Selective Neck Dissection for Node-Positive Oral Cavity Squamous Cell Carcinoma: A Retrospective Cohort Study

Syed Salman Hashmi[1]   Akbar Abbas[2]   Amna Bukhari[3]   Javeria Saeed[4]   Ali Shafqat[3]
Atif Hafeez Siddique[5]   Ahmed Raheem Buksh[6]   Ghulam Murtaza[7]

[1] ENT Department, Peterborough City Hospital, Northwest Anglia NHS Foundation Trust, Peterborough, England
[2] Department of ENT, Aga Khan University Hospital, Karachi, Sindh, Pakistan
[3] Department of ENT and Head and Neck Surgery, Patel Hospital, Karachi, Sindh, Pakistan
[4] Department of Orthopedics, Aga Khan University Hospital, Karachi, Sindh, Pakistan
[5] Department of Otolaryngology, Dow University of Health Sciences, Karachi, Sindh, Pakistan
[6] Department of Pathology and Laboratory of Medicine, Aga Khan University Hospital, Karachi, Sindh, Pakistan
[7] Department of General Surgery, Patel Hospital, Karachi, Sindh, Pakistan

Address for correspondence Syed Salman Hashmi, MBBS, FCPS, ENT Department, Peterborough City Hospital, North West Anglia NHS Foundation Trust, Peterborough PE3 9GZ, England (e-mail: salmanhashmi1404@gmail.com).

Abstract

Introduction Selective neck dissection in clinically node-negative neck is considered the standard of care for oral squamous cell carcinomas (SCCs). Controversy still prevails in node-positive disease regarding the extent of neck dissection. In our part of the world, comprehensive neck dissection is mostly considered to be the minimal optimal treatment for palpable neck disease.

Objective To compare regional control and disease-specific survival between clinically node-positive and node-negative patients undergoing selective neck dissection for oral SCC.

Methods This was a retrospective cohort study conducted in the department of ENT, Head and Neck surgery at a tertiary care hospital. All patients with biopsy-proven oral and lip SCC, with or without nodal disease, who underwent selective neck dissection between April 2006 and July 2015 were included in the study.

Results During the study period, 111 patients with oral SCC underwent selective neck dissection, of whom 71 (62%) were clinically node-negative and 40 (38%) patients had clinically positive nodes in the neck. The mean follow-up was 16.62 months (standard deviation [SD]: 17.03). The overall regional control rates were 95 versus 96% for clinical negative versus positive nodes, respectively ($p = 0.589$). The disease-specific survival was 84.5% in the node negative group versus 82.5% in the node-positive group ($p = 0.703$).

Keywords
► carcinoma
► squamous cell/surgery
► mouth neoplasms/therapy
► neck dissection/methods
► neoplasm recurrence, local
► survival rate

Conclusion Selective neck dissection in node-positive neck oral SCC has similar regional control rates when compared with node-negative neck SCC. The difference in disease-specific survival between the two groups is also not significant.

Introduction

Oral cancer is among the commonest cancers in some parts of South Asia.[1,2] Over 95% of oral cancers are squamous cell carcinomas (SCCs).[3] The estimated incidence of cervical metastasis in this group is of up to 40%.[4] Multiple studies have shown that the presence of neck metastasis is the most important prognostic factor in the management of oral cancers.[5,6] The presence of neck metastasis reduces the survival by up to 50%.[7,8] Therefore, neck dissection is considered a standard of care in the treatment of oral cancers. However, morbidity associated with neck dissection remains a challenge.[9,10] Currently, by consensus, supraomohyoid neck dissection (SND), as well for node negative oral SCC. However, the role of selective neck dissection in clinically palpable nodes is controversial, as many surgeons still recommend comprehensive neck dissection in patients with node-positive disease.[11,12]

In the past 2 decades, many clinicians have explored the role of selective neck dissection in node-positive SCC. In the beginning of the present century, Loree et al[13] showed that the overall regional control rates with selective neck dissection were 88 versus 71% for pathologically negative versus positive-node neck disease, respectively. Two recent review articles on the same subject have also concluded that SND can be an adequate substitute for comprehensive neck dissection (CND) without compromising oncological efficacy.[14,15] Interestingly, studies have also shown that < 50% of the clinically palpable nodes turn positive pathologically.[16] The reason for this lymphadenopathy can be superimposed infection at the cancer site or tuberculosis (TB) lymphadenitis, especially in the regions where TB is endemic.[17] Based on these observations, a recent article from the All India Institute of Medical Sciences has also proposed that comprehensive neck dissection in all clinically palpable oral cancers may not be warranted.[16]

