Original Research Article

Prognostic factors in carcinoma of the oral cavity in Eastern India: a clinico pathological study

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Abstract

Oral and oro pharyngeal malignancy is the most common malignant tumour in Asia with higher incidence in males. It mostly affects persons above 60 years of age. Majority of the oral cancers are squamous cell carcinoma which accounts for 85% of patients. The probable explanation of squamous cell carcinoma is an agent such as tobacco and its constituents that causes irreversible damage in the DNA(Deoxyribonucleic Acid)of the affected cells. Surgery and radiotherapy are the modes of treatment. The aim of this study was to assess the prognostic significance of clinico pathological factors on the overall survival rate and disease free survival rate in oral cavity carcinoma. History, clinical examination with indirect laryngoscopy and upper GI Endoscopy was done for diagnosing the tumours initially. After ethical clearance, diagnosed persons of oral cavity carcinoma were selected for the study by applying the inclusion and exclusion criteria and after taking consent from them. Prospective analysis was done for 38 and 42 diagnosed patients, but 11 patients were lost to follow up, so the study was conducted with 69 patients. Diagnosis was done by history, physical examination, indirect laryngoscopy and Upper GI Endoscopy. The clinical factors assessed were gender, presenting age, tumour site, consumption of tobacco in different forms, alcohol consumption and habit of chewing betel quid, premalignant lesions, metachromous and synchronous tumours and staging. Pathological factors were histology and grade of tumour . The study showed that most of the clinico pathologic factors had prognostic impact on overall survival in diagnosed oral cavity cancer cases. Gender, anatomical location, size of the tumour, nodal status, betel quid chewing, tobacco consumption and grade of the tumour had an effect on the prognosis of these patients.

Keywords: Oropharyngeal cancer ,prognosis, clinicopathologic factors.

Introduction

NCCN guidelines depict Head and Neck Cancers to all malignant tumors arising from lip, oral cavity, oropharynx; hypopharynx , glottic and supraglottic larynx, paranasal sinuses , nasopharynx and salivary glands, as well as occult primary cancer[1].

Incidence: In global terms, oropharyngeal cancer is the sixth most common malignancy. In the west, it accounts for only 2% - 4% of all malignant tumors, although there is evidence to show that incidence is increasing, mostly in younger people The majority of oral cavity cancers comprises of squamous cell variety whereas, a small percentage consists of malignant tumors of salivary glands, lymphoreticular disease, bone tumors, melanomas, sarcomas, malignant odontogenic tumors and oral metastasis of tumors from other locations. In contrast, in Asia, oral and oropharyngeal malignancy is the most common malignant tumor, accounting in parts of India, for no less than 40% of all malignancies. The incidence is higher in men accounting for 30% of cancers in males, 13% in females and 50% of admissions in major cancer hospitals. It is predominately a disease of the elderly population is age >60 years.

Anatomy of oral cavity: The oral cavity extends from the vermilion border of the lips to the anterior tonsillar pillar[2].For staging purpose the following subsites are considered part of the oral cavity: lip, oral tongue (anterior two thirds), floor of the mouth, buccal

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mucosa, upper and lower alveolus, hard palate, retromolar trigone. There is rich lymphatic supply for the tissues of the oral cavity and regional nodal metastases are typically the first site of spread for squamous cell carcinoma of head and neck. The primary lymphatic drainage basins are the perifacial, upper jugular submandibular & the submental nodes. Secondary lymphatic drainage basins include the parotid, mid and lower jugular and posterior cervical nodes. Sites close to the midline often drain bilaterally. The deep tongue and palate commonly have bilateral lymphatic drainage.

Anatomy of cervical lymphatics: Cervical lymph nodes are classified according to the system developed at Memorial Sloan's Kettering Cancers Centre in 1930s[1]from Level 1 to 5.

Pathology: Majority of oral cavity cancers are squamous cells carcinomas (85%).Other types are lymphoepithelioma,spindle cell carcinoma,verrucous cell carcinoma,undifferentiated carcinoma,lymphoma etc.

