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Original

Ten-year analysis of oral cancer focusing on young people in northern Thailand

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Abstract: The objective of the present study was to assess the current situation of oral squamous cell carcinoma (OSCC) in northern Thailand, with an emphasis on patients <40 years of age. Medical records of patients histologically diagnosed with OSCC were collected from the Cancer Registry of Maharaj Nakorn Chiang Mai Hospital, Thailand between 2001 and 2010. The clinico-demographic data of patients aged <40 years (young group) and those aged ≥40 years (old group) were compared. A total of 874 patients were included in this study, of which 4.1% were <40 years of age. The tongue was the most common cancer site in both age groups. Most patients in both age groups were diagnosed with oral cancer at stage IV. Tobacco smoking (62.3%) and alcohol consumption (52.3%) were the most common risk factors in both age groups. However, the rates of betel quid chewing (17.5%) had decreased from those found in our study in the previous decade (50.2%); these rates were not found in the young group. The 5-year survival rate was 27.4% for the old group and 56.2% for the young group. OSCC remains a serious oral health problem in northern Thailand, and it has not been resolved among young adults.
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Keywords: oral cancer; squamous cell carcinoma; Thailand; young people.

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Introduction

Cancer of the oral cavity accounts for approximately 3% of the cancer burden worldwide (1), and it is the 8th most common cancer in males and the 14th in females (1). Squamous cell carcinoma is the most common type of oral carcinoma (1), representing more than 90% of all tumors in the oral cavity (1). Oral squamous cell carcinoma (OSCC) becomes more prevalent with increasing age (2). It is commonly observed after the 5th decade of life and has male predominance with a male-to-female ratio of 3:1 (3,4). Recently, many studies have reported an increasing incidence of OSCC in younger people (5,6). Despite the advancements in treatment modalities in the recent years, the 5-year survival rate of OSCC has not improved compared with other malignant tumors, which is probably because it is usually diagnosed during the more advanced stages of the disease (5).

Oral cancer is a multifactorial disease (6), and the risk factors for OSCC are tobacco use, high alcohol consumption, betel quid chewing, and low dietary intake of fresh

fruit and vegetables (7,8). Exposure to certain factors can result in the development of tumors at specific sites in the oral cavity. OSCC mostly involves the tongue (41%), followed by the floor of the mouth (21.1%) and other parts of the mouth (20.5%). In south-central Asia, where tobacco chewing is widely practiced, the most common site of OSCC is the buccal mucosa. In western and eastern Europe, where alcohol consumption and tobacco smoking habits are popular, the most common sites for OSCC are the tongue and the floor of the mouth (1). Because OSCC is a lifestyle-related disease, much evidence suggests that reduction of exposure to the risk factors lowers the incidence of OSCC (9).

In Thailand, oral cancer was among the ten most common cancers (10). Regarding oral cancer in northern Thailand, Iamaroon et al. (11) reviewed 587 medical records of patients with OSCC between 1991 and 2000 at Maharaj Nakorn Chiang Mai Hospital, which is considered to be the biggest cancer treatment center in northern Thailand. The percentage of patients <45 years of age with OSCC was 12.8%, which is 2-fold higher than the rates reported in most studies (4%-6%) (12). The comparatively high incidence in young patients probably is the consequence of exposure to traditional risk factors at a very young age. The incidence ratio between males and females was 1.3:1 (11). Most of the patients were diagnosed with OSCC at stage IV. The tongue (42.8%) was the most common site of the OSCC followed by the buccal mucosa (16%). These sites are related to the most common risk factors among northern Thai people, which are tobacco smoking and betel quid chewing. In young patients, OSCC is rarely found in the buccal mucosa (11), which is probably because betel quid chewing is less popular among the younger population. Iamaroon et al. (11) reported an association between risk factors and sexes: tobacco smoking was more common among males, whereas betel quid chewing was more common among females.