Despite the changing trends toward performing selective neck dissection internationally, the practice is still different in our part of the world. Most of our local surgeons still recommend comprehensive neck dissection as the standard of care for node-positive SCC, with specific reference to studies by Ehsan ul Haq et al.[18] and Shaikh et al.[19] There is severe scarcity of local published literature available on the subject of selective neck dissection in node-positive oral cancers. Therefore, the role of selective neck dissection in node-positive neck needs to be explored in our set of patients.

Based on this background, we intend to evaluate the role of selective neck dissection in clinically positive oral SCC, and to compare it with node-negative oral cancers in terms of regional control and disease-free survival.

Material and Methods

First, approval of the study was obtained from the Ethics Review Committee of the hospital (approval form no 36). A review of the prospectively collected oral cancer database of the Department of Otolaryngology Head and Neck Surgery at a tertiary care hospital was performed. All patients who underwent selective neck dissection for SCC involving the oral cavity and lip between April 2006 and July 2015 were reviewed. The medical records of these patients were also reviewed to confirm findings of the database. Only patients with primary SCC of the lip or of the oral cavity were included. Non-SCC cancers, patients who underwent resection of nonlymphatic structures such as the sternocleidomastoid muscle (SCM), the spinal accessory nerve (XI Nerve), the internal jugular vein (IJV), or the skin, and patients who underwent comprehensive neck dissection (that is, radical or modified radical neck dissection) and/or preoperative chemoradiation were excluded from the study.

Selective neck dissection for SCC of the oral cavity or of the lip involves the systematic and comprehensive removal of lymph nodes and lymphatic-bearing tissue from neck levels I, II, III and/or IV.[20,21] Nonlymphatic structures such as the SCM, the XI nerve, and the IJV are preserved. The extent of SND in the present study corresponded to this definition.

All patients were divided into two groups, one with clinically node-negative and the other clinically node-positive, irrespective of the site and stage of the primary site. Both groups underwent selective neck dissection and postoperative radiotherapy, except for those in early T stage with pathologically N0 disease. All patients were regularly followed-up in the ear, nose, and throat (ENT) clinic. Data was prospectively collected by a dedicated research officer either face to face in the clinic, or by telephonic interviewing of the patients.

Categorical variables are analyzed as proportions and compared between groups with the chi-squared test. Continuous variables are analyzed as means with standard deviations (SDs). Both groups were analyzed separately in terms of disease-specific survival and regional recurrence/residual rates with Kaplan Meier curves.

Results

A total of 124 patients were retrieved from our database. On review of their medical records, 13 patients were excluded because of the exclusion criteria outlined above. A total of 111 patients were analyzed; 70 patients belonged to the clinically node-negative group and 40 patients belonged to the clinically node-positive group. Their mean age was 47 (SD: 11.97) years old. Eighty-five (76.6%) patients were male

Table 1 Demographics and other variables from node-negative and node-positive groups

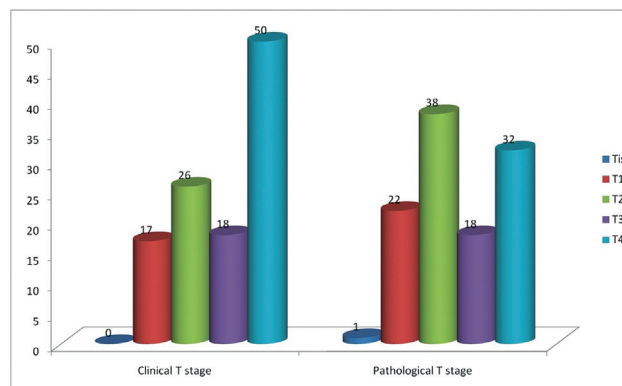| Variable	Node-negative	Node-positive
Total patients	71	40
Age (years old)*	49 (25–85)	43.70 (22–64)
Male	55 (77.5%)	30 (75%)
Female	16 (22.5%)	10 (25%)
Total number of nodes*	35	34.3
Follow-up (months) (SD)*	16.21 (14.48)	17.35 (21)
RTx Dose#	66 Gy	66 Gy