Carcinogenesis: Simplest explanation of the causation of squamous cell carcinoma is an initiating agent (perhaps some contaminant or metabolite of tobacco) than induces an irreversible change in DNA of the affected cells).

Diagnosis: History and physical examination are the most important considerations in the diagnosis of carcinoma of the upper aero digestive tract. Visualization of the entire upper aero digestive tract is the sine-qua-non of diagnosis.A systematic approach was done that includes inspections of the facial and cervical surface anatomy and contour, intraoral examination, and indirect (mirror) laryngoscopy with nasopharyngoscopy is essential for diagnosis and staging. Examination of the neck revealed the presence or absence of metastatic lymph nodes. The site of the primary tumor should predict the most likely site of disease.Distant metastasis was evaluated by history, physical examination, laboratory procedures and radiology.Before treatment planning, definitive histologic confirmation of disease is necessary. If a primary site is visible a wedge biopsy was taken at the edge of the tumor to include some adjacent normal tissue.The value of triple endoscopy (panendoscopy) – bronchoscopy, oesophagoscopy and direct laryngo-scopy – has been debated but is advisable for the ideal work up of an advanced head and neck cancer in a patient with long history of tobacco and alcohol use.Radiology of intraoral disease usually involves assessment of the mandible. Ortho pantomograms show the extent of the disease by cortical disruption and widening of the inferior alveolar canal or mental foramen.Technetium 99m radionuclide bone scans have been advocated for diagnosis of mandibular involvement.However, it lacks specificity with false positive rate of 53% and faces negative rate of 12%.CT is highly sensitive method of diagnosing cortical invasions, but the presence of metal tooth fillings interfered with accuracy.MRI is probably the most accurate and useful method in detecting perineural disease and mandibular bone marrow invasion.

Staging: Stage at diagnosis is the most important predictive factor of survival[1]. The TNM staging systems was developed by the American Joint Committee on Cancer (AJCC) for the lip and oral cavity, pharynx (nasopharynx, oropharynx and hypopharynx), & larynx,In general, stage I or stage II disease defines a relatively small primary tumor with no nodal involvement.Stage III and stage IV cancers including larges primary tumors, which may invades underlying structures and / or spread to regional nodes. Distant metastases are uncommon at presentation as carcinoma of head neck basically a loco-regional disease. In general, the survival rate of patients with locally advanced (stage III or stage IV) disease is less than 50% of the survival rate of patients with early stage disease.

Management approaches: Single modality treatment with surgery or radiotherapy is generally recommended for approximately 40% of patients who present with early stage diseases (stage I and stage II). The two modalities result in similar survival in these individuals.

In contrast, for 60% of patients with locally advanced disease at diagnosis, combined modality therapy is generally recommended.

Recurrent disease: Surgery is recommended for resectable recurrent disease, usually followed by radiations if it has not been administered[1].If the recurrence is unresectable & the patient did not have prior RT, then radiotherapy with concurrent cisplatin or carboplatin based chemotherapy is recommended.Over expression of EGFR and / or common ligands has been observed in greater than 90% oral of squamous cell carcinomas which has led to the development of EGFR inhibitors such as the monoclonal antibodies cetuximab and nimotuzumab and small molecule tyrosine-kinase inhibitors such as erlotinib and gefitinib.

Metastatic disease: Palliative adjunctive measures include radiotherapy to areas of symptomatic disease along with analgesics and investigational agents[1]. Most active agents include cisplatin, carboplatin, paclitaxel, docetexel, 5FU, ifosfamide, gemcitabine and cetuximab.

Aim and objectives

The aim of this analytical, retrospective as well as prospective study was to evaluate the prognostic significance of clinico-pathological variables on the overall survival and disease free survival in patients with oral cavity carcinoma

Material and methods

Inclusion Criteria-The study populations comprised of all patients diagnosed with oral cavity carcinoma at General Surgery Unit, Central Hospital, S.E. Rly, Kolkata.

