Original Research Paper

Clinical Research

EXPERIENCE THE TREATMENT OF GINGIVAL/ALVEOLAR RIDGE MUCOSA SQUAMOUS CELL CARCINOMA IN VIETNAM

Le Ngoc Tuyen	National Hospital of Odonto-Stomatology in Hanoi
Pham Dang Bach*	Thanh Hoa General Hospital *Corresponding Author
Dong Ngoc Quang	National Hospital of Odonto-Stomatology in Hanoi

ABSTRACT The study was conducted on 35 patients who were diagnosed with squamous cell carcinoma of the gingiva/alveolar ridge mucosa in the National Hospital of Odonto-Stomatology in Hanoi and Hanoi Medical University Hospital. This study described the clinical and para-clinical manifestations of squamous cell carcinoma of the gingiva/alveolar ridge mucosa in these 35 patients. It was a retrospective study to review patients record and direct interview. The results show that males is more than a half of pateints (18/35; 51.4%). The age ranged from 26 to 79 years with the mean age of 49.1 years. The proportion of smoker was 37.1%. The betel chewers accounted for 14.3%. The tumor was more common in the lower jaw (57.1%) than the upper jaw (42.9%). The posterior dental sites (74.3%) were more likely to have tumor than the anterior sites (25.7%). Almost of the tumor size was T4 (80.0%), follow with T2 (17.1%) and T1 (2.9%). Nodal metastasis was assessed as the highest stage with 74%, while N1 and N2 was lower 14.3% and 11.4%. The most commonly used surgical method is tumor resection with neck dissection and reconstruction (74.2%), followed by with neck dissection (22.9%) and sole tumor resection (2.9%). After surgery, recurrence rate was 25.7%, in which the local tumor recurrence was higher than the recurrence nodal level (77.8% vs 22.2%, p <0.05). Average survival time after surgery was 57.8 months. Five-year survival was high with 66.4% of patients. The 3-year survival rate of patients without node was higher than that of nodal metastasis group (80.6% vs. 20.8%, p <0.05). Patients should be screened before the age of 50. When detecting surgical intervention in time to limit lymph node metastasis to improve the survival of the patient.

INTRODUCTION

Oral carcinoma is a disease caused by the malignant transformation of the mucosal lining of the oral cavity such as the mucosa of lips, cheek, tongue, gingiva, retromolar trigone, palate and floor of the mouth . In the world oral carcinoma accounts for around 2-4% cases of cancer. In some areas, especially in Asia, the prevalence of oral carcinoma is even higher, as in Pakistan it is about 10% and in India it is even up to 45% . Several studies have shown that oral carcinoma contributes 90% to the total malignant lesions of the mouth [3]. In Asia, the habit of chewing betel leaf with areca nut present in some countries in addition to the increased exposure to risk factors such as tobacco, alcohol and chemicals in foods lead to the rising trend of oral cancer and the younger age of the patients . In oral cancer, the cancer of the gingiva/alveolar ridge mucosa accounts for about 2 to 18% and is more likely to occur in the lower jaw than the upper jaw. Nodal metastases are more common in lower alveolar ridge mucosa cancer compared to the upper gingiva . Similarly to the oral cancer in general, the most commonly seen cancer of the gingiva/alveolar mucosa is the squamous cell carcinoma (SCC) [6]. Every year, there are approximately more than 500,000 new cases of oral SCC in the world [7]. Gingival SCC accounts for 20% of all oral SCC [8]. Presently, there are several methods for early detection of oral carcinoma. However, the ability to diagnose gingival SCC is still limited. The reason for this is because the gingival SCC is often misdiagnosed with gingivitis, periodontitis, odontogenic abscess or denture pain and sores. The early detection and treatment of gingival SCC will have positive impact on the treatment outcome. The 5-year survival rate is 85% for T1 tumor while it is only 20% for T4 .

PARTICIPANTS AND METHODS
1. Target group, time and place of study
The study was conducted based on the records of patients who were diagnosed with gingival/alveolar mucosa SCC at the National Hospital of Odonto-Stomatology in Hanoi and Hanoi Medical University Hospital from January 2012 to August 2018.

1.1. Inclusion criteria
• Complete patient's record could be found.
• Patient was diagnosed with gingival/alveolar mucosa SCC.
• Histopathological result was present.

