Comparison of Clinical Characteristics and Outcome of Young and Older Patients with Oral Squamous Cell Carcinoma

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Oral squamous cell carcinoma (SCC) is relatively uncommon in patients less than 40 years of age. Of 411 patients with oral SCC treated, 27 patients (6.6%) were less than 40 years of age. These cases of young age were compared with those of older age concerning their clinical characteristics and outcome. The five-year overall survival rate was 92.6% for young and 68.8% for older patients, respectively ($P = 0.027$). Using logistic multivariate regression analysis, including age, gender, primary site, TN category and treatment modality, only TN category and treatment modality were significant and independent predictive variables for recurrence, but age was not ($P < 0.05$). It was concluded that better prognosis observed in young patients with oral SCC was significantly determined by their characteristics of TN category and treatment modality, but not by their age.

Key words: oral cancer, squamous cell carcinoma, young patients, oral cavity

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Introduction

Oral squamous cell carcinoma (SCC) is relatively uncommon in patients less than 40 years of age. It has been estimated that less than 3% of all oral cavity SCCs occur in patients younger than 40 years of age (1-3). There have been a few reports regarding the outcome of patients younger than 40 years of age with oral tongue SCC (4-6). Some authors (4-5) reported that patients younger than 40 years old with SCC of the tongue had a higher rate of locoregional recurrence rate than did older patients. Other authors (6) have found young patients to have a prognosis similar to their older counterparts. However, these reports have been limited, mostly due to small numbers of patients, which has precluded meaningful statistical analysis and limited our understanding of etiology, natural history, and optimal therapeutic management, and outcome. Resolution of these issues is important because if age-related differences exist, treatment strategies for young patients may potentially be different. Our purpose, therefore, is to evaluate possible predictive variables for patients younger than 40 years of age with oral SCC by comparison with older patients.

Patients and methods

Patients

Four hundred eleven patients consisting of 270 males and 141 females with oral SCC treated at the First Department of Oral and Maxillofacial Surgery, Tokyo Medical and Dental University Hospital, from January 1988 to December 1997, were included in this study. The mean age of these patients was 59.6 ± 13.1 years (mean $\pm$ SD), with a range from 23 to 88 years (Fig. 1). Of these patients, 27 patients (6.6%; 20 males, 7 females) were less than 40 years of age and were defined as young patients in this analysis. The mean age of the young patients was 31.7 ± 4.9 years, with a range from 23 to 39 years. The number of patients older than or equal to 40 years of age was 384 patients (250 males, 134 females) and the mean age was 61.6 ± 11.1 years, with a range from 40 to 88 years. All patients had a minimum 2-year follow-up.

Definitive diagnoses and histologic grading were rendered by biopsy. Histologic grading was classified into three types (Grade I, numerous epithelial pearls; Grade II, epithelial pearls infrequent or even absent; and Grade III, epithelial pearls rarely seen) according to the World

Fig. 1: Distribution of 411 patients of oral squamous cell carcinomas by age and gender
Mean $\pm$ standard deviation, 59.6 $\pm$ 13.1 years; range 23 to 88 years

