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Comparison of Regional Recurrence in Patients with Tongue Squamous Cell Carcinoma (T1-3N_0) between Levels I-III and I-IV Neck Dissection Methods

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Abstract

Objective and aim: There is an ongoing controversy between supporters of levels I-III neck dissection and levels I-IV neck dissection in N_0 tongue SCC as the key step of its treatment. Thus, we aimed to evaluate and compare these two groups' local recurrence, regional recurrence, and occult metastasis.

Methods and materials: This retrospective study was conducted on patients with T1-3 N_0 tongue cancer who had undergone tongue surgery and neck dissection during 2010 to 2019 at IKHC (level I-III neck dissection) and Amiralam hospital (I-IV neck dissection). Demographic data (age and gender), histopathologic parameters, postoperative radiotherapy, brachytherapy, and chemotherapy were recorded. Recurrence sites local and regional recurrences were evaluated. Time to development of recurrence was also measured. SPSS 26 was used for data analysis.

Results: 88 patients (53.02 ± 14.87 years old, 56.8% females) were evaluated in our study. Local and regional recurrence was detected in 31.8% and 11.4% of patients, respectively. One case (1.1%) of IV level involvement was observed. Regional recurrence was signi icantly associated with close margin and pathologic node status (p-value<0.05). T stage and perivascular invasion were signi icantly associated with pathologic node status. Two groups of neck dissection did not differ signi icantly in any study parameters.

Conclusion: Level IV neck dissection is not bene icial in improving local and regional recurrence in tongue SCC. Thus, level I-III neck dissection is recommended in N_0 tongue SCC cases.

Keywords: Tongue; SCC; Metastasis; Recurrence; Neck dissection; Level IV

Introduction

Squamous cell carcinoma is the most common malignancy in the oral cavity, accounting for approximately 4% of cancers in the body [1]. The involvement of cervical lymph nodes is the most important prognostic factor in oral SCC, found in more than 40% of patients on presentation [2,3]. The impact of lymph nodes in oral SCC is signi icant, with around a 50% reduction in survival rates of patients. Thus, diagnosis and management of the involvement of lymph nodes are critical in these patients.

Neck dissection is the main treatment for controlling lymph node metastases. The approach to neck dissection has evolved during past decades from radical neck surgeries to more selective methods of neck dissection [4]. In selective neck dissection, lymph nodes in levels I to III are removed as the highest risk of metastasis [5]. This type of neck dissection is routinely performed in neck negative oral SCC (N_0), which has yielded similar efficacy in managing oral SCC compared to neck dissection with more extent [6-8]. Despite favorable outcomes with selective neck dissection, the extent of this procedure is a matter of debate for two reasons. First, the prevalence of metastasis to level IV in oral SCC is also controversial. Second, skip metastasis is a phenomenon that can make surgeons underestimate the incidence of involvement in level IV. Thus, some authors have recommended that level IV be included in neck dissection due to skip metastasis and high rates of level IV involvement [9].

On the other hand, many researchers report that rates of level IV metastasis are meager. Thus, removal of level IV is not bene icial in terms of survival, recurrence, and occult metastasis. In addition, they claim that surgical removal of level IV lymph nodes is associated with several morbidities, which cannot be justi ied by the relatively low chance of metastasis to level IV lymph nodes [10,11]. In summary, some authors believe that neck recurrence is diminished with extensive levels of I-IV neck dissection, while others oppose this theory and state that levels I-III neck dissection is adequate, and level IV is not necessary with signi icant complications.

Given the ongoing controversy between supporters of levels I-III neck dissection and levels I-IV neck dissection, we aimed to evaluate and compare local recurrence, regional recurrence, and occult metastasis between these two groups.

Materials and Methods

This retrospective study was conducted at Imam Khomeini Hospital Complex (IKHC) and Amiralam hospital in 2020. The study sample included patients with T1-3 N_0 tongue cancer who had undergone tongue surgery and neck dissection from 2010 to 2019 at these centers. The routine surgical procedure was level I-III neck dissection at IKHC, while level I-IV neck dissection was the surgical routine at Amiralam hospital. Patients undergoing surgery at these centers were routinely examined by ultrasonography and CT scan to evaluate cervical node recurrence for at least a 1 year follow up period. Patients with recurrence of primary tumor and death due to reasons other than tongue cancer were excluded from the study. Demographic data (age and gender) were recorded. Histopathologic parameters including T stage involved margin, close margin, depth of invasion, perineural invasion, perivascular invasion, pathologic node status, and extracapsular node. Postoperative radiotherapy, brachytherapy, and chemotherapy were recorded. Recurrence sites were also retrieved from medical records. Local and regional recurrences were also considered as study outcomes. Time to development of recurrence was also measured.

IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA) was used for data analysis. Frequency and percentage were used for reporting descriptive analysis. *Chi-square* test and Fisher's exact test were applied to compare categorical variables. ANOVA or t-test analysis was used to compare continuous parameters between two groups. P-value <0.05 was considered statistically significant.

Results

Eighty eight patients were enrolled in our study. The mean age of patients was 53.02 ± 14.87 years (range=22-80). Thirty eight patients (43.2%) were males, while 50 patients (56.8%) were females. Forty ive patients (51.1%) underwent level I-IV neck dissection in Amiralam hospital (group A). The mean age of patients in this group was 52.53 ± 15.39 years (range=22-80). Twenty three patients (51.1%) were males, while 22 patients (48.9%) were females. Forty three patients (48.9%) were treated with level I-III neck dissection at IKHC (group B). The mean age of patients was 53.53 ± 14.47 years (range=26-77). Fifteen patients (34.9%) and 28 patients (65.1%) were males and females, respectively.

Overall, 34 cases (38.6%) belonged to the T1 stage, while 43 (48.9%) and 7 (8%) cases were in T2 and T3 stage groups, respectively. Five cases (5.7%) had involved margin, and a close margin was seen in 19 patients (21.6%). The mean depth of invasion was 10.12 ± 4.67 mm (range=2.50-20).

Forty patients (45.5%) underwent level I-III neck dissection, and 41 patients (46.6%) underwent level I-IV neck dissection. 6 level I-V neck dissections and one bilateral level I-III neck dissection were also performed. 40 (88.9%) level I-IV and 5 (11.1%) level I-V neck dissections were done in group A. In group B, 40 level I-III neck dissections were conducted. One (2.3%) level I-IV, one (2.3%) level I-V and one (2.3%) bilateral level I-III dissections were also performed.

Perineural invasion, perivascular invasion, and status of pathologic nodes are also evaluated. Extracapsular node was also found in one patient (1.1%). The details of these parameters are presented in Table 1.

Table 1: Histopathologic parameters in two surgery groups.

Parameter	Group A	Group B	Total
Perineural invasion	10 (22.2%)	19 (44.2%)	29 (33%)
Perivascular invasion	1 (2.2%)	12 (27.9%)	13 (14.8%)
Pathologic node	1 (2.2%)	14 (32.6%)	15 (17%)

Postoperative radiotherapy was performed in 68 patients (77.3%). Postoperative brachytherapy was done in 9 patients (10.2%). Chemotherapy after surgery was found in 8 patients (9.1%).

Local recurrence was observed in 28 patients (31.8%), while regional recurrence had occurred in 10 patients (11.4%). The status of recurrence in our patients is displayed in Table 2.

Table 2: Rates of recurrence.

Recurrence status	Frequency (%)
No recurrence	55 (62.5%)
Local recurrence	23 (26.1%)
Regional recurrence	5 (5.7%)
Local and regional recurrence	5 (5.7%)

The pattern of involved levels is as follows: Level I (2 patients, 20%), level II-III (7 patients, 70%), and level IV (one patient, 10%). Recurrence sites were also tongue in 22 patients (78.6%), the loor of the mouth in 3 patients (10.7%), contralateral side of tongue in 2 patients (7.1%) and combined retromolar and buccal areas in one patient (3.6%). Overall, the most common recurrence pattern in our study was tongue (17 patients, 51.5%) followed by combined tongue and level II-III (4 patients, 12.1%) and loor of mouth (3 patients, 9.1%) or level II-III (3 patients, 9.1%). The complete list of recurrence locations is presented in Table 3.

Table 3: Recurrence sites.

