Research Article

Risk Factors Assessment for Cervical Lymph Node Metastasis in Head and Neck Squamous Cell Carcinoma: A Cross-Sectional Study

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Abstract

Background: Head and neck cancer in one of the most disturbing health problems considering morbidity and mortality. Detecting and treating occult lymph node metastasis have the most influence on patients' survival in head and neck squamous cell carcinoma (SCC). This article aimed to introduce some potential risk factors for cervical node metastasis in this type of malignancy.

Subjects & Methods: 164 patients with head and neck SCC who underwent cervical node dissection of all types from 2001 to 2011were enrolled in this study. Then the effect of the assumed risk factors including age, sex, smoking, alcohol, and opium, primary site of tumor and extra-capsular extension of involved lymph node son cervical lymph node involvement frequency were evaluated.

Results: This study showed that cervical node metastasis was more frequent in older patients (mean age of 58.83 y/o) (P=0.038). On the other hand there was no significant difference in cervical lymph node metastasis in presence or absence of other assumed risk factors (P >0.05) in this series. There was no significant relationship between extra-capsular extension of involved lymph nodes with primary tumor site and levels of cervical node involvement too.

Conclusion: This study revealed that maybe older patients (mean age of 58.83 y/o) with head and neck SCC are at higher risk for involvement of cervical nodes and they may receive more aggressive approach for detecting and treating occult cervical node metastasis.

Keywords: Head and neck; SCC; Cervical lymph node; Metastasis; Cancer; Risk factor

Introduction

The prevalence of head and neck malignancies has been increasing since 1970 [1]. Among different types of the head and neck malignancies, squamous cell carcinoma (SCC) is the most common carcinoma, which are capable of metastasis [2]. So this study aimed to evaluate the risk factors of the lymphatic metastasis in the cases of head and neck SCC.

There are several surgical approaches for treating head and neck SCC, including radical cervical lymph node dissection, modified radical cervical lymph node dissection, and selective lymph node dissection. The most important factor for predicting the prognosis of head and neck SCC is neck metastasis [3,4]. Several studies have attempted to describe the correlation of neck lymph node metastasis with histopathology and/or clinical findings in patients with head and neck SCC. In one study in Taiwan the incidence of cervical node metastasis was higher in tongue cancer with moderate or poor differentiation, an invasion depth more than 3 mm, and positive perineural invasion or lymphovascular permeation at the time of presentation [5].

Some authors suggest that elective neck treatment should be done in tongue cancer regardless of a small primary and negative neck examination [6]. Similar result was achieved in a study on patients with SCC of oral tongue and floor of the mouth at the Emory university hospitals [7]. In other study there was a relationship between combined expression of Ki-67, VEGF-A and occult lymph node metastasis [1]. One other study recommended treating the contra lateral neck in the cases with the primary tumor of more than 3.75 mm thickness [8]. According to above mentioned studies, the importance of the neck metastasis on patients' survival are considered by the most of researchers.

Regarding the immense prognostic value of detecting and treating occult cervical lymph node metastasis in patients with head and neck SCC [4,6,9-11], this study aimed to show some probable predictive risk factors for cervical lymph node involvement in patients with head and neck SCC.

Subjects and Methods

This study, as a Descriptive-Analytic Cross Sectional one, performed in three tertiary referral Academic hospitals in Tehran, Iran (Iran National Cancer Institute, Valiasr hospital, and Amir-Alamhospital) between 2001 and 2011.

Subjects

Eligible participants in this study were 164 patients selected among patients who underwent cervical lymph node dissection (of

all types) through their surgical treatment for head and neck SCC. Patients were excluded from this study if they had a recurrent head and neck SCC.

Ethical approval

The protocol of this study was approved by the Institutional Review Board of the Tehran University of Medical Sciences. All aspects of the study were conducted according to the Declaration of Helsinki.

Variables measurement

During a comprehensive review of case records, all needed information including: demographic data, family history for head and neck malignancies, smoking history, drug abuse history, alcohol drinking history, the history of radiation to head and neck, and pathologic findings were extracted.

The stage of the tumor, involvement of the different cervical node levels, absence or presence of nodal metastasis, and extra capsular lymph node extension were assessed in the pathologic specimens.

Statistical analysis

Data were analyzed via Chi-Square test and paired sample t-test, using the Statistical Package for the Social Science 20 (SPSS 20). A p value of less than 0.05 considered significant. Data are presented as mean ± standard deviation, and percentage.

Statistical calculation for the volume required for sampling done via following method:

$$n = \frac{Z_{1-\frac{\alpha}{2}}^2 pq}{d^2}$$

$Alfa = 0.05$ $Z_{1-\frac{\alpha}{2}} = 1.961150776$

$d = 0.03$

$p = 0.03$ $n = 100$

Results

Regarding our criteria 164 patients was enrolled in this study. 110 (67%) of our participants were male and the remainder were female. The mean age was 57.92±15.135 years old and ranged between 21-97 years old. Descriptive analysis of the other measured variables is shown in Table 1 and Table 2. About the nodal involvement two of our patients had occult metastasis which was detected with permanent pathology so the percentage of no nodal involvement in Table 2 is different and decreased.