Exclusion Criteria-Malignancy of oropharynx; hypopharynx, glottic and supraglottic larynx, paranasal sinuses (ethmoid and maxillary), nasopharynx and salivary glands, as well as occult primary cancer[1].

A retrospective analysis was performed of 38 cases diagnosed .A prospective study of 42 cases was done .It was possible to select and review 69 case histories; 11 cases were lost to follow up. The sample size therefore reduced to 69 cases. Stress was given on proper history taking, thorough clinical examination including indirect laryngoscopy, and upper gastro intestinal tract endoscopy for initial diagnosis of the tumor.

Confirmation of diagnosis was done with either,

a) incision or wedge biopsy or,
b) excision biopsy depending on the site and size of the tumor.

Computed tomography was used to detect cortical invasion of mandible and maxillary antrum and to analyze the extent of lymph nodal spread, and encasement or infiltration of the carotid vessels if any. As carcinoma oral cavity is primarily a loco-regional disease, distant metastases being unusual, metastatic work up was done in cases with significant positive history. Distant metastasis was evaluated by proper history taking, physical examination, laboratory procedures and radiology. A clinico-pathological staging and grading of the cancer was performed.

After initial work up the patients were subjected to single or multimodality therapy that included:

- Surgery alone.
- Surgery with radiotherapy as a pre operative or post operative adjuvant.
- Concurrent chemo radiotherapy was used in selected cases depending upon the stage of the disease and performance status of patients (ECOG - O or I).

Follow up / survelliance: On completion of treatment the patients were asked to attend the Surgical Oncology Clinic as follows:

Table 1: Follow up and post treatment(years)

Years post treatment	Follow up
1st year	3 months
2nd years	3 months
3rd years	6 months
4th years	6 months.
After 5 years	Annually

Prognostic factors: The prognostic factors in oral cancers were broadly classified into :

- Clinical factors.
- Pathological factors.

Clinical factors:

1. Sex
2. Age at presentation
3. Site of tumor.
4. Consumption of tobacco in any form.
5. Consumption of alcohol.
6. Habit of chewing betel quid.
7. Presence of premalignant lesions like leukoplakia, erythroplakia, oral candidiasis and submucous fibrosis.
8. Synchronous or metachronous tumors.
9. Staging.

Pathological factors:

1. Tumor histology
2. Tumor Grade

2002 American Joint Committee On Cancer (AJCC) TNM Staging Systems For The Lip and Oral Cavity was used for staging.

Histologic grade (G): G_x-Grade cannot be assessed.

G_1-Well differentiated

G_2-Moderately differentiated

G_3-Poorly differentiated

In this study on oral cavity carcinoma cases, a correlation of the above mentioned clinico-pathological factors with overall survival rate and disease free survival rates was carried out.

Results and analysis

An analytical, observational, retrospective as well as prospective study of 69 oral cavity cancer patients was carried out at. Central Hospital, South Eastern Railway,

Garden Reach, Kolkata.The aim was to evaluate the role of clinico-pathological prognostic factors on the overall survival and disease free survival in these patients treated with single or multimodality therapy.

The results obtained are as follows:

1)Table 2 depicts survival distribution. Overall survival rate was lowest in age groups 61-70 years (73%) and 71-80 years (60%)(Table 3). Disease free survival rate was also lowest in the same age groups-61-70 years (57.9%) & 71-80 years (40%)(Table 4)

2) Males with oral cancer tend to survive for shorter periods (OSR: 78%) compared to women (OSR: 85%). Disease free survival rate was slightly higher for females.

3) Oral carcinoma located in the upper alveolar ridge (OSR: 71%, DFS: 57%), lower alveolar ridge (OSR: 63%,

DFS: 62.5%), and retromolar trigone (OSR: 62%, DFS: 50%) had greatest risk of mortality and locoregional recurrence.

4) Overall survival rate was 50% in cases with tumor size >4 cm compared to 92% in cases with tumor size <2 cm on presentation.