Recurrence site	Frequency (%)
Tongue	17 (51.1%)
Level I	1 (3%)
Level II-III	3 (9.1%)
Level IV	1 (3%)
Floor of mouth	3 (9.1%)
Contralateral side of tongue	2 (6.1%)
Retromolar and buccal areas	1 (3%)
Tongue and level II-III	4 (12.1%)
Tongue and level I	1 (3%)

The association of study parameters with recurrence was also analyzed. In patients with a close margin, the regional recurrence rate was 26.31%, while in patients without a close margin, only 7.69% of patients experienced regional recurrence (p=0.037). Regional recurrence was 26.66% and 8.21% in patients with and without pathologic node (p=0.040). Two surgery groups did not differ in terms of recurrence (p=0.900). A trend toward a higher frequency of perivascular invasion in local and regional recurrence (p=0.065 and 0.053) was observed, but it could not reach statistical signi icance. The details of the correlation of study parameters with recurrence rates can be seen in Table 4.

Table 4: Rates of recurrence according to different study parameters.

Local recurrence				
Close margin	Absent	35 (67.30%)	17 (32.69%)	0.124
	Present	17 (89.47%)	2 (10.52%)	
Surgery group	Group A	32 (71.11%)	13 (28.88%)	0.546
	Group B	28 (65.11%)	15 (34.88%)	
Perineural invasion	Absent	39 (66.10%)	20 (33.89%)	0.55
	Present	21 (72.41%)	8 (27.58%)	
Perivascular invasion	Absent	54 (72%)	21 (28%)	0.065
	Present	6 (46.15%)	7 (53.84%)	

Pathologic node	Negative	49 (67.12%)	24 (32.87%)	0.638
	Positive	11 (73.33%)	4 (26.66%)	
Postoperative brachytherapy	Absent	48 (70.58%)	20 (29.41%)	0.809
	Present	6 (66.66%)	3 (33.33%)	
Postoperative chemotherapy	Absent	47 (63.51%)	27 (36.48%)	0.911
	Present	2 (66.66%)	1 (33.33%)	
Regional recurrence				
Close margin	Absent	48 (92.30%)	4 (7.69%)	0.037
	Present	14 (73.68%)	5 (26.31%)	
Surgery group	Group A	40 (88.88%)	5 (11.11%)	0.939
	Group B	38 (88.37%)	5 (11.62%)	
Perineural invasion	Absent	55 (93.22%)	4 (6.77%)	0.053
	Present	23 (79.31%)	6 (20.68%)	
Perivascular invasion	Absent	68 (90.66%)	7 (9.33%)	0.149
	Present	10 (76.92%)	3 (23.07%)	
Pathologic node	Negative	67 (91.78%)	6 (8.21%)	0.04
	Positive	11 (73.33%)	4 (26.66%)	
Neck dissection	Level I-III	37 (88.09%)	5 (11.90%)	0.9
	Level I-IV	34 (87.17%)	5 (12.82%)	

As mentioned above, pathologic node status was significantly correlated with regional recurrence. Perivascular invasion and T stage had a significant impact on pathologic node status. The details are presented in Table 5.

Table 5: Analysis of association of pathologic node with perivascular invasion and T stage.

Pathologic node				
Parameter		**Absent**	**Present**	
Perivascular invasion	Absent	68 (90.66%)	7 (9.33%)	0
	Present	5 (38.46%)	8 (61.53%)	
T stage	1	32 (94.11%)	2 (5.88%)	0.029
	2-3	38 (76%)	12 (24%)	

The median recurrence time in patients with only local recurrence was 16.00 months, while the median of patients with regional recurrence with or without local recurrence was 10.00 months (p=0.026). The details of recurrence time according to recurrence status are presented in Table 6.

Table 6: Recurrence time in different types of recurrence.

Recurrence status	Median	Mean	Minimum	Maximum
Local recurrence	16	28.39	2	96
Regional recurrence	11.1	10.4	8	12
Local and regional recurrence	8	9.6	6	15
Total	12	22.81	2	96

