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Age and stage as determinants of treatment for oral cavity and oropharyngeal cancers in the elderly

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SUMMARY

Background: We investigate treatment selection for oral cavity and oropharyngeal (OC&OP) cancers to understand factors that influence treatment selection.
Methods: We studied 7023 patients, ⩾66 years, diagnosed with a first primary OC&OP cancer using SEER–Medicare data. Multinomial logistic regression was to model treatment selection, controlling for other factors.
Results: Most patients with OC cancer were treated with surgery alone (56.5%); most patients with OP cancer were treated with chemotherapy and radiation (28.9%). Age, stage and site were the most important predictors of treatment selection. As age increased from 70 to 81 (the interquartile range), treatment shifted toward surgery alone (OR = 1.26; CI: 1.08–1.46) and no treatment (OR = 1.5, 95% CI: 1.25–1.80), and away from combined surgery, radiation and treatments involving chemotherapy.
Conclusions: Age, stage, and site are the most important determinants of treatment selection for patients with OC&OP cancers. Increasing age and stage drive treatment toward non-surgical options and no treatment at all.

Introduction

The increasing prevalence of human papilloma virus (HPV) infection has led to a rapid increase in cancers of the oral cavity and oropharynx (OC&OP) among people aged 40–59 [1]. However, OC&OP cancers are most concentrated among older patients, with a median age at diagnosis of 62 years [2]. Additionally, more than half of the approximately 7890 OC&OP cancer deaths in 2012 occurred in patients 65 years of age and older [2].

As with most malignant neoplasms, the prognosis for patients with cancers of the OC&OP is based primarily on the extent of the tumor and specific subsite at the time of presentation as well as the presence of regional or distant metastasis. Five-year survival rates range widely, from 73% for localized tumors of the lip to only 12% for metastatic tumors of the oropharynx [3]. It has been shown that cancers of the OC&OP carry a different prognosis despite similar morphologic stage [3–7]. Furthermore, recent evidence indicates that age >65 years is independently associated with poor prognosis among patients with OP cancer [8].

The treatment paradigm for OC differs from that of OP cancer. OC cancer is typically treated with surgery, while radiation is reserved for adjuvant therapy to enhance loco-regional control, primary treatment in patients unable to tolerate or unsuited for surgery, or salvage treatment of recurrent or persistent disease [9]. In contrast, until recently chemotherapy and radiation was used primarily for all but the smallest OP tumors, in part because of the potential morbidity of OP resections. Moreover, surgery, chemotherapy, and radiotherapy may be frequently complicated by locoregional disease persistence and significant long-term functional deficits in speech and swallowing [10,11]. While the treatment options for OC&OP are well-known, treatment choice has not been systematically studied, particularly in the elderly population. In this study we use data from the combined Surveillance Epidemiology and End Results (SEER) and Medicare data to systematically study factors that affect choice of treatment for

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OC&OP cancers to better understand which treatments patients receive and what variables influence the treatment selection.

Methods

Data

Data for this study were obtained from the SEER–Medicare linked database, which combines tumor registry data from the National Cancer Institute's (NCI) SEER program for patients who are covered by Medicare with their Medicare billing records [12]. The SEER–Medicare data contain tumor registry data on 54,955 patients who were diagnosed with a first primary tumor of the OC (lip, tongue, floor of mouth, gum, and other mouth) or OP (tonsil and oropharynx) between 1973 and 2005. Claims data are only available beginning in 1986 and are only available for certain types of services since 1994. We therefore limited our sample to patients who were diagnosed with a first primary tumor of the OC or oropharynx between 1995 and 2005. We further restricted cases to patients aged 66 and older and excluded patients for whom the diagnosis of cancer was obtained on autopsy or from a death certificate only. In addition, patients enrolled in a health maintenance organization (HMO) at or after the cancer diagnosis were excluded since these patients do not have any Medicare billing records. The final sample contained 7023 patients. The human subjects protocol and procedures were reviewed and approved by The Pennsylvania State University Institutional Review Board.