The aim of the present study was to identify the current situation of OSCC among northern Thai patients, including demographic distribution, tumor status at diagnosis, related risk factors, and the survival rate of patients, and to compare these variables between patients <40 years (young group) and those ≥40 years (old group). We believe that our study will provide important insights into OSCC in northern Thailand, thus aiding the development of efficient methods for cancer prevention and control.

Materials and Methods

We analyzed the medical records of patients histologically diagnosed with OSCC at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand in 2001-2010. The medical records were obtained from the Cancer Registry at Maharaj Nakorn Chiang Mai Hospital, which is a tertiary hospital in northern Thailand. The OSCC cases included in the present study had primary tumors located in the oral cavity. Metastatic tumors, oropharyngeal tumors, salivary gland tumors, sarcomas, verrucous carcinomas, and other variants of OSCC were excluded. All tumors were biopsied and inspected microscopically by qualified pathologists.

The data collated in the present study included demographic distribution, status of the tumors at diagnosis, histories of risk factors, and vital status. For demographics, we collected data on age, sex, race, and the province of domicile of the patients at the time of diagnosis. The status of the tumors included the site, clinical stage, histologic grade, and mode of treatment. The tumor sites were categorized in accordance with the International Classifications of Diseases for Oncology (ICD-O-3): C00 (lip), C01 and C02 (tongue), C03 (gingiva), C04 (floor of mouth), C05 (palate), C06.0 (buccal mucosa), C06.2 (retromolar area), C06.9 (mouth, not otherwise specified), and multiple sites.

The clinical stages of tumors were stratified with the tumor node metastasis staging system according to the American Joint Committee on Cancer (13). The histologic grade categories were as follows: well differentiated, moderately differentiated, poorly differentiated, and undifferentiated.

The risk factors included in the present study were tobacco smoking, alcohol consumption, and betel quid chewing, which were also reported as the major risk factors among the northern Thai population in the previous decade (11). We assessed the exposure history of the patients to these risk factors in terms of their frequency and duration. Furthermore, the vital status was collected to perform the survival analysis. Deaths caused by cancer were included in the data set. The time to death was measured from the time of diagnosis to the death date. The time to death of the patients who were alive at last date of follow up and the patients who died with other causes were right censored. We excluded the patients who died with unknown cause of death. The patients were divided into two groups based on their ages at the time of diagnosis: patients <40 years of age (young group) and patients ≥40 years of age (old group). We considered 40 years as an appropriate cut-off age because the incidence of OSCC is significantly higher in patients ≥40 years (5,14).

We transferred the patient and tumor data to a Windows-

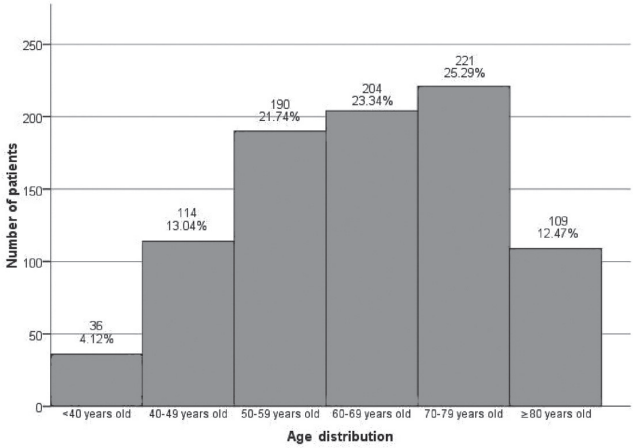

Fig. 1 Age distribution of all patients.

