (2016) The impact of marital status at diagnosis on cancer survival in patients with differentiated thyroid cancer. Cancer Med 5: 2145–54. [https://doi.org/10.1002/cam4.778]

21. Alamanda VK, Song Y, Holt GE (2014) Effect of marital status on treatment and survival of extremity soft tissue sarcoma. Ann Oncol 25: 725–29. [https://doi.org/10.1093/annonc/mdt583]

22. Nelles JL, Joseph SA, Konety BR (2009) The impact of marriage on bladder cancer mortality. Urol Oncol 27: 263–67. [https://doi.org/10.1016/j.urolonc.2008.04.016]

23. Jatoi A, Novotny P, Cassivi S et al (2007) Does marital status impact survival and quality of life in patients with non-small cell lung cancer? Observations from the mayo clinic lung cancer cohort. Oncologist 12: 1456–63. [https://doi.org/10.1634/theoncologist.12-12-1456]

24. Ding Z, Yu D, Li H, et al (2021) Effects of marital status on overall and cancer-specific survival in laryngeal cancer patients: a population-based study. Sci Rep 11:723. [https://doi.org/10.1038/s41598-020-80698-z]

25. Aizer AA, Chen MH, McCarthy EP, et al (2013) Marital status and survival in patients with cancer. J Clin Oncol 31:3869-76. [https://doi.org/10.1200/JCO.2013.49.6489]

26. Jin JJ, Wang W, Dai FX, et al (2016) Marital status and survival in patients with gastric cancer. Cancer Med 5:1821-9. [https://doi.org/10.1002/cam4.758]

27. Wang R, Zhu Y, Liu X, et al (2019) The Clinicopathological features and survival outcomes of patients with different metastatic sites in stage IV breast cancer. BMC Cancer 19:1091. [https://doi.org/10.1186/s12885-019-6311-z]
28. Yao JC, Shah MH, Ito T et al (2011) Everolimus for advanced pancreatic neuroendocrine tumors. N Engl J Med 364: 514–23. https://doi.org/10.1056/NEJMoa1009290.

29. Iwashyna TJ, Christakis NA: Marriage, widowhood, and health-care use. Soc Sci Med, 2003; 57(11): 2137–47

30. Baine M, Sahak F, Lin C et al (2011) Marital status and survival in pancreatic cancer patients: A SEER based analysis. PLoS One 6: e21052. https://doi.org/10.1371/journal.pone.0021052.

31. Rana M, Kanatas A, Herzberg PY, et al (2015) Prospective study of the influence of psychological and medical factors on quality of life and severity of symptoms among patients with oral squamous cell carcinoma. Br J Oral Maxillofac Surg 53:364-70. https://doi.org/10.1016/j.bjoms.2015.01.019.

32. DiMatteo MR, Lepper HS, Croghan TW (2000) Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med 160: 2101–7. https://doi.org/10.1001/archinte.160.14.2101.

33. Kugaya A, Akechi T, Okamura H, et al (1999) Correlates of depressed mood in ambulatory head and neck cancer patients. Psychooncology 8:494–9. https://doi.org/10.1002/(sici)1099-1611(199911/12)8:6<494::aid-pon403>3.0.co;2-m.

