Editorial

Editorial for nomograms-based prediction of overall and cancer-specific survivals for patients diagnosed with major salivary gland carcinoma

Ameya A. Asarkar[1], Brent A. Chang[2]

[1]Department of Otolaryngology/Head and Neck Surgery, LSU Health, Shreveport, LA, USA; [2]Department of Otolaryngology/Head and Neck Surgery, Mayo Clinic, Phoenix, AZ, USA

Correspondence to: Ameya A. Asarkar, MD, FACS. Assistant Professor, Department of Otolaryngology/Head and Neck Surgery, LSU Health, 1501 Kings Highway, Shreveport, LA 71103, USA. Email: ameya.asarkar@lsuhs.edu.

Comment on: Guo Z, Wang Z, Liu Y, *et al.* Nomograms-based prediction of overall and cancer-specific survivals for patients diagnosed with major salivary gland carcinoma. Ann Transl Med 2021;9:1230.

Submitted Oct 11, 2021. Accepted for publication Nov 19, 2021.
doi: 10.21037/atm-2021-10
View this article at: https://dx.doi.org/10.21037/atm-2021-10

Salivary gland cancer is a relatively rare group of cancers (1 case per 100,000) with a heterogenous histology comprised of up to 22 subtypes (1). The prognosis depends on certain factors including the histological subtype, grade, and regional metastasis. Literature quotes survival rates ranging from 19.6% to 84.7% (2,3). This wide range underlines the need for a better understanding of prognostic factors in these cancers. As a clinician, due to the rarity of these cancers, formulating treatment algorithms and counselling patients is often challenging. Thus, availability of reliable predictive algorithms is helpful for evidence based clinical decision making. Multiple studies that have looked at variables influencing the survival in individual subtypes of salivary gland cancers. Studies have shown that histological grade is a more relevant predictor of prognosis and response to treatment in salivary gland cancers compared to histological subtype (4,5). A predictive nomogram developed by Ali *et al.* in 2013, using a cohort of 301 patients, described vascular and perineural invasion, nodal status, grade, and age as the most predictive variables for recurrence in salivary gland cancer (6). Compared to traditional methods including the American Joint Committee on Cancer (AJCC) TNM (tumor node metastasis) staging system, nomograms may do a better job of predicting risk in patients (7). Staging using the TNM system is effective in predicting outcome for a patient population, however, it is less effective when applied to an individual patient.

Guo *et al.* in the current study have used data of major salivary gland cancer (MGSC) patients from the Surveillance, Epidemiology, and End Results (SEER) database and developed a predictive nomogram model for overall survival (OS) and cancer-specific survival (CSS) (8). The study included 11,362 patients with 7,953 and 3,409 patients in the training and validation groups, respectively. The results of Cox regression model during the multivariate analysis showed that age, race, gender, AJCC stage, T and N stage, tumor size, type of treatment modality used (namely surgery), and histological type significantly correlated with OS ($P<0.001$). Previous studies have shown several of these factors to adversely affect survival (6). For OS, the area under the curve (AUC) of the training dataset using the nomogram was 83.5 (82.4–84.7), and the AUC of the AJCC staging was 71.6 (70.2–73.0). This was similar to the results for CSS with the nomogram yielding AUC of 83.9 (82.6–85.2) versus the AUC of 73.9 (72.4–75.3) using the AJCC staging for the training dataset. The nomogram also had a higher concordance (C-index) for OS 0.796 (0.788–0.804); 0.787 (0.774–0.799) compared to AJCC stage (0.751, 0.739–0.762; 0.730, 0.712–0.748) in the training group and validation group, respectively. C-index of the nomogram was also superior in predicting CSS when compared to the AJCC staging with 0.806 (0.797–0.815) in training group and 0.798 (0.78–0.81) in validation group and 0.781 (0.769–0.793) and 0.769 (0.750–0.788) in training set and validation set, respectively for AJCC staging. Further, the Brier score of the nomogram

was a better predictor of OS and CSS in both training and validation sets. Overall, these results suggest the superiority of the nomogram to the AJCC staging in predicting both 3- and 5-year survival in MSGC. Further, the calibration curves deduced by the current nomogram were congruent with the reference line making them highly accurate when compared to the other systems.

Certain salivary gland cancers like adenoid cystic carcinoma and salivary duct carcinoma have predilection for perineural invasion (PNI). Studies have shown that PNI is associated with aggressive cancers (9). PNI along with variables like lymphovascular emboli, tobacco, and alcohol use have prognostic importance in salivary gland cancer. However, the SEER database does not capture these variables and thus are not included in developing the nomogram in this study. The role of targeted therapy in MSGC is evolving (10,11). Although surgery with or without adjuvant radiotherapy is the mainstay of treatment of MSGC, availability of other treatment options adds to the repertoire of the treating physician especially for patients who are unable to tolerate traditional treatment measures. Again, this information is not captured by the SEER database which is an inherent limitation of using this type of population-based database.

