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Original Research Article

In Patients with Resectable Oral Squamous Cell Carcinoma of the Tongue, Prognostic Factors, Failure Patterns, and Survival Analysis Were Examined

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Abstract

Purpose: Resectable oral tongue squamous cell carcinoma has little evidence on treatment results (OTSCC). In this investigation, treatment outcomes for resectable OTSCC were evaluated, failure patterns were investigated, and potential clinicopathological prognostic variables influencing treatment outcomes were identified.

Materials and Methods: It is a retrospective review of 202 patients with resectable OTSCC who underwent main upfront surgery, adjuvant radiation, and concomitant chemotherapy as needed.

Results: The average follow-up period was 35.2 months (range, 1.2 to 99.9 months). Locoregional control (LRC) lasted an average of 84.9 months (95% confidence interval: 67.3-102.4). The LRC rate across three and five years was 68.5% and 58.3%, respectively. Increased pT stage, increased pN stage, and the presence of extracapsular extension (ECE) were substantially linked with worse LRC, according to multivariate analysis. At the time of study, the median overall survival time (OS) had not been attained. The 3- and 5-year OS rates were, respectively, 70.5% and 66.6%. Increasing pT stage and the presence of ECE were strongly related with a worse OS, according to multivariate analyses.

Conclusion: In resectable OTSCC, locoregional failure continues to be the primary factor in treatment failure. Given the low LRC and OS, there is potential to significantly improve the prognosis. Strong prognostic variables include the pathological T-stage, N-stage, and ECE. To confirm whether adjuvant therapy improves treatment outcomes in instances with lymphovascular invasion, depth of invasion and perineural invasion and to assist doctors in customising adjuvant therapy, more study is needed.

Keywords: Head neck, Oral cancer, Tongue, Radiotherapy, Treatment outcome, Prognosis.

Introduction

The prevalence of oral tongue squamous cell carcinoma (OTSCC), particularly in younger people, is rising, most likely as a result of increased cigarette and alcohol use. While locally progressed resectable disease is treated with mixed modality therapy, which involves surgery followed by adjuvant radiotherapy (RT) or chemoradiation (CRT), early stage OTSCC is treated with single modality

therapy, preferably surgery [1,2,3,4]. Several clinicopathological prognostic variables for oral cavity squamous cell carcinoma (OCSCC) have been discovered, although the majority of these have only been reported in research on mixed patient populations that included all oral cavity subsites [5,6]. Data is limited for OTSCC per se. Since OTSCC is on rise and treatment outcome of OTSCC has been found to be poorer than that of carcinoma arising from other subsites of oral cavity [7,8], it is important to identify clinicopathological factors for carcinoma arising from this subsite. The aim of this study was to measure the treatment outcomes, explore the failure patterns, and identify the potential clinicopathological prognostic factors affecting treatment outcomes for resectable OTSCC.

Methods

The study was authorised by our institution's institutional ethics committee. Patients with locally advanced and resectable OTSCC who underwent primary surgical resection of the original tumour and regional lymph nodes at this institution between January and February 2022, with or without cervical nodal involvement, met the inclusion criteria.

An Eastern Cooperative Oncology Group performance status of 2, neoadjuvant chemotherapy given before primary surgical resection, surgical resection carried out with palliative or debulking intent, recurrent head and neck cancers, and a prior history of radiation therapy to the head and neck area were among the exclusion criteria. Although the staging and management of the study were conducted using the American Joint Committee on Cancer (AJCC) 7th edition, prognostic variables were examined using the AJCC 8th edition. Adjuvant RT was administered within 4 to 6 weeks from the date of surgery depending on the high-risk features recorded in the histopathological report of the resected specimen. As per institutional policy, the following were the indications for adjuvant RT: pathological T3 or T4 stage, node positivity (even a single node), positive resection margins (<1.0 mm), close surgical margins (≥1.0 mm to ≥4.0 mm), perineural invasion (PNI), and lymphovascular invasion (LVI). Depth of invasion (DOI) of >4.0 mm was considered as an indication for adjuvant RT depending on the individual policy of treating physicians. For patients with positive resection margins or extracapsular extension, weekly cisplatin (40.0 mg/m2) or carboplatin (area under the curve 2) treatment was given (ECE). Patients' weekly cisplatin doses were first taken into account when planning adjuvant CRT. Elderly patients or those deemed ineligible for cisplatin received carboplatin or cetuximab instead.

Patients received simultaneous-integrated boost intensity-modulated RT or two-dimensional conventional RT as treatment (SIB-IMRT). All patients received standard fractionation. Surgery bed with a positive margin or a nodal area with ECE received 66 Gy for SIB-IMRT. 30 portions of 60 Gy were administered to surgical beds lacking positive margins or nodal areas without ECE. Elective nodal regions were given 54 Gy in 30 fractions. When two-dimensional parallel opposed shrinking field technique was used, we delivered 50 Gy in 25 fractions to elective nodal regions and boosted surgical bed without margin positive or nodal regions without ECE to 10 Gy in 5 fractions. Surgical bed with positive margin or nodal region with ECE was boosted to another 6 Gy in 3 fractions.