• Patient consented to participate in the study.

1.2. Exclusion criteria
• Lack of record
• Patient or family did not agree to participate.
• Patient received treatment before the initiation of the research.

2. METHODS: This was a retrospective study. Thirty five patients were selected according to the inclusion and exclusion criteria . Patient data is retrieved as age, gender, chief complaints (pain, bleeding, exophytic lesion, gingival ulcer, unhealed extraction socket). Risk factors for disease are also designed to collect as history of exposure to risk factors such as alcohol, tobacco and betel chewing or no risk factor, onset time (the period from the notice of the first symptom to hospitalization) counted in month, lesion sites: maxilla and mandible). Evaluate disease spread based on clinical evaluation and CT or MRI, the tumor size was classified into 4 categories according to the 2010 AJCC TNM classification.

3. Data collection and analysis
Data collection form specifically designed for this study.
The data were input to and analyzed by SPSS software version 20.0. χ^2 test was used to check if these was statistical significance.

RESULTS
In the total of 35 participants, there were 18 males (51.4%) and 17 females (48.6%); the minimum and maximum age were 26 and 78 years, respectively. The most common age group was from 51 to 69 with 12 patients (34.3%).

Table 1. Patients distribution by age and gender

Age group	Male	Female	Total	
			No.	Per. (%)
<30	1	0	1	2.9
30 – 40	0	1	1	2.9
41 – 50	4	1	5	14.3
51 – 60	5	7	12	34.3
61 – 70	4	5	9	25.7
>70	4	3	7	20.0
Total	18	17	35	100

The male to female ratio was 1.06:1. The age group with largest number of patients was from 51 to 69 with 12 patients (34.3%).

Table 2. Risk factors in male and female pateints

Risk factor	Male		Female	
	No.	Per. (%)	No.	Per. (%)
Tobacco	3	16.7	0	0
Alcohol	3	16.7	0	0
Tobacco and Alcohol	10	55.5	0	0
Betel chewing	0	0.0	5	29.4
No risk factor	2	11.1	12	70.6
Total	18	100	17	100

The male patients with history of tobacco, Aztec tobacco and alcohol use had the highest proportion of 55.5%. The percentages of patients who consumed alcohol or tobacco were equal and were 16.7%. There were 2 (11.1%) in 18 male patients who had no history of exposure to risk factors. In female, betel chewers contributed 5 in 17 patients which were 29.4%. The rest of them were not exposed to risk factors.

Table 3. Onset time of the study pateints

Disease onset	No.	Per. (%)
< 3 months	18	51.4
3 – 6 months	10	28.6
6 -12 months	2	5.7
>12 months	5	14.3
Total	35	100

Most of the patients (18 patients – 51.4%) sought medical examination within 3 months from the first symptom. The minimum detection time was 2 weeks, the maximum was 3 years.

Table 4. Location of the gingival/alveolar muocsa SCC

Location	Anterior area		Posterior area		Total
	No.	Per. (%)	No.	Per. (%)	
Maxilla	3	8.6	12	34.3	15 (42.9)
Mandible	6	17.1	14	40	20 (57.1)
Total	9	25.7	26	74.3	35 (100)

The tumor was more likely to occur in the lower jaw (57.1%) than in the upper jaw (42.9%). However, the difference was not statistically significant. Tumor was more commonly located in the posterior teeth area (74.3%) than the anterior teeth area (25.7%).

Table 5. Classify by tumors size and lymph node

Tumors	No.	Per. (%)	Node	No.	Per. (%)
T1	1	2.9	N0	26	74.3
T2	6	17.1	N1	5	14.3
T3	0	0	N2	4	11.4
T4	28	80.0	N3	0	0
Total	35	100	Total	35	100

The most common tumor size was T4 with 28 patients (80.0%). There was 6 patients with T2 (17.1%) and 1 patient with T1 (2.9%). The proportion of patient without nodal metastasis was highest with 74.3%. The total number of patient with positive lymph nodes were 9 patients (25.7%) in which N1 was 14.3%, N2 was 11.4% and no patient had N3.