Abbreviations: RTx, Radiation therapy; SD, standard deviation.
*mean, # Mode.

and 26 (23.4%) were females. Our mean follow-up period was 16.62 months (SD: 17.03), ranging from 1 to 78 months. All patients underwent selective neck dissection along with resection of the primary tumor. The mean total number of lymph nodes dissected in our patients was 34.75 (SD: 15.12). All patients beyond stage I disease were advised to undergo postoperative radiotherapy. Eight patients from the node-negative group and two from the node-positive group did not receive radiation. Distributions of different variables in both groups are shown in ►Table 1.

The most common primary site was the buccal mucosa (56.7%), followed by the tongue (25.2%). The different sub-sites and their association with node-negative and node-positive groups is depicted in ►Table 2. In both groups, the buccal mucosa remains the most common site, followed by the tongue. Most of the patients in the present study had stage IV disease, mainly because of their T Stage. The distribution of T stage in our patients is shown in ►Fig. 1. Both in the node-negative and in the node-positive group, T4 remains the most common stage, followed by T2 and T3, respectively. Further details are shown in ►Table 3. Thus, the majority of our patients had locally advance disease.

All patients, irrespective of the primary site, were treated with resection of the primary tumor with grossly negative margins, selective neck dissection, and reconstruction of the defect with microvascular free flap, if required. A total of 101 out of 111 (91%) patients received adjuvant postoperative radiation.

The statistics related to the clinical and pathologic nodal staging of our patients is shown in ►Table 4. A graphical presentation of the statistics is shown in ►Fig. 2. One very important finding is the conversion rates of clinical versus

Fig. 1 Tumor (T) staging of the patients.

Table 3 Tumor stage distribution among node-positive and node-negative groups

Tumor stage	Node-negative	Node-positive
T1	13 (18.3%)	4 (10%)
T2	21 (29.6%)	5 (12.5%)
T3	9 (12.7%)	9 (22.5%)
T4	28 (39.4%)	22 (55%)
Total	71 (100%)	40 (100%)

Table 4 Nodal staging and conversion of nodal staging patients

N Stage	Clinical	Pathological
N0	72(64.9%)	65(58.6%)
N1	28 (25.2%)	15 (13.5%)
N2a	06 (5.4%)	02 (1.8%)
N2b	05 (4.5%)	27 (24.3%)
N2c	0	02 (1.8%)
N3	0	0

pathological staging. Twenty-one out of the 71 (29.5%) patients of the clinically node-negative group turned out to be positive for cervical metastasis on histopathology. Most of the clinically missed nodal metastasis staging was N2b. Fifteen out of 40 clinically node-positive patients were pathologically N0. This conversion is of high statistical significance, with p value < 0.001, as shown in ►Table 4.

All patients had no evidence of distant metastasis prior to treatment. The main outcome measures of our patients were

Table 2 Oral cavity subsite distribution among node-positive and node-negative groups