Tables

Table 1. Baseline clinicopathological and socioeconomic characteristics of OPSCC patients
| Characteristics | Total n=37023 | Married n=21049(%) | Single n=7554(%) | Divorced n=5428(%) | Widowed n=2992(%) | P value |
|-----------------|--------------|---------------------|------------------|--------------------|-------------------|---------|
| Age             |              |                     |                  |                    |                   | <0.001  |
| <60             | 17745        | 10082(47.9%)        | 4694(62.1%)      | 2607(48.0%)        | 362(12.1%)        |         |
| ≥ 60            | 19278        | 10967(52.1%)        | 2860(37.9%)      | 2821(52.0%)        | 2630(87.9%)       |         |
| Sex             |              |                     |                  |                    |                   | <0.001  |
| Female          | 9247         | 4342(20.6%)         | 1685(22.3%)      | 1347(24.8%)        | 1873(62.6%)       |         |
| Male            | 27776        | 16707(79.4%)        | 5869(77.7%)      | 4081(75.2%)        | 1119(37.4%)       |         |
| Race            |              |                     |                  |                    |                   | <0.001  |
| Black           | 2976         | 964(4.6%)           | 1263(16.7%)      | 505(9.3%)          | 244(8.1%)         |         |
| White           | 32064        | 18773(89.2%)        | 5989(79.3%)      | 4745(87.4%)        | 2557(85.5%)       |         |
| Other           | 1983         | 1312(6.2%)          | 302(4.0%)        | 178(3.3%)          | 191(6.4%)         |         |
| Location        |              |                     |                  |                    |                   | <0.001  |
| Tongue          | 16719        | 9778(46.4%)         | 3329(44.1%)      | 2309(42.5%)        | 1303(43.5%)       |         |
| Oropharyn       | 12582        | 7301(34.7%)         | 2651(35.1%)      | 1988(36.6%)        | 642(21.5%)        |         |
| Others          | 7722         | 3970(18.9%)         | 1574(20.8%)      | 1131(20.8%)        | 1047(35.0%)       |         |
| Grade           |              |                     |                  |                    |                   | <0.001  |
| Low             | 22852        | 12588(59.8%)        | 4791(63.4%)      | 3355(61.8%)        | 2118(70.8%)       |         |
| High            | 14171        | 8461(40.2%)         | 2763(36.6%)      | 2073(38.2%)        | 874(29.2%)        |         |
| SEER stage      |              |                     |                  |                    |                   | <0.001  |
| Local           | 11007        | 6546(31.1%)         | 1936(25.6%)      | 1301(24.0%)        | 1224(40.9%)       |         |
| Regional        | 20005        | 11577(55.0%)        | 4094(54.2%)      | 3042(56.0%)        | 1292(43.2%)       |         |
| Distant         | 6011         | 2926(13.9%)         | 1524(20.2%)      | 1085(20.0%)        | 476(15.9%)        |         |
| Composite SES   |              |                     |                  |                    |                   | <0.001  |
| Low             | 7398         | 3886(18.5%)         | 1757(23.3%)      | 1117(20.6%)        | 638(21.3%)        |         |
| High            | 29625        | 17163(81.5%)        | 5797(76.7%)      | 4311(79.4%)        | 2354(78.7%)       |         |
| Insurance       |              |                     |                  |                    |                   | <0.001  |
| None            | 1684         | 575(2.7%)           | 677(9.0%)        | 359(6.6%)          | 73(2.4%)          |         |
| Insurance(medicaid) | 35339     | 20474(97.3%)        | 6877(91.0%)      | 5069(93.4%)        | 2919(97.6%)       |         |
| Treatment       |              |                     |                  |                    |                   | <0.001  |
| None            | 2526         | 929(4.4%)           | 774(10.3%)       | 473(8.7%)          | 350(11.7%)        |         |
| Surgery alone   | 10082        | 5865(27.9%)         | 1887(25.0%)      | 1220(22.5%)        | 1110(37.1%)       |         |
| Radiation alone | 12796        | 7182(34.1%)         | 2693(35.6%)      | 2093(38.6%)        | 828(27.7%)        |         |
| Surgery with radiation | 11619     | 7073(33.6%)         | 2200(29.1%)      | 1642(30.2%)        | 704(23.5%)        |         |
| Cancer-specific death |         |                     |                  |                    |                   | <0.001  |
| Events   | 9130 | 4093(19.4%) | 2306(30.5%) | 1662(30.6%) | 1069(35.7%) |
|----------|------|-------------|-------------|-------------|-------------|
| Censored | 27893| 16956(80.6%)| 5248(69.5%) | 3766(69.4%) | 1923(64.3%) |