Outcomes and covariates

Our aim was to identify factors associated with treatment choice for patients with OC&OP cancers. The dependent variables for these analyses were treatment indicators. Treatment indicators were mutually exclusive for surgery alone, radiation alone, a combination of surgery and radiation, chemotherapy in combination with radiation (regardless of surgery), chemotherapy without radiation (regardless of surgery), and absence of any treatment. Radiation and surgery were defined according to the SEER tumor registry data. Chemotherapy was determined from Medicare billing records. Specifically, all Medicare claims files were searched for any record with a Healthcare Common Procedure Coding System (HCPCS) code of 964.xx, 965.xx, or Q0083-Q0085, an ICD-9 diagnosis code of V58.1, V66.2, V67.2, or an ICD-9 procedure code of 99.25 [13]. Patients with at least one of these claims in the window ranging from 1-month prior to diagnosis up to 4 months after diagnosis were classified as having received chemotherapy. Patients in which a chemotherapy claim was made at least 2 months prior to diagnosis were excluded from the analysis. Claims prior to diagnosis were included because there can be lags in reporting. There were only 2 patients in the final data set who had chemotherapy listed prior to diagnosis; the remaining patients had chemotherapy beginning on the date of diagnosis or later (within 4 months).

We distinguished between OC cancer, which included tumors of the lip, oral tongue, floor of mouth, and gum and other mouth, and tumors of the OP, which included tumors of the base of tongue, tonsils, and oropharynx. Our analyses controlled for demographic characteristics, disease characteristics, and comorbidities. Demographic variables included patient age at diagnosis, gender, race/ethnicity (black, white, other), year of diagnosis, marital status, and geographic location. Disease variables included cancer site and morphologic extent of malignant disease defined using the SEER historic stage (local, regional, distant metastasis, unstaged) [14]. We controlled for comorbidities using the sum of the number of Agency for Health Care Research and Quality (AHRQ) comorbidities for each patient up to one year prior to diagnosis [15,16].

Statistical methods

The statistical analysis was designed to model the relationship between treatment choice, age, stage, and site of disease, controlling for demographic characteristics and comorbidities. We first presented descriptive statistics to summarize the sample. We used chi-squared tests to test whether the distribution of disease variables across treatment types was significantly different.

We used multinomial logistic regression, which is a generalization of logistic regression to outcomes with more than two categories, to model the probability of treatment choice by age, site, stage and other patient characteristics. First, we tested several models of probability of treatment choice as a function of age and site. The best fitting model was a quadratic function of age (i.e. age and age squared) with no interaction term. Next, we added stage to the model as a categorical effect with localized and in situ stages combined and specified as the reference group. Again several model specifications were tested, but the best fitting model was the one with no interactions, a quadratic effect for the log odds of age, and main effects for site and stage. Lastly, we included all other demographics and patient characteristics in the model, to determine whether the associations we observed among age, site and stage remained significant after adjusting for other factors.

Results

The characteristics of patients with OC&OP cancers are summarized in Table 1. The average age is almost 76 years, and patients were predominantly male (58.8%), white (85.9%) and living in a metropolitan area. Most patients had no comorbidities (82.8%), however, among those who did the most common were hypertension (10.5%) and chronic pulmonary disease (5.9%).

Among patients with OC disease, the primary treatment was surgery alone (56.5%), followed by combined surgery and radiation (16.8%) or single modality radiation therapy (11.8%) (Table 2). Patients with OP cancer were primarily treated with chemotherapy and radiation (28.9%) or with single modality radiation therapy (27.9%), followed by surgery plus radiation (17.1%). Nearly 8.1% of patients with OC cancers and 12.4% of patients with OP cancers received no treatment at all.

Site and stage of disease were strongly associated with treatment choice. Single modality surgery was the primary treatment for patients with disease of the lip (87.4%), oral tongue (54.5%), floor of mouth (44.4%) and gum and other mouth (43.0%) (Table 2). Treatment choice for the OC was also largely driven by stage of disease. Single modality surgery was the most common treatment for all stages but other treatments were also used.

The most frequent treatments for OP cancers were radiation alone or in combination with chemotherapy. Increasing stage was associated with lower likelihood of radiation alone, and greater likelihood of chemotherapy plus radiation. Approximately 12.4% of patients with disease of the oropharynx (across all stages) received no treatment; of patients with distant disease of the oropharynx, 20.2% received no treatment at all.

Fig. 1A presents the trends in treatment between 1995 and 2005. Among patients with OC cancers, treatment choice has remained largely stable, with most patients receiving surgery alone. Patients with OP cancers, however, were more likely to be treated with chemotherapy and radiation, and less likely to be treated with surgery and radiation as time progressed.

The predicted probabilities of treatment choice from the multinomial regression model that included age and site as predictors are shown for OC diseases in Fig. 1B. For OC cancers, as age increased a patient's probability of receiving surgery alone was relatively unchanged. However, the probability the patient was