Disease free survival rate was significantly lower (38.9%) for tumors >4 cm.

5) Lowest overall survival rates were found in cases with nodal status N_{2b}, N_{2c} and N_3 being 63%, 62%, and 50% respectively.N_{2b} and N_3 tumors showed greater recurrence rates with mean disease free intervals of 14.2 months and 5.5 months respectively.

6) Premalignant lesions were present in 18.8% of cases with OSR of 76%; being lower than those unaffected (OSR: 81%).Locoregional recurrence was higher (DFS: 33.3%) in cases with chronic hyperplastic candidiasis.

7) Tobacco consumption in any form was associated with increased risk of death (OSR: 72%).

8) In cases consuming tobacco for >20 yrs mortality rate was highest; (OSR: 54%).

Disease free survival rate was significantly lower for those consuming tobacco for >25 yrs. (DFS: 43.8%).

9) Consumption of alcohol did not seem to have significant prognostic value in this study.

10) Patients with habit of betel quid chewing suffered from increased risk of death & locoregional recurrence (OSR: 73%); compared to those who abstained from it (OSR: 90%).

11) Further analysis showed that those addicted from an younger age (<20 yrs) suffered increased risk of death and locoregional recurrence (OSR: 60%, DFS: 59.2%).

Similar results were found in those patients addicted for a longer duration i.e. >20 years. (OSR: 62%, DFS: 52.3%).

12) Patients with Stages IVA and IVB showed marked decrease in OSR and DFSR.. OSR was 75% and 43% for stages IVA and IV B respectively. DFS rate was exceptionally low for stage IV B, being 28.5% only

13) Majority of the cases belonged to squamous cell carcinoma variety with OSR of 78% and DFS rate of 71.8%. OSR was 100% for the small populations (n=4) of verrucous cell carcinoma variety.

14) Tumor differentiation (histological grade) was found to be an important independent prognostic factor. Cases of grade III showed OSR of 62% and DFS rate 50%. Disease free interval for grade III was 6.4 months on average.

Table 2:Estimation of survival distribution using kaplan-meier method

Months after beginning of the study	No. alive at the beginning of the interval	No. died during the interval	Effective no. exposed to risk of dying just before end of interval	Proportion dying	Proportion surviving	Cumulative proportions surviving through end of interval.
0-6	69	0	69	0	1.0	1.0
6-12	69	1	69	.01	.99	.99
12-18	68	1	68	.01	.99	.98
18-24	67	0	67	0	1.0	.98
24-30	67	2	65	.03	.97	.95
30-36	65	0	65	0	1	.95
36-42	65	2	65	.03	.97	.92
42-48	63	2	63	.03	.97	.89
48-54	61	3	61	.05	.95	.84
54-60	58	1	58	.02	.98	.82
60-66	57	2	57	.04	.96	.78

Table 3:Site Of Tumour(OSR)

Site	No. of cases	% of cases	No. of deaths	Cumulative proportion of survivors	Overall Survival Rate (OSR)
Lips	7	10.1	0	1.0	100%
Oral tongue (ant 2/3rd)	11	15.9	2	0.81	81%
Floor of the mouth	5	7.3	1	0.80	80%
Buccal mucosa	21	30.5	3	0.83	83%
Upper alveolus	7	10.1	2	0.71	71%
Lower alveolus	8	11.6	3	0.63	63%
Hard palate	2	2.9	0	1.0	100%
Retromolar trigone	8	11.6	3	0.62	62%

Table 4:Site of tumour(DFS)

Site	No. of cases	No. of cases with locoregional recurrence	Mean disease free interval (in months)	Disease free survival rate (DFS)
Lips	7	×	×	100%
Oral tongue (ant 1/3 rd)	11	2	14	81%
Floor of the mouth	5	2	6.5	60%
Buccal mucosa	21	4	15.2	80.9%
Upper alveolus	7	3	8.2	57.1%
Lower alveolus	8	3	9.5	62.5%
Hard palate	2	1	10	50%
Retromolar trigone	8	4	13.2	50%