Discussion

The extent of neck dissection in patients with neck-negative (N_0) oral squamous cell cancers is a matter of debate in the available literature. We compared neck dissections with levels I-III and I-IV in two centers, and no difference in any parameters was found between the two neck dissection routines. 31.8% and 11.4% of patients developed local and regional recurrence, but no significant difference was observed between surgery groups in terms of any recurrence. Regional recurrence in level IV was 1.13%. Based on our findings, the rate of involvement of IV level is meager and inclusion of level IV in neck dissection did not yield additional benefits for SCC patients, which could not decrease recurrence rates in comparison to the supraomohyoid neck dissection of levels I-III. The clinical decision of dissection of selected levels of lymph nodes is related to the chance of metastasis in these levels. Levels I, II, and III of the neck are the most susceptible areas for occult metastasis from cancers in the oral cavity [12,13]. Detection of occult metastasis is not feasible through clinical examination or imaging techniques due to the relatively small sizes of these metastases. In addition, the skip metastasis phenomenon adds to the complexity of the problem because of the unpredictable behavior of metastasis development. Classically, a famous paper by Byers, et al. has reported that the rate of involvement of level IV lymph nodes through skip metastasis has been 15.8%. This high rate of skip metastasis led them to a recommendation of extending neck dissections to level IV in early stage squamous cell carcinomas of the oral cavity. However, that study had included patients from all stages of N and T in their analysis. Another look at their data shows that the prevalence of level IV metastasis in negative neck patients has only been 4.8%. Later, Shah, et al.'s study showed a rate of 3% for level IV metastasis in N_0 patients, while this rate was 17% in N+patients. They suggested that the extent of the neck dissection strategy must be modified according to the presence or absence of lymph node involvement. Nithya, et al. study reported lymph node metastasis in 35.6% of patients with no isolated involvement of level IV in N_0 cases. Khafif, et al. also reported that only one case was positive in 17 patients who underwent dissection of level IV. In a 4.1 years follow-up, only one patient had a recurrence in level IV.

Additionally, only 2% of patients without dissection of level IV developed recurrence in level IV. Vishak, et al., reported a 1.5% rate for skip metastasis in level IV [15]. Metastasis to levels III and IV was found in 8.5% of patients. Motive Langroudi, et al. also reported that occult metastasis was found in 28% of patients with T1-3N_0M_0 tongue SCC who underwent level I-IV neck dissection [16]. Level IV metastasis was found in only 6.25% of cases, and finally, dissection of levels I-III was recommended. Yuen, et al. yielded results indicating that while the rate of lymph node metastasis has been 34% in neck negative patients, involvement of IV level has been 0% [17]. They also suggested level I-III neck dissection in N_0 cases. Although many studies are consistent with our findings and suggest that dissection of IV level is not advised, some studies do not support this idea. For instance, Oscar, et al. reported a relatively high rate of 52% for lymph node metastasis in primary head and neck cancers [18]. They revealed that 15% of patients had level IV metastasis and thus, neck dissection must always include level IV, particularly in cases of tongue involvement. In order To have more inclusive and definite results, a recent meta-analysis in 2020 on level IV neck dissection for oral tongue cancers was performed. The study concluded that the rate of IV involvement is roughly 2.8%, and accordingly, the prevalence of skip metastasis to level IV is low. At last, they recommended level I-III neck dissection in N_0 oral cavity cancers.

An important point to consider in managing these patients is that clinical decisions for performing or extending neck dissection cannot be only based on one factor of the prevalence of metastasis. Numerous factors in the studies have been evaluated as predictors of recurrence in these patients. Regional recurrence was significantly correlated with close margin and pathologic node status in our study. Pathologic node status itself was correlated with perivascular invasion and T stage. A trend toward higher rates of perivascular invasion was also noted in patients with recurrence, but this association did not reach statistical significance. Sittitrai, et al., revealed that surgical margin <5 mm, perilymphatic invasion, and perivascular invasion were significantly correlated with local recurrence, while perilymphatic and perivascular invasion were significant predictors of regional recurrence [19]. O-Charoenrat, et al. reported that tumor thickness >5 mm had been significantly associated with poorer survival and higher recurrence rates [20]. Keski-Santti, et al. concluded that the T stage significantly correlated with local recurrence. D'Cruz, et al. reported that perineural invasion and tumor grade were significant predictive factors for recurrence. Troeltzsch, et al. indicated that poor histologic differentiation is significantly correlated with regional recurrence [21]. As can be concluded from the studies, various histopathologic parameters have been reported as predictors of recurrence, survival, and occult metastasis in tongue SCC cases,

and there is no general agreement regarding these predictive factors.

The main limitation of our study was the relative sample size. Larger sample sizes in upcoming studies can yield more inclusive results. In addition, retrospective study design limits the power of the study in the analysis of data and interpretation of results.

Conclusion

Level IV neck dissection is not beneficial in improving local and regional recurrence in neck negative tongue SCC. Thus, level I-III neck dissection is recommended in N_0 tongue SCC cases.

Conflicts of Interest

The authors declare no conflict of interest.

Financial Disclosures

None.

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Ethical Approval

This study was approved by the ethics committees of the collaborating hospitals. Informed consent was obtained from all participants (IR.TUMS.REC.1399.499).

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