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Impact of Neck Dissection in the Treatment of Oral Squamous Cell Carcinoma

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ABSTRACT

The clinical outcome of the overall recurrence after SND and RND in the treatment of oral squamous cell carcinoma; relate the recurrence rate of pathological staging and the significance of PORT in reducing recurrence. Fifty-eight Neck Dissection (ND) was done in 57 patients with oral squamous cell carcinoma in Ramadi Teaching Hospital, Iraq from 2008 to 2014. In the first group there were 33 SND which were done in the clinically negative neck (cN0) and in the second group there 25 RND which were done in the clinical positive neck (cN+). Postoperative radiotherapy was given to six patients with cN0 and to 19 patients with cN+. There were four recurrences in the first group (3 cases, ND without PORT, 1 case ND with PORT) and 6 recurrences in the second group (4 cases ND without PORT, 2 cases ND with PORT). there is a significant difference in tumor recurrence in the pathological positive neck (pN+) than the pathological negative neck (pN0) (9.6 times more recurrences in pN+). Tumor recurrence was not influenced statistically with the use of postoperative radiotherapy PORT in the clinically negative neck. There was a significant difference in recurrence in the clinical positive neck (cN+) (p- value >0.05). These findings support general acceptance of the use of END in the clinically negative neck without PORT and RND for clinical positive neck combined with PORT in selected cases to obtain a low recurrence.

Keywords: Oral cancer, Elective neck dissections; Squamous cell carcinoma; Clinical negative neck, Neck dissections

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INTRODUCTION

One of the most important prognostic factors in head and neck carcinoma is the presence or absence of metastatic neck disease [1]. It has been estimated that the presence of lymphatic metastases indicates a 50% decrease in survival rate with contralateral nodal disease, indicating another 50% decrease in survival rate [2]. Lymph node metastases appear to be predictable and follow constant routes in patients with previously untreated squamous cell carcinoma of the head and neck [3, 4]. Various characteristics of the primary tumor may influence the frequency of cervical nodal metastases. Such characteristics include the site of origin, size, tumor thickness, tumor stage, location, and histomorphologic presentation [5]. A radical neck dissection was the gold standard procedure in treatment of metastatic neck, but with anatomical and functional disadvantages. The first radical neck dissection was performed by George Washington Crile at the Cleveland Clinic in 1906 [6]. Recently, supraomohyoid neck dissection (SOHND) is recommended for patients with oral cavity cancer who are at risk of harboring occult nodal disease. Also, selective neck dissection (SND) can be performed for patients with low-volume nodal disease (N1) located in the upper neck provided that postoperative radiation therapy is part of the treatment plan. Metastasis have been interpreted in a Darwinistic perspective as being a process [7].

The aim of this article is to evaluate the recurrence in relation to pathological negative and positive neck and to assess the role of postoperative radiotherapy in reducing of recurrence of oral cancer.

PATIENTS AND METHODS

Between February 2008 and April 2014, 57 patients (38 males and 19 females) were enrolled from the consultative clinic of the department of Oral and Maxillofacial Surgery in Ramadi Teaching Hospital.

All patients were diagnosed with oral squamous cell carcinoma after comprehensive examination, including history (medical, family, dental and social), clinical examination, radiological (Figure 1A, a-d) and histopathological examination to evaluate the clinical staging and patient fitness to any proposed treatment. An inclusion criterion was previous untreated patients with squamous cell carcinoma of the oral cavity. The patients with non-squamous malignancy, prior treatment with surgery, radiotherapy and chemotherapy were excluded. The patients classified according to age, sex, primary site, clinical (pretreatment) and pathological(postsurgical histopathological) staging.

The tumor sites were the tongue (39 cases, 68.4%), the gingiva (9 cases, 15.7%), the floor of mouth (5 cases, 8.7%) and the retromolar region (4 cases, 7%) (Table 1). The clinical staging of patients was done according to the TNM stage (2009) (Table 2). Stage I – 2 cases (3.5%), Stage II – 15 cases (26.3%), Stage III – 17 cases (29.8%) and Stage IV - 23 cases (40.3%). All of the patients underwent elective/ treatment of the primary tumor and the neck simultaneous. Surgery was modified radical or selective neck dissection as shown in Figures (1B, a-d and 2a-f). The patients classified into two groups:

The first group (n=32 patients with 33ND) includes patients with the clinically negative neck (cN0) and those treated by SOHND (removal of cervical nodal level I, II & III) or extended SOHND (removal level I through IV) if the primary tumor was in tongue. The elective neck dissection was only performed if there was 15-20% chance of occult neck disease (tumor thickness >4mm, poorly differentiated SCC, tumor T stage >T1 or the neck is hard to assess). Patients with advanced T stage (T3/T4), the presence of lymphovascular invasion, the presence of perineural invasion, positive surgical margins, lymph node involvement, extracapsular nodal extension, and bone involvement were received postoperative radiotherapy [8]. The PORT was not given to N1 with any capsular spread. According to these criteria, the postoperative radiotherapy (PORT) is given to 6 patients where 3 of them were pN+ and three were pN0 but had adverse features of primary tumors that mandate PORT.

The level of lymph nodes, which included in radiotherapy was ipsilateral I-IV and also guided by positive histopathology.

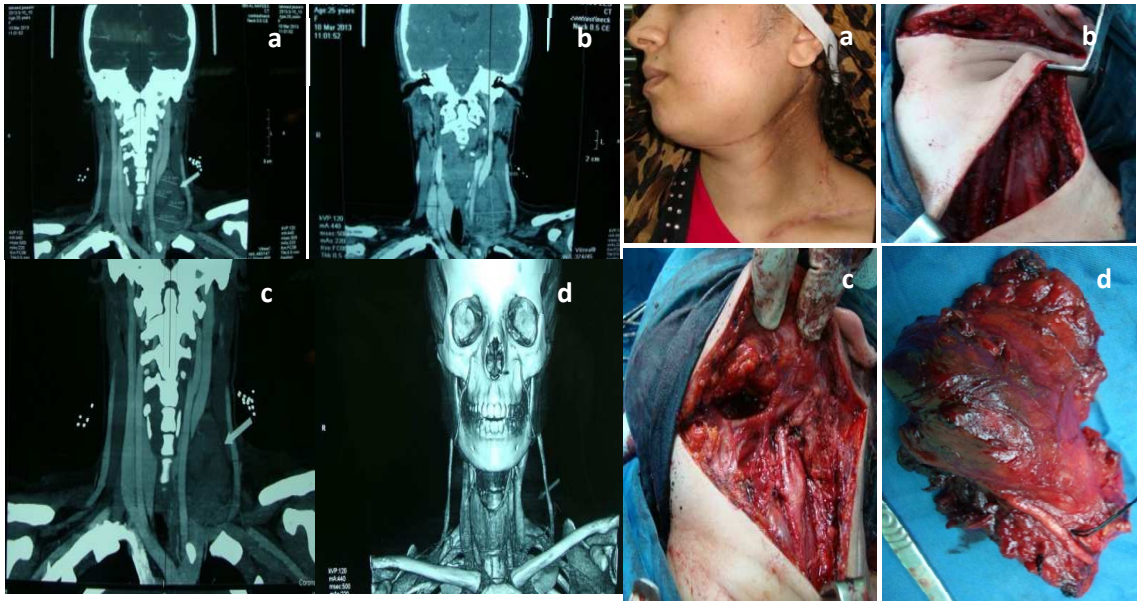

Figure (1A, a-d): CT scan axial section, include enlargement of neck, showing the cervical regional metastasis. Figure (1B, a-d): Stages of operation in a patient with OSCC.

Figure (2 a-f): Stages of operation in a patient with tongue SCC.

The second group Included 25 patients with clinically positive necks (cN+) and those treated by modifying RND (removal of level I-V with preservation of one or all of non-lymphatic structures: SAN, IJV & SCM). Postoperative radiotherapy was given to 19 patients who satisfied the same criteria in the first group. Patients with the N1without extracapsular spread are treated by surgery alone (no PORT).

The external beam PORT protocol for indicating patients involve total dose 65Gy delivered in fraction two Gy/day, five days per week for 6-7 weeks. The overall recurrences (local, regional and loco-regional) were assessed with follow-up period for two years as shown in Figure 1 (A and B).

