A Clinical Comparison of the Efficacy of Level I-III Versus Level I-IV Neck Dissection in N0 Early Stage Tongue Squamous Cell Carcinoma

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Abstract- In this study, we compared regional recurrence in patients who had a dissection of levels I-III or levels I-IV. Patients with tongue SCC who were node-negative both clinically and radiologically, and underwent elective supraomohyoid neck dissection (SOHND) or extended supraomohyoid neck dissection (ESOHND) between March 2012, and March 2015 were retrospectively reviewed. The two therapeutic groups were analyzed for the incidence of tumor recurrence and survival. The two groups had statistically similar demographic qualities. Surgery duration and complications were the same in both groups. Complications mainly included internal jugular vein and thoracic duct injury. Tumour size was 46.2% T_1, 40.4 % T_2, and 13.3% T_x, being statistically similar in both groups. Tumour size had no meaningful correlation with the occurrence of occult neck metastasis in both groups. Local recurrence was more in ESOHND patients, but regional recurrence was similar in both groups. The survival rate was alike in both groups. No significant differences in tumor recurrence and mortality rate were found between patients treated with SOHND versus ESOHND. Thus, SOHND could be considered as a sufficient treatment for early-stage tongue SCC.

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Keywords: Neck dissection; Tongue; Squamous cell carcinoma; Tumor recurrence; Mortality rate

Introduction

Oral mucosa neoplasms (with the exception of lip neoplasms) account for 14% of all head and neck cancers, and more than 85% of cases are squamous cell carcinoma (SCC) (1,2). The tongue is the most common site of primary SCC in the oral cavity (3). Mostly, the standard treatment for oral cavity SCC at the early stages (stage I and II) is surgery. Interestingly, the incidence of occult neck metastasis to neck lymph nodes is high in tongue SCC (7%-28% of patients with T1 and 28%-40% of T2 with clinical N0) (4). The mortality rate rises up to 50% in the presence of neck metastasis (5). Thus, the management of neck is crucial even in node-negative (N0) patients, and elective neck dissection (ND) is part of treatment in such patients. However, there is still no consensus on the extension of neck surgery for N0 patients with tongue SCC. Hence there is controversy in performing level IV ND.

Byer suggested the ND for levels I-IV or extended supraomohyoid neck dissection (ESOHND) considering the 15.8% rate of metastasis to levels III and IV in the absence of involvement of the levels I or II (6). While the National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology states that the selective neck dissection (SND) of levels I-III or supraomohyoid neck dissection (SOHND) is sufficient in this setting (7). An increasing number of studies have evaluated the oncologic outcomes of patients who underwent level I-III ND. They found that considering the low probability of skip or occult metastasis to level IV, maybe the routine inclusion of level IV in an elective ND is not necessary for N0 patients with tongue SCC (8,9). A retrospective study was done by Iype *et al.*, revealed that level I-III ND is enough for early-stage oral SCC (10). Additionally, Yu *et al.*, assessed the rates of occult metastasis, regional disease-free survival, overall and disease-free survival, and distant metastasis-free survival and had the same findings (11). It has also been demonstrated that the neck nodal recurrence is comparable between the neck dissection of levels I-III and levels I-IV (12). Furthermore, dissection of level IV

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is associated with more complications, including nerve injury or flap necrosis, and results in poor cosmetic outcomes (13). Taken together, level I-III ND has been newly considered as an appropriate treatment for early-stage N0 tongue SCC. So, here we investigated neck nodal (regional) recurrence and survival rate among patients who undergone ND for levels I-III or levels I-IV in a retrospective cohort study.

Materials and Methods

All of the methods applied in this project were in accordance with the declaration of Helsinki principles. Also, this retrospective cohort study was approved by the ethics committee of Tehran University of Medical Sciences (IRB code: 31878). The medical records of patients with tongue SCC (T1-T2N0M0) who underwent partial glossectomy and level I-III or level I-IV neck dissection between March 2012 and March 2015 was assessed. The staging was evaluated according to the 2010 American Joint Committee on Cancer (AJCC) criteria. Pre-treatment evaluations included physical examination, chest radiographs, and Computed tomography scans or magnetic resonance imaging obtained to determine the stage of the disease and cervical lymph node involvement.

