Original Article

Marital Status and Head and Neck Cancer Outcomes

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BACKGROUND: The objective of this study was to examine the effects of marital status on stage at presentation, receipt of treatment, and survival in patients with head and neck cancer (HNC). **METHODS:** The Surveillance, Epidemiology, and End Results database was used to analyze 51,272 patients who were diagnosed with HNC from 2007 to 2010. The impact of marital status on cancer stage at presentation, receipt of definitive treatment, and HNC-specific mortality (HNCSM) was determined using multivariable logistic and Fine and Gray competing-risks regression models, as appropriate. **RESULTS:** Marriage had a protective effect against metastatic presentation of oral and laryngeal cancers (oral cancer: adjusted odds ratio [AOR], 0.72; 95% confidence interval [CI], 0.60-0.87; $P<.001$; laryngeal cancer: AOR, 0.53; 95% CI, 0.42-0.67; $P<.001$) but not against oropharyngeal, hypopharyngeal, or nasopharyngeal cancers. Among patients with nonmetastatic disease, married patients were more likely to receive definitive treatment (overall AOR, 1.77; 95% CI, 1.60-1.95; $P<.001$) and had a lower risk of HNCSM (overall adjusted hazard ratio, 0.72; 95% CI, 0.68-0.77; $P<.001$); these associations remained significant across all HNC sites. **CONCLUSIONS:** Among patients with oral and laryngeal cancers, those who are married are less likely to present with metastatic disease. In addition, married patients are more likely to receive definitive treatment and less likely to die from HNC across all HNC sites. This suggests that spousal support may have a role in the surveillance of visual and symptomatic HNC types and leads to higher rates of treatment and better survival across all HNC sites. ***Cancer*** **2015;121:1273-8.** *© 2014 American Cancer Society.*

KEYWORDS: head and neck cancer, marriage, Surveillance, Epidemiology, and End Results, cancer outcomes, cancer social support.

INTRODUCTION

There are an estimated 55,070 newly diagnosed cases of head and neck cancer each year.[1] Once diagnosed, social support for a patient diagnosed with head and neck cancer is of particular importance. Survivors of head and neck cancer often endure treatment that results in visual disfigurement, psychological distress, and functional disruption in mastication, swallowing, breathing, and speech.[2-4] Therefore, it has been demonstrated that social support positively affects the recovery of patients with head and neck cancer.[3,4]

The benefits of social support also extend to cancer outcomes. The protective effects of marriage on cancer stage at presentation and survival have been demonstrated across several major cancer sites, including breast, prostate, ovarian, and colon cancers as well as head and neck cancers.[5-12] Although the benefits of marriage on head and neck cancer outcomes have been suggested previously, the site-specific differences that potentially exist for cancers of the oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx have not been examined, making it is difficult to derive specific conclusions about the association between marital status and head and neck cancer outcomes.[5,13]

Examining and understanding the effects of marriage on head and neck cancer site-specific outcomes are pertinent to the construction of effective social support networks and head and neck cancer screening programs and guidelines. Therefore, the objective of this study was to examine the effects of marital status on stage at presentation, receipt of treatment, and survival in patients with oral, oropharyngeal, nasopharyngeal, hypopharyngeal, and laryngeal cancers.

MATERIALS AND METHODS

Study Population

We used the Surveillance, Epidemiology, and End Results (SEER) Program to identify 51,272 patients who were diagnosed with head and neck cancer from 2007 to 2010. The National Cancer Institute's SEER Program collects information on cancer incidence, prevalence, survival, and mortality of patients with cancer.[14] The SEER Program captures

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approximately 97% of incident cancers, and the 17 SEER tumor registries encompass approximately 28% of the US population. The inclusion period for this study was limited to the years from 2007 to 2010, because 2007 represents the year when additional, pertinent covariates were introduced into SEER.