**Table 2.** Univariate and multivariate survival analysis for marital status on CSS of patients with OPSCC
| Variables                  | 5-year CSS | Univariate analysis | Multivariate analysis |
|---------------------------|------------|---------------------|-----------------------|
|                           | Log rank $\chi^2$ test | P         | HR(95%CI) | P         |
| Age                       |            | 272.436             | <0.001               |           |
| <60                       |            | 72%                 | Reference            |           |
| ≥60                       |            | 63%                 | 1.401(1.340-1.464)   | <0.001    |
| Sex                       |            | 73.511              | <0.001               |           |
| Female                    |            | 65%                 | Reference            |           |
| Male                      |            | 69%                 | 0.825(0.785-0.866)   | <0.001    |
| Race                      |            | 610.992             | <0.001               |           |
| Black                     |            | 48%                 | Reference            |           |
| White                     |            | 70%                 | 0.684(0.642-0.728)   | <0.001    |
| Other                     |            | 66%                 | 0.844(0.759-0.939)   | <0.05     |
| Location                  |            | 174.319             | <0.001               |           |
| Tongue                    |            | 66%                 | Reference            |           |
| Oropharynx                |            | 73%                 | 0.703(0.669-0.738)   | <0.001    |
| Other                     |            | 64%                 | 1.238(1.172-1.308)   | <0.001    |
| Grade                     |            | 26.698              | <0.001               |           |
| Low                       |            | 67%                 | Reference            |           |
| High                      |            | 69%                 | 0.802(0.767-0.839)   | <0.001    |
| Seer stage                |            | 2992.176            | <0.001               |           |
| Local                     |            | 81%                 | Reference            |           |
| Regional                  |            | 68%                 | 2.152(2.006-2.309)   | <0.001    |
| Distant                   |            | 42%                 | 4.304(3.993-4.639)   | <0.001    |
| Composite SES             |            | 109.128             | <0.001               |           |
| Low                       |            | 63%                 | Reference            |           |
| High                      |            | 69%                 | 0.889(0.846-0.933)   | <0.001    |
| Insurance                 |            | 134.827             | <0.001               |           |
| None                      |            | 55%                 | Reference            |           |
| Insurance(medicaid)       |            | 68%                 | 0.787(0.724-0.856)   | <0.001    |
| Treatment                 |            | 5375.402            | <0.001               |           |
| None                      |            | 28%                 | Reference            |           |
| Surgery alone             |            | 80%                 | 0.179(0.165-0.194)   | <0.001    |
| Radiation alone           |            | 64%                 | 0.263(0.247-0.279)   | <0.001    |
| Surgery with Radiation    |            | 71%                 | 0.214(0.201-0.229)   | <0.001    |
| Marital status            |            | 1037.044            | <0.001               |           |
| Marital Status | 5-Year CSS | SEER Stages | Univariate Analysis | Multivariate Analysis |
|----------------|-----------|------------|---------------------|----------------------|
|                |           |            | Log rank $\chi^2$ test | P & HR(95%CI) & P |
| Married        | 85%       | Localized  | 126.885             | <0.001 & Reference   |
| Single         | 79%       |            |                     | 1.397(1.213-1.609) & <0.001 |
| Divorced       | 76%       |            |                     | 1.599(1.378-1.856) & <0.001 |
| Widowed        | 74%       |            |                     | 1.607(1.372-1.882) & <0.001 |
| Married        | 76%       | Regioned   | 689.966             | <0.001 & Reference   |
| Single         | 61%       |            |                     | 1.570(1.460-1.689) & <0.001 |
| Divorced       | 63%       |            |                     | 1.457(1.345-1.577) & <0.001 |
| Widowed        | 48%       |            |                     | 1.887(1.703-2.090) & <0.001 |
| Married        | 52%       | Distant    | 233.965             | <0.001 & Reference   |
| Single         | 36%       |            |                     | 1.407(1.279-1.547) & <0.001 |
| Divorced       | 37%       |            |                     | 1.409(1.273-1.560) & <0.001 |
| Widowed        | 24%       |            |                     | 1.499(1.307-1.719) & <0.001 |

**Table 3.** Subgroup survival analysis for marital status on CSS of OPSCC according to SEER stages

**Table 4.** Subgroup survival analysis for marital status on CSS of OPSCC based on C-SES
| Composite socioeconomic status | 5-year CSS | Univariate analysis | Multivariate analysis |
|-------------------------------|------------|---------------------|-----------------------|
|                               | Log rank $\chi^2$ test | $P$ | HR(95%CI) | $P$ |
| Low                           | 267.150    | <0.001             |                       |     |
| Married                       |            | Reference           |                       |     |
| Single                        | 53%        | 1.584(1.423-1.763)  | <0.001                |     |
| Divorced                      | 56%        | 1.513(1.342-1.707)  | <0.001                |     |
| Widowed                       | 51%        | 1.685(1.446-1.963)  | <0.001                |     |
| High                          | 760.968    | <0.001             |                       |     |
| Married                       | 76%        | Reference           |                       |     |
| Single                        | 63%        | 1.494(1.404-1.588)  | <0.001                |     |
| Divorced                      | 62%        | 1.475(1.381-1.575)  | <0.001                |     |
| Widowed                       | 56%        | 1.762(1.623-1.914)  | <0.001                |     |
Table 5 The baseline characteristics of patients with OPSCC after PSM

