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Clinico-pathological features of squamous cell carcinoma of the oral cavity in patients <40 years of age

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BACKGROUND: Considerable controversy exists in the literature regarding the clinical course of young patients with oral squamous cell carcinoma (SCC). The purpose of this study was to evaluate the clinico-pathological features of oral SCC among young people.
METHODS: From a cohort of 529 patients diagnosed with SCC, 35 (6.6%) were under the age of 40 years. This group was compared to a control group of 110 cases aged over 40 to determine if there were any differences in clinicopathological features between the two groups.
RESULTS: In the young group there were 20 males and 15 females. The site was most frequently the tongue (51.3%), followed by the floor of the mouth, the buccal mucosa, and the upper and lower alveolus and gingiva. The local and regional control rate was 64.8% which was similar to that of older patients in this series.
CONCLUSIONS: The prognosis of oral SCC in the young patients does not appear to be different from that of the older population. Univariate analysis showed that clinical stage and the mode of invasion were the most significant prognostic factors in both younger and older patients.
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Keywords: oral carcinoma; prognostic factors; young patients

Introduction

It is generally considered that oral cancer is most common in men in the sixth to eighth decades of life and is rare in patients younger than 40 years. The incidence of oral squamous cell carcinoma (SCC) in patients younger than 40 years has been reported to range from 0.4 to 3.9% of all cases (1). In the cancer registries of the UK and USA oropharyngeal cancers (IDC10 C00-C14) in persons <40 years account for 4.6% and 5.2% of all registrations respectively (2, 3). A review of literature reveals no consensus regarding the clinical course or prognosis of younger patients when compared with older patients. There is a generally held view that oral cancers in young people are more aggressive and have a worse prognosis. Although this is supported by some studies (4–7), others have shown that the 5-year survival rate of younger patients is better than for older individuals (2, 8, 9). Other studies, however, suggest that young patients have a similar clinical course and their survival rate generally resembles that reported for patients of all ages when compared stage-for-stage (10–12).

It has even been suggested that oral cancer in younger persons may be a distinct disease entity, on the basis of different biological behaviour and aetiological factors (5–7). With regards to smoking and alcohol habits, it has been estimated that smoking and alcohol consumption account for 75% of all cases of oral SCCs. However, the significance of these risk factors among young patients is still controversial. Franceschi et al. (13) reported results of a case–control study showing that smoking is strongly associated with the development of oral cancer in older patients but is not generally considered to be a significant aetiological agent in younger patients. This view is shared by a number of descriptive studies (6, 7, 14) but more recently, Llewellyn et al. (15) have reported conflicting evidence in a comprehensive literature review. A case–control study (16) have shown that young patients exhibit similar behavioural risk factors as older patients.

It seems therefore that recent studies suggest that oral cancer in young and old patients is a similar disease with a similar outcome. Few studies have analysed the pathology of these lesions to confirm whether or not lesions are histologically similar. The purpose of this study was to compare clinicopathological features of oral SCCs in a group of young patients with similar lesions in a cohort of older patients.

Methods

Between 1990 and 1999, 529 patients with SCC affecting the oral cavity were diagnosed at the Eastman Dental

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Institute. Of these, 35 (6.6%) were aged <40 years at the time of initial diagnosis. The original biopsies of all these patients were available for review and clinical details relating to tumour stage were obtained from the pathology records. As a group for comparison, 110 of the remaining 494 cases were selected for review. The larger sample size of the older patients was used to increase the statistical power for comparisons. Stratified random sampling was undertaken to ensure that the older cases represented all ages over 40 years, but that clinical and pathological features did not influence sampling probability.