Patient Characteristics

Patient characteristics were analyzed using the independent samples *t* test and the chi-square test, as appropriate. Age at diagnosis and sex were determined as provided by the SEER database.[14] Race was categorized into African American, non-Hispanic white, nonblack Spanish/Hispanic/Latino, Asian or Pacific Islander, Native American, and other as provided by the SEER data set.[14] Income was calculated as the median household income, whereas educational level was categorized as the percentage of residents aged $\geq$25 years who had at least a high school diploma; both were determined at the county level by linking to the 2000 US Census.[15] Residence type also was determined at the county level by linking to the 2003 US Department of Agriculture rural-urban continuum codes.[16] Insurance status was analyzed as a bivariate value (insured vs uninsured) as determined by the SEER data set.[14] Tumor classification (according to the American Joint Committee on Cancer [AJCC] TNM classification) and grade of tumor were determined as provided in the SEER data set.[14,17]

Study Variables

Head and neck cancer outcomes were analyzed in a site-specific manner and were broken into 5 cancer types: squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, nasopharynx, and larynx. The primary variable of interest was marital status, which was captured at the time of diagnosis and analyzed as a bivariate value (married vs unmarried). The outcomes of interest for each cancer type were cancer stage at presentation (metastatic vs nonmetastatic), receipt of definitive treatment, and head and neck cancer-specific mortality. Metastases were recorded according to the TNM classification system as defined by the *AJCC Cancer Staging Manual* (sixth edition).[17] Definitive treatment included surgery, radiation therapy, or a combination of surgery and radiation therapy in accordance with the National Comprehensive Cancer Network guidelines for head and neck cancers.[18] Head and neck cancer-specific mortality was determined according the SEER database.[14]

Statistical Analysis

Multivariable logistic regression was applied to measure the effect of marital status on presentation with metastatic disease. The multivariable model was adjusted for patient demographics (age at diagnosis, sex, and race) and socioeconomic factors (income, level of education, and residence type). After restricting the cohort to patients with nonmetastatic disease, multivariable logistic regression was applied determine whether there was an association between marital status and receipt of definitive treatment for patients with nonmetastatic disease. The multivariable model was adjusted for patient demographics (as listed above), socioeconomic factors (as listed above), and tumor characteristics (tumor classification and grade).[19] A multivariable sensitivity analysis also was completed in which we used other-cause mortality within 5 years of follow-up as a proxy for comorbidity to determine whether comorbidity had any influence on any observed association between marital status and receipt of treatment.[20]

Fine and Gray competing-risks regression was then used to model the impact of marital status on mortality from head and neck cancer among patients who had nonmetastatic disease after adjusting for the previously listed variables as well as receipt of definitive therapy.[21] Finally, the cumulative incidence of head and neck cancer-specific mortality stratified by marital status was generated from the competing-risks regression models described above and displayed graphically.[22] Point estimates and associated confidence intervals (CIs) were generated and compared using the Gray k-mean *P* value.

All *P* values were 2-sided. *P* values $\leq$ .05 were considered statistically significant. All CIs were stated at the 95% confidence level. All statistical analyses were computed using STATA 13.0 (StataCorp, College Station, Tex). This study was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board.

RESULTS

Cohort Characteristics

Of the 51,272 patients in the study cohort, 27,012 patients (52.7%) were married, and 24,260 (47.3%) were unmarried. In general, married patients were more likely to be men, non-Hispanic white, and come from a region with a higher education and median income level ($P < .001$ for all characteristics) (Table 1).