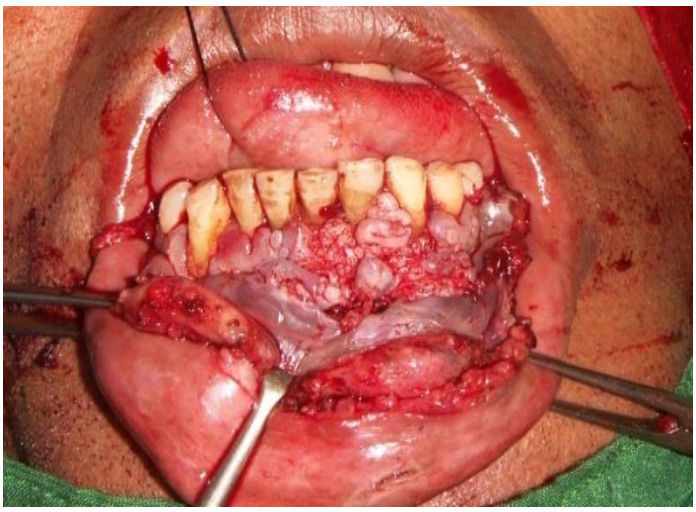

Fig 1:Oral cancer

Discussion

In this study a univariate analysis was done on the prognostic significance of clinico-pathological factors on the OSR and DFSR of 69 patients with oral cavity carcinoma.In this study the incidence of oral cavity carcinoma was highest in the age group 51 to 60 yrs. (33.3%). The highest and lowest age of the patients was 35 yrs and 73 yrs respectively. The OSR was lowest in the age groups 61-70 yrs and 71-80 yrs. Disease free interval (DFI) was highest in the age group 41-50 yrs and DFS rate was lowest in age group 61-70 yrs. and 71-80 yrs.Seoane J. et al.in his series recognized a prognostic importance for advanced age of the patients[3].Regarding gender this study indicated that men with oral cancer tend to survive for shorter periods (OSR: 78%) than women (OSR: 85%). Mean DFI were comparable between the groups, DFS being slightly higher for females Pugliano et al. speak of greater survival in women[4], however, Shah et al. showed that survival in females is lower[5]. On studying importance of the site of primary tumor on prognosis this study indicated that carcinoma in upper and lower alveolar ridge and retromolar trigone carried highest risk of mortality.Locoregional recurrence was higher in retromolar trigone (DFS: 50%) followed by upper and lower alveolus and floor of the mouth.Study results of Seoane J. et al. matched with this study.In this study OSR was lowest in cases with N_{2b}, N_{2c} and N_3 disease. (63%, 62% and 50% respectively). DFSR were low for N_{2b}, and N_3 tumors with mean disease free interval of 14.2 months and 5.5 months respectively.Kalnins IK. et al. in 1977 concluded that presence of lymphadenopathy reduced 5 yr survival rates to 45%[6]. Study by Seoane J. et al. showed that tumors in stage N_{2a} – N_{2b} had lower survival than those who were in stage N_0 – N_1 (P=0.0035). In this study the pre-malignant lesions, i.e. leukoplakia, erythroplakia and chronic hyperplastic candidiasis was present in 13 of 69 cases; majority being leukoplakia (10 cases). OSR in cases with premalignant lesions (76%) was slightly lower that those without (81%). On further study overall survival rate for leukoplakia (80%) was higher than chronic hyperplastic candidiasis (67%). Locoregional recurrence was higher in cases with chronic hyperplastic candidiasis.However, the sample size was not sufficiently powered to demonstrate significance.