Statistical Analysis

The statistical programme for the social science system (SPSS version 20; IBM SPSS, Armonk, NY, USA) was used for all statistical analyses, and a p-value of less than 0.05 was regarded as statistically significant. All of the provided p-values refer to two-sided testing. Clinical and pathological categorical baseline data were presented as frequencies and

corresponding percentages. The outcomes were determined using the Kaplan-Meier product-limit approach and were locoregional control (LRC) and overall survival (OS). Univariate analysis of LRC and OS was performed on the following clinical and histopathological factors selected based on results from previous studies on oral cavity cancer: age, sex, addictions (tobacco smoking, tobacco chewing and/or alcohol consumption), tumor grade, pathological T (pT) stage, pathological N (pN) stage, PNI, LVI, resection margin status, DOI, and ECE. Multivariate Cox proportional hazards regression analysis was performed to estimate the impact of known relevant prognostic factors.

Results

202 patients who met the inclusion and exclusion criteria had their medical records examined. The average follow-up period was 35.2 months (range, 1.2 to 99.9 months). 95% confidence interval: 67.3-102.4 months; the median length of LRC was 84.9 months. The rates for the 3- and 5-year LRC were, respectively, 68.5% and 58.5%. Increased pT stage, increased pN stage, and the presence of PNI, LVI, and ECE were all significant unfavourable prognostic variables for LRC, according to a univariate analysis. However, multivariate analysis revealed that worsening LRC was substantially correlated with worsening pT stage, worsening pN stage, and the presence of ECE. The median duration of OS was not reached at the time of analysis. The 3- and 5-year OS rate was 70.5% and 66.6, respectively. Univariate analysis revealed that increasing pT stage, increasing pN stage, presence of LVI, DOI of >20 mm, and ECE were poor prognostic factors for OS. However, multivariate analysis using Cox proportional hazard ratios showed that increasing pT stage and the presence of ECE were significantly associated with a poorer OS.

Majority of percent patients completed planned treatment. At the time of analysis, 74 patients (36.6%) had developed recurrence. Of these, 33 patients (44.5%) experienced tumor recurrence in the primary site alone, 23 (31.1%) experienced recurrence in the nodal region alone, 3 (4.0%) experienced recurrence in the primary site and nodal region, and 15 (20.2%) had distant metastases most common being lung followed by bone.

Discussion

In this study, LRC and OS, failure patterns, and numerous prognostic clinical and pathological variables affecting LRC and OS for OTSCC are explored. Given that over a third of recurrence in this analysis was locoregional, the study provided additional proof that locoregional recurrence continues to be a key cause of treatment failure in this population of patients. Therefore, careful consideration should be given to identifying patients with a high risk of recurrence based on clinical and pathological criteria, since these patients may benefit from further therapy in the form of adjuvant RT or CRT. Although there were 38.6% patients in the current study who were found to have pathological stage III/IV, more than two-thirds of patients from the entire cohort received adjuvant RT because of combination of other risk factors on surgical histopathological specimen examination. Approximately one-fourth amongst those who received adjuvant RT also received concurrent chemotherapy (CCT).

According to numerous studies with sizable sample populations, including all subsites of the oral cavity taken together [9–12], gender may have an impact on the treatment's result. According to this research, women have a higher chance of surviving. The current study did not show any association with outcomes in line with Garavello et al. [13] who particularly looked at the influence of gender on OTSCC similar to our study and found that

gender does not influence prognosis in this subsite. Age whether as continuous or categorical variable was not found to affect outcome in OTSCC in this study. [14]

Alcohol use and smoking are predictive factors for head and neck cancer, according to a number of studies [15–18]. In a prospective research, Sawabe et al. [19] examined OTSCC as a whole and found that patients with OTSCC who underwent surgery had a strong inverse relationship between alcohol intake and prognosis. However, we did not find these habits be a prognostic factor in Indian population particularly looking at OTSCC. Our results are similar to that of a study done by Thiagarajan et al. [20] on similar cohort of patients as ours (Indian patients with OTSCC), that habits (including alcohol, smoking and tobacco chewing) does not affect the OS. [21-23]

The reported 5-year OS was 65% in the investigation by El-Husseiny et al. [39] on OTSCC (T1-4 N0-3). Patients treated for T1-2 N0 OTSCC had a 5-year OS of 60.9%, according to Rusthoven et al. [7]. Even though OTSCC had a worse prognosis than malignancies that originated in other parts of the oral cavity, this study's 5-year OS and LRC figures were 66.6% and 58.3%, respectively. This study showed the survival outcome of OTSCC to be affected by increasing T stage, more than two clinically positive nodes, ECE of lymph node metastasis and LVI on univariate analysis. These findings have also been reported by others [24]. However, multivariate analysis revealed increasing pT stage and presence of ECE to be significantly associated with overall survival. [25]

This study's shortcomings include possible bias brought on by its retrospective nature. Although the treatment protocols used at our institute are standardised, there are still significant variations in the indications for adjuvant therapy in OCSCC dependent on the treating oncologist's personal experiences, particularly with relation to DOI. A strength of this study is its large cohort of patients with squamous cell carcinoma limited to oral tongue subsite only, taken from one of the largest and most exclusive cancer research centers in the country. Furthermore, the fact that all surgical and histopathological reporting was done at a single institute may have helped to reduce bias. [26-28]

Conclusion

In summary, locoregional failure continues to be the major contributing factor to treatment failure in resectable OTSCC. Given the low LRC and OS, there is potential to significantly improve the prognosis. Strong prognostic variables include the pathological T-stage, N-stage, and ECE. If adjuvant therapy improves treatment results in patients with LVI, PNI, and DOI and assists doctors in customising adjuvant therapy, more study is needed to validate this.

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