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Importance of tumour thickness measurement in prognosis of tongue cancer

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Abstract

Eighty-one patients who underwent surgery for cancer of the tongue were retrospectively studied to evaluate the influence on survival of some clinical and pathologic parameters. These parameters and data on the patient's current status were gathered by the study of tissue sections, using haematoxylin-eosin staining, and from medical records. The 5-year survival rate was 68.5%. Univariate analysis showed that the parameters influencing survival were: T ($P<0.01$), pathologic T ($P<0.01$), N ($P<0.05$), pathologic N ($P<0.05$), extracapsular nodal spread ($P<0.05$), locoregional recurrence ($P<0.01$), and tumour thickness ($P<0.05$). Multivariate analysis showed that tumour thickness had the greatest influence on survival. Patients with tumour thickness of $\leqslant 3$ mm had a 5-year survival of 85.7%, significantly greater ($P<0.05$) than the rates of 58.3 and 57% for patients with tumour thickness of 4–7 mm and >7 mm, respectively. Wider studies are required to unify criteria for the measurement of this important prognostic parameter.

Keywords: Prognosis; Tongue neoplasm; Tumour thickness measurement

1. Introduction

The prognostic value of the TNM system has been widely reported as inadequate in patients with oral squamous cell carcinoma (OSCC) [1–3]. Among the parameters that make up the TNM system, the maximum superficial diameter (*T*) is especially controversial [4] for several reasons: (a) the clinical measurement of tumours in the upper aerodigestive tracts can be difficult; (b) the size of tumours is not necessarily related to the prognosis, so that some large tumours progress satisfactorily, whereas some small tumours can kill the patient despite treatment; (c) most oral and pharyngeal SCC are T2 with superficial diameters ranging from 20 to 40 mm, and it seems unlikely that tumours so varied in size could have the same prognosis [5]; and (d) some carcinomas of the aerodigestive tracts are multicentric, complicating further the measurement of the superficial diameter.

Attempts have been made to improve the measurement of the tumour size, in order to increase its value as a predictive prognostic factor in OSCC. Measurement of the maximum diameter of the tumour on the operative specimen (pathologic T) has been proposed [6], whereas other studies [4,7–11] have focused on the predictive value for OSCC of the tumour thickness considered alone. The aim of the present work was to compare the prognostic value of widely used clinical and pathologic parameters such as N, M, extracapsular nodal spread, and tumour size, measured as maximum superficial diameter (T), maximum diameter of operative specimen (pathologic T), and tumour thickness, in a retrospective study of patients with cancer of the tongue, an OSCC site associated with an especially poor prognosis [12].

2. Material and methods

The study was performed in 2000 on 81 squamous carcinomas of the tongue treated at our university

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hospital before 1996. The patients' clinical data were obtained from the hospital medical records, including the values of the T parameter, the increase in cervical lymph node involvement determined by clinical methods (N), and the presence of distance metastasis according to IUAC and AJCC criteria [13].

Locoregional tumour recurrence and the time period between treatment and recurrence were recorded. The survival after the surgery was recorded in months. The status of the patient at the time of the study was registered as "alive without disease", "alive with disease", "death from tongue cancer".

The pathologic T measurement was taken from the pathology report in the patient's medical record. The histopathologic data and the measurement of the tumour thickness were obtained by studying tissue sections of the operative specimen, using hematoxylin-eosin staining. The involvement of cervical lymph nodes by the tumour (pathologic N) was evaluated following the IUCC and AJCC criteria [14]. The extracapsular nodal spread of the tumour were also assessed. For evaluation of the tumour thickness, multiple sections were studied, selecting the thickest tissue section in which mucosa adjacent to the tumour could be observed and which was not considered to have been cut tangentially. An optical micrometer was used to measure the distance (to the nearest mm) from an imaginary line reconstructing the basal membrane of the healthy oral mucosa to the deepest point of tumour invasion, both in exophytic and ulcerated lesions, disregarding any superficial keratin layer or inflammatory infiltrate that may exist. Of the 81 tumours studied, 22 failed to meet our requirements for a reliable measurement of their thickness, so that 59 patients comprised the final study sample for this parameter. The patients were classified in three groups according to their tumour thickness: $\leqslant 3$ mm, 4–7 mm, and > 7 mm.

Statistical Analysis. The disease-specific survival rate was determined with the Kaplan–Meier product-limit actuarial method. Comparison of two or more survival curves was performed with the log rank test. Prognostic factors were evaluated with a multivariate analysis, using the Cox proportional hazards regression model.

3. Results

We studied 81 patients with cancer of the tongue, 64 males and 17 females, with a mean age of 58 years (range, 37–87 years).

The results for the T, pathologic T, and tumour thickness parameters are shown in Table 1.

Table 2 lists the results for the lymph node involvement and the presence of distance metastasis.

Forty-six patients (63%) showed no recurrence of the tumour, 17 (23.3%) had recurrence in the tongue, and 10 patients (13.7%) had recurrence in the cervical lymph nodes. Eight patients were lost to the follow-up.

Table 1
Results obtained in the determination of different variables related to the T parameter

Variable		Frequency (%)
T[a]	T1	22 (28.2)
	T2	33 (42.3)
	T3	10 (12.8)
	T4	13 (16.6)
Pathologic T[a]	T1	24 (30.7)
	T2	34 (43.6)
	T3	11 (14.1)
	T4	9 (11.5)
Thickness[b]	$\leqslant 3$ mm	10 (16.9)
	4–7 mm	15 (25.4)
	> 7 mm	34 (57.6)

[a] Three lost to follow-up.
[b] Twenty-two lost to follow-up.

