Optimal Treatment for the High-Risk Salivary Gland Cancer

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Carcinomas of the major salivary glands constitute a heterogeneous group of rare malignant neoplasms, with 24 distinct histological types recognized by the World Health Organization classification. As a consequence of this heterogeneity, the literature lacks prospective studies with high-quality evidence from large groups of patients. This deficiency has made it challenging to achieve progress in the management of these patients. As a result, complete macroscopic surgical resection remains the definitive treatment of choice for patients with operable salivary gland cancer [1].

Multiple studies have identified poor prognostic factors of salivary gland cancer, such as high tumor grade, advanced T and N stages, advanced age, lymphovascular invasion, and positive surgical margins. Of these factors, tumor grade and nodal metastasis were found to be common independent factors in multivariate analyses with effects on survival, as well as locoregional spread and distant metastasis [2]. Regional metastatic disease has long been known to have prognostic and therapeutic implications [3]. Since high-grade tumors have a higher incidence of regional and distant metastasis, tumor grade has been described in the literature as one of the most compelling risk factors of treatment failure [4,5].

Since several reports have shown a positive role of postoperative radiotherapy (RT) in patients with poor prognostic factors,

it is generally agreed that complete surgical resection of high-risk salivary gland cancer, followed by RT, is a rational approach to improve treatment outcomes [6]. The current National Comprehensive Cancer Network (NCCN) guidelines support surgery as the standard definitive treatment for these malignant neoplasms, with RT indicated for high-risk patients. Despite the addition of RT, the incidence of distant metastases in malignant salivary gland tumors is estimated to be around 20%–30% [7], and distant metastasis is the most common cause of treatment failure [8].

Although surgery followed by RT may result in excellent lo-

coregional control, the high mortality rate associated with high-risk salivary gland cancer underscores the need for more aggressive treatment approaches, such as adjuvant chemotherapy or targeted therapy. Effective systemic therapies that address the high rate of distant metastasis must be developed to improve clinical outcomes. The rationale for adjuvant concurrent chemoradiotherapy (CCRT) for managing high-risk salivary gland malignancies draws from squamous cell carcinoma treatment.

However, few studies have aimed to assess the benefit of CCRT for high-risk salivary gland cancer treatment [9]. Since no randomized prospective study of CCRT has been conducted, this treatment option is still a subject of debate [10]. The current NCCN guidelines list CCRT as a category 2B recommendation that can be considered for high-risk patients. Fortunately, the role of CCRT in the setting of high-risk salivary gland cancer is currently under investigation (RTOG 1008: a randomized phase II study of adjuvant concurrent radiation and chemotherapy versus radiation alone in resected high-risk malignant salivary gland tumors, clinical trial registry: NCT01272037). This is the first prospective trial attempting to answer this question for high-risk salivary gland cancer.

Combining future molecular-driven therapies with more sophisticated RT techniques and technologies may be another way to improve the outcomes of high-risk salivary gland tumors. Furthermore, given the likelihood that toxic effects related to treatment may contribute to negative outcomes, it is critical to identify which high-risk patients may benefit the most from a combined treatment modality.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Received November 22, 2019
Accepted November 23, 2019