Table 7. The rate of surgical methods has been applied

| Surgical method	No.	Per. (%)	P -value
Tumor resection	1	2.9	< 0.05
Tumor resection and neck dissection	8	22.9	
Tumor resection + neck dissection + reconstruction	26	74.2	
Total	35	100	

The most common surgical method was tumor resection with neck dissection and reconstruction (74.2%). Tumor resection with neck dissection accounted for 22.9%. Tumor resection only was

performed on 1 patient with the percentage of 2.9%.

**Table 8. Local recurrence and nodal recurrence**

	No.	Per. (%)	P -value
*Type of recurrence (n=35)			
No recurrence	26	74.3	<0.05
Recurrence	9	25.7	
* Reccurence site (n=9)			
Local recurrence	7	77.8	<0.05
Nodal recurrence	2	22.2	
Local and Nodal recurrence	0	0	

The rate of recurrence was 25.7%. In which, the rates of local and nodal recurrence were 77.8% and 22.2%, respectively. No patient had both local and nodal recurrence.
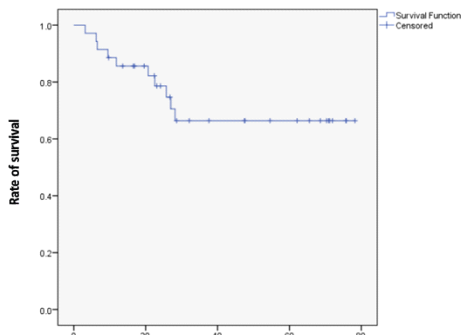
Additional survival time (month)
Figure 1. Chart of survival

The mean additional survival time was 57.8 months. The rates of 1-year, 2-year and 5-year survival were 85.6%, 78.6% and 66.4%, respectively.
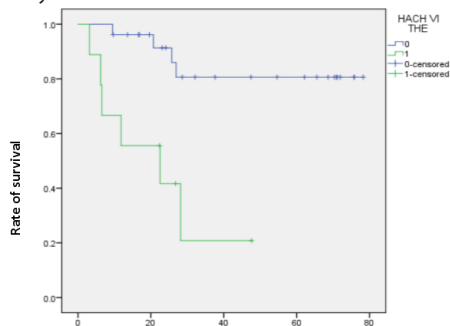
Survival time (month)
Figure 2. Chart of survival according to node status
Note: 0: N(-)
1: N(+)

The mean survival time of patients with positive nodes was 22 months which was lower than the negative nodes group with the mean of 67.2 months. The 3-year survival rate of negative node patients was 80.6%. Whereas, the 3-year survival rate of positive node patients was 20.8%. This difference was statistically significant.

DISCUSSION
Oral carcinoma in general and SCC of the gingiva/alveolar mucosa in particular are common in people over 40 years old. In our study, the rate of SCC of the gingiva/alveolar mucosa in the age over 40 accounted for 94.3% The peak was between 51-60 years old (34.3%). In the age group ≤ 40, the proportion was low (5.7%). The mean age of acquiring disease was 60.2 years. In general, the age ranged from 26 to 78 years. The findings of our study are similar to other research such as the work of Pires F.R and colleagues where the mean age was 62.3 years, the proportion of patients over 40 years was 96.7% [8]. According to research by Feng Z and co-workers, the mean age was 64.2 years [9]. Wang T.C and colleagues found that the mean age of acquiring the diseease was 56.2 years [10]. In the studies of oral SCC

and gingival/alveolar ridge mucosa SCC, the proportion of males was always higher than that of females. The male/female ratio varies according to the studies, the were 1.08/1 in the work of Subapriya R et al. [11], 1.2/1 according to Arduino G.P and colleagues [12],and 1.4/1 in the research of Sankaranarayananl R and co-workers [13]. In our study, the male/female ratio was 1.1/1. The higher rate in males than females might due to more exposure to risk factors in males. Among all male patients, the ones with a history of consuming tobacco, Aztec tobacco and alcohol had the highest proportion of 55.5%. The rates of patients who drank and who smoked were equal (16.7%). Only 2 in 18 male patients (11.1%) had no risk factors exposure. In female patients, 5 in 17 patients had the risk factor of betel chewing accounted for 29.4%. The rest were not exposed to risk factors.