Impact of Marital Status on Head and Neck Cancer Outcomes

Once adjusted for patient demographics and socioeconomic factors, married patients with cancers of the oral cavity and larynx were significantly less likely to present with metastatic disease (oral cavity cancers: adjusted odds ratio [AOR], 0.72; 95% CI, 0.60-0.87; $P < .001$;

TABLE 1. Cohort Characteristics

	No. of Patients (%)		
Characteristic	Unmarried, N = 24,260	Married, N = 27,012	P^a
Age at diagnosis: Mean ± SD, y	60.9 ± 13.8	61.0 ± 12.0	.61
Sex			< .001
Men	16,908 (69.7)	21,500 (79.6)	
Women	7352 (30.3)	5512 (20.4)	
Insurance status			< .001
Insured	22,969 (94.7)	26,406 (97.8)	
Uninsured	1291 (5.3)	606 (2.2)	
Income: Mean ± SD, USD[b]	45,100 ± 11,200	46,300 ± 11,800	< .001
Completed HS: Mean ± SD, %[b]	78.9 ± 7.7	79.4 ± 7.8	< .001
Race			< .001
Non-Hispanic white	17,020 (70.2)	20,620 (76.3)	
African American	3983 (16.4)	1833 (6.8)	
Non-black Hispanic	1851 (7.6)	2007 (7.4)	
Asian/Pacific Islander	986 (4.1)	2246 (8.3)	
Native American	168 (0.7)	129 (0.5)	
Other	252 (1)	177 (0.7)	
Site			< .001
Oropharynx	744 (3.1)	613 (2.27)	
Hypopharynx	1358 (5.6)	1125 (4.2)	
Nasopharynx	1330 (5.5)	1810 (6.7)	
Larynx	7242 (29.9)	7964 (29.5)	
Oral cavity	13,586 (56)	15,500 (57.4)	
Metastatic disease			< .001
Yes	1050 (4.3)	807 (3)	
No	23,210 (95.7)	26,205 (97)	
Tumor classification[c]			< .001
T1	3865 (31.8)	5527 (40.2)	
T2	3585 (29.5)	4345 (31.6)	
T3	1956 (16.1)	1855 (13.5)	
T4	2746 (22.6)	2021 (14.7)	
Grade[c]			< .001
Well differentiated	1847 (15.2)	2199 (16)	
Moderately differentiated	6222 (51.2)	6751 (49.1)	
Poorly differentiated	3670 (30.2)	4345 (31.6)	
Undifferentiated	413 (3.4)	453 (3.3)	

Abbreviations: HS, high school; SD, standard deviation; USD, US dollars.
Continuous data were analyzed using independent-samples *t* tests, and chi-square tests/Fisher exact tests were used for categorical measurements.
County-level data were used for the income and education variables.
Data for tumor classification and grade indicate the proportions among patients who had nonmetastatic disease (N = 25,900; unmarried, n = 12,152; married, n = 13,748).

laryngeal cancers: AOR, 0.53; 95% CI, 0.42-0.67; $P < .001$). This association was not observed for cancers of the oropharynx, hypopharynx, or nasopharynx (AOR range, 0.88-0.97; $P \geq .630$ for all sites) (Fig. 1). After adjusting for the aforementioned variables in addition to tumor characteristics, married patients with nonmetastatic disease were significantly more likely to receive definitive treatment (overall AOR, 1.77; 95% CI, 1.60-1.95; $P < .001$) (Fig. 2). This association remained significant on sensitivity analysis when adjusting for other-cause mortality within 5 years as a proxy for comorbidity (AOR, 1.74; 95% CI, 1.58-1.93; $P < .001$) and remained significant when stratified across all 5 cancer types (AOR range, 1.59-2.49; $P \leq .020$).

Adjusting for the same factors plus receipt of definitive treatment, multivariable Fine and Gray competing-risks regression revealed a significantly lower risk of head and neck cancer-specific mortality for married patients (overall adjusted hazard ratio [AHR], 0.72; 95% CI, 0.68-0.77; $P < .001$). Again, this association remained significant across all 5 sites (AHR range, 0.64-0.77; $P \leq .037$) (Fig. 3). After a median follow-up of 19 months, cumulative incidence estimates of cancer-specific mortality were significantly lower for married patients compared with unmarried patients ($P < .001$) (Fig. 4). The 3-year cancer-specific mortality rate was 21.6% for married patients (95% CI, 20.6%-22.6%; $P < .001$) and 37.4% for unmarried patients (95% CI, 35.9%-38.9%; $P < .001$).