All patients were staged according to the UICC TNM system (17). Biopsy specimens obtained prior to treatment were graded as well, moderately or poorly differentiated according to the World Health Organization (WHO) criteria (18). All specimens were also graded according to the method of Anneroth et al. (19), applied to the invasive front of tumours as described by Bryne et al. (20). Five individual parameters were scored on a 4-point scale: degree of keratinization, number of mitoses, mode of invasion, depth of invasion and lympho-plasmacytic infiltration. As a measure of outcome, tumours were defined as 'controlled' or 'uncontrolled'. Controlled tumours were defined as those in which there had been no recurrence or metastasis for more than 2 years after treatment. The uncontrolled group was those tumours with development of local recurrence or cervical lymph node metastasis or distant metastasis within 2 years of first diagnosis. Differences between patient groups were compared using chi-square test except in the comparison of outcomes for young and old patients when ANOVA was used. Statistical significance was considered when the P-value was <0.05. The statistical analyses were performed with STAT VIEW 4.0 statistical software.

Results

In the young group, there were 20 male and 15 female patients. The distribution by aged showed that the number of patients increased with increasing age (Table 1) as would be expected. The youngest patient was a 19-year-old female. The male–female ratio (1.33:1) was the same as that of the older group (1.39:1). Most lesions (54.3%) in the young group involved the tongue as floor of mouth, buccal mucosa and alveolar ridge and others each account for 11.4%. In the older group, more lesion affected the alveolar ridge, but still the tongue is most involved, just like in the young group.

A comparison of the clinical stage between the younger and older groups is shown in Table 2. There was a statistically significant difference between the size of tumours at presentation ($P = 0.027$) with a greater number of patients in the older group presenting with large (T4) lesions. However, there were no significant differences in the lymph node status or overall TNM staging.

The analysis of histopathological findings is shown in Table 3. In the young group, most tumours (65.7%) were well-differentiated SCCs compared with only 32.7% in the older group. This difference was statistically significant ($P < 0.001$). Grading of different pathological parameters, according to the Anneroth et al. (19) method, showed some variations but there were no significant differences between the two groups (Table 3).

The local and regional control rates of the younger and older groups and the results of the univariate analysis and ANOVA concerning prognosis are shown in Tables 4 and 5. Univariate analysis showed that size of tumour (T stage), degree of differentiation and the mode of invasion were significantly associated with prognosis in the younger patients. In older patients, nodal status (N stage), and the mode and depth of invasion were significant factors. Stage was significantly associated with prognosis in both groups, but there were no significant differences between the young and old patients.

Discussion

The incidence of oral cancer in the young is relatively low. We retrospectively reviewed the pathology of lesions from young patients with carcinoma of the oral cavity and compared them with lesions from older patients in order to determine if there were any defining characteristics in the young population. In this study,

Table 1 Age and gender distribution

Age group (years)	*Male*	*Female*
Young group		
<20	0	1
21–30	9	4
31–40	11	10
Total	20	15
Old group		
41–50	10	6
51–60	19	10
61–70	22	12
71–80	9	10
81–90	4	5
91+		3
Total	64	46

Table 2 Distribution of clinical factors

	Number (%) in each group		
Factor	*Patients <40*	*Patients >40*	*P-value*
T-classification			0.0269
T1	17 (48.6)	49 (44.5)	
T2	8 (22.9)	21 (19.1)	
T3	5 (14.3)	4 (3.6)	
T4	5 (14.3)	36 (32.7)	
N-classification			0.6836
N0	30 (85.7)	85 (77.3)	
N1	3 (8.6)	18 (16.4)	
N2	2 (5.7)	7 (6.4)	
N3	0 (0.0)	0 (0.0)	
Stage-classification			0.4014
I	17 (48.6)	47 (43.1)	
II	7 (20.0)	16 (14.7)	
III	4 (11.4)	10 (9.2)	
IV	7 (20.0)	37 (33.9)	

