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Tumor thickness versus depth of invasion – Analysis of the 8th edition American Joint Committee on Cancer Staging for oral cancer

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ABSTRACT

Objectives: The primary aim of this study is to compare the effect of using tumor thickness versus depth of invasion (DOI) to determine the 8th edition AJCC T-category on survival in a large cohort of OSCC.
Materials and methods: A retrospective cohort study of patients whose clinicopathologic information had been collected prospectively into a dedicated head and neck database. 927 patients with oral SCC were identified in this cohort, with the final study population including 456 patients with complete information on DOI, tumor thickness, T and N staging and follow-up.
Results: 26 (5.7%) patients had a different AJCC 8 T category when using thickness instead of depth. 15 were upstaged from T1 to T2, 10 upstaged from T2 to T3 and 1 down staged from T2 to T1. Additionally, similar stratification of disease-specific and overall survival curves were found for T category based on DOI and thickness.
Conclusion: The T category and TNM stage prognostic performance of 8th edition AJCC staging of oral cancer is similar regardless of whether DOI or thickness is used as the T-category modifier.

In centers without complete DOI data it is reasonable to impute thickness for retrospective survival analyses using the 8th edition of the AJCC staging system.

Introduction

One of the most important changes in the recently proposed 8th edition of the American Joint Committee on Cancer (AJCC) staging system for oral cavity squamous cell carcinoma (OSCC) is the addition of depth of invasion (DOI) as a modifier for the T category [1]. The new staging manual emphasizes that it is important to distinguish between tumor thickness and DOI and stipulates the use of the latter for staging purposes (Table 1).

There have been numerous studies examining the impact of both DOI and tumor thickness in OSCC [2–17]. This has led to a general consensus that tumors with a larger DOI or thickness are associated with an increased risk of nodal metastasis and worse survival outcomes [5,11,18].

Many institutions have measured tumor thickness instead of DOI historically and recorded these in large prospective research databases. It is unknown whether on a population basis it is reasonable to substitute tumor thickness for DOI when retrospectively analyzing the effect of T category or AJCC stage, either as the variable of interest or when adjusting for its effect as a confounder (covariate) in multivariable analyses. The primary aim of this study is to compare the effect of using tumor thickness versus DOI to determine the 8th edition AJCC T-category on survival in a large cohort of OSCC.

Methods

Study population

Clinicopathological data were extracted from the Sydney Head and Neck Cancer Institute (SHNCI) database for all patients with OSCC treated with curative intent between 1987 and 2016 with surgery ± adjuvant therapy. Collection of data on thickness started in 1987 and

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Table 1
Definitions of 8th edition AJCC TNM. Definition of primary tumor (T-category).

T Category	T Criteria
TX	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor ≤ 2 cm, ≤ 5 mm depth of invasion (DOI) DOI is depth of invasion and not tumor thickness
T2	Tumor ≤ 2 cm, DOI > 5 mm and ≤ 10 mm *or* tumor > 2 cm but ≤ 4 cm, and ≤ 10 mm DOI
T3	Tumor > 4 cm *or* any tumor > 10 mm DOI
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease (lip) Tumor invades through cortical bone or involves the inferior alveolar nerve, floor of mouth, or skin of face (i.e., chine or nose) (oral cavity) Tumor invades adjacent structures only (e.g.., 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

collection of depth of invasion in 1995. Exclusion criteria were absence of follow-up data, perioperative mortality or incomplete data on primary tumor features or nodal status to permit staging.

Depth of invasion and tumor thickness

Depth of invasion and tumor thickness were measured during histopathologic examination of the tumors as per the AJCC 6th edition guidelines and the College of American Pathologists (CAP) protocol [19,20]. Multiple sections were studied to identify the deepest point of invasion.

Depth of invasion was measured as the perpendicular distance from the basement membrane region to the deepest point of the infiltrative front of the tumor in millimeters (Fig. 1A). Thus, this measurement took into account only the infiltrative component of the tumor. Tumor thickness was measured as the perpendicular distance between the highest point of the tumor surface to the deepest point of the infiltrative front of the tumor in millimeters. The tumor thickness measurement also took into account both the exophytic and the infiltrative component of the tumor (Fig. 1B).