The inclusion criteria were: (1) a T1-T2 tumor located in the oral tongue; (2) no evidence of distant or neck metastasis in evaluations; (3) negative margin status in pathologic specimens; (4) no previous treatment for the neck.

Partial glossectomy with 1.5-2 cm margin and elective ND of levels I-III or levels I-IV was done for patients. The difference in the extent of neck surgery was due to the fact that the patients were operated in two different medical centers (Amir Alam hospital and Imam-Khomeini hospital, both affiliated to Tehran University of Medical Sciences).

Patients with metastatic lymph nodes, which were confirmed by frozen-section during the surgery, had been excluded from the study. The patients from other medical centers who underwent glossectomy and were referred for the prophylactic ND were classified as Tx group if fulfilled inclusion criteria. The patients were followed on return visits and by telephone interviews. The data of overall survival, the cause of death, the recurrence of the disease, and the place of recurrence were evaluated during follow up (till November 2016).

All the data was finally analyzed using SPSS 24. The quantitative and qualitative data are presented mean±SD and percentage, respectively. Normally distributed data were analyzed by parametric tests otherwise analyzed by nonparametric ones. To compare the mean of quantitative variables based on qualitative variables, a *t*-test was used. For qualitative variables, the *chi*-square test was used. In all tests, $P<0.05$ was considered significant.

Results

Patients demographics

This study included 52 patients, 28 males (53.8%) and 24 females (46.2%) compared in two groups of neck dissection. The mean age for level I-III ND group was 54.7±12.2 years, while it was 54.7±17.1 years in the level I-IV ND group. Patients' sex and age were not statistically different between these two groups. The mean age for level I-III ND group was 54.7±12.2 years, while it was 54.7±17.1 years in the level I-IV ND group. Patients' sex and age were not statistically different between these two groups.

Duration of surgery

Comparing the duration of surgery between the applied neck dissection methods revealed that the mean duration of Level I-III ND (310.5±105.5 minutes) was not significantly different from Level I-IV neck dissection (333.1±56.2 minutes) (P=0.3).

Surgical complications

Surgical complications of both neck dissection groups are described in table 1. Our results revealed that while most surgeries (>87%) were not associated with any complications. In those surgeries which lead to complications, the majority of reports included damage to the internal jugular vein and thoracic (or lymphatic) duct. Furthermore, comparing the occurrence of these complications, results showed that while more complications occurred in the level I-IV ND, the dissimilarity was not statistically considerable. (P=0.8)

Tumour size and metastasis

Tumour size (T) was evaluated as 46.2% T_1, 40.4 % T_2, and 13.3% T_x in the study population. Table 2 shows the distribution of different tumor sized in our study groups. According to our analysis, there was no significant difference in the distribution of Tumor size in the two study groups (P=0.7). A total of 9 patients (17%) in this research were involved with hidden metastasis in their pathology report, 3 among the Level I-III ND (2 T_1 and one T_2) and 6 in the Level I-IV neck dissection group (4 T_1, 1 T_2, and 1 T_x). Data analysis showed that there was no significant difference between the applied ND

methods regarding the detection of hidden metastasis (*P*=0.7). Also, Tumor size had no meaningful correlation with the occurrence of hidden metastasis in both groups (*P*>0.3). (Table 2)

Table 1. Surgical complications according to the therapeutic group

Side effect (%)	Group		*P*
	level I-III neck dissection	level I-IV neck dissection	
Injury to the internal jugular vein	5%	3.1%	0.8
Injury to the thoracic duct	5%	9.4%	
No side effect	90%	87.5%	

Table 2. T stage in study groups

No. of patients	Group		Total	*P*
	level I-III neck dissection	level I-IV neck dissection		
T1	8 (40%)	16 (50%)	24 (46.2%)	0.7
T2	8 (40%)	13 (40.6%)	21 (40.6%)	
Tx	4 (20%)	3 (9.4%)	7 (13.5%)	
Hidden metastasis	3 (15%)	6 (18.8%)	9 (17.3%)	>0.99