Studies of SCC of the gingiva/alveolar mucosa have so far shown that tumors are more common in the lower jaw than in the upper jaw and in the posterior than in the anterior. In our study, the percentages of maxillary tumors, mandibular tumors, posterior teeth area, and anterior teeth area were 42.9%, 57.1%, 74.3% and 25.7%, respectively. This rate was comparable to that of Gomez D colleagues, with 36% in the upper jaw and 64% in the lower jaw, 18% in the anterior and 82% in the posterior [14]. The location of tumors are very important in planning for the surgical resection, reconstrucsion as well as neck dissection.

The most commonly seen tumor size was T4 (80%), the next was T2 with 17.1%. 2.9% of the participants were diagnosed with T1 and no patient had T3 tumor. These proportions were higher than other studies. According to Gomez D et al. (2000), the rate of T4 was 69.9% [14]. In the work of Lubek J and colleagues (2010), T4 accounted for 54.2% [15].

Lymph node metastasis is an important factor to decide the management attitude and is also a significant factor affects the treatment outcome. The nodal status of patients in this study was as following: N0 dominated with 74.3% of patients while 14.3% of patients had N1 lymph nodes. Patients with N2 accounted for 11.4% and there was no patient with N3.

According the the study of Gomez D et al., the percentages of N0, N1, N2 and N3 were 72%, 17%, 6% and 5%, respectively [14]. In the research of Mourouzis C and co-workers (2010), the proportions of N0, N1, N2 and N3 were 76,5%, 5,9%, 17,6% and 0%, respectively [16]. Therefore, the rate of patients withouth nodal metastasis in our study was similar to other research.

Regarding the surgical methods, most of the patients underwent neck dissection with the rate of 97.1% while only one patient received tumor resection only without neck dissection. This patient was the only one who was in Stage I. According to Yang X and colleagues (2015), the rate of neck dissection was 74.2% [17]. The research of Gomez D et al. Showed that the percentage of neck dissection was 81.1% [14]. Thus, the proportion in our study was higher because the work of Yang was conducted on the group of patients with SCC of the maxillary gingiva and hard palate.

In our study, there were 9 patients suffered recurrence (22.2%) in which the percentages of local recurrence, nodal recurrence and both local and nodal recurrence were 77.8%, 22.2% and 0%. These rates were quite similar to the research of Lubek and co-workers (2010) with 78.7% local recurrence and 21.3% nodal recurrence [15]. In 9 patients with recurrence, 6 received postoperative radiotherapy and only one had nodal recurrence after surgery and this patient has N2 lymph nodes. The other 3 patients did not receive postoperative radiotherapy and one of them suffered nodal recurrence although the initial node classification was N0.

The total 1-year and 5-year survival rate were 85.6% and 66.4%, respectively. The mean additional survival time was 57.8 months. According to the research of Gomez D and colleagues, the total 1-year and 5-year survival rate were 72.9% and 42.7%, respectively

[14]. So the 5-year survival rate in our study was higher than that of Gomez D. In the study of Want T.C and co-workers (2010), the 5-year survival rate of patients who received tumor resection with selective neck dissection was 72%, in no selective neck dissection, the rate was 56.9% [10]. These percentages were similar to ours.

Lymph node metastasis is also an important and a main prognostic factor the treatment of gingival/alveolar mucosa SCC. If there is no metastatic nodule, the prognosis is very good but if there is metastatic nodes, the prognosis is worse and the survival rate decreases. According to our study, the 3-year survival rate of the negative lymph node group was 80.6%, and the positive lymph node group was 20.8% (p = 0.001). According to Lubeck et al. (2010), the 5-year survival rate for the negative lymph node group was 85%, and the positive lymph node metastasis group was 59% [15]. In the study of Yang X and partners (2015), the 3-year survival rate of patients without lymph node metastasis was 71.3%, and with lymph node metastasis was 36.9% (p = 0.006) [17]. Overall, studies have shown that the survival rates of positive lymph node subgroups are significantly lower than those without lymph node metastases.