This study showed that consumption of tobacco in any form (cigarettes, bidis, Khaini, Gutkha, Guraku) has significant impact on long term survival and disease free survival rate.OSR was 92% in those consuming tobacco compared to 72% in those who abstained from it. 15 out of 43 cases suffered locoregional recurrence. Duration of consumption also found to have prognostic significance. OSR was lowest in those consuming tobacco for >20 yrs (54%) compared to those consuming for 5-10 yrs (80%). Disease free survival rate was significantly lower (43.8%) for those consuming tobacco for >25 yrs.In a study by Bundgaard T. et al. patients consuming tobacco above the median had 5 yr cause specific survival of 55+/- 6% compared to 39+/-6% for those who abstained from it. (P=0.056) (borderline significance)[7] Browman et al. demonstrated that patients who continued smoking during radiotherapy had lower survival than others[8].In relation to consumption of alcohol, 56% of the cases in this study were alcoholics with OSR of 77% whereas, the non alcoholics had OSR of 83% (not statistically significant on further evaluation it was found that duration of alcohol intake did not prognosticate OSR or DFI and DFS rates. In this study 68% of the cases were habituated to betel quid chewing with OSR of 73% being significantly lower than those who abstained from it (OSR: 90%) .16 of 47 cases suffered from locoregional recurrence.Further analysis revealed the prognostic effect of betel quid chewing was dependent on the duration of addiction. OSR for those chewing betel quid for >20 yrs was 62% compared to 83% for those using it for 10-15 yrs. Locoregional recurrence was highest in the study groups chewing betel quid for >25 yr (DFS: 52.3%).Age for starting this habit was also found to be significant. Those who started, at the age of <20 yrs had an OSR of 60% and DFS rate of 59.2%. where as, those who started at an age >30 yrs. had better OSR (86%) and DFS (87%) rates.In a study by Lee JJ. et al. betel quid chewing had a significant prognostic influence on multivariate analysis (P<0.05)[9]

The risk of death was 31.4 fold higher in heavy users (duration >30 yrs, daily consumption >30 quids, age at starting <20 yrs) compared to those habituated to a milder degree (duration <10 yrs, daily consumption <15 quids, age of starting ≥20 yrs) (P<0.001)[10].In a study by Huang CH. et al. patients showed 5 yrs disease specific survival rates of 90%, 77%, 52% and 47% for stage I, II, III and IV oral squamous cell carcinoma. (P<0.001)[10].

In this study TNM staging was found to be statistically significant as a prognostic factor. OSR was lowest in stage IV (75% for stage IVA and 43% for stage IVB respectively) whereas, for stage I OSR was 100%.DFSR rates were lowest in stages IVA and IVB being 65.3% and28.5% respectively. Mean disease free interval were 8 months and 5.5 months for these

stages.This study found that majority of the cases (92.8%) belonged to squamous cell carcinoma variety. Only 5.8% cases were of verrucous cell carcinoma type. OSR was comparatively less (78%) for squamous cells carcinoma variety .Locoregional recurrence was higher for squamous cell carcinoma variety (DFS: 71.8%).In this study 52% of cases had well differentiated tumors with OSR and DFS rates of 88% each.11.6% cases belonged to poorly differentiated type with OSR and DFS rates of 62% and 50% respectively. In an article by Choikk et al. emphasis has been given on the fact that prognosis of oral squamous cell carcinoma might depend directly on cancer stage[11]. In a study conducted on Taiwanese population by Ping-Ho-Chin et al. the impact of morphological type on death was marked particularly for Hakka and Hokkien communities[12].

In another article by Marlide A. et al. a higher rate of metastasis and recurrence was observed in cases of lip cancers belonging to grades II and III[13].Other studies by Nemeth Z. et al[14], Zhao H. et al[15] and Huang CH. et al highlighted histological grade as one of the most important[10].

Conclusion

In conclusion it can be stated that in this study most of the clinico-pathological variables showed prognostic impact on the overall survival and disease free survival in patients with oral cavity carcinoma. There are indications that out of the different variables age at diagnosis, gender, anatomical site, tumor size, nodal status, habit of betel quid chewing, consumption of tobacco and tumor grade had an effect on the prognosis of these patients.However, statistical significance was observed with regards to tumor size, nodal status and histological grade only.