DISCUSSION

In this study, we observed that marriage had a significant protective effect against metastatic oral cancer and laryngeal cancer. Among patients with nonmetastatic disease,

married patients were more likely to receive definitive treatment across all 5 head and neck cancer sites. In addition, we observed that married patients with nonmetastatic disease had a lower risk of head and neck cancer-specific mortality across all head and neck cancer sites. The importance of this study is that the results highlight the significant impact marriage can have on stage of diagnosis, treatment, and survival of head and neck cancer by site. Previous literature examining the benefit of marriage on cancer outcomes for other cancer types have demonstrated that social support protects against late stage of presentation.[6,23-26] For oral and laryngeal cancers, this relation held true, because married patients were 28% to 47% less likely to present with metastatic cancer. In contrast, marriage did not have a protective effect for patients who were diagnosed with oropharyngeal, nasopharyngeal, or hypopharyngeal cancers. We hypothesize that these differences are a result of the visual and symptomatic changes that take place for both oral and laryngeal cancers, respectively. Specifically, oral cancers have the benefit of a visual diagnosis and, thus, may be detected at an earlier stage by a spouse. In a similar manner, hoarseness, dysphagia, otalgia, and changes to the voice are common symptoms of laryngeal cancer that can lead to early detection by partners or spouses.[27] This form of "spousal surveillance" may lead to subsequent encouragement to visit a physician, enabling patients to receive proper diagnosis and treatment in a timely manner.

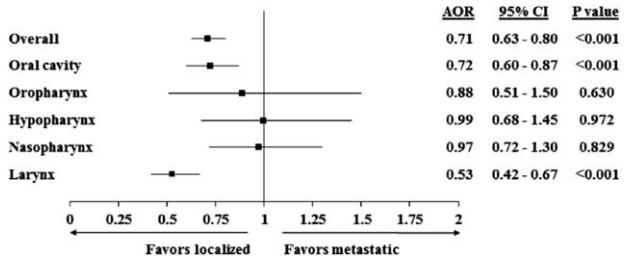

Figure 1. The effect of marriage on disease stage at presentation is illustrated in patients who were diagnosed with head and neck cancer from 2007 to 2010 (N = 51,272). AOR indicates adjusted odds ratio; CI, confidence interval.

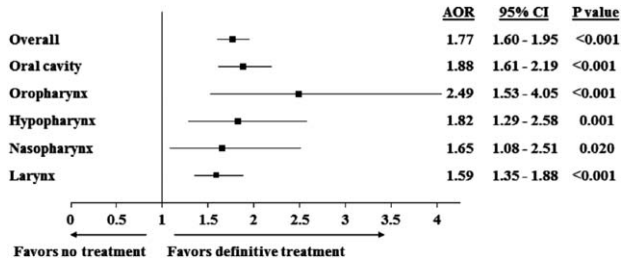

Figure 2. The effect of marriage on receipt of definitive treatment is illustrated in patients who were diagnosed with head and neck cancer from 2007 to 2010 (N = 25,900). AOR indicates adjusted odds ratio; CI, confidence interval.

If marriage exerts its beneficial effects through social support, then our data suggest that the integration of targeted social support mechanisms into the care of patients with head and neck cancer may improve treatment compliance and outcomes. Social support can also lead to the pursuit of immediate and aggressive treatment options.[6] The compounded detrimental effects on speech, nutrition, and appearance from head and neck cancer place an additional burden on an affected individual's spouse and, thus, may prompt a spouse to provide social support and advocate for effective treatment. In addition, the continual support provided by a spouse encourages adherence to prescribed treatment regiments.[5,28,29] With regard to treatment, we observed that married patients were from 59% to 149% more likely to receive definitive treatment. In turn, adherence to treatment regimens may have a significant effect on differences in cancer-specific survival by marital status. In our study, married patients with head and neck cancer had a 23% to 36% reduced risk of

