

Modified Tumor Classification With Inclusion of Tumor Characteristics Improves Discrimination and Prediction Accuracy in Oral and Hypopharyngeal Cancer Patients Who Underwent Surgery

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Abstract: Several histopathological characteristics have a significant prognostic impact on recurrence and survival rates in head and neck squamous cell carcinoma (HNSCC). We conducted a retrospective study on patients with HNSCC to compare traditional pathological T (pT) classification to a new T classification system that incorporates these histopathological characteristics.

Newly diagnosed patients with HNSCC (n=349) post major surgery were identified from the cancer registry database between 2004 and 2013. The pT and new T classification systems were compared with respect to recurrence-free survival (RFS), disease-specific survival (DSS), and survival rates using the Cox proportional hazards model with adjustments. The discriminatory ability of these 2 classification systems was evaluated using the adjusted hazard ratio (HR) and Akaike information criterion (AIC) in a multivariate regression model. The prediction accuracy was assessed using Harrell's C-statistic.

The new T classification, which incorporated tumor size, extent, and location with histopathological features had better discriminatory ability and monotonicity of gradients than did pT classification. The new T4 classification yielded a higher adjusted HR in RFS (HR, 4.11; 95% confidence interval [CI], 7.75–9.65) and in DSS (HR, 4.39; 95% CI, 1.6–12.03), and a lower AIC in recurrence (927 vs 969) and survival rates (791 vs 833).

The new T classification system had better discriminatory ability in RFS and DSS compared with the routinely used American Joint Committee on Cancer (AJCC) pT classification system. Therefore, this new T classification system, which includes tumor size, location, extent, and histopathological features, could be used as an alternative to AJCC pT classification for patients with HNSCC.

Editor: Haijun Zhang.

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The authors have no funding and conflicts of interest to disclose.

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DOI: 10.1097/MD.0000000000001114

(*Medicine* 94(27):e1114)

Abbreviations: AIC = Akaike information criterion, AJCC = American Joint Committee on Cancer, CI = confidence interval, DMFS = distant metastasis-free survival, DSS = disease-specific survival, HNSCC = head and neck squamous cell carcinoma, HPV = human papillomavirus, HR = hazard ratio, ICD-9 = International Classification of Diseases, 9th revision, pN = pathological N, PNI = perineural invasion, pT = pathological T, RFS = recurrence-free survival.

INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) is among the 10 most common forms of cancer, with a rising incidence in Western and Asian countries.^{1,2} Despite advances in clinical treatment, long-term outcomes of patients with HNSCC have not improved significantly in the last decades.^{3,4} Improvement and adjustment of the present TNM staging system may be necessary to identify high-risk groups.

The American Joint Committee on Cancer (AJCC) TNM classification system is widely applied to mucosal cancers of the head and neck. Within this system, the present pathological T (pT) classification for HNSCC is based on tumor size, extension, anatomic location, and cranial nerve involvement.⁵ Despite consideration of clinical prognostic factors such as tumor size or stage, prediction of the clinical outcome of HNSCC is difficult. Patients who have a small tumor may still have a poor outcome.⁶ Evaluation of the histopathological characteristics of resected tumor specimens plays an important role in the diagnostic process and prediction of patient outcomes. Multiple histopathological factors predicting survival have been identified in the literature, including tumor thickness, grade, pathological nodal classification, extracapsular spread, margin status, and perineural invasion (PNI).⁷ Thus, incorporation of these additional prognostic factors may be helpful for refinement of the classification system to improve its prediction accuracy.

Several prediction models have been proposed. Among oral SCCs, poor differentiation was associated with neck metastasis, extracapsular spread, PNI, neck recurrence, and distant metastasis.^{8,9} However, the differentiation grade was not regarded as a risk factor in determining adjuvant therapy in the latest NCCN guidelines.¹⁰ Brandwein-Gensler et al validated the prognostic influence of histological findings, such as PNI, lymphocyte infiltrate at the interface, and worst pattern of tumor invasion in head and neck cancer (HNC).^{11–13} The depth of invasion, tumor budding, and worst pattern of invasion were