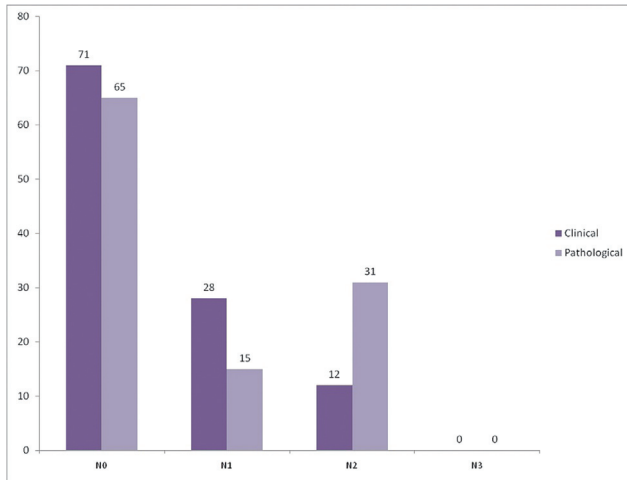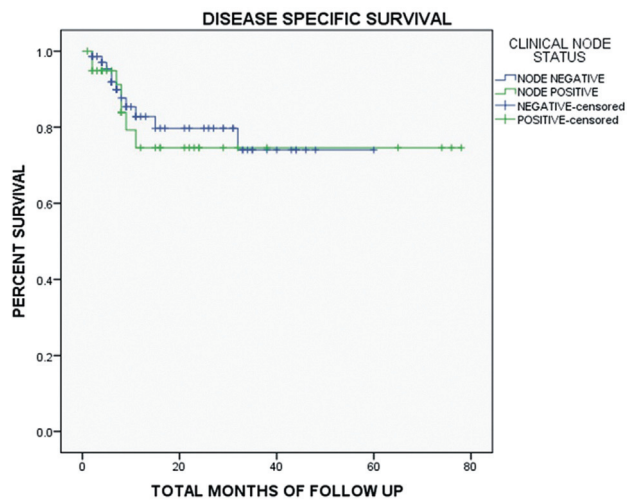| Node Status	Lip	Buccal mucosa	Oral tongue	Hard palate	Lower alveolus	Floor of mouth	Retromolar trigone	Total
Node-negative	3 (4.22%)	38 (53.5%)	21 (29.6%)	3 (4.22%)	2 (2.8%)	1 (1.4%)	3 (4.22%)	71 (100%)
Node-positive	1 (2.5%)	26 (65%)	6 (15%)	1 (2.5%)	4 (10%)	0 (0%)	2 (5%)	40 (100%)

Fig. 2 Nodal (N) staging of the patients.

Fig. 3 Comparison of disease specific survival in node positive and node negative group.
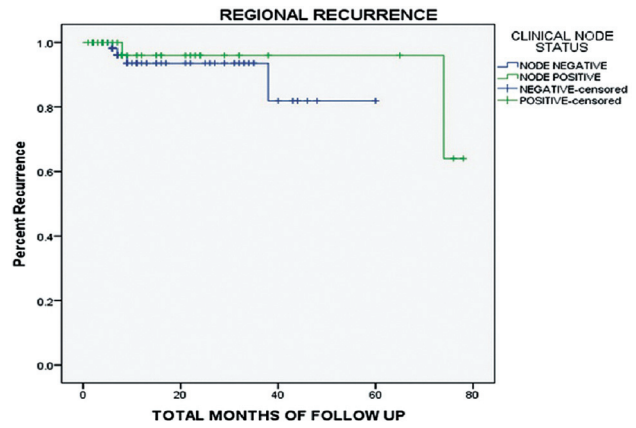

Fig. 4 Comparison of regional recurrence in node positive and node negative group.

of surgery), while 3 presented with recurrence (that is, after 6 months of surgery). Interestingly, 4 of them were from the node-negative group and all presented residual disease, except for one who presented with recurrence at 1 year postoperatively. The cases in the node-positive group presented with recurrences at 7 and 57 months (postoperatively), respectively. The second case also had second primary SCC. The statistical difference of both groups in this regard is also insignificant ($p = 0.47$ not significant [NS]). The comparison of outcomes in both groups along with distant metastasis is shown in ►Table 5. Further description as Kaplan Myer graphs are shown in ►Figs. 3 and 4.

Discussion

In summary, disease-specific survival and regional control rates were statistically similar both in the node-positive and in the node-negative groups. Another important finding of the present study is the significant conversion rates of clinical nodal staging versus pathological staging. This shows that clinical staging alone is not sufficient to decide the type of neck dissection. Therefore, instead of exposing the patients to radical surgeries, we should look into other aspects of cancer biology to optimize the quality of life (QOL) of our patients, without negatively impacting the oncological outcome.