References

1. Arlene A. Forastiere, Nancy Y. Lee. Guidelines Index, Head and Neck cancers Toe, Staging MS, Reference. Head and Neck cancers, NCCN Practice guidelines in oncology – V.l. 2006: MS 1-24.
2. William R. Carroll. Surgery for cancer of the Oral Cavity Mastery of Surgery. Tosef E. Fischer 2007 4th Edition. Volume 1, Chapters 25: 307-17.
3. Varela – Centelles PT, Seoane J, Vasquez Fernandez F, DE La Cruz A, Garcia Asenzo TA. Survival to oral cancer. A study of clinical risk markers with independent prognostic value. Bue Group Int. Rech Sci Stonatol Odontol. 2002; 44 (2): 46-51.
4. Pugliano FA, Picciritto JF, Zequira MR, Fred Riskson JM, Perez CA, Simpson JR. Clinical severity staging systems form oral cavity cancers; 5 yrs survival rates. Otolaryngol. Head Neck, Surg. 1999 ;120 (1): 38-45.
5. Shah JP, Cendon RA, Farr HW, Strong EW. Carcinoma of the oral cavity. Factors affecting treatment failure at the primary site and neck. Am J. Surg. 1976; 132 (4): 504-7
6. Kalnins IK, Leonard AG, Sako K, Rajaek MS, Shedd DP. Correlation between prognosis and degree of lymph node involvement in carcinoma of oral cavity. Am. J. Surgery 1977 ; 134 (4): 450-4
7. J. Hibbert, N.J., Marks, PJ. Winter, O.H. Shaheen. Prognostic factors in oral squamous cell carcinoma and their relation to clinical surgery. Clinical otolaryngology 1983; 8(3): 197-203
8. Browman GP, Wong G, Hodson I, Sathya J, Russel R, Mc Alpine L, et al. Influence of cigarette smoking on the efficacy of radiation therapy in head and neck cancer. N Engl J Med. 1993; 328 (3): 159-63
9. Lee JJ, Jeng JH, Wang HM, Chang HM, Chiang CP, Kuo YS, Lan WH, Kok SH. Univariate and multivariate analysis of prognostic significance of betel quid chewing in squamous cell carcinoma of buccal mucosa in Taiwan. J Surg. Oncology 2005 ; 91 (1): 41-7.
10. Huang CH, Chu ST, Ger LP, Huo YY, Sun CP. Clinico-pathological evaluation of prognostic factors for squamous cell carcinoma of the buccal mucosa. Head Neck, 1997; 19 (6): 506-12
11. Choi KK, Kim MJ, Yun PY, Lee JH, Moon HS, Lee TR, Myoung H. Independent prognostic factors for 861 cases of oral squamous cells carcinoma in Korean adults. Oral Oncol. 2006 ; 42 (2): 208-17
12. Ping Ho Chin, Tien-YO Shieh, Pei-Shantto, Chi-chang Tsai, Yi-sin Yang, YIng-Chu Lim, Min-Shan KO, Pei-chien Tsai, Shang-lun Chian G, Hung-Pin TU, Ying-Chin KO. Prognostic factors associated with survival of oral and pharyngeal carcinoma in Taiwan, BMC Cancer 2007,7(1): 22
13. 10. Marlide A, MM Abrue, Dalva R, N. PimenteL, Olga M.P. Silva. Squamous cell carcinoma of the lip: assessment of prognostic factors. Rev. Bras. Otorhinolaryngology.2007;70(6): 765-70
14. Nemeth Z, Velich N, Bodgdan S, Ujpal M, Szalo G; Susa ZS. The prognostic role of clinical morphological and molecular markers in oral

squamous cells tumors. Neoplasma 2005, 52 (2): 95-102
15. Zhao H, Zeng ZY, Chin FJ, Xugp, Wu GH, Guo ZM, Zhag O. Multivariate analysis for prognostic predictors in the cN0 squamous cell carcinoma of the tongue. Ai Zheng 2003; 22 (2): 206-9

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