Table 1 Demographic data of patients with oral squamous cell carcinoma

		Age <40 years $n = 36$	(%)	Age ≥40 years $n = 838$	(%)	*P* value
Sex	Male	23	(63.9)	494	(58.9)	0.555
	Female	13	(36.1)	344	(41.1)	
Race	Thai	36	(100)	822	(98.1)	0.507
	Non-Thai	0	(0)	16	(1.9)	
Occupation	Retired	1	(2.8)	453	(54.1)	0.000*
	Independent labor	23	(63.9)	153	(18.3)	
	Agriculture	5	(13.9)	130	(15.5)	
	Merchant	0	(0)	40	(4.8)	
	Housewife	1	(2.8)	22	(2.6)	
	Civil servant	1	(2.8)	16	(1.9)	
	Student	2	(5.6)	0	(0)	
	Others or unknown	3	(8.3)	24	(2.9)	

*Significant at the 0.05 level.

based PC and performed the statistical analysis using the SPSS statistical package, version 17 for Windows (IBM Corp., Armonk, NY, USA). The data were analyzed using descriptive statistics. The associations between sex/age groups and the demographic distribution, tumor status, and the related risk habits were analyzed by the chi-square test at $P = 0.05$. We analyzed the survival function of patients using the Kaplan-Meier estimator. The 5-year survival distributions of sex, age, and stage groups were analyzed by the log-rank test.

Patient confidentiality is a concern. To protect the patients' privacy, any patient medical information at Maharaj Nakorn Chiang Mai Hospital was collected, stored, and used for research only. The research obtained international-standard ethic approval from the Human Experimentation Committee of the Faculty of Dentistry, Chiang Mai University (reference number: 20/2014).

Results

Eight hundred and seventy-four patients were histologically diagnosed with OSCC at Maharaj Nakorn Chiang Mai Hospital between 2001 and 2010. There were 517 (59.2%) male patients and 357 (40.8%) female patients. The age range of the patients was 15-97 years (Fig. 1), and the median age for the patients was 64 years (IQR = 84-44 years). The male-to-female ratio for all patients was 1.4:1. Of the overall patient population, 36 patients (4.1%) were diagnosed at <40 years of age. In the young group, 23 patients (63.9%) were male and 13 (36.1%) were female; the male-to-female ratio was 1.8:1. The youngest male patient was 15 years old, and the youngest female patient was 18 years old. The median age in the young group was 33.5 years (IQR = 42.5-24.5), and the male-to-female ratio was 1.8:1. The demographic data of the patients by age group are shown in Table 1.

In all patients, the most common sites of the tumors were the tongue (38.4%) and gingiva (17.8%). In the young group, the tongue was the most common site, which accounted for 75.0% of all the cases, followed by the palate, buccal mucosa, and the floor of the mouth. In both the overall patients and young group, most of the patients were diagnosed with oral OSCC at stages III and IV, and most tumors were histologically defined as being well differentiated. Table 2 shows the histologic differentiation, site, clinical stage, and mode of treatment stratified by age groups.

Risk factor exposure was related to the sex and age of the patients. Both tobacco smoking ($P < 0.01$) and alcohol consumption ($P < 0.01$) were more frequently observed in males, whereas betel quid chewing was more frequently observed in females ($P < 0.01$). There was a higher proportion of patients who smoked ($P < 0.05$) or chewed betel quid ($P < 0.01$) in the old group than in the young group, whereas there was no significant difference in the proportions of patients who had a history of alcohol consumption ($P = 0.767$) between the two groups. Table 3 shows the numbers and percentages of patients who had been exposed to risk factors, stratified by frequency of exposure. The percentage of patients with concurrent tobacco smoking and alcohol consumption habits was 33.6%. The combinations of risk habits are displayed in Table 4.

One hundred and eighty-eight patients (21.5%) were alive till the last follow-up date. Five hundred and fifty-one patients (63%) died as a result of cancer, and 89 patients (10.2%) died from an unknown cause. For all patients, the 5-year survival rate was 28.7%, and the median survival time was 1.16 ± 0.07 years (Fig. 2). In the young group, the 5-year survival rate was 56.2%, which was significantly better than that in the old group