Table 3 Distribution of histopathological factors

Factor	*Number (%) in each group*		*P-value*
	Patients < 40	*Patients > 40*	
Differentiation			0.0009
Well	23 (65.7)	36 (32.7)	
Moderately	5 (14.3)	51 (46.4)	
Poorly	7 (20.0)	23 (20.9)	
Keratinization			0.5616
Grade 1	21 (60.0)	63 (57.3)	
Grade 2	3 (8.6)	8 (7.3)	
Grade 3	6 (17.1)	15 (13.6)	
Grade 4	5 (14.3)	24 (21.8)	
Mitosis			0.0925
Grade 1	24 (68.6)	86 (78.2)	
Grade 2	10 (28.6)	15 (13.6)	
Grade 3	1 (2.9)	4 (3.6)	
Grade 4	0 (0.0)	5 (4.5)	
Mode of invasion			0.4891
Grade 1	5 (14.3)	8 (7.3)	
Grade 2	8 (22.9)	34 (30.9)	
Grade 3	9 (25.7)	22 (20.0)	
Grade 4	13 (37.1)	46 (41.8)	
Depth of invasion			0.1118
Grade 1	4 (11.4)	3 (2.7)	
Grade 2	7 (20.0)	33 (30.0)	
Grade 3	8 (22.9)	19 (17.3)	
Grade 4	16 (45.7)	55 (50.0)	
Lympho-plasmacytic infiltration			0.3068
Grade 1	6 (17.1)	25 (22.7)	
Grade 2	14 (40.0)	36 (32.7)	
Grade 3	10 (28.6)	41 (37.3)	
Grade 4	5 (14.3)	8 (7.3)	

Table 4 Local and regional control rate according to clinical factors

Factor	*Patients < 40*		*Patients > 40*		*P-value (≤40 vs. > 40)*[a]
	Percentage controlled	*P-value*	*Percentage controlled*	*P-value*	
T-classification		0.0051		0.0739	0.1815
T1	82.4		78		
T2	87.5		68.2		
T3	33.3		75		
T4	16.7		51.4		
N-classification		0.1009		0.0206	0.799
N0	70		74.1		
N1	50		55.6		
N2	0		28.6		
N3					
Stage-classification		0.0012		0.0243	0.1325
I	81.3		80.9		
II	100		75		
III	50		63.6		
IV	12.5		50		

[a]Comparison of young and old groups by two-factor factorial ANOVA.

patients with oral SCC younger than 40 represented 35 (6.6%) of the total number of 529 patients who were diagnosed between 1990 and 1999. Saito et al. (21) reported that 19 (5.8%) of 326 patients with oral carcinoma were younger than 40 years old, while others have suggested it is very rare. McGregor et al. (22) reported that only 36 patients with SCC of the tongue and oral cavity were treated between 1944 and 1982, while in another study (23) only 39 patients aged < 40

Table 5 Local and regional control rate according to histopathological factors

Factor	*Patients < 40*		*Patients > 40*		*P-value (≤40 vs. > 40)*[a]
	Percentage controlled	*P-value*	*Percentage controlled*	*P-value*	
Differentiation		0.0324		0.0702	0.1347
Well	69.6		80.6		
Moderately	100		66.7		
Poorly	33.3		52.1		
Keratinization		0.0617		0.1551	0.0266
Grade 1	85		65.6		
Grade 2	33.3		100		
Grade 3	71.4		53.3		
Grade 4	20		73.1		
Mitosis		0.406		0.743	0.4889
Grade 1	68		66.3		
Grade 2	60		71.4		
Grade 3	50		100		
Grade 4			60		
Mode of invasion		0.0078		0.0329	0.3374
Grade 1	100		100		
Grade 2	75		79.4		
Grade 3	88.9		66.7		
Grade 4	33.3		41.6		
Depth of invasion		0.0721		0.0317	0.303
Grade 1	100		100		
Grade 2	57.1		80		
Grade 3	88.9		61.1		
Grade 4	47		57.4		
Lympho-plasmacytic infiltration		0.3638		0.1042	0.0804
Grade 1	33.3		80		
Grade 2	71.4		74.3		
Grade 3	72.7		63.4		
Grade 4	66.7		37.5		

[a]Comparison of young and old groups by two factor factorial ANOVA.

presented between 1964 and 1983. In the USA, a recent analysis of the National Cancer Institute, Surveillance, Epidemiology and End Results (SEER) data shows 5.2% of tongue cancer patients were under 40 years (2). The proportion of younger patients in the present study is larger. However, this probably does not reflect increasing or larger numbers in the UK, because UK registration data (3) shows 5.2% and 4.6% in 1992 and 2000 respectively. Data for London registries show 6% of cases were under 45 years (14). The proportion in the present study is probably representative or may reflect the specialist nature of the unit which is a tertiary referral centre.