Table 1: Summary of 27 cases of patients less than 40 years of age

Age/Gender	UICC / WHO	Treatment	Time/site of recurrence	Salvage	Outcome (months)
Primary site					
23/F tongue	T1N0M0 / Grade I	Partial glossectomy	None		NED(31)
24/M tongue	T1N0M0 / Grade I	Partial glossectomy	None		NED(69)
25/M tongue	T1N0M0 / Grade I	Partial glossectomy	None		NED(24)
26/F tongue	T1N0M0 / Grade I	Partial glossectomy	None		NED(96)
29/F tongue	T1N0M0 / Grade I	Partial glossectomy	None		NED(28)
30/M tongue	T1N0M0 / Grade I	Partial glossectomy	5 months/neck	RND(pN2b)	NED(101)
30/M tongue	T1N0M0 / Grade II	Partial glossectomy, RND(pN0)	None		NED(36)
30/M tongue	T1N0M0 / Grade II	Partial glossectomy	None		NED(56)
31/M tongue	T1N0M0 / Grade I	Partial glossectomy	None		NED(57)
38/M tongue	T1N0M0 / Grade II	Partial glossectomy	None		NED(80)
26/M tongue	T1N2bM0 / Grade II	Partial glossectomy, RND(pN2b)	None		NED(44)
31/M tongue	T2N0M0 / Grade II	Preoperative XRT(30Gy), Hemiglossectomy, Reconstruction, RND(pN0)	7 months/neck	None	DOD(12)
32/M tongue	T2N0M0 / Grade I	Partial glossectomy	None		NED(76)
33/M tongue	T2N0M0 / Grade II	Hemiglossectomy, Reconstruction, RND(pN0)	None		NED(39)
35/F tongue	T2N0M0 / Grade I	Partial glossectomy	None		NED(29)
37/F tongue	T2N0M0 / Grade II	Hemiglossectomy, Reconstruction, RND(pN0)	None		NED(53)
39/F tongue	T2N0M0 / Grade II	Hemiglossectomy, RND(pN0)	None		NED(122)
38/M tongue	T2N1M0 / Grade I	Partial glossectomy, RND(pN1)	None		NED(49)
34/M tongue	T3N0M0 / Grade I	Hemiglossectomy, Reconstruction, RND(pN0)	None		NED(33)
35/M tongue	T3N0M0 / Grade II	Hemiglossectomy, Reconstruction, RND(pN0)	None		NED(60)
29/F tongue	T3N1M0 / Grade I	Hemiglossectomy, RND(pN1)	15 months/lung	XRT	DOD(19)
27/M tongue	T4N2cM0 / Grade II	Preoperative XRT(20Gy), Hemiglossectomy, Reconstruction, RND(pN2c)	None		NED(62)
35/M lower gingiva	T1N0M0 / Grade II	Marginal resection	None		NED(31)
39/M lower gingiva	T1N0M0 / Grade II	Marginal resection	None		NED(67)
27/M lower gingiva	T4N0M0 / Grade I	Segmental resection, Reconstruction, RND(pN0)	None		NED(93)
34/M upper gingiva	T1N0M0 / Grade I	Partial maxillectomy	None		NED(32)
39/M upper gingiva	T1N0M0 / Grade I	Partial maxillectomy	None		NED(91)

UICC: TNM classification, WHO: Histologic grading, M: male, F: female, RND: radical neck dissection, XRT: radiotherapy, NED: no evidence of disease, DOD: dead of disease

Health Organization (WHO) histologic grading system (7). TNM classification of the Union Internationale Contre le Cancer (UICC, 1997) was used to stage the disease(8). Clinical indication to therapeutic modalities was determined in our hospital by clinical conference of oral surgeons and radiation oncologists on an individual patient basis. In general, surgical resection alone for early stage and composite resection with reconstruction for advanced stage were performed, and radiotherapy alone was performed for the patients who had serious histories, such as cerebrovascular accidents, and who may not tolerate more aggressive surgical therapy.

Statistical analysis

Chi-square test with Fisher's exact test was used for the statistical significance. The statistical correlation between data was assessed by Spearman's rank correlation test. Overall survival time was determined as the time interval in months between initial treatment and death or until the date of follow-up. The overall survival rates were calculated with the Kaplan-Meier method. The log-rank test was used to test for the statistical signifi-

cance of differences in overall survival curves.

The prognostic factors in recurrence (primary, regional and distant failure) were evaluated by logistic multivariate regression analysis. Variables included for the analysis were age, gender, primary site, TN category, and treatment modalities. P values < 0.05 were considered statistically significant.

Results

Summary of 27 cases of patients less than 40 years of age is shown in Table 1. Distribution of primary site of the tumors is shown for both young and older patients in Table 2. The incidence of tongue carcinoma was significantly different between young (81.5%) and older (56.8%) patients (P = 0.012). Male to female ratio was 2.9:1 in young and 1.9:1 in older patients (P = 0.343). Table 3 showed patient distribution according to stage and TN category in young and older patients. The incidence of T1 of oral SCC was significantly different between young (55.6%) and older (32.5%) patients (P = 0.015). The incidence of N0 of oral SCC was not significantly different between young (85.2%) and older (79.2%) patients (P =

Table 2: Distribution of primary site of young and older patients

Site	Young (< 40 years old)				Older (≥ 40 years old)			
	M	F	Total	(%)	M	F	Total	(%)
Tongue	15	7	22	(81.5)	147	71	218	(56.8)
Lower gingiva	3	0	3	(11.1)	37	24	61	(15.9)
Upper gingiva	2	0	2	(7.4)	10	16	26	(6.8)
Buccal mucosa	0	0	0	(0.0)	25	18	43	(11.2)
Floor of mouth	0	0	0	(0.0)	27	1	28	(7.3)
Hard palate	0	0	0	(0.0)	4	4	8	(2.0)
Total	20	7	27	(100.0)	250	134	384	(100.0)