Table 2 Clinico-pathologic data of patients with oral squamous cell carcinoma

		Age <40 years		Age ≥40 years		*P* value
		n = 36	(%)	*n* = 838	(%)	
Histologic grading	Well differentiated	18	(50.0)	487	(58.1)	0.509
	Moderately differentiated	11	(30.6)	235	(28.0)	
	Poorly differentiated	5	(13.9)	62	(7.4)	
	Undifferentiated	0	(0)	3	(0.4)	
	Unknown	2	(5.6)	51	(6.1)	
Site	Lip	1	(2.8)	63	(7.5)	0.001*
	Tongue	27	(75.0)	309	(36.9)	
	Gingiva	0	(0)	156	(18.6)	
	Floor of the mouth	2	(5.6)	69	(8.2)	
	Palate	2	(5.6)	91	(10.9)	
	Buccal mucosa	2	(5.6)	119	(14.2)	
	Retromolar area	1	(2.8)	12	(1.4)	
	Mouth, NOS	1	(2.8)	16	(1.9)	
	Multiple sites	0	(0)	3	(0.4)	
Clinical stage	I	3	(8.3)	83	(9.9)	0.409
	II	11	(30.6)	169	(20.2)	
	III	1	(2.8)	105	(12.5)	
	IV A	12	(33.3)	275	(32.8)	
	IV B	0	(0)	17	(2.0)	
	IV C	1	(2.8)	14	(1.7)	
	Unknown	8	(22.2)	175	(20.9)	
Treatment	S**	1	(2.8)	119	(14.2)	0.055
	R**	9	(25)	242	(28.9)	
	C**	1	(2.8)	26	(3.1)	
	S + R**	12	(33.3)	156	(18.6)	
	S + R + C**	2	(5.6)	26	(3.1)	
	S + C**	0	(0)	7	(0.8)	
	R + C**	6	(16.7)	58	(6.9)	
	Palliative	2	(5.6)	108	(12.9)	
	Unknown	3	(8.3)	96	(11.5)	

*Significant at the 0.05 level.
**S = surgery, R = radiotherapy, C = chemotherapy, NOS = not otherwise specified

Table 3 Related risk habits

	Age <40 years					Age ≥40 years				
	Male		Female		*P* value	Male		Female		*P* value
	n	(%)	*n*	(%)		*n*	(%)	*n*	(%)	
Tobacco smoking										
Non-smoker	3	(13)	6	(46.2)	0.083	25	(5.1)	92	(26.7)	0.000*
Occasional use	1	(4.3)	0	(0)		15	(3)	10	(2.9)	
Frequent use (1-10 years)	4	(17.4)	0	(0)		24	(4.9)	9	(2.6)	
Frequent use (>10 years)	10	(43.5)	3	(23.1)		328	(66.4)	141	(41)	
Unknown	5	(21.7)	4	(30.8)		102	(20.6)	92	(26.7)	
Alcohol consumption										
Non-drinker	3	(13)	6	(46.2)	0.101	51	(10.3)	143	(41.6)	0.000*
Occasional use	4	(17.4)	2	(15.4)		88	(17.8)	52	(15.1)	
Frequent use (1-10 years)	3	(13)	0	(0)		23	(4.7)	8	(2.3)	
Frequent use (>10 years)	8	(34.8)	1	(7.7)		225	(45.5)	43	(12.5)	
Unknown	5	(21.7)	4	(30.8)		107	(21.7)	98	(28.5)	
Betel quid chewing										
Non-chewer	14	(60.9)	9	(69.2)	0.727	252	(51)	127	(36.9)	0.000*
Occasional use	0	(0)	0	(0)		23	(4.7)	15	(4.4)	
Frequent use (1-10 years)	0	(0)	0	(0)		4	(0.8)	16	(4.7)	
Frequent use (>10 years)	0	(0)	0	(0)		30	(6.1)	65	(18.9)	
Unknown	9	(39.1)	4	(30.8)		185	(37.4)	121	(35.2)	

*Significant at the 0.05 level.

