

Clinico-Pathological Prognostic Factors in Patients with Resectable Locally Advanced Oral Squamous Cell Carcinoma

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Abstract

Clinical and pathological prognostic factors are valuable tools for proper planning the strategy of adjuvant treatment and determining prognosis of oral cancer patients. The standard treatment of patients with locally advanced oral cavity cancers is surgical resection which is followed by adjuvant radiotherapy or simultaneous chemoradiation therapy [1]. Considerable progress has been made in the diagnosis and treatment patients with oral squamous cell carcinoma (OSCC). Nonetheless, the overall 5-year survival rate has remained stagnant at about 45-50% in most countries over the past decades [2]. A further insight into the factors contributing to the progression of the disease can be advantageous for the properly reasoned judgment of the most appropriate post-surgical treatment modes in order to gain better patient survival [3-5].

Therefore, the objective of this study was to determine the clinical and pathological prognostic factors affecting the prognosis of the disease in patients with resectable locally advanced oral squamous cell carcinoma. It is a retrospective analysis of outcomes of 234 patients with resectable locally advanced OSCC, which was performed in order to study the impact of clinical and pathological factors on disease-free survival (DFS) and overall survival (OS). The study included stage III-IVa-b OSCC patients, who underwent surgical treatment followed by radiotherapy or chemoradiation therapy. The patients who had received immunotherapy, chemotherapy or radiation therapy before the surgical treatment and those with distant metastases and tumor recurrence after previous treatment were not eligible for the study.

Results

The research involved the investigation of clinical and pathological prognostic factors in 234 patients with stages III-IVa-b OSCC. The patients had plastic reconstructive surgery for repair of post-surgical deformities with free or regional flaps. Surgical complications occurred in 47 (20.1%) patients. Patients having histologically verified factors associated with high risk of recurrence (positive resection margins or extracapsular nodal extension) received adjuvant chemoradiotherapy. Those with intermediate risk factors (multiple lymph node involvement, perineural invasion, lymphovascular invasion, primary tumor of pT3/4, high-grade tumor) underwent adjuvant radiation therapy. Seventy-seven (32.9%) patients had chemoradiation therapy. Radiation therapy was employed in 157 (67.1%) patients. A 5-year follow-up analysis showed that the rates of overall and disease-free survival were 55.4% and 59.6%, respectively.

The evaluation of pathological prognostic factors revealed positive resection margins in 15 (6.5%) patients, extracapsular nodal extension in 64 (27.3%) patients, multiple lymph node involvement in 89 (38.0%) patients, perineural invasion in 121 (51.7%) patients, and lymphovascular invasion in 150 (64.1%) patients. Seventy-two (30.7%) patients were diagnosed with 6-10 mm thick tumors; 116 (49.6%) patients had 11-20 mm thick tumors; in 46 (19.7%) patients, tumor thickness was >20 mm. G1 tumor grade was found in 62 (26.5%) patients; G2 grade was in 145 (62.0%) patients; G3 tumor grade was identified in 27 (11.5%) patients.

A multivariable analysis of clinical factors revealed a statistically significant effect of stage IVa-b and the presence of surgical complications on DFS (hazard ratio (HR) = 4.9 (95% confidence interval (CI) 2.9 - 8.3), $p < 0.001$), (HR = 1.6 (95% CI 1.0 - 2.6), $p = 0.047$), respectively. Stage IVa-b, the occurrence of surgical complications and the retromolar trigone subsite were found to have a statistically significant impact on OS (HR = 4.0 (95% CI 2.5 - 6.5), $p < 0.001$), (HR = 1.8 (95% CI 1.1 - 2.8), $p = 0.01$), (HR = 1.9 (95% CI 1.1 - 3.2), $p = 0.02$), respectively. A multivariable analysis of pathological factors showed a statistically significant effect of positive resection margins, the multiple lymph node involvement and high-grade tumor on DFS (HR = 3.7 (95% CI 2.0 - 6.6), $p < 0.001$), (HR = 4.3 (95% CI 2.8 - 6.7), $p < 0.001$), (HR = 1.6 (95% CI 1.1 - 2.2), $p = 0.01$), respectively. Besides, positive resection margins and multiple lymph node involvement were found to cause a statistically significant impact on the OS (HR = 3.6 (95% CI 2.0 - 6.5), $p < 0.001$), (HR = 3.7 (95% CI 2.5 - 5.6), $p < 0.001$), respectively. A tumor grade tended to worsen OS (HR = 1.4 (95% CI 1.0 - 1.9), $p = 0.053$).

Conclusion

Stage IVa-b, the presence of surgical complications, the retromolar trigone subsite, positive resection margins multiple lymph node involvements and high-grade tumor were found to be significant clinical and pathological prognostic factors in patients with resectable locally advanced OSCC. Further studies addressing the feasibility of adjuvant chemoradiotherapy in patients with multiple lymph node involvement and high-grade tumors would be beneficial.

References

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