| Variables          | Married n=2992 | Widowed n=2992 | P  | Divorced n=2992 | Widowed n=2992 | P  | Single n=2992 | Widowed n=2992 | P  |
|-------------------|---------------|---------------|----|----------------|---------------|----|---------------|---------------|----|
| Age, years        | 0.874         | <0.001        | 0.020    | 0.874         | <0.001        | 0.020    | 0.874         | <0.001        | 0.020    |
| <60               | 357           | 362           | 540       | 362           | 424           | 362       | 2568          | 2630          | 2568       |
| ≥ 60              | 2635          | 2630          | 2452      | 2630          | 2568          | 2630      | 2568          | 2630          | 2568      |
| Sex               | 0.831         | <0.001        | 0.020    | 0.831         | <0.001        | <0.001   | 0.831         | <0.001        | <0.001   |
| Female            | 1864          | 1873          | 1091      | 1873          | 910           | 1893      | 1882          | 1119          | 1893     |
| Male              | 1128          | 1119          | 1901      | 1119          | 2082          | 1119      | 2082          | 1119          | 2082     |
| Race              | 0.247         | <0.001        | 0.020    | 0.247         | <0.001        | <0.001   | 0.247         | <0.001        | <0.001   |
| Black             | 223           | 244           | 250       | 244           | 271           | 244       | 271           | 244           | 271       |
| White             | 2601          | 2557          | 2635      | 2557          | 2576          | 2557      | 2576          | 2557          | 2576     |
| Others            | 168           | 191           | 107       | 298           | 145           | 191       | 145           | 191           | 145      |
| Location          | 0.027         | <0.001        | 0.020    | 0.027         | <0.001        | <0.001   | 0.027         | <0.001        | <0.001   |
| Tongue            | 1271          | 1303          | 1216      | 1303          | 1296          | 1303      | 1296          | 1303          | 1296     |
| Oropharyn         | 728           | 642           | 1012      | 642           | 951           | 642       | 951           | 642           | 951      |
| Others            | 993           | 1047          | 764       | 1047          | 745           | 1047      | 745           | 1047          | 745      |
| Grade             | 0.669         | 0.020         | <0.001   | 0.669         | 0.020         | <0.001   | 0.669         | 0.020         | <0.001   |
| Low               | 2134          | 2118          | 2034      | 2118          | 1944          | 2118      | 1944          | 2118          | 1944     |
| High              | 858           | 874           | 958       | 874           | 1048          | 874       | 1048          | 874           | 1048     |
| Stage             | 0.943         | <0.001        | <0.001   | 0.943         | <0.001        | <0.001   | 0.943         | <0.001        | <0.001   |
| Localized         | 1237          | 1224          | 929       | 1224          | 877           | 1224      | 877           | 1224          | 877      |
| Regional          | 1283          | 1292          | 1576      | 1292          | 1596          | 1292      | 1596          | 1292          | 1596     |
| Distant           | 472           | 476           | 487       | 476           | 519           | 476       | 519           | 476           | 519      |
| Treatment         | <0.001        | <0.001        | <0.001   | <0.001        | <0.001        | <0.001   | <0.001        | <0.001        | <0.001   |
| None              | 244           | 350           | 339       | 350           | 325           | 350       | 325           | 350           | 325      |
| Surgery alone     | 1147          | 1110          | 866       | 1110          | 855           | 1110      | 855           | 1110          | 855      |
| Radiation alone   | 837           | 828           | 1073      | 828           | 1056          | 828       | 1056          | 828           | 1056     |
| Surgery with Radiation | 764   | 704           | 714       | 704           | 756           | 704       | 756           | 704           | 756      |
| Insurance         | 0.568         | 0.934         | 0.335    | 0.568         | 0.934         | 0.335    | 0.568         | 0.934         | 0.335    |
| None              | 80            | 73            | 75        | 73            | 85            | 73        | 85            | 73            | 85       |
| Insurance(medicaid) | 2912     | 5831          | 2917      | 2919          | 2907          | 2919      | 2907          | 2919          | 2907     |
| Composite SES     | 0.728         | 0.925         | 0.950    | 0.728         | 0.925         | 0.950    | 0.728         | 0.925         | 0.950    |
| Low               | 626           | 638           | 635       | 638           | 641           | 638       | 641           | 638           | 641      |
| Column 1 | Column 2 | Column 3 | Column 4 | Column 5 | Column 6 | Column 7 |
|---------|----------|----------|----------|----------|----------|----------|
| High    | 2366     | 2354     | 2357     | 2354     | 2351     | 2354     |
Continue Table 5 The baseline characteristics of patients with OPSCC after PSM