Table 4 Combined risk habits

	Age <40 years		Age ≥40 years		*P* value
	n	(%)	*n*	(%)	
Tobacco smoking + alcohol consumption	12	(33.3)	282	(33.7)	0.992
Tobacco smoking + betel quid chewing	0	(0)	86	(10.3)	0.067
Alcohol consumption + betel quid chewing	0	(0)	40	(4.8)	0.308
Tobacco smoking + alcohol consumption + betel quid chewing	0	(0)	37	(4.4)	0.322

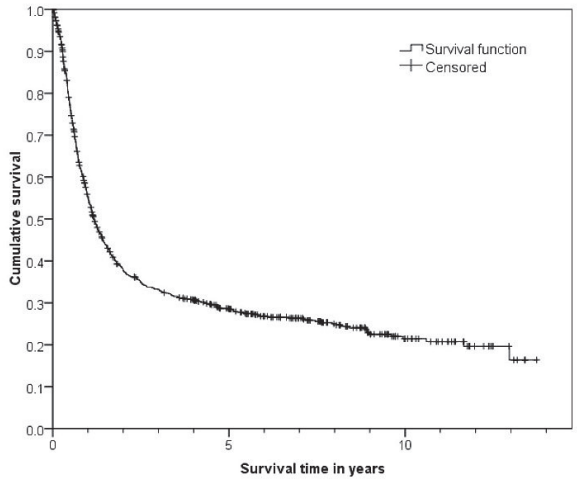

Fig. 2 Survival curve for all patients (Kaplan-Meier method).

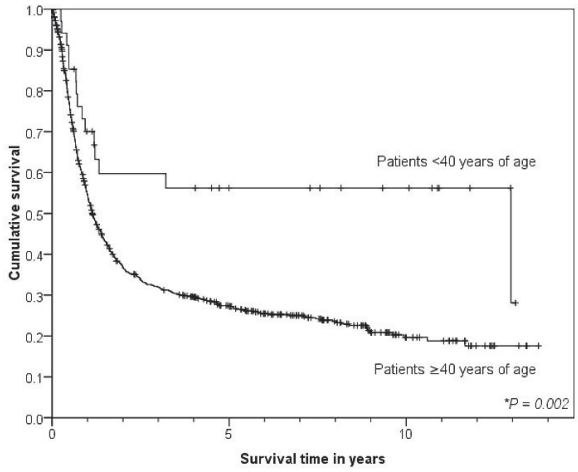

Fig. 3 Survival curve for the young (<40 years) and old (≥40 years) groups (Kaplan-Meier method) (*log rank test).

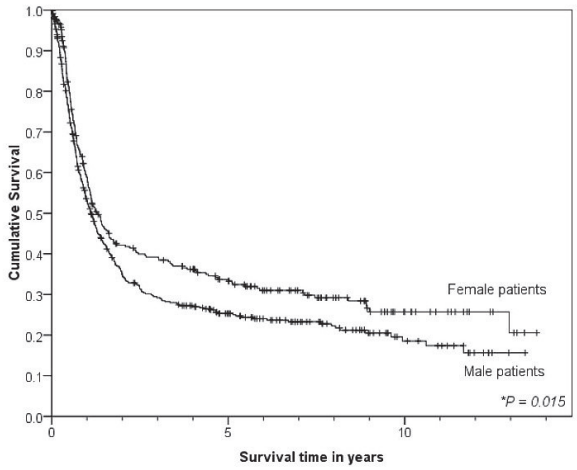

Fig. 4 Survival curve for the two sex groups (Kaplan-Meier method) (*log rank test).

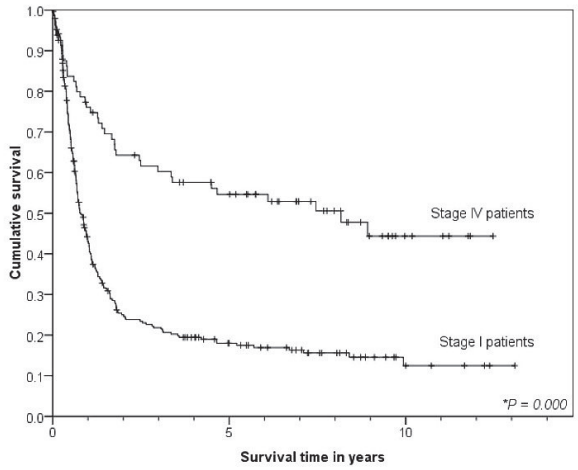

Fig. 5 Survival curve for the patients who were diagnosed with tumors at stages I and IV (Kaplan-Meier method) (*log rank test).

