EDITORIAL COMMENT

The effect of depth of invasion on node negative tongue cancer staging

Staging of cancer is an important tool for understanding and combating this disease on a global scale. The goal of staging is multifactorial. Assessment of cancer epidemiology, global burden of disease, entry into clinical trials, and prognosis are among the most important outcomes. Modifications to the system should be undertaken cautiously, with evidence to support changes and at relatively infrequent intervals. This was the goal of the American Joint Committee on Cancer (AJCC) head and neck task force. Additionally, worldwide acceptance must be accomplished. To achieve this aim, the head and neck task forces of the AJCC and the Union for International Cancer Control (UICC) worked together on the 8th edition by utilizing a UICC liaison member in development. Publication of the 8th edition AJCC Cancer Staging Manual occurred in October 2017, 15 months prior to the implementation of the staging system which occurred on January 1, 2019.[1] After publication, additional conversations were held with UICC head and neck task force members and additional adjustments were made to oral cavity staging as it relates to depth of invasion (DOI) to hold assiduously to the data presented by Ebrahimi et al.[2] These were reported in an errata available on the AJCC website (Table 1). The results of the errata were transmitted to the College of American Pathologists as they created the templates for staging.[3] The new criteria are thus reflected in the staging sheets available to clinicians.

TNM was developed in the middle of the twentieth century with the goal of providing clinicians with a means of categorizing patients with cancer to achieve the aims set out above. To be successful, a staging system should try to maximize the four characteristics described by Groome et al of hazard consistency, hazard discrimination, predictive power, and numerical balance.[4] Hazard consistency is a statistical reflection that each patient with a similar stage should have a similar outcome and behavior. Hazard discrimination implies that each stage group should behave differently than the one above or below. Survival predication is the main clinical outcome of staging systems. Numerical balance is a reflection of a relatively even distribution of subjects in each group to maximize the utility of the staging system. The addition of DOI to oral cavity staging is aimed at enhancing hazard consistency and discrimination as well as predictive power while hopefully enhancing the numerical balance.

Dang and coworkers examine these goals with respect to stage I and II disease.[5] Dang et al examined 1277 patients from the National Cancer Database (NCDB) to determine the impact of the (AJCC) 8th edition Head and Neck Staging in a subset of oral cavity cancers that arose in the oral tongue and were staged T1-3N0. This group was chosen to examine the effect of the addition of DOI on overall staging of patients with oral tongue cancer. They found that 17.1% of patients were upstaged due to DOI with an approximately equal number moving from pT1 to pT2 and pT2 moving to pT3. As would be hoped, the authors found a slight improvement in survival in the pT1 (stage I) cohort and slightly worse outcome in the pT2 (stage II) cohort. The addition of DOI thus yields better hazard discrimination, hazard consistency, and predictive power in this cohort. Examining the numerical balance, we also find some improvement where 68.7% were stage I in the 7th edition and this was reduced to 56.3% in the

TABLE 1 Updated 8th edition T categorization

Definition of primary tumor (T)	
T Category	**T Criteria**
TX	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor ≤2 cm with ≤5 mm depth of invasion (DOI)*
T2	Tumor ≤2 cm with >5 mm DOI
	or tumor >2 cm and ≤4 cm with ≤10 mm DOI
T3	Tumor >2 cm and ≤4 cm with >10 mm DOI
	or tumor >4 cm with ≤10 mm DOI
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease
	Tumor >4 cm with >10 mm DOI
	or tumor invades adjacent structures only (eg, through cortical bone of the mandible or maxilla or involves the maxillary sinus or skin of the face)
	Note: Superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4
T4b	Very advanced local disease
	Tumor invades masticator space, pterygoid plates, or skull base, and/or encases the internal carotid artery

8th while stage II disease increased from 26.6% to 32.3%. These findings support the recent addition of DOI to TNM for oral cavity.

The issue of the pT3N0 group deserves special comment. As the authors note, the majority of cases of oral tongue cancer in the NCDB did not have DOI, so significant bias may be introduced especially in the advanced stages. Second, pT3N0 may represent a biologically different entity that is less aggressive as suggested by a lack of nodal involvement. This hypothesis deserves further study. TNM are components of the overall staging system which is reflected in the stage groupings. These are the actual stage of the individual. The T is a category not a stage. T1N0M0 and T2N0M0 encompass stage I and II disease. Stage III, however, is not merely composed of T3N0 so assessment of the four Groome parameters is not possible in this study. Only a hint of how this might affect stage III can be gleaned. Stage III also includes those patients with pT1-3N1 disease and these patients may be expected to have a worse prognosis. The work of Dang et al does suggest that T3N0 may need additional scrutiny as it may not be providing adequate hazard discrimination. More work needs to be done on this specific question.

As discussed above, the oral cavity staging has been somewhat modified since the publication of the 8th edition. Errata were issued to reflect these changes to serve the critical aim of agreement among international stakeholders. Thus, the current staging is slightly different than that studied by Dang. What effect this had on the study results is not clear. Careful analyses of the data, such as this work by Dang et al, are crucial to continue refinement of the staging system to help clinicians and scientists combat this devastating disease.

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