RESULTS

Fifty-seven patients with OSCC underwent resection of the primary tumor with elective/therapeutic neck dissections as shown in Table 1. There were 66.6% male patients (n=38) and 33.3% female patients (n=19). The male: female ratio was 2:1. The mean age was 53.5 years with minimum age was 26 years, and the maximum age was 81 years. According to T classification, most cases were of T2 (n=25, 43, 1%) while T3, T4 and T1 sized-lesions were 14 (24.1%), 14 (24.1%) and 5 (8.6%) cases, respectively (Table 1). Regional metastasis was clinically and pathologically staged (Table 2, 3). According to metastatic lymph node level, the highest incidence of histopathologically positive lymph node level was level I that is, 50%, n=14 (Table 4).

Table 1: Distribution of primary lesion according to the site

Tongue	Lower gingiva	Floor of the mouth	Retromolar tumors	Total
39	9	5	4	57

Table 2:Clinical T and N staging (cT and cN) of 58 ND of Oral Squamous Cell Carcinoma

Clinical stage	cN0	cN1	cN2a	cN2b	cN2c	cN3	cNx	TOTAL
cT1	5	0	0	0	0	0	0	5
cT2	17	8	0	0	0	0	0	25
cT3	7	3	1	1	1	1	0	14
cT4	4	2	5	2	0	1	0	14
cTx	0	0	0	0	0	0	0	0
TOTAL	**33**	**13**	**6**	**3**	**1**	**2**	**0**	**58**

**T = staging of the primary tumor - TNM. N = staging of lymph node metastasis – TNM*

Table 3: Pathological (post-treatment) staging of cervical node metastases

Pathological N stage	pN0	pN1	pN2a	pN2b	pN2c	pN3	pNx	Total pN+
	30	9	7	8	1	3	0	28

**pN=pathological stage*

Table 4: Distribution of cervical node metastases

Nodal level	Number	Percentage
I	14	50%
I,II	8	28.5%
I,II,III	4	14.3%
I,II,III,IV	2	7.2%
total	28	100%

Table 5: The Types of recurrence

Tumor recurrence	Local	Regional	Local-regional
SOHND (33)	0	2	2
Modified RND (25)	0	2	4

Table 6: Recurrence according to type of neck dissection

Type of neck dissection	State	Surgery alone	Surgery + PORT	Total	Yates' X^2	d.f.	p-value
SOHND	Recurrence	3 (11.11%)	1 (16.67%)	4 (12.12%)	0.099	1	0.753 (NS)
	Cure	24 (88.89%)	5 (83.33%)	29 (87.88%)			
	Total	27 (100%)	6 (100%)	33 (100%)			
Modified RND	Recurrence	4 (66.67%)	2 (10.53%)	6 (24%)	5.102	1	0.024 (S)
	Cure	2 (33.33%)	17 (89.47%)	19 (76%)			
	Total	*6 (100%)*	*19 (100%)*	*25 (100%)*			

**PORT: Postoperative Radiation Therapy, SOHND: SupraOmoHyoid Neck Dissection, Modified RND: Modified Radical Neck Dissection*

Table 7: Recurrence about pathological staging of cervical nodes

Stage	State	Neck Dissection only	Neck Dissection + PORT	Total	Yates' X^2	d.f.	p-value
pN0	Recurrence	1 (3.70%)	0 (0%)	1 (3.7%)	1.839	1	0.175 (NS)
	Cure	29 (96.30%)	0 (0%)	29 (96.67%)			
	Total	30 (100%)	0 (0%)	30 (100%)			
pN+	Recurrence	3 (50%)	6 (27.27%)	9 (32.14%)	0.318	1	0.573 (NS)
	Cure	3 (50%)	16 (72.73%)	19 (67.86%)			
	Total	6 (100%)	22 (100%)	28 (100%)			

**ND: Neck Dissection*

**pN: pathological stage of cervical node (negative or positive)*

In the first group (SOHND group): (among the total 33), which was done in the clinically negative neck (cN0): The regional recurrence had been occurred in four cases (12.1%), of these one case was pN0 and three cases were pN+. The regional recurrence was distributed between level I (one case) and level II (3 cases). Of these recurrent cases, three cases were not irradiated (because not fit the criteria for indications of PORT) and 1 case was irradiated.

In the second group (modified RND group): (among the total 25), which were done in the clinically positive neck (cN+), six cases have recurred. Of these the recurrence was regional in two cases (there was metastasis at level II & III), 4 cases were local-regional (level I metastasis in 1 case, level II metastasis in 2 cases and level III

metastasis in 1 case). The rates of local, regional and local-regional of tumor recurrence shown in Table 5 while the recurrence, according to the type of neck dissection with or without postoperative radiotherapy was given in Table 6 and according to pathological staging as in Table 7 using Yates' chi-square test.