(27.4%) ($P < 0.01$). Female patients had a higher 5-year survival rate (33.7%) (Fig. 3) than male patients (25.3%) ($P < 0.05$) (Fig. 4). Moreover, the 5-year survival rate of patients who were diagnosed at stage I (54.6%) was significantly higher than that in patients who were diagnosed at stage IV (18%) ($P < 0.01$) (Fig. 5).

Discussion

Many studies have reported an increasing incidence of OSCC in various parts of the world in the last few decades (6,15-17). The present study showed a markedly increased number of northern Thai patients with OSCC over the period between 2001 and 2010 when compared with a previous study in a similar population of patients with OSCC in the same region over the period between

1991 and 2000 (11). We have several hypotheses for why the prevalence of OSCC has increased in northern Thailand. Cancer registration may have improved at Maharaj Nakorn Chiang Mai Hospital, the population may have increased in Chiang Mai city, or the incidence of OSCC may in fact have increased. Moreover, the patients probably had better knowledge about oral health and also health in general or better access to health care services.

Generally, patients are commonly diagnosed with OSCC after the age of 40 years (11,18-20). The disease is infrequently observed in younger patients. However, high numbers of OSCC in younger patients have recently been reported in many parts of the world (6,11,17,19,21). In this study, the percentage of patients <40 years (4.1%) was similar to those reported worldwide (1%-6%) (6,12,14,22).

Sex distribution or the male-to-female ratio in the present study (M:F = 1.4:1) was similar to that found in our previous study a decade ago (M:F = 1.3:1) (11) and is in agreement with the results of many previous studies worldwide (5,7,14,23). Males are more often affected by OSCC than females, probably because males are more likely to heavily indulge in major risk habits (5,6,24). In some areas where the betel quid chewing habit is common among women, such as some regions of India and northeastern Thailand, the prevalence of OSCC in females is higher than in males (5,15,25,26).

The 5-year survival rate for oral cancer in most countries is approximately 50% (6). A study in some Asian countries by Rao et al. (15) showed survival rates ranging from 38%-42% in India and 61% in Taiwan. However, the 5-year survival rate in our study (28.7%) was relatively low. The low survival rate in our study may be because of the fact that most of the patients came for treatment at later stages (stages III and IV) of the disease (48.6%), which is consistent with the findings of many previous studies (6,15,20). However, these findings show an improvement of the disease situation when compared with the percentage of late-stage patients found in our previous study a decade ago (67%) (11) and may imply that the patients in the present study had more awareness about the disease and more access to health care services. In addition, early detection by healthcare practitioners could play a role in improving this situation (7,27). Our study also shows that in stage IV disease, the percentage of male patients (41.8%) was significantly higher than that of female patients (28.9%). The reason for this may be that the female patients had better health awareness and took better care of themselves, which is consistent with the results from studies by Llewellyn et al. (23) and Scott et al. (28).

The most common site of OSCC in both age groups in our study was the tongue, which is in agreement with the findings of many previous studies (14,15,23,29,30). This result is also in line with the analysis from multinational cancer registries in both developed and developing countries in all regions of the world except for south-central Asia, where the most common sites were found to be the gingiva and buccal mucosa (1). In the old group in the present study, the second and third most common sites of OSCC were the gingiva and buccal mucosa, accounting for 18.6% and 14.2%, respectively. However, in the young group, the percentage of tumors on the buccal mucosa (5.6%) was relatively low, and no tumors were found on the gingiva. The discrepancy of these results between the old and young groups may be because of different risk factors in these two groups. Accordingly, some studies have reported that the tumor site is related to specific risk factors (5,6,15,18,30-32). Tumors of the tongue and the floor of the mouth may be associated with excessive alcohol consumption and cigarette-smoking habits (1,6,29,32), whereas lesions on the buccal mucosa and gingiva may be related to tobacco/betel quid chewing habits (1,6,18,30). Taken together, these factors could explain the low percentages of tumors on the gingiva and buccal mucosa in the young group in our study.