Table 2
Results obtained in the determination of different variables related to the N and M parameters

Variable		Frequency (%)
N[a]	N0	46 (59.0)
	N1	18 (23.1)
	N2a	3 (3.8)
	N2b	11 (14.1)
Pathologic N[a]	N0	50 (64.1)
	N1	17 (21.8)
	N2a	2 (2.6)
	N2b	7 (9.0)
	N2c	1 (1.3)
	N3	1 (1.3)
Extracapsular spread	Yes	16 (57.1)
	No	12 (42.9)
M[a]	M0	72 (100.0)
	M1	0 (0.0)

[a] Three lost to follow-up.

The mean time period between the surgery and locoregional recurrence was 15.74 months (range, 1–48 months).

The survival rate at 5 years of the series was 68.5% (50 patients alive after 5 years). The mean survival of the patients who died from oral cancer was 30.5 months (range, 1–84 months). Eight patients were lost to the follow-up.

The survival rate at 5 years of the 10 patients with tumour thickness of $\leqslant 3$ mm was 85.7%, significantly higher ($P < 0.05$) than the 58.3% 5-year rate for the 15 patients with thickness of 4–7 mm and the 57% rate for the 34 patients with thickness of > 7 mm.

Univariate analysis showed that the variables influencing survival were T ($P<0.0001$), pathological T ($P<0.01$), N ($P<0.05$), pathologic N ($P<0.05$), extracapsular spread ($P<0.05$), locoregional recurrence ($P<0.01$), and tumour thickness ($P<0.05$)

Multivariate analysis showed that the parameter with greatest influence on survival was the tumour thickness.

4. Discussion

Multivariate analysis of the results of our study revealed that the most influential parameter in the prognosis of a patient with cancer of the tongue is the tumour thickness. Many authors have found that the thickness of the tumour correlates better with survival and involvement of the lymph nodes than does its superficial diameter [5,9,10,12,15,16]. The first report on the importance of tumour thickness in prognosis was published by Breslow [17], who studied malignant melanomas and measured from the deepest part of the invasion to the height of the layer of granular cells in the overlying epidermis, cutting sections perpendicularly.

Tumour thickness has not been uniformly measured to date. Although most authors used an optical micrometer to measure the thickness [6,8,10,11], others do not specify how the data were obtained [9,12]. Some authors [10,11] measured the distance from the deepest point of tumour invasion to the most protruding part of the tumour (tip of the papilla) in exophytic lesions and to the ulcer base in ulcerated lesions, whereas others [8,11,12] measured from the deepest point of the tumour to an imaginary line that reconstructed the healthy mucosa. Furthermore, some authors [10,11] ignored the keratin layer and inflammatory infiltrate, while others provided no data on this issue [9]. Assuming that healthy tissue presents greater resistance to the vertical than to the superficial growth of the tumour [6], it is reasonable to think that the most aggressive tumours are those with the greatest capacity to grow downwards vertically. Thus, in our view, the tumour mass that reveals the vertical growth capacity of the tumour and its aggressiveness is that which can be observed below an imaginary line reconstructing the healthy oral mucosa, because below this line the tumour must destroy healthy tissue in order to invade. The exophytic growth of the tumour should not be considered, because it does not represent the overcoming of tissue resistance, whereas the space left by the ulcerated tumour should be included, because it represents tissue destroyed by the downwards growth of the tumour. We therefore consider that the reference measurement of tumour thickness should be the distance between the maximum depth of the tumour and the imaginary mucosal line described above. The drawbacks of using the tumour thickness parameter include the absence of mucosa in some samples, the tangential cutting of some tissue sections, and samples that are inadequate to allow measurement of the maximum tumour depth. The thickness of 22 tumours in the present series could not be evaluated for these reasons.

There is also controversy regarding the thickness values that differentiate patients according to their survival. The present data indicate that patients with tumours of $\leqslant 3$ mm thickness have a significantly higher ($P<0.05$) survival rate (85.7% at 5 years) than do those with tumours of greater thickness. We observed no differences in survival between patients with tumours of 4–7 mm thickness (58.3% at 5 years) and those with tumours of >7 mm thickness (57% at 5 years). The multivariate analysis showed that the thickness of the tumour had the greatest influence on the survival of the present patients, more significant than that of the superficial measurement of the tumour or the pathologic T. Other studies have reported the influence of tumour thickness on survival. Brown et al. [10] also described the cut-off point as being 3 mm, whereas Spiro et al. [8] concluded that patients showed a significantly lower survival rate above a tumour thickness of 2 mm. Moore et al. [4] differentiated five groups of patients according to their tumour thickness and found that the survival reduced significantly with increasing tumour thickness, without identifying a cut-off point. Finally, Urist et al. [16] performed a survival analysis and concluded that a thickness of 6 mm was the cut-off point to divide patients with tumours of the oral mucosa according to their survival.

Other studies that did not include a survival analysis reported a significant association between the tumour thickness and the presence of cervical lymph node recurrence [8,10,12,18–21]. Only one study found no relationship between tumour thickness and locoregional recurrence [22]. The main conclusion of these works was the need for surgical treatment of the neck when the thickness of the tumour reaches a certain dimension, variously defined as being 2, 3, or 4 mm [8,10,12,18,19], given that the possibility of cervical metastasis is significantly increased above these thicknesses.

We conclude that the thickness of the tumour is the most influential parameter on the survival of patients with cancer of the tongue, and that the survival significantly reduces above a thickness of 3 mm. Wider studies are required to unify criteria for the measurement of this important prognostic parameter.

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