DISCUSSION

The decision regarding the optimal treatment of neck is subject to debate. Traditionally, selective neck dissection indicated in clinically negative neck (cN0) while (modified) radical neck dissection used in the clinical positive neck (cN+). However, the management of head and neck SCC varies both within and between countries alongside with the large number of published researchers. In the present study, cervical nodes level I was the most common site of lymphatic metastasis for OSCC (pN+ 50% of cases) followed by level I & II (28.5% of cases), level I, II, III (14.2% cases) then level I, II, III, IV (7.1% cases). The cervical nodes level I, II, III represent the first echelon nodes at highest risk for initial metastasis although skip metastasis may be present [9]. The level V was not involved in our case series and this may be explained by lack of lymphatic drainage to posterior cervical nodes from jugular chain nodes due to presence of valves in cervical lymphatics [10, 11]**.** SOHND procedure is intended for removal cervical nodes level I, II, III for oral SCC and extended for level IV in case of tongue lesions because of the risk of skip metastasis. Clinical staging usually underestimates the extent of lymph node metastasis as additional or occult pathologic lymph nodes were identified by light microscopy after neck dissection (pathological stage). There were 33 cN0 and 25 cN+ while there were 30 pN0 and 28 pN+ and this stage migration had impact on subsequent treatment and outcome [12]. Almost the cases of OSCC were presented in stage III & IV with equal prevalence 31.03% (n=18) for each stage while 29.3% (n=17) presented in stage II and 8.6 % (n=5) presented in stage I. This can be attributed to delay in diagnosis of OSCC due to patient (delay in looking treatment) and/or professional factors (delay or missed diagnosis). This study comes in accordance with other studies [13, 14, and 15]. The primary objective of our study is how many recurrences that occur in clinical and pathological negative and positive neck, and what is the role of postoperative radiotherapy in decreasing the recurrences in N0 and N+. Many factors may influence the recurrence of OSCC such as clinical T and N stage, tumor site, histological factors (differentiation, perineural and vascular invasion),resection margins, age, sex, race, genetic factors (like p53 gene mutation is responsible for locoregional recurrence despite clear histopathology of surgical margin and lymph node). 1- Overall recurrence (local, regional, and loco-regional) had occurred in ten patients (17.2%) of total 58 ND. In the first group (cN0=33 ND) the regional recurrence was 11.1% and 16.6% without and with PORT respectively. In cN0 group, the postoperative radiation (PORT) didn't influence neck recurrence statistically while in cN+ group there is significant difference statistically in recurrence among patients who receive PORT and those who didn't (p value = 0.024). These findings are in agreement with studies [16, 17] and the study of MSKCC [18]. The PORT was given when there is two or more positive lymph nodes, whereas, it wasn't given to (N0) even if there is micro-metastasis or (N1) without ECS (2). The analysis of recurrence between pN0 and pN+, there had shown 3.3% for pN0 and 32.1% for pN+. These results were agreement with the kind of literatures in which recurrence for pN0=3-7% irrespective type of treatment partially. While for pN+ was ranged from 10% for N1, 20-30% for N2 to 85% for N3 [19, 20, and 21]. In the present study, the recurrence can be interpreted by an underestimate of T and N stage. So that residual disease can cause recurrence like clinical staging T3N0M0 while pathological staging T3N2M0. Furthermore, incomplete removal of all lymph nodes that harbor metastases may cause recurrence and this may explain recurrence in cases despite RND was performed.

CONCLUSION

The pathological staging of the neck is an important predictor of recurrence because there is the significant difference in tumor recurrence in the pathological positive neck (pN+) than the pathological negative neck (pN0) (9.6 times more recurrences in pN+). Tumor recurrence was not influenced statistically with the use of PORT in the clinical negative neck while there was a significant difference in the clinical positive neck (cN+). These findings support general acceptance of the use of END in the clinical negative neck without PORT and (modified) RND for the clinical positive neck combined with PORT in selected cases to obtain good results with low recurrence.

Patient consent for publication Written and informed consent was obtained from the patients for publication and any accompanying images.

Ethics approval the study was approved by the Committee of Ethics of Ramadi Teaching Hospital (Reference number: 641 on 23/03/ 2017).

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