Several risk factors are associated with OSCC. Heavy tobacco smoking, excessive alcohol consumption, and betel quid chewing have been characterized as major risk factors of OSCC among the Thai population (11,25). In our study, the percentages of patients with histories of tobacco smoking (59.3%) and alcohol consumption (35.4%) were relatively high compared to the general population. However, the percentage of patients with a history of betel quid chewing in our study was quite low (13%), and none of the patients in the young group had ever chewed betel quid. We found a lower percentage of patients with a betel quid chewing habit in our study compared with in our previous study (50.2%) (11), which suggests that the popularity of betel quid chewing has decreased in northern Thailand. This finding is in line with Reichart's report that betel quid chewing habit is decreasing in Thailand (33). In our study, the percentage of patients with concurrent habits of tobacco smoking and alcohol consumption (33.6%) was notably higher than that with other combinations of risk factors. A relationship between tobacco smoking and alcohol consumption has been presented in some reports (25,31). These findings confirmed that these two disease-associated habits are related to each other and are still major risk factors among the northern Thai population.

Low socioeconomic status is an independent risk factor

for OSCC (1,5,6,15) and has been suggested as being interrelated with other patient factors (for example, diet, health care, education, and living conditions) that may indirectly increase the risk of OSCC in patients. In order to assess patients' socioeconomic status, Jansson et al. (34) suggested that data be collected on education, region of residence, and occupation (employment length, workplace, and work tasks for each occupation). However, in our study we only assessed patients' occupations and found that most patients appeared to have low socioeconomic status, which supports the idea that low socioeconomic status is an important risk factor for northern Thai people. Other parameters of socioeconomic status in Thai people need to be further investigated.

As shown previously, the 5-year survival rate in the young group was significantly higher than in the old group. This finding is in agreement with those from studies by Udeabor et al. (14), Warnakulasuriya et al. (6), and Fan et al. (26), which reported better prognoses for younger patients. Some studies reported that comorbidities in older patients affected the 5-year survival rate (14,29). Moreover, the young group was more tolerant to treatment than the old group (14,26,29). However, some studies found no difference in the 5-year survival rate between different age groups (22,29,35).

The knowledge obtained from our study may aid in proper cancer prevention and control in northern Thailand. In terms of primary prevention, it is suggested that the major risk habits, including tobacco smoking and alcohol consumption, should be minimized by promoting more anti-tobacco/alcohol campaigns and establishing more smoking/alcohol cessation clinics for patients who need to discontinue these habits. In terms of secondary prevention, it is recommended that dental practitioners perform oral soft tissue examinations during routine dental check-ups. Potentially malignant disorders, such as oral leukoplakia, erythroplakia, lichen planus, and submucous fibrosis, should be recognized, and suspicious lesions should be biopsied for further histologic evaluation (20,24). Furthermore, clinical detection during the early stages of OSCC when the tumors are small would allow less aggressive treatment to be used and could result in greater therapeutic efficacy, improved survival rates of patients, and decreased economic burden (7,20,31).

In conclusion, OSCC remains a serious oral health problem in the northern Thai population, which is characterized by high prevalence and low survival rates. In addition, the high rates of this disease among young adult patients have not been resolved. The situation of OSCC in northern Thailand can be ameliorated by limiting exposure to associated risk factors, particularly tobacco smoking and alcohol consumption. Anti-tobacco/alcohol campaigns for all age groups should be conducted as a public concern. Moreover, increasing disease awareness among dental practitioners and public could lead to early detection, thus improving the OSCC situation in northern Thailand.

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Conflict of interest

The authors declare no conflict of interest.

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