CONCLUSION

After conducting a research on 35 patients with SCC of the gingiva/alveolar mucosa, we conclude the followings:

- The most common age range was from 51 to 60 years which accounted for 34.3%. The mean age of participants was 60.2 ± 11.9. The male pateint was higher than female.
- The most common tumor site was in the lower jaw (57.1%) and in the posterior teeth area (74.3%). The most common tumor sizes were T4 (80%), T2 (17.1%) và T1 (2.9%). The percentages of nodal metastasis were as follow : N0 (74.3%), N1 (14.3%), N2 (11.4%). Almost of patients (97.1%) underwent neck dissection. The reccurence rate was 25.7%, in which local reccurence and nodal recurrence were 77.8% and 22.2%, respectively.
- The total of the five-year survival rate was 66.4%. The 3-year survival rate of negative and positive lymph node patients were 80.6% and 20.8%, respectively.

REFERENCE:

1. Le Ngoc Tuyen (2016). Oral cancer, Medical Publishing House, Hanoi (by Vietnamese).
2. Williams H.K (2000). Molecular pathogenesis of oral squamous carcinoma. J. Clin Pathol: Mol Pathol, 53, 165 – 172.
3. Johnson N.W, Jayasekara P, Amarasinghe A.A.H.K (2000). Squamous cell carcinoma and precursor lesions of the oral cavity: epidemiology and aetiology. Periodontology, 57, 19 – 37.
4. Siddiqui I.A, Farooq M.U, Siddiqui R.A et al (2006). Role of toluidine blue in early detection of oral cancer. Pak J Med Sci, 22(2), 184 – 187.
5. Miloro M (2004). Peterson's principles of oral and maxillofacial surgery, 2nd, BC Decker, London.
6. Dhanuthai K, Rojanawatsirivej S, Thosaporn W et al (2018). Oral cancer: A multicenter study. Med Oral Patol Oral Cir Bucal, 23 (1), 23 – 29.
7. Palasz P, Adamski L, Gorska – Chrzatek M et al (2017). Contemporary diagnostic imaging of oral squamous cell carcinoma. J Pol Radiol, 82, 193 – 202.
8. Pires F.R, Ramos A.B, Oliveira J.B.C et al (2013). Oral squamous cell carcinoma: clinicopathological features from 346 cases from a single Oral Pathology service during an 8-year period. J Appl Oral Sci, 21 (5), 460 – 467.
9. Feng Z, Li J.N, Li C.Z et al (2013). Elective neck dissection versus observation for cN0 neck of squamous cell carcinoma primarily located in the maxillary gingiva and alveolar ridge: a retrospective study of 129 cases. Oral Surg Oral Med Oral Pathol Oral Radiol, 116, 556 – 561.
10. Wang T.C, Hua C.H, Lin C.C et al (2010). Risk factor affect the survival outcome of hard palatal and maxillary alveolar squamous cell carcinoma: 10 – year review in a tertiary referral center. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2010, 110, 11 – 17.
11. Subapriya R, Thangavelu A, Mathavan B et al (2007). Assessment of risk factors for oral squamous cell carcinoma in Chidambaram, Southern India: a case - control study. European Journal of cancer prevention, 16, 251 – 256.
12. Arduino P.G, Carrozzo M, Chiecchio A et al (2008). Clinical and histopathologic independent prognostic factors in oral squamous cell carcinoma: A retrospective study of 334 cases. Journal of oral & maxillofacial surgery, 66, 1570 – 1579.
13. Sankaranarayananl R, Duffy S.W, Padmakumary G et al (1989). Tobacco chewing, alcohol and nasal snuff in cancer of the gingiva in Kerala, India. Br J Cancer, 60, 638 – 643.
14. Gomez D, Faucher A, Picot V et al (2000). Outcome of squamous cell carcinoma of the

gingiva: a follow – up study of 83 cases. Journal of Cranio – Maxillofacial, 28, 331 – 335.

15.　Lubek J, El – Hakim M, Salama A.R et al (2010). Gingival carcinoma: retrospective analysis of 72 patients and indications for elective neck dissection. British Journal of Oral and Maxillofacial Surgery, 49, 182 – 185.

16.　Mourouzis C, Pratt C, Brennan P.A (2009). Squamous cell carcinoma of the gingiva, alveolar, and hard palate: is there a need for elective neck dissection. British Journal of Oral and Maxillofacial Surgery, 48, 345 – 348.

17.　Yang X, Song X, Chu W (2015). Clinicopathological characteristics and outcome predictors in squamous cell carcinoma of the maxillary gingiva and hard plate. Journal Oral Maxillofacial Surgeons, 1 – 8.