| Variables     | Married n=5428 | Divorced n=5428 | P   | Married n=7554 | Single n=7554 | P   |
|---------------|----------------|-----------------|-----|---------------|---------------|-----|
| Age, years    |                |                 | 0.833 |               |               | 0.091 |
| <60           | 2595           | 2607            |      | 4593          | 4694          |     |
| ≥60           | 2833           | 2821            |      | 2961          | 2860          |     |
| Sex           |                |                 | 0.608 |               |               | 0.938 |
| Female        | 1323           | 1347            |      | 1680          | 1685          |     |
| Male          | 4105           | 4081            |      | 5874          | 5869          |     |
| Race          |                |                 | 0.777 |               | <0.001        |     |
| Black         | 498            | 505             |      | 923           | 1263          |     |
| White         | 4764           | 4745            |      | 6352          | 5989          |     |
| Others        | 166            | 178             |      | 279           | 302           |     |
| Location      |                |                 | 0.931 |               | 0.484         |     |
| Tongue        | 2297           | 2309            |      | 3264          | 3329          |     |
| Oropharyn     | 2007           | 1988            |      | 2717          | 2651          |     |
| Others        | 1124           | 1131            |      | 1573          | 1574          |     |
| Grade         |                |                 | 0.828 |               | 0.531         |     |
| Low           | 3367           | 3355            |      | 4829          | 4791          |     |
| High          | 2061           | 2073            |      | 2725          | 2763          |     |
| Stage         |                |                 | 0.756 |               | 0.907         |     |
| Localized     | 1283           | 1301            |      | 1957          | 1936          |     |
| Regional      | 3030           | 3042            |      | 4069          | 4094          |     |
| Distant       | 1115           | 1085            |      | 1528          | 1524          |     |
| Treatment     |                |                 | 0.581 |               | <0.001        |     |
| None          | 437            | 473             |      | 636           | 774           |     |
| Surgery alone | 1241           | 1220            |      | 2036          | 1887          |     |
| Radiation alone | 2126       | 2093            |      | 2653          | 2693          |     |
| Surgery with Radiation | 1624 | 1642 | 2229 | 2200 |       |
| Insurance     |                |                 | 0.532 |               | <0.001        |     |
| None          | 342            | 359             |      | 542           | 677           |     |
| Insurance(medicaid) | 5086   | 5069 | 7012 | 6877 |       |
| Composite SES |                |                 | 0.636 |               | 0.384         |     |
| Low           | 1137           | 1117            |      | 1711          | 1757          |     |
| High          | 4291           | 4311            |      | 5843          | 5797          |     |
**Figure 1**

Forest plot for CSS of patients with OPSCC according to Cox-regression multivariate analysis
Figure 2

Survival curves of patients with OPSCC according to marital status: A KM, $\chi^2=1037.044$, $P<0.001$; B Cox-regression method after controlling confounding factors, $\chi^2=9314.649$, $P<0.001$
Figure 3

Survival curves of patients with OPSCC according to marital status in different SEER stages. (A) localized stage: $\chi^2=126.885$, $P<0.001$ (B) regional stage: $\chi^2=689.966$, $P=0.001$; (C) distant stage: $\chi^2=233.965$, $P<0.001$. 
Figure 4

Survival curves of patients with OPSCC according to marital status in different composite socioeconomic status. (A) CSS in Low C-SES: $\chi^2=267.150, P<0.001$; (B) CSS in High C-SES: $\chi^2=760.968, P<0.001$.

Figure 5

Cancer-specific survival curves of patients with OPSCC before and after PSM. (A) Before PSM between married and widowed status, $\chi^2=658.938, P<0.001$; (B) After PSM between married and widowed status, $\chi^2=62.498, P<0.001$; (C) Before PSM between widowed and divorced, $\chi^2=49.389, P<0.001$; (D) After PSM between widowed and divorced, $\chi^2=18.673, P<0.001$. (E) Before PSM between single and widowed, $\chi^2=401.810, P<0.001$; (F) After PSM between single and widowed, $\chi^2=49.701, P<0.001$; (G) Before PSM between married and divorced, $\chi^2=43.256, P<0.001$; (H) After PSM between married and divorced, $\chi^2=27.428, P<0.001$; (I) Before PSM between married and single, $\chi^2=557.810, P<0.001$; (J) After PSM between married and single, $\chi^2=117.609, P<0.001$. 