Tumour recurrence

In these 52 patients, a total of 20 patients (38.4%) suffered from tumor recurrence. In the mean 23 months follow up period for the level I-III ND group, recurrence occurred in 6 patients while in the Level I-IV neck dissection patients, 14 cases of recurrence were verified. Although more patients suffered from a recurrence in the second group, this dissimilarity was also not significant (*P*=0.3). In this study, recurrence was categorized into three subgroups of Local, regional (in the neck) and distant recurrence. Local recurrence occurred in two cases (10%) who underwent level I-III ND and ten patients (31.2%) who were in the level I-IV ND group, the analysis showed that this type of recurrence was significantly higher in the second group (*P*=0.03). Data showed that there was no substantial difference in the regional or distant recurrence between the study groups (*P*=0.4). (Table 3)

Table 3. Tumor recurrence according to the therapeutic group

No. of patients with recurrence	Group		Total	*P*
	level I-III neck dissection	level I-IV neck dissection		
Recurrence*	6 (30%)	12 (37.5)	18 (34.66%)	0.3
Local	2 (10%)	10 (31.2%)	12 (23%)	0.03
Regional (neck)	3 (15%)	3 (9.4%)	6 (11.5%)	0.4
Distant	2 (10%)	4 (12.5%)	0 (11.5%)	0.4

**Includes the presence of any type of recurrence in any region, regardless of the number of regions*

Mortality

In the follow-up period in this research, the survival rate for Level I-III ND patients was about 90%, with only two recorded demises (10%) at that time. Moreover, the Level I-IV ND group had a survival rate of 78% survival, with 7 recorded cases of death. Comparing the mortality rate between these two methods, our results indicated that there was no significant difference between Level I-III and Level I-IV neck dissection in tongue SCC patients. (Table 4).

Table 4 The mortality rate according to the therapeutic group

No. of patients	Group		Total	*P*
	level I-III neck dissection	level I-IV neck dissection		
Death	2 (10%)	7 (21.8%)	9 (17.3%)	0.5
Live	17 (85%)	23 (71.9%)	40 (76.9%)	
Un-known	1 (0.5%)	2 (6.3%)	3 (5.8%)	

Discussion

In the current study, two different neck dissection approaches for early-stage tongue SCC were evaluated in two groups of patients with similar ages. Sex, tumor size, and the prevalence of hidden metastasis were also similar in these groups. Our results revealed that both Level I-III and Level I-IV ND had similar operative time. The incidence of surgical complications was also similar in these groups, while their majority included damage to the internal jugular vein and thoracic (or lymphatic) duct. Furthermore, patients' follow up revealed that while regional and distant recurrence was similar in both groups, patients who underwent level I-IV ND suffered from a greater incidence of local recurrence, although survival rates were similar in both neck dissection methods applied in this research.

Previous studies have reported a wide range of operative time for neck dissection methods. According to a recent review on different neck dissection methods, it has been indicated that the duration of conventional open ND is between 78 to 218 minutes while robotic-assisted surgeries require a longer duration (136-382 min) (14). On the other hand, another study has indicated that tumor resection and neck dissection surgeries may require a longer period of time, depending on different tumor and patient properties (130-880 min). The study also suggests that longer durations of surgery might be associated with more comorbidities (15). Our results indicate that the mean times for surgery were not significantly different between the two study groups. Thus, it could be concluded that any difference in complications would have been independent of this factor. Moreover, the meantime for surgery was about 310 and 333 minutes in SOHND and ESOHND, respectively. Although, as similar surgical times have been previously reported, the relatively prolonged recorded duration could have occurred due to the different applied techniques and also time recording methods in this study (14,15).

Surgical complications described in all of the patients in this study had a total prevalence of less than 13% and included mainly damages to the internal jugular vein and thoracic (or Lymphatic) duct. Thoracic duct injury is one of the major complications of neck surgeries, which can lead to death in some cases (16). Recent studies have indicated that the incidence of this complication is usually between 2-8% in neck dissections (17). It has also been indicated that the incidence rate is correlated with the extent of the procedure (16). Bleeding and internal jugular vein injury are also reported as major complications in neck dissection. Bleeding is reported to occur in 10% of cases, while studies have indicated that internal jugular vein (IJV) complications may take place in up to 14% of neck dissections (18,19). In our study, injury to the thoracic duct had a statistically similar prevalence of 5% in SOHND and 9.4% in ESOHND. Moreover, the incidence of IJV complications was 5% in Level I-III ND, which was not significantly different from the 3.1% incidence rate in ESOHND. Thus, it could be concluded that both of these methods could be evaluated as similar regarding the incidence of major complications. It would also be noteworthy to mention that the difference in the incidence rates between the current study and the previous evaluation could have occurred due to the dissimilarities in the population and the applied surgical and data recording method between these studies (18,20).