Statistical analysis

Statistical analysis was performed using Stata version 12.0 SE (StataCorp LP, College Station, Texas). All statistics were 2-sided and $P < 0.05$ was considered statistically significant. The end points for analysis included disease-specific survival (DSS) and overall survival (OS). Overall survival was calculated from the date of surgery to the date of death or last follow-up visit. For DSS, patients who died from causes other than oral SCC were censored at the time of death.

Patients were classified into AJCC 8 T category and TNM Stages using both thickness and DOI. The prognostic performance of the staging system using thickness versus DOI was evaluated using the Akaike Information Criterion (AIC), Harrel concordance index (C-index) and visual inspection for stratification into distinct prognostic categories on Kaplan-Meier curves. The C-index provides a measure of model discrimination, with a value of 1 indicating perfect prediction, whilst 0.5 is equivalent to the toss of a coin. Discrimination is the ability of a model to distinguish individuals who experience the end-point of interest from those who remain event free. For a prognostic model, the C-index is the chance that given two individuals, one who will develop the event and one who will remain event free, the prediction model will assign a higher probability of the event to the former.

Results

Patient demographics

Our unit database search identified 927 patients with oral SCC. There were 663 patients with data available on thickness. Of these, 207 were missing data on depth and were therefore excluded from the main analysis. The final study population includes 456 patients with complete information on DOI, tumor thickness, T and N staging and follow-up.

There were 260 men and 196 women, with a median age of 63.9 years (range, 18.2–97.6 years) and median follow-up of 2.1 years. All patients underwent surgery with curative intent, with 201 patients also receiving adjuvant radiotherapy ± chemotherapy. There were 92 deaths in the study population, 65 of which were due to oral SCC. Relevant patient demographic and clinicopathological data are summarized in Table 2.

Depth versus thickness

The median DOI was 9.5 mm and median thickness 10 mm. The median difference between thickness and depth was 0 mm and the mean difference 0.7 mm (thickness > DOI). Thickness and depth were the same in 263 patients (57.7%) and the difference was < 1 mm in a further 93 (21.2%) patients. There were only 18 pts in whom the difference between thickness and depth was > 5 mm. It was unusual in our study cohort for DOI to exceed thickness.

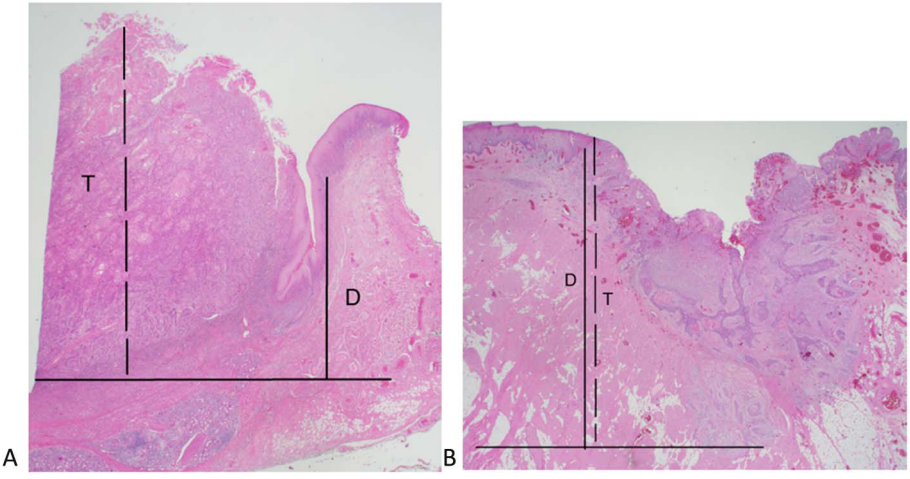

Fig. 1. A + B: Depth of invasion and tumor thickness measurements as per the AJCC 6th edition guidelines and the College of American Pathologists. D (—) = DOI, T (– – –) = Thickness. A: exophytic growth of SCC. B: ulcerated growth of SCC.