Neck dissection still remains the most important part of oral cancer treatment. Since its introduction in the literature by Crile,[22] the extent of neck dissection has been the subject of significant debate and discussion. Over the past 3 decades, there has been a significant increase in the amount of literature supporting conservative or selective neck dissection. The concept of selective neck dissection first came from the studies done by Shah et al. when the mapping of lymphatic spread was shown from different subsites of the

disease-specific survival and regional control rates. Additionally,, distant survival rates were also calculated. Disease-specific survival in the node-negative group was 84.5 compared with 82.5% in the node-positive group ($p = 0.703$). Seven out of 40 patients in the node-positive group expired because of the disease, 2 of whom were pathologically N0, and rest were N2. The earliest dip in the graph is at 2 months, because of 2 patients, both belonging to N1 stage clinically. This is shown as a Kaplan-Myer depiction of survival in ►Fig. 3.

The regional control rate was of 94.4% in the node-negative group versus 95% in the node-positive group. In total, 6 patients developed neck disease; 3 of them presented with residual disease (that is, disease coming back within 6 months

Table 5 Outcome measures of the two groups

Clinical node status	Disease-specific survival (%)	Regional control (%)	Distant metastasis (%)
Node-negative	84.50	94.40	2.80
Node-positive	82.50	95	10

Table 6 Regional control rates after selective neck dissection in node-positive and node-negative groups

Authors	Node-negative (%)	Node-positive (%)	Follow-up (months)
Loree et al.[13]	88	71	24 (min)
Chepeha et al.[33]	84.6	92.3	24.5#
Iqbal et al.[27]	91.1	86.9	29>
Shimura et al.[11]	——	94	42 (min)
Our Results	94.4	95	16.62#

*Regional control in node-negative was not described in the present study, # mean follow-up, > median follow-up, (min) minimum follow-up.

Table 7 Disease-specific survival after SND in node-positive oral squamous cell carcinoma

Author	DSS (%)	Follow-up period
Shah et al.[32]	68.8>	40.8*
Shin et al.[28]	70	47 months*
Feng et al.[33]	52.8	68 months#
Shimura et al.[11]	61	42 (min)
Our Results	82.5	16.62*

Abbreviation: DSS, disease-specific survival.
>actuarial survival, * mean follow up, # median follow up, (min) minimum follow up.

head and neck. Shah et al. demonstrated in their remarkable study of 501 oral SCC patients that level IV metastasis only occurs in ∼ 15% of patients with oral SCC and in < 4% of patients on level V.[21] He also concluded that level V metastasis is almost always associated with metastasis at other levels. Other researchers have also supported the finding that that skip metastasis to level IV and V is rare.[16,23] In general, it is recommended to include all those levels in nodal dissection, in which the chances of occult metastasis are > 20%.[24,25] Therefore, elective neck dissection in clinically node-negative disease requires minimum clearance from level I to III.

Controversy prevails in the proper surgical management of the node-positive patient. As discussed above, many institutions, especially in our part of the world, are still performing comprehensive or modified versus radical neck dissection. This is despite the plethora of literature over the past few decades that have supported the less morbid selective neck dissection, which is still an oncologically sound operation. Mclean et al. published a systematic review on prophylactic level V dissection in node-positive mucosal head and neck SCC. They have shown that, irrespective of the site, the incidence of occult metastasis is not > 2.56%. On this basis, they have concluded that elective dissection of level V in absence of clinical involvement may be an extra morbidity for the patient.[26]

Recently, a study from the Shuakat Khanum memorial hospital has shown that SND can provide similar results in node-positive disease, if combined with postoperative radiotherapy.[27] These results from South Asia match with the ones published by many authors in the European and American literature over the last 2 to 3 decades.

It is also debated in the literature whether the regional control of the disease in oral cancers after SND is due to radiation

therapy or to chemoradiation therapy.[28] However, in a systematic review published in 2018 Rodrigo et al have concluded that adjuvant chemoradiation is elemental in achieving regional control after SND.[15] As the National Comprehensive Cancer Network (NCCN) recommends radiation therapy in every node-positive oral cancer,[29] this would also be an argument against performing a more radical neck dissection surgery. The main concern in performing a comprehensive neck dissection is the increased incidence of multiple complications and of sequelae, as described in the literature, for radical and modified radical neck dissection, such as damage to the spinal accessory nerve, to the phrenic nerve, to the brachial plexus, and to the thoracic duct. Comparatively, complication rates are much lower in selective neck dissection, as opposed to comprehensive neck dissection. Apart from complications, comprehensive neck dissections usually lead to neck and upper limb dysfunction despite sparing the spinal accessory nerve, mainly because of its excessive manipulation.[30]