An accurate predictive algorithm is paramount to assess the survival among cancer patients and a well-constructed nomogram plays an important role in this regard. The nomogram presented in the current study has a C-index of close to 0.8 for both training and validation sets; this was higher than the prediction with the AJCC classification. A nomogram developed by Lu *et al.* used six predictive factors that showed significance on the Multivariate Cox regression model (12). These included tumor grade, lymphatic invasion, PNI, smoking habit, pathologic T and N classification. These factors, although reported in literature as being high risk in predicting tumor recurrence, have not been consistent across the board (13-15). These factors are similar to the ones used in the development of the nomogram by Memorial Sloan Kettering Cancer Center (MSKCC) (6). The MSCKCC nomogram did well with predicting recurrence rates in low-risk groups but generally overestimated the 5-year recurrence-free probability in high-risk groups (16). Further, the MSKCC nomogram did not have significant advantage over the AJCC staging in stages III and IVa. Consistent with the previous nomograms, the results presented in the current study have similar C-index scores in both the validation and training datasets (6-8,17). Further, external validation in future studies will help in gauging the utility of this nomogram in a wider population. The current study included histological subtype as one of the variables which was not included in the externally validated MSKCC nomogram.

Overall, this is an important study to formulate a reliable predictive algorithm for survival in MSGC. The superiority of the current and previously published nomograms over more universally accepted systems like the AJCC system underlines the importance of considering several other risk factors in stratifying and prognosticating patients with major salivary gland cancers.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Translational Medicine*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/atm-2021-10). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Seethala RR, Stenman G. Update from the 4th Edition of the World Health Organization Classification of Head and Neck Tumours: Tumors of the Salivary Gland. Head Neck Pathol 2017;11:55-67.

2. McHugh CH, Roberts DB, El-Naggar AK, et al. Prognostic factors in mucoepidermoid carcinoma of the salivary glands. Cancer 2012;118:3928-36.
3. Iqbal H, Bhatti AB, Hussain R, et al. Ten year experience with surgery and radiation in the management of malignant major salivary gland tumors. Asian Pac J Cancer Prev 2014;15:2195-9.
4. Haderlein M, Scherl C, Semrau S, et al. High-grade histology as predictor of early distant metastases and decreased disease-free survival in salivary gland cancer irrespective of tumor subtype. Head Neck 2016;38 Suppl 1:E2041-8.
5. Kim BY, Hyeon J, Ryu G, et al. Diagnostic accuracy of fine needle aspiration cytology for high-grade salivary gland tumors. Ann Surg Oncol 2013;20:2380-7.
6. Ali S, Palmer FL, Yu C, et al. A predictive nomogram for recurrence of carcinoma of the major salivary glands. JAMA Otolaryngol Head Neck Surg 2013;139:698-705.
7. Kattan MW. Nomograms are superior to staging and risk grouping systems for identifying high-risk patients: preoperative application in prostate cancer. Curr Opin Urol 2003;13:111-6.
8. Guo Z, Wang Z, Liu Y, et al. Nomograms-based prediction of overall and cancer-specific survivals for patients diagnosed with major salivary gland carcinoma. Ann Transl Med 2021;9:1230.
9. Huyett P, Duvvuri U, Ferris RL, et al. Perineural Invasion in Parotid Gland Malignancies. Otolaryngol Head Neck Surg 2018;158:1035-41.
10. Takahashi H, Tada Y, Saotome T, et al. Phase II Trial of Trastuzumab and Docetaxel in Patients With Human Epidermal Growth Factor Receptor 2-Positive Salivary Duct Carcinoma. J Clin Oncol 2019;37:125-34.
11. Falchook GS, Lippman SM, Bastida CC, et al. Human epidermal receptor 2-amplified salivary duct carcinoma: regression with dual human epidermal receptor 2 inhibition and anti-vascular endothelial growth factor combination treatment. Head Neck 2014;36:E25-7.
12. Lu CH, Liu CT, Chang PH, et al. Develop and validation a nomogram to predict the recurrent probability in patients with major salivary gland cancer. J Cancer 2017;8:2247-55.
13. Gallo O, Franchi A, Bottai GV, et al. Risk factors for distant metastases from carcinoma of the parotid gland. Cancer 1997;80:844-51.
14. Harbo G, Bundgaard T, Pedersen D, et al. Prognostic indicators for malignant tumours of the parotid gland. Clin Otolaryngol Allied Sci 2002;27:512-6.
15. Carrillo JF, Vázquez R, Ramírez-Ortega MC, et al. Multivariate prediction of the probability of recurrence in patients with carcinoma of the parotid gland. Cancer 2007;109:2043-51.
16. Chou WC, Chang KP, Lu CH, et al. Complementary role of the Memorial Sloan Kettering Cancer Center nomogram to the American Joint Committee on Cancer system for the prediction of relapse of major salivary gland carcinoma after surgery. Head Neck 2017;39:860-7.
17. Wei Z, Zhang Z, Yang L, et al. Development and validation of nomograms for predicting survival and recurrence in patients with parotid gland cancer. Gland Surg 2021;10:2398-407.

Cite this article as: Asarkar AA, Chang BA. Editorial for nomograms-based prediction of overall and cancer-specific survivals for patients diagnosed with major salivary gland carcinoma. Ann Transl Med 2021;9(23):1709. doi: 10.21037/atm-2021-10