M: male, F: female

P=0.012 for the difference between young and older patients in "Tongue" site group

Fig. 2: Overall survival rates in young and older patients, P= 0.027 (Kaplan-Meier analysis)

Table 3: Patient distribution according to stage, TN category

		Young (%) n=27	Older (%) n=384
Stage	I	14 (51.9)	116 (30.2)
	II	6 (22.2)	136 (35.4)
	III	4 (14.8)	54 (14.1)
	IV	3 (11.1)	78 (20.3)
T category	T1	15 (55.6)	125 (32.5)
	T2	7 (25.9)	178 (46.4)
	T3	3 (11.1)	43 (11.2)
	T4	2 (7.4)	38 (9.9)
N category	N0	23 (85.2)	304 (79.2)
	N1	2 (7.4)	30 (7.8)
	N2a	0 (0.0)	0 (0.0)
	N2b	1 (3.7)	37 (9.6)
	N2c	1 (3.7)	13 (3.4)

All cases were M0

P=0.019 and 0.015 for the difference between young and older patients in "Stage I and T1" group, respectively

0.454). The incidence of stage I of oral SCC was significantly different between young (51.9%) and older (30.2%) patients ($P = 0.019$). The correlation between age and stage was not significant ($R = 0.087$, $P = 0.078$).

Table 4 showed patient distribution according to initial treatment modalities for primary tumor. In young patients, the composite surgical resection with reconstruction and the resection alone were performed in 13.6% and 86.4% for T1-T2 group, respectively. None of young patients received either radiotherapy alone or chemotherapy alone. On the other hand, in older patients, the composite resection with reconstruction and others (resection alone, brachytherapy alone, and external radiotherapy alone) were performed in 13.9% and 86.1% for T1-T2 group, respectively. The difference of treatment modality between young and older patients in T1-T2 group was not significant ($P = 0.999$). The composite resection with reconstruction for T3-T4 group was performed for 80.0% in young and 44.4% in older patients, respectively ($P = 0.179$).

Primary recurrence was found in none of the 27 young patients. Of 3 patients (11.1%) with regional or distant recurrence, 2 died of disease. On the other hand, as for 384 older patients, 302 patients are alive with no evidence of disease, while 64 patients died of oral carcinoma (33 with primary failures, 19 regional failures, and 12 distant failures) and 18 patients died with other disease. The five-year overall survival rate was 92.6% for younger and 68.8% for older patients, respectively (Fig. 2, $P = 0.027$).

Logistic multivariate regression analysis demonstrated that T category ($P = 0.003$; odds ratio = 1.63) and N category ($P < 0.001$; odds ratio = 2.00) were significant and independent predictive variables for recurrence (Table 5). When the multivariate analysis was performed for young and older patients separately, again T category ($P = 0.003$; odds ratio = 1.62) and N category ($P < 0.001$; odds ratio = 2.03) were significant and independent predictive variables for recurrence in older patients. On the other hand, there was no significant predictive variable for recurrence in younger patients.

Furthermore, when the multivariate analysis was performed by excluding N category, T category ($P = 0.001$; odds ratio = 1.71) and treatment modality ($P = 0.048$; odds ratio = 1.90) had significant and independent predictive variables for recurrence (Table 6). When the multivariate analysis was performed for young and older patients separately, again T category ($P = 0.001$; odds ratio = 1.69) and treatment modality ($P = 0.045$; odds ratio = 1.93) were significant and independent predictive variables for recurrence in older patients. On the other hand, nothing was a significant predictive variable for recurrence in younger patients.

The correlations between T category and N category, between T category and treatment modality, and between N category and treatment modality of young and older patients with oral SCC were significant ($R = 0.268$; $P < 0.001$, $R = -0.374$; $P < 0.001$, $R = -0.394$; $P < 0.001$, respectively).