In this study there was no significant relationship between the frequency of the cervical node involvement with these risk factors: the

history of the smoking (P >0.05), history of opium using (P= 1.00), familial history of head and neck cancer (P= 0.383), and history of radiation to head and neck (P= 1.00). Frequency of cervical node metastasis was not significantly different regarding the primary site of tumor (P= 0.686), and sex (P= 0.083), too. There was a significant positive relationship between frequency of cervical node metastasis and age (P= 0.038) (Table 3) and the stage of the tumors (P= 0.0001); so cervical node involvement was more frequent by increasing the patients' age and the stage of the head and neck SCC.

Extra capsular extension was not significantly different between different primary tumor sites (P= 0.511) and different cervical node levels involvement (P= 0.119).

Discussion

SCC was reported as the most common type of head and neck malignancies by many authors [12,13]. Also, neck lymph node involvement and occult metastasis are highly probable in patients with clinical negative lymph nodes [7]. Besides, cervical node metastasis is one of the most important factors in the head& neck cancer survival rate [4]. Recently it is shown the LNR (lymph node ratio) can be a valuable additional prognostic factor for risk assessment in the treatment of oral squamous cell carcinoma [14]. It is more beneficial to treat cervical node involvement in occult metastasis stage rather than clinically positive lymph nodes [9,15]. Moreover, regarding the importance of the cervical node metastasis on surveillance of this type of cancer, it seems to be valuable to know more about its possible risk factors, which helps us to use more aggressive treatment in presence of these risk factors.

Also, the specific characteristics of Iranian population regarding geographical location, specific risk factors like opium usage and lesser amount of alcohol usage may cause a different pattern of the cancers epidemiology, which needs to be much paid attention [16-18].

In our study, lymph node involvement was more prevalent in older patients. Similarly Antonio et al. showed that older patients had more severe lymph node involvement and were not suitable candidates for selective lymph node dissection [19].

Our study showed that cervical node involvement was more common in level I and II and less common in Level IV. Similarly Nithya C et al. [12] found that metastasis is less common in Level IV and more common in level II but the level I placed in the second common site for metastasis.

In our review of literature other authors have introduced some risk

Table 1: Descriptive analysis of variables.

Variables	Positive Number (percent)	Negative Number (percent)
Alcohol user	0(0)	164(100)
Smoker†	113(68.9)	43(26.2)
Opium user	36(22)	128(78)
Hx of the radiation to head and neck	13(7.9)	151(92.1)
Family history of head and neck malignancies	14(8.5)	150(91.5)
Extra capsular nodal extension	62(37.8)	102(62.2)
Nodal metastasis	144(87.80)	20(12.2)*

†8 persons were ex-smokers
*According to preoperative assessment included PH/E and radiology

Table 2: Descriptive statistics of variables.

Variable		Total count (%)
	Level I	17(10.4)
	Level II	17(10.4)
	Level III	16(9.8)
	Level IV	2(1.2)
Level(s) of the cervical lymph node involvement*	No involvement	18(11)
	I+II	23(14)
	II+III	25(15.2)
	III+IV	9(5.5)
	II+III+IV	37(22.6)
	Tongue	64(39)
	Larynx	24(14.6)
	Glottic and supra glottic	2(1.2)
Primary site of SCC	Mandibular area	9(5.5)
	Lip	34(20.7)
	Buccal& maxillary area	24(14.6)
	Scalp	6(3.7)
	Orbit	1(0.6)
	I	4(2.4)
Stage of tumor	II	14(8.5)
	III	117(71.3)
	IV	29(17.7)

*Confirmed by pathology examination

Table 3: The relation between age and lymph node involvement.

Nodal metastasis	Number	Mean age (y)	Std. Deviation	P-value
No	18	51.35	14.321	**0.038**
Yes	146	58.83	15.066	

factors for lymph node metastasis in head and neck SCC including: 1) combined expression of Ki-67 and VEGF-A by Boonkitticharoen et al. [1], 2) primary tumor thickness >3.75 mm by Bier-Laning et al. [8], 3) tongue cancer with moderate or poor differentiation, an invasion depth more than 3 mm, and positive perineural invasion or lymphovascular permeation at the time of presentation by Chen et al. [5], 4) tumor depth, desmoplasia and degree of immunosuppression by J Drugs et al. [2].

In this study extra capsular extension did not have significant relationship with primary tumor site and levels of cervical node involvement, which can be explained by the advanced stage of the most of the evaluated cases in this series.

Authors suggested that maybe older patients (with mean age of 58.83 y/o) need to undergo a more aggressive therapy due to the high incidence of the neck involvement in head & neck SCC. But it is needed to design a study with clear definition of old age and enough sample size to compare the characteristics of their malignancy with younger ones. In a study, Clayman et al. have shown that there was no significant difference between lymph node metastases in two groups of patients with the median age of 83 years old and 56 years old [20].

It seems to determine a comprehensive pattern of the risk factors for lymph node metastasis in head and neck SCC, additional studies are necessary.

Conclusion

This study revealed that maybe older patients (mean age of 58.83 y/o) with head and neck SCC are at higher risk for involvement of cervical nodes and they may receive more aggressive approach for detecting and treating occult cervical node metastasis.

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