The results of our study strongly support the notion that selective neck dissection can provide very good oncologic outcomes in most of the cases of oral SCC. Although our study is retrospective, all of our data bank was prospectively collected with a dedicated team continuously following patients from the initial evaluation to the most recent follow-up visit. We only evaluated lip and oral cancer patients undergoing selective neck dissection to minimize the bias, as different sites of the head and neck have different routes of spread. Another strong point of our study is that the results are from a single surgeon. The most significant limitations of the present study were that selective neck dissection was not compared with comprehensive neck dissection and that the mean follow-up was of < 2 years. Furthermore, around 5% of patients were lost to follow up and level of neck recurrence was not recorded in the data. The importance of the level of recurrence is obvious, as it can show the exact relation with the inclusion of different levels in neck dissection.

The results of our study are also consistent with the international literature. We have compared our outcomes – regional control and disease specific survival – in ►**Tables 6** and **7**[31–33]

Conclusion

Selective neck dissection in neck node-positive oral SCC has similar regional control rates when compared with node-negative neck SCC. The difference in disease-specific survival

between the two groups is also not significant. Furthermore, the study also reveals a high conversion rate of clinical node-negative to pathological node-positive. Therefore, we suggest that selective neck dissection can provide results comparable to those of node-negative patients in oral SCC. Therefore, we suggest that SND should be performed in all early node-positive patients, followed by postoperative radiation.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Cancer Registry and Clinical Data Management (CRCDM)—Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC)—Report Based on Cancer Cases Registered at SKMCH & RC from December 1994–December 2019 and in 2019 [Internet]. 2020

2 García-Martín JM, Varela-Centelles P, González M, Seoane-Romero JM, Seoane J, García-Pola MJ. Epidemiology of oral cancer. Oral Cancer Detection Springer; 2019:81–93

3 Ayaz B, Saleem K, Azim W, Shaikh A. A clinico-pathological study of oral cancers. Biomedica 2011;27(01):29–32

4 Noguti J, De Moura CFG, De Jesus GPP, et al. Metastasis from oral cancer: an overview. Cancer Genomics Proteomics 2012;9(05):329–335

5 Shaha AR. Neck dissection: an operation in evolution. World J Surg Oncol 2005;3(01):22

6 Pantvaidya G, Rao K, D'Cruz A. Management of the neck in oral cancers. Oral Oncol 2020;100:104476

7 De Cicco C, Trifirò G, Calabrese L, et al. Lymphatic mapping to tailor selective lymphadenectomy in cN0 tongue carcinoma: beyond the sentinel node concept. Eur J Nucl Med Mol Imaging 2006;33(08):900–905

8 Henriques V, Breda E, Monteiro E. Discrepancy between clinical and pathological neck staging in oral cavity carcinomas. Acta Otorrinolaringol Esp (Engl Ed) 2018;69(02):67–73

9 Kuntz AL, Weymuller EA Jr. Impact of neck dissection on quality of life. Laryngoscope 1999;109(08):1334–1338

10 Gane EM, McPhail SM, Hatton AL, Panizza BJ, O'Leary SP. The relationship between physical impairments, quality of life and disability of the neck and upper limb in patients following neck dissection. J Cancer Surviv 2018;12(05):619–631

11 Shimura S, Ogi K, Miyazaki A, et al. Selective neck dissection and survival in pathologically node-positive oral squamous cell carcinoma. Cancers (Basel) 2019;11(02):269

12 Kakei Y, Komatsu H, Minamikawa T, et al. Extent of neck dissection for patients with clinical N1 oral cancer. Int J Clin Oncol 2020;25(06):1067–1071

13 Kolli VR, Datta RV, Orner JB, Hicks WL Jr, Loree TR. The role of supraomohyoid neck dissection in patients with positive nodes. Arch Otolaryngol Head Neck Surg 2000;126(03):413–416

14 Liang L, Zhang T, Kong Q, Liang J, Liao G. A meta-analysis on selective versus comprehensive neck dissection in oral squamous cell carcinoma patients with clinically node-positive neck. Oral Oncol 2015;51(12):1076–1081