In this study, the male–female ratio was 1.33:1. The male–female ratio in the total cases treated during the same period was 1.39:1. Some previous studies have suggested that there is a predominance of females in the younger age groups (7, 24), but most have reported a similar higher number of males (2, 3, 15, 16, 25, 26). Analysis by site showed that 54.3% of cancers arose on the tongue in young patients, compared with 30.9% in older patients, supporting previous studies suggesting that tongue may be more commonly affected in younger patients (reviewed in 15).

No difference was observed in the 2 year control rate of SCCs between the younger and the older patients. Byers (7) suggested that cancer in younger adults tended

to be more frequently anaplastic (48% vs. 22%) resulting in a more virulent behaviour and poorer prognosis. Amsterdam and Strawitz (27) reported a poorer survival in T1 and T2 oral cancers for the age group younger than 35 years. Yung and Daniel (28) showed that oral cavity and oropharyngeal cancer in young adults carried a dismal prognosis with a 3-year survival of 17% and loco-regional failure rate of 91%. Many reports, however, show comparable stage-for-stage survival between young and old patient groups (10–12, 29, 30). Although there has been no overall consensus about the difference in prognosis between the younger and older groups, these latter studies, and more recent studies, indicate that there are no differences and even suggest that there may be improved survival among younger individuals (2, 8, 9, 22, 31).

In the present study, univariate analysis showed that clinical stage and the pattern of invasion were the most significant prognostic factors in both younger and older patients. This is in agreement with a number of previous studies in which stage has been shown to be the single most important prognostic factor for oral carcinoma (1, 32–36) regardless of age. The strong influence of clinical stage on prognosis emphasizes the importance of early diagnosis and treatment of oral malignancies, but the similar findings in both groups does not suggest that younger patients should be managed any differently. As Byers (7) has pointed out the management of each patient must be on an individual basis regardless of emotional or subjective factors.

With regard to pathological features, in this study there was a tendency for tumours in younger individuals to be well differentiated in contrast to lesions in the old group which were more often moderately differentiated. Histological grading of oral SCC is used as a routine tool for predicting prognosis in individual patients and the results support previous studies showing that differentiation and pattern of invasion are significant predictors of outcome. In a number of studies however, pattern of invasion has been shown to be a more significant indicator than simple differentiation alone (37–40). For example, in a study of 102 patients with intra-oral carcinoma, Yamamoto et al. (37) reported an association between the pattern of invasion and frequency of metastases. Sasaki (38) also showed that the pattern of invasion was the most significant factor for survival in their multivariate analysis of prognostic factors for oral SCCs. Overall, however, there was little evidence that lesions in younger individuals were more aggressive or in any way histologically different from those in older patients. This confirms previous studies, which have been unable to detect any pathological differences between lesions in young and old persons (11). More recent studies of genetic alterations have also shown no differences between the age groups (41, 42).

In conclusion, this study shows that there are no specific pathological characteristics of carcinomas in young adults. The outcome of oral SCC in the young patients does not appear to be different from that of the older population. For all age groups, clinical stage and the pattern of invasion were the most significant prognostic factors. Questions still remain, however, as to factors associated with carcinomas in younger individuals. Although exposure to behavioural risk factors is similar, in younger persons these have less time to act and yet the lesions are still similar in terms of stage and pathology, although they are more common on the tongue. Further research is still needed to investigate possible confounding or potentiating factors including genetic and hereditary factors and diet, as well as possible demographic factors (15).

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