Nine patients (17.3%) in this research had hidden metastasis, 3 among the SOHND, and 6 Among ESOHND patients. The most common areas for metastasis were levels I and II. Tumour size had no meaningful correlation with the occurrence of hidden metastasis in both groups. Our results were in accordance with previous findings such as a study by Mantsopoulos *et al.*, which indicated that the prevalence of hidden metastasis of oral cavity cancers is 20.2 % and also the study of Thomas Mücke *et al*., in 327 patients with $T_1-T_2N_0$ oral cavity cancer had an 18.65% rate of hidden metastasis (21,22). The similar incidence rate of hidden metastasis in our study groups could also rule out the probability of patients' tumor dissimilarities affecting the comparison of the applied methods.

Previous studies have indicated that the rate of recurrence in early-stage tongue cancers varies between 18.3-45.3% (23,24). Inconsistency with these studies, our follow up evaluations revealed that that the rate for recurrence was (34.66%) in the study population. Moreover, while the incidence of recurrence was in the normal range for both study groups, our results revealed that there was no significant difference in overall recurrence between level I-III (30%) and I-IV (37.5%) ND methods. However, Relapse in primary tumor site (Local recurrence) was seen in 10% of I-III ND patients, which was significantly less than the 31.2% rate in ESOHND patients (P=0.03). Previous studies have indicated that one of the necessities for neck dissection is to prevent further cancer spread in head and neck tumors in which local recurrence and also the incidence of second primary tumors are relatively high. Thus, although there is a significant difference in local recurrence between the

ND groups in our study, this result could not be considered as a major factor for comparison of these methods efficacy (25). Moreover, it has ensued from technical or histological issues, *e.g.* the proximity of the surgical margins or high-grade malignancy of tumor cells. Moreover, considering the relatively high local recurrence rate, it would be noteworthy to mention the fact that various studies have implied that local recurrence is more prevalent than other types of relapses in this regard (23,24).

Regional (Neck) recurrence occurred in 15% of patients who underwent SOHND and 9.4% of patients of ESOHND; this difference was not significant. Our finding was consistent with the study of different neck treatment methods for cancers of the oral cavity in which SOHND, radical neck dissection, functional ND, and observation were compared. These studies revealed that all of the applied methods were effective, and there was also no statistical difference between them (12).

As demonstrated in this distant study, metastasis took place statistically indifferently in SOHND (10%) and ESOHND (12.5%). Prior studies suggest a 5 to 25% distant metastasis rate associated with 4.3% mortality in surgical treatments applied for similar tongue cancer. Comparing these results, it could be concluded that although neck dissection is an effective therapeutic approach, there is not much difference in the occurrence of distance metastasis when applying different ND methods (26).

Finally, our results indicated that the overall survival rate in level I-III neck dissection was 85%. Although apparently higher than the ESOHND group (71.9 %), further analysis revealed that the difference was not significant. Our results were in accordance with the previous investigation that indicated that neck dissection could increase the survival rate of early-stage tongue cancer from 49 to 72% (27,28). Nevertheless, as there were no significant differences between the achieved survival rates through the different applied methods and also considering the similarity in tumor recurrence and surgical complications in these groups, our study suggests that extended supraomohyoid neck dissection may not have any advantages compared to the conventional SOHND in early-stage tongue SCC. The limitation of the current study is that detailed investigation of histopathological differences in the therapeutic effects of these surgical methods was not performed. Also, considering other potential complications, cost-benefits of each method, and also longer surveillance periods may affect the outcomes concluded in this research. Thus, it would be essential to perform further investigations in order to find the most beneficial neck dissection approach for patients suffering from tongue SCC.

In tongue SCC, considering the high possibility of occult metastasis, elective neck dissection is highly recommended to reduce recurrence and mortality. This study shows that surgical complications, tumor recurrence, and survival rates are not statically different in SOHND and ESOHND. Hence it could be concluded that SOHND does not differ from the extended form and could be chosen as a sufficient approach for patients with N0 tongue SCC.

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