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Prognosis of oral cancer: a comparison of the staging systems given in the 7th and 8th editions of the American Joint Committee on Cancer Staging Manual

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Abstract

The 8th edition of the American Joint Committee on Cancer (AJCC) Staging Manual introduces "depth of invasion" and "extranodal extension" into the head and neck section, and our aim was to find out if these changes have an impact on prognosis. We evaluated 174 patients who had had oral squamous cell carcinomas (SCC) resected between 2003 and 2012. The clinical records were reviewed, the patients' tumours restaged according to the 8th edition of the AJCC, and we analysed five-year survival to verify whether different correlations were made between the T and N stages and disease-specific survival using the 7th and 8th editions. We excluded seven cases because information was incomplete, and the final sample was 167 patients. The five-year overall survival was 68% and the five-year disease-specific survival was 78%. The variable pT was upstaged in 51 patients (31%), and no tumour was downstaged. When we used the 7th edition, the pT category did not correlate with survival ($p = 0.055$), but when we used the 8th edition, there was a significant association between increased pT categories and disease-specific survival ($p = 0.01$). In the pN category 23 cases were upstaged (14%) and this affected disease-specific survival using both the 7th and the 8th editions ($p = 0.001$). When patients were restaged, there was an improvement in discrimination between T categories in relation to disease-specific survival, and confirmation of the prognostic impact of the variable pN. T stage and depth of invasion are complementary predictors of disease-specific survival, and their combination results in the new AJCC staging system giving a better prognosis.

Keywords: oral cancer; survival; TNM classification; depth of invasion; extranodal extension; prognosis

Introduction

Since its introduction, the TNM staging system of malignant tumours has been extensively used for the selection of treatment, assessment of prognosis, and evaluation of results. Some authors have highlighted its limitations in definition of the primary tumour, in that it considers almost exclusively the anatomical extent/size of the tumour, and does not account for perineural invasion, lymphocytic response, and depth of invasion.[1] Unlike cutaneous melanoma and cutaneous squamous cell carcinoma (SCC), depth of invasion was not included in the 7th edition of the staging system for oral SCC.[2] An inaccurate staging system may lead to incorrect staging of patients with cancers of the head and neck, with the consequent risk of overtreatment or undertreatment. It could also explain the unchanged survival after oral cancer in recent years.[3]

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The American Joint Committee on Cancer (AJCC) has recently published the 8th edition of its staging system, which has some modifications in the head and neck section.[4] Among the changes, depth of invasion has been incorporated into the staging of oral cancer, and extranodal extension has been added to the lymph node category (N). Tumours less than 2 cm in size with a depth of invasion of 5 cm or less are now staged as pT1; tumours less than 2 cm with a depth of invasion between 5 and 10 mm, or tumours between 2 and 4 cm and a depth of invasion of less than 10 mm, are grouped as pT2; and tumours that exceed 4 cm or with a depth of invasion of more than 10 mm are classified as pT3. If there is extranodal extension of less than 3 cm in diameter in a single node, tumours are staged as pN2a; and all other cases with extranodal extension are classified as pN3b.[4]

Although previous studies have shown that the thickness of the tumour is related to the risk of metastases in the neck[5,6] and the prognosis of the tumour,[7] depth of invasion has recently been shown to be a more reliable predictor.[8,9] It is defined as the distance between the level of the basement membrane of the closest adjacent normal mucosa and the deepest point of invasion of the tumour.[10]

The role of extranodal extension in prognosis is well known,[11–13] as it is associated with a higher risk of locoregional recurrence and distant metastases.[14] It is defined as "the extension of metastatic carcinoma from within a lymph node through the fibrous capsule and into the surrounding connective tissue, regardless of the presence of stromal reaction".[15]

The importance of depth of invasion and extranodal extension in the staging system of cancers of the oral cavity was first validated by a retrospective analysis of a large database of patients treated in North America[15] and, more recently, by Matos et al who externally validated the results.[14,15]

The aim of the present study was to evaluate (using the new AJCC classification) patients whose oral SCC were resected at our hospital, and find out whether correlations in terms of survival differed between the 7th and 8th editions of the staging system. The decision to analyse disease-specific survival was made because the N stage has such a considerable influence on prognosis.

Patients and methods

The clinical and histopathological records of 174 patients operated on for oral SCC from 2003 and 2012 were collected retrospectively. The histopathological specimens were re-evaluated by a single pathologist, and the depth of invasion measured. We also considered the following data: T and N categories using the 7th and the 8th editions of the AJCC staging system, the size and number of lymph nodes, and the presence of extranodal extension.

To define the impact of the introduction of a different staging system, the significance of the differences in the relation between disease–specific survival and the T and N categories obtained using the 7th and the 8th editions was tested with the help of the dedicated software SPSS (version15, SPSS Inc, Chicago, IL, USA). Kaplan–Meier survival curves were used to estimate the disease-specific and overall survival for each group, and the log-rank test was used to assess the significance of differences between the survival curves. The same method was used to assess the differences in disease-specific survival, with depth of invasion as an independent prognostic factor. Probabilities of less than 0.05 were accepted as significant.

Table 1
Distribution of the sample by site of tumour.

Tumour site	No. (%) of cases
Tongue	72 (43)
Floor of the mouth	48 (29)
Hard palate	6 (4)
Retromolar trigone	17 (10)
Cheek	24 (14)
Total	167 (100)

Results

We excluded seven patients for whom we had insufficient information to assess the primary depth of invasion or whose specimens were unavailable. The sample therefore comprised 167 patients (108 men and 59 women, mean (range) age 64 (29–93) years) who were followed up for at least five years, and Table 1 summarises the distribution of the sites of the tumours.

The five-year overall survival was 68% and the five-year disease-specific survival was 78%. There were 37 deaths from oral cancer (Fig. 1).

Table 2 summarises the changes in the histopathological T and N categories, and shows the comparison between the TNM categories according to the 7th and 8th editions. The pT was unchanged in 116 patients (70%), upstaged in 51 patients (31%), and downstaged in none. Table 3 shows the sample stratified by pT categories and the relative disease-specific survival defined according to the TNM classifications in both the 7th and 8th editions of the AJCC handbook.

The pT category did not correlate significantly with survival when the 7th edition was used ($p = 0.055$), and only the difference between pT1 and pT4 was significant in terms of disease-specific survival ($p = 0.029$). With the application of the new TNM staging system, there was a significant association between increasing pT categories after adjusting for depth of invasion and disease-specific survival ($p = 0.01$) (Table 3). When depth of invasion was considered to be an independent prognostic factor of survival, there was significantly worse disease-specific survival when it was greater than 10 mm ($p = 0.001$).

Most of the histopathological N category (90%) was pN0, and 61 (10%) patients presented with metastases. Because of the paucity of the latter subgroup, we pooled pN2 and

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