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The effects of geography on survival in patients with oral cavity squamous cell carcinoma

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SUMMARY

Objective: To assess the survival outcomes of oral cavity squamous cell carcinoma (OCSCC) by differing geographical location.
Methods: Demographic, pathologic, treatment, and survival data was obtained from OCSCC patients from 1998–2010 in Alberta, Canada. 554 patients were included from 660 OCSCC patients. Overall, disease-specific, and disease-free survivals were estimated with Kaplan–Meier and Cox regression analyses. Patients were grouped by geographic locations.
Results: Patients from urban locations had improved overall, disease-specific, and disease-free survival compared to rural locations ($p < 0.05$). Two and five year estimates of overall survival were significantly higher in the urban cohort at 84% and 78%, versus rural with 48% and 44%, respectively ($p < 0.05$). Disease-specific and disease-free survival rates were also superior in the urban group ($p < 0.05$). Diagnosis to treatment time for all 3 geographical groups was not found to be statistically significant ($p > 0.05$).
Conclusion: This study shows that patients with OCSCC living in urban settings have improved survival compared to rural groups.

Introduction

Cancer has become the leading cause of death in Canada [1]. Increasing disparities in socio-economic status as well as access to cancer care services are some of the primary driving forces behind this rise [2]. These inequities are especially prevalent in head and neck mucosal cancers (HNC) where access to treatment programs and end-of-life care are linked to a variety of socioeconomic, demographic and geographic factors [1,2].

Rural residence has traditionally been associated with lower than average life expectancy compared with urban residence [3]. Due to their unique geographical location, rural HNC patients are often theorized to be far away from tertiary care cancer centers and thus at a disadvantage in access to advanced medical care [4,5]. Additional burdens including disruptions in family life, work, and financial security not only influences quality of life but are some of the major disparities that differ between rural and urban HNC patients [2].

This is especially pertinent in oral cavity squamous cell carcinoma (OCSCC). Being the most common site for HNC, over 3000 new cases will be diagnosed in Canada in 2012 alone [1]. To date, there is no conclusive study to show any disparities between geographical locations in HNC patients, especially those that are site specific for the oral cavity. Therefore, the objective of this study was to assess survival outcomes in OCSCC for different geographical locations in Alberta, Canada. The primary goal was to determine if residing in an urban center improved survival. The secondary goal was to identify factors associated with survival differences.

Methods

Ethics approval was granted by the University of Alberta's Health Research Ethics Board (HREB) and the Alberta Cancer Board.

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[1] NB: The corresponding author has full access to the data in this study and takes responsibility for the integrity of the data and accuracy of the data analysis.

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Patients

Inclusion criteria were defined as:

1. Biopsy-proven OCSCC.
2. Treatment in Alberta with curative intent.
3. Residents of Alberta > 18 years of age.

Exclusion criteria were defined as

1. Previous HNC with or without treatment.
2. Refusal of prescribed treatment.
3. Treatment with palliative intent.
4. Incomplete data sets from chart review.

Data collection

Cancer surveillance data was retrieved by a clinical data analyst from Alberta Health Services medical records. All patients diagnosed with an OCSCC between January 1, 1998 and January 1, 2010 were identified in the Alberta Cancer Registry (ACR). The ACR, established in 1942, is a population-based registry that records and maintains data of all new cancer cases, their treatments, and resulting deaths occurring in the province. The ACR is operated by Alberta Health Services Cancer Care and follows patients longitudinally and prospectively [6].

Demographic, survival and clincopathologic data were extracted from the ACR database. A physical review of outpatient, inpatient, and cancer clinic records was undertaken to confirm data accuracy and extract relevant patient, tumor, treatment, follow-up, survival data, as well as Eastern Cooperative Oncology Group (ECOG) performance scores [7]. Age adjusted Charlson Comorbidity Index (CCI) scores [8], which were not included in the ACR database, were calculated using relevant comorbidities taken from chart review. Tumors were staged via AJCC criteria and reported by a head and neck pathologists [9]. Date of diagnosis was defined as the date of pathologically confirmed OCSCC. Inclusion criteria followed by exclusion criteria were then applied to each patient's data within the database to create a final data set for analysis.

Grouping

Groups were created based on where a patient was residing at the start of cancer treatment. Two types of groups were created,

Geographic groups

Three geographical groups were created for the province of Alberta: (1) Rural, (2) Intermediate, and (3) Urban. Rural was defined as any location with a population of less than 10,000. Intermediate locations were defined as populations between 10,000 and 100,000. A city was any location with a population greater than 100,000. Geographic grouping was based on Statistics Canada 2011 Survey classifications [10].

Distance from cancer center groups

Three distances from cancer centers were set as: (1) within 50 km (<50 km), (2) between 50 and 100 km (50–100 km), and (3) greater than 100 km (>100 km). Distances were calculated from the place of residence to the cancer center responsible for patient treatment and follow-up.

Treatment

A total of five treatment groups were analyzed: (1) primary surgery (S), (2) primary radiotherapy (RT), (3) primary chemoradiotherapy (CRT), (4) surgery followed by adjuvant radiotherapy (S-RT), and (5) surgery followed by adjuvant chemoradiotherapy (S-CRT). Surgical resections consisted of tumor ablation with variations of primary closure, locoregional or free tissue transfer reconstruction, and uni- or bilateral neck dissection. Patients receiving RT or CRT for metastases or palliation were not included. Failed CRT or RT patients that had salvage surgery were analyzed in an intent to treat style as part of their original group. S-RT patients underwent surgical resection and adjuvant RT within 6–8 weeks post-operatively. S-CRT patients received surgical resection followed by adjuvant CRT within 6–8 weeks of their operation. Doses for curative RT ranged from 6300 to 8000 Gy and for adjuvant RT from 5500 to 7000 Gy. Cisplatin or carboplatin based CRT protocols were used exclusively for all patients.

Outcomes

The primary outcome measure was overall survival. This was calculated as the time from the first date of primary treatment to the date of death or last known date the patient was alive. Secondary outcomes included disease-specific and disease-free survival as per geographic groups. Disease-specific survival was defined as the time from the first day of treatment to death as a result of OCSCC. Death caused by the primary cancer was therefore considered to be disease-specific death. Disease-free survival was calculated from the first day of primary treatment to the date of OCSCC recurrence anywhere in the body. Thus, if patients died without any evidence of disease, they were considered disease free at the time of death.

Follow-up

All patients were followed at regional cancer treatment centers at regular intervals following treatment. Dates of follow-up, up to November 1, 2012 were recorded. Patients who were suspected to have disease recurrence underwent a metastatic workup including appropriate imaging, endoscopy and biopsy as per standardized institutional guidelines.

Statistical analysis

Baseline characteristics were compared using standard modes of comparison between multiple groups. Continuous data was analyzed using analysis of variance (ANOVA), with a Bonferoni correction factor for multiple comparisons. Categorical data was compared using the chi-squared test. Overall, disease-specific and disease-free survival rates were performed using Kaplan–Meier analyses to determine estimated actuarial survival rates. The log-rank test was employed to determine the presence of significant differences between different demographic groups. Cox regression analysis, with covariates of age, gender, CCI, overall staging, treatment modalities, and ECOG performance scores was performed for overall, disease-specific, and disease-free survival. Patients were analyzed by group: (1) geographical locations and (2) distance from cancer center. Level of significance was set as $p < 0.05$. Analyses were performed with SPSS Statistics 19.0 (SPSS Inc, Chicago, IL).

Results

660 Patients were diagnosed with OCSCC in Alberta from 1998 to 2010. 106 were excluded for the following reasons: 21 refused