

Abstract

Malignancies of the retromolar trigone (RMT), an oral cavity subsite, are often diagnosed at late stage and carry a poor prognosis. This retrospective cohort study evaluated the difference in overall survival (OS) in 2,877 patients with RMT squamous cell carcinoma (SCC) treated with surgery alone versus surgery plus postoperative radiotherapy (PORT) versus surgery plus postoperative chemoradiotherapy (POCRT) using a multivariate Cox proportional hazards model. Treatment with surgery + PORT +/- chemotherapy appears to be associated with significantly improved OS compared to treatment with surgery alone for advanced malignancies of the RMT.

Introduction

The RMT is a relatively uncommon location for oral cavity squamous cell carcinoma (OCSCC). The triangular mucosal area of the oral cavity lies posterior to the region of the third molars and is in continuity with the anterior tonsillar pillar and buccal mucosa.¹ Most tumors are diagnosed as SCC.² In a review of 20,647 patients with OSCC, RMT was the primary subsite in only 1,879 (9.1%) cases.³ Often presenting in a late stage, RMT primaries portend a poor prognosis.^{1,4} Management of RMT SCC can be controversial, until recently guided by individual case series.

In 2018, Rizvi et al. published the first multicenter population-based study of RMT SCC treatment, finding improved survival in patients treated with surgery. However, combined surgery and adjuvant radiation therapy (RT) did not independently predict improved survival.⁵ Others have suggested favorable outcomes with primary non-surgical treatment.⁶ Given the contradictory data from these studies, a larger, more robust data set is needed to guide treatment. This study gleaned a large sample of multicenter data to conduct survival analysis of patients with RMT SCC treated with either surgery alone, surgery plus (PORT), or surgery plus POCRT. The primary objective was to determine which treatment combination provides improved overall survival.

Methods

Patients (age >18) with a diagnosis of SCC of the RMT, who were treated with surgery as the primary treatment modality between 2010-2015 as recorded in the National Cancer Database (NCDB) were included in the cohort. Patients were treated with surgery alone as primary modality or received PORT vs POCRT. Exclusion criteria included those with metastatic disease (M0) or unresectable disease.

The primary outcome was OS, which was defined as the duration of time following the initial diagnosis at which the patient passed away or contact was lost following definitive treatment. Secondary outcomes included 2-and-5-year OS. Subgroup analyses were performed among groups of patients with T1/2 tumors versus T3/4 tumors, and overall stage I/II disease versus overall stage III/IV.

Statistical Analysis

Multivariate Cox proportional hazards model was constructed to compare OS among patients in the 3 treatment groups. Covariates included age, sex, presence of histological lymphovascular invasion (LVI), facility setting (academic/community), surgical margins, T classification and C/D Score. Subgroup analyses were performed in which patients were stratified by tumor classification (T1/T2 or T3/T4) and overall stage (stage I/II or stage III/IV) to compare OS between patients treated with surgery alone vs surgery with PORT vs surgery with POCRT. Analysis was performed in Stata (StataCorp, LLC, College Station, Texas). Statistical significance was considered at $p < 0.05$.

Results

2,877 patients with primary SCC of the RMT were included in the final cohort. There were 1,415 (50%) patients treated with surgery alone, 870 (30%) patients treated with surgery plus PORT, and 572 (20%) treated with surgery plus POCRT between years 2010-2015. 2,153 patients (75%) had complete data on overall clinical staging. Of these patients, 468 (22%) were clinically stage I, 435 (20%) were classified as stage II, 263 (12%) were stage III, and 987 (46%) were stage IV.

Treatment Group Analysis

Patients treated with surgery + PORT had significantly improved OS compared to patients who underwent definitive treatment with surgery alone (relative hazard: 1.25, 95% CI: 1.01, 1.54, $p=0.042$). In addition, patients in the surgery + POCRT group had significantly improved OS compared to surgery alone (relative hazard: 1.89, 95% CI: 1.45, 2.43, $p<0.001$), Figure 1.

Subgroup Analysis

Patients with T1 or T2 classifications had no significant difference in adjusted OS with surgery plus PORT ($p=0.331$), nor with surgery plus POCRT ($p=0.134$) compared to surgery alone. Patients with T3 or T4 tumor classifications experienced significantly improved adjusted OS in the surgery plus PORT group (relative hazard 1.39, 95% CI: 1.05, 1.84, $p=0.022$) and in the surgery plus POCRT group (relative hazard 2.27, 95% CI: 1.66, 3.15, $p<0.001$) compared to with surgery alone.