15 Rodrigo JP, Grilli G, Shah JP, et al. Selective neck dissection in surgically treated head and neck squamous cell carcinoma patients with a clinically positive neck: Systematic review. Eur J Surg Oncol 2018;44(04):395–403

16 Deo SV, Shukla NK, Jha D, Khanna P, Pandit A, Thulkar S. Are we over-treating neck in buccal & alveolo-buccal cancers: experience from a tertiary cancer care center. Indian J Surg Oncol 2012;3(04):272–275

17 Iqbal M, Subhan A, Aslam A. Papillary thyroid carcinoma with tuberculous cervical lymphadenopathy mimicking metastasis. J Coll Physicians Surg Pak 2011;21(04):207–209

18 Ehsan-ul-Haq M, Warraich RA, Abid H, Sajid MAH. Cervical lymph node metastases in squamous cell carcinoma of tongue and floor of mouth. J Coll Physicians Surg Pak 2011;21(01):55–56

19 SHAIKH AA. Shafique S, Shafi M, Punjabi SK. COMPLICATIONS OF MODIFIED RADICAL NECK DISSECTION TYPE III IN ORAL SQUAMOUS CELL CARCINOMA. Pak Oral Dent J 2014;34(02):

20 Manikantan K, Bang B, Sharan R, Mallick I, Chatterjee S, Arun P. Therapeutic Neck Dissection in Oral Squamous Cell Carcinoma: Is Selective Neck Dissection the Way Ahead? Kathmandu Univ Med J (KUMJ) 2016;14(55):221–225

21 Shah JP, Candela FC, Poddar AK. The patterns of cervical lymph node metastases from squamous carcinoma of the oral cavity. Cancer 1990;66(01):109–113

22 Crile GW. On the surgical treatment of cancer of the head and neck. Transactions Southern Surg Gynecol Assoc 1905;18:109–127

23 Rahim DU, Siddiqui AH, Ahmed Z, Marfani MS. Frequency of Cervical Metastasis in Oral Cancer. Pak J Otolaryngol 2013;29:80–83

24 Medina JE, Byers RM. Supraomohyoid neck dissection: rationale, indications, and surgical technique. Head Neck 1989;11(02):111–122

25 Spiro JD, Spiro RH, Shah JP, Sessions RB, Strong EW. Critical assessment of supraomohyoid neck dissection. Am J Surg 1988;156(04):286–289

26 McLean T, Kerr SJ, Giddings CEB. Prophylactic dissection of level V in primary mucosal SCC in the clinically N positive neck: A systematic review. Laryngoscope 2017;127(09):2074–2080

27 Iqbal H, Bhatti ABH, Hussain R, Jamshed A. Regional failures after selective neck dissection in previously untreated squamous cell carcinoma of oral cavity. Int J Surg Oncol 2014;2014:205715

28 Shin YS, Koh YW, Kim S-H, Choi EC. Selective neck dissection for clinically node-positive oral cavity squamous cell carcinoma. Yonsei Med J 2013;54(01):139–144

29 Pfister DG, Ang K-K, Brizel DM, et al; National Comprehensive Cancer Network. Head and neck cancers, version 2.2013. Featured updates to the NCCN guidelines. J Natl Compr Canc Netw 2013;11(08):917–923

30 Gane EM, O'Leary SP, Hatton AL, Panizza BJ, McPhail SM. Neck and upper limb dysfunction in patients following neck dissection: looking beyond the shoulder. Otolaryngol Head Neck Surg 2017;157(04):631–640

31 Andersen PE, Warren F, Spiro J, et al. Results of selective neck dissection in management of the node-positive neck. Arch Otolaryngol Head Neck Surg 2002;128(10):1180–1184

32 Feng Z, Li JN, Niu LX, Guo CB. Supraomohyoid neck dissection in the management of oral squamous cell carcinoma: special consideration for skip metastases at level IV or V. J Oral Maxillofac Surg 2014;72(06):1203–1211

33 Chepeha DB, Hoff PT, Taylor RJ, Bradford CR, Teknos TN, Esclamado RM. Selective neck dissection for the treatment of neck metastasis from squamous cell carcinoma of the head and neck. Laryngoscope 2002;112(03):434–438