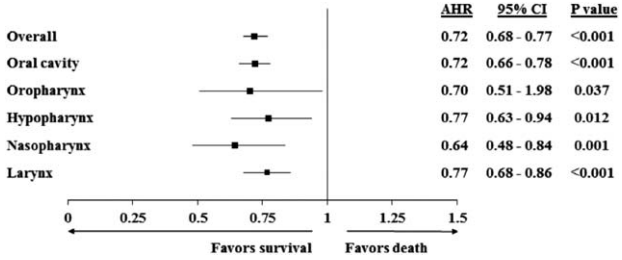

Figure 3. The effect of marriage on cancer-specific mortality is illustrated in patients who were diagnosed with head and neck cancer from 2007 to 2010 (N = 25,900). AOR indicates adjusted odds ratio; CI, confidence interval.

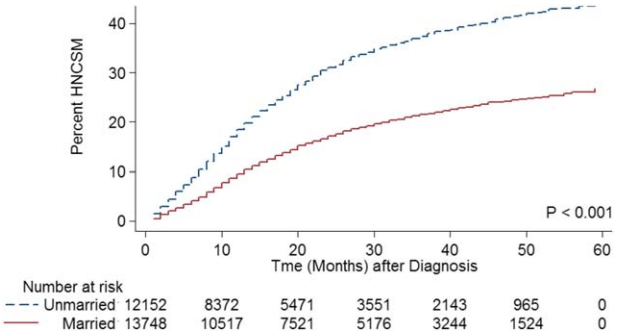

Figure 4. The cumulative incidence of head and neck cancer-specific mortality (HNCSM) is illustrated according to marital status in patients who were diagnosed with head and neck cancer from 2007 to 2010 (N = 25,900; Gray k-mean $P < .001$).

cancer-specific mortality. It is noteworthy that our results are consistent with a previous study in which married patients with head and neck cancer had the greatest relative reduction in cancer-related death among the top 10 leading causes of cancer-related death.[5] In this study, we examined a more current cohort that was twice in size and identified differences in stage at presentation when stratified by site.

These results should be viewed within the limitations of the data. First, the SEER database does not collect information on etiologic factors of head and neck cancer, such as smoking, alcohol, and the presence of human papillomavirus (HPV) type 16, which disproportionately affects white, middle-aged men and is associated with improved treatment outcomes and survival when detected with oropharyngeal cancer.[30-33] Although it is unclear whether the prevalence of HPV in oropharyngeal cancer differs between married and unmarried patients, a very small number of patients (approximately 5%) in the current study had oropharyngeal cancer; thus, any potential effect of HPV status would have been limited. SEER also does not provide information on the quality of treatment at various institutions, and this may contribute to differences in outcomes. In addition, dental benefit status is not captured within SEER. Subsequent lack of surveillance by an oral health provider may have contributed to the differences in stage of presentation observed in this study. The inclusion of medical insurance status also limited our study period (2007-2010) and median follow-up (19 months). Despite the short follow-up, significant differences in cancer-specific mortality and other-cause mortality were observed. Future studies with the benefit of longer follow-up should examine whether our trends hold over time.

Despite the stated limitations, our study demonstrates that, compared with unmarried patients, married patients are less likely to present with metastatic oral and laryngeal cancers, more likely to receive definitive treatment across 5 head and neck cancer sites, and less likely to die from 5 head and neck cancer sites, suggesting that spousal support may have a role in the surveillance of visual and symptomatic head and neck cancers and leads to higher rates of treatment and better survival across all head and neck cancer types. Integrating social support mechanisms into the comprehensive treatment and care for patients with head and neck cancer should be a targeted priority for providers and policymakers.

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