Cox regression analysis revealed no significant survival improvement for patients with RMT SCC treated at an academic center compared to those treated at a non-academic center ($p=0.313$),

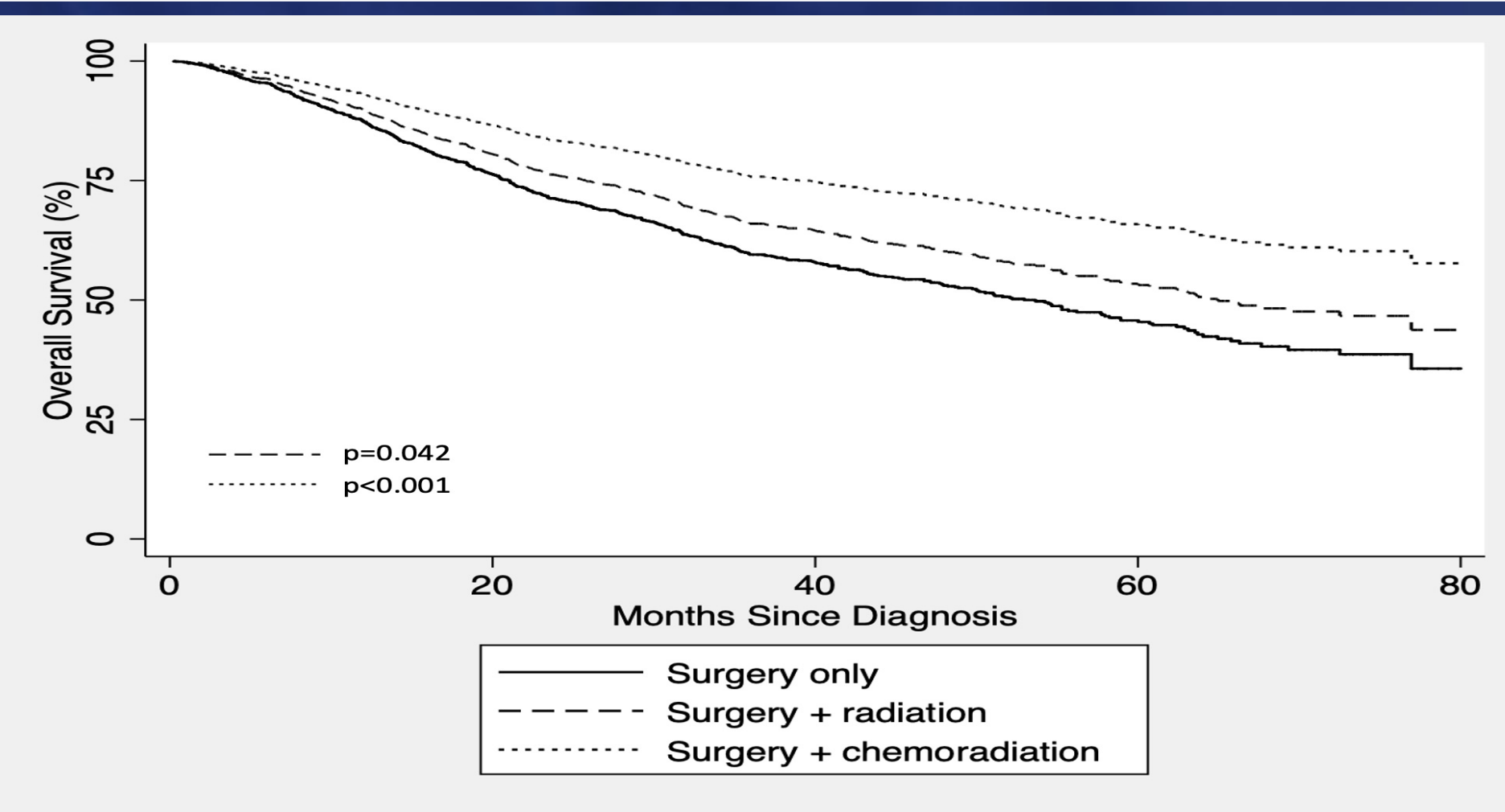


FIGURE 1. Cumulative Survival Stratified by Treatment Subtype. The inverse Cox proportional hazard was plotted at average values for all covariates in our model. Probability of overall survival is shown on the Y axis, and time since diagnosis (in months) is shown on the X axis.

Discussion

1. The primary outcome of this study suggests improved OS for patients with malignancies of the RMT when treated with surgery and postoperative adjuvant therapies, especially amongst those with advanced disease (T3/T4).
2. This finding is consistent with that of Rizvi et al, who showed that in patients with tumors > 4cm, those treated with surgery and PORT had improved disease-specific survival.⁵
3. Our study provides a unique perspective as the NCDB allows access to data across multiple institutions, thus providing a large sample size of patients for a relatively uncommon oral cavity malignancy.
4. This study can help to optimize treatment for an otherwise historically elusive and controversial target.

Conclusions

Advanced RMT SCCs appear to have better survival outcomes when treated with surgery + PORT vs either modality alone

References

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