Discussion

It has been reported that the percentage of SCC of the oral cavity and oropharynx in patients under 40 years of age ranges from 0.9% to 2.7% of oral SCC of all ages (1-

Table 4: Patient distribution according to treatment modalities and T category

Initial treatment of primary tumor	Young (%)		Older (%)	
	T1-T2 (%)	T3-T4 (%)	T1-T2 (%)	T3-T4 (%)
Resection with reconstruction	3 (13.6)	4 (80.0)	42 (13.9)	36 (44.4)
Resection alone	19 (86.4)	1 (20.0)	197 (65.0)	27 (33.3)
Brachytherapy alone	0 (0.0)	0 (0.0)	53 (17.5)	5 (6.2)
External radiotherapy alone	0 (0.0)	0 (0.0)	11 (3.6)	13 (16.1)
Total	22 (100.0)	5 (100.0)	303 (100.0)	81 (100.0)

Table 5: Prognostic factors in oral SCC by logistic multivariate regression analysis

	Odds ratio	95%CI	P value
Age (years): <40 vs. 40f	0.46	0.12-2.17	.328
Gender: male vs. female	0.79	0.44-1.42	.433
Primary site: tongue vs. others	1.02	0.57-1.85	.938
T categories: T1-T4	1.63	1.19-2.24	.003
N categories: N0-N2	2.00	1.40-2.86	<.001
Treatment modality: resection with reconstruction vs. others	1.21	0.60-2.42	.595
95% CI: 95% confidence interval			

Table 6: Prognostic factors in oral SCC by logistic multivariate regression analysis excluding N category

	Odds ratio	95%CI	P value
Age (years): <40 vs. 40f	0.41	0.09-1.88	.252
Gender: male vs. female	0.75	0.43-1.33	.332
Primary site: tongue vs. others	0.97	0.54-1.73	.919
T categories: T1-T4	1.71	1.25-2.32	.001
Treatment modality: resection with reconstruction vs. others	1.90	1.01-3.58	.048
95% CI: 95% confidence interval			

3). The incidence of oral SCC in patients younger than 40 years old is 6.6% in our present study, which is somewhat higher than the reported rate. As for site distribution, our result indicates that the incidence of tongue carcinoma is significantly different between young (81.5%) and older (56.8%) patients. Although the roles of smoking and drinking alcohol in the aetiology of oral cancer are common knowledge among the medical community (9-10), it seems that there is a strong association with population-specific aetiological agents, particularly chronic stimulus by teeth, regarding tongue carcinoma in young patients. We report also that the incidence of T1 of oral SCC is significantly different between young (55.6%) and older (32.5%) patients. It is considered that early detection and medical examination are possible because young patients may have better oral health care than older patients.

An aggressive therapeutic approach to young patients with oral SCC appears warranted in an attempt to improve to ultimate survival (1-2,4). Son *et al.* (1) showed that oral cavity and oropharyngeal cancer in young adults carried a dismal prognosis with a 3-year actuarial survival of 17% and locoregional failure rate of 91%. Cusumano *et al.* (2) showed that all five patients with stage I and II of oral cavity carcinoma as young adults survived 5 years, compared with only one of six patients with stage III and IV disease. Sarkaria *et al.* (4) showed that five of six patients with tongue cancer as young adults had developed locoregional failure and four patients had died from their cancer.

The present study showed that the composite re-

section with reconstruction for T3-T4 cases was performed for 80.0% in young and 44.4% in older patients, respectively. This is because young patients could tolerate aggressive operations whereas some older patients with serious histories, such as cerebrovascular accidents, may have not received more aggressive surgical therapy.

The prognostic factors of young patients with SCC of the oral cavity and oropharynx are still controversial (1-6). Although age has been reported as a significant factor, some authors (4-5) reported that patients younger than 40 years old with SCC of the tongue had a higher rate of locoregional recurrence rate than did older patients. Other authors (6) have found young patients to have a prognosis similar to their older counterparts. This study indicated that the five-years overall survival rates of young and older were 92.6% and 68.8%, respectively. Further, this study demonstrated that using logistic multivariate regression analysis with including age, gender, primary site, TN category and treatment modality, only TN category and treatment modality were significant and independent prognostic factors, but the age was not.

Although the prognosis of young patients with oral SCC was better than the older patients in this study, this is strongly suggested because young patients could be performed more aggressive therapy for advance stage. It was concluded that the prognostic factors of young patients with oral SCC were TN category and treatment modality, rather than the age. This suggests that improvement of therapeutic outcome may be possible for older patient by careful selection of the treatment modality. Further analysis for this hypothesis should be continued.

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