

Role of Elective Neck Dissection in Clinically Negative Neck Nodes in Head and Neck Malignancies

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Abstract

Background : In this study, we wanted to evaluate accuracy of clinical intra operative lymph node assessment in patients with head and neck cancer, define the degree of correlation between clinical preoperative assessment and histopathological examination in patients with head and neck cancer, determine as to whether the use of a selective neck dissection used electively on all patients presenting with head and neck cancer and clinically N0 necks improve survival, disease-free survival and loco-regional disease control rates.

Materials and Methods: This was a hospital-based study conducted among 50 patients who presented with head and neck malignancy to a tertiary care hospital, between August 2012 and August 2014 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Results: 42 (60 %) of 70 sides of neck in 30 patients were negative for lymph node metastases. 28 (40 %) of 70 sides of neck in 20 patients were positive (or suspect) for lymph node metastases. Histopathological examination was done for the 70 selective neck dissection specimens obtained in our study. Lymph nodes were positive for malignant metastases in 30 (43 %) of 70 sides of neck in 18 patients. Lymph nodes were negative for malignant metastasis in 40 (57 %) of 70 sides of neck in 32 patients. Stage III and IV patients had a higher incidence of lymph node metastases compared with stage I and II patients. 38 patients (60 %) received post-operative radiotherapy, 18 patients received post-operative radiation because post-operative histopathological examination was positive for metastasis.

Conclusion: The neck must be properly managed at the same time with the primary tumour. The decision to use elective neck dissection or elective neck irradiation is guided by the

treatment of the primary tumour. Intra operative lymph node assessment alone is not an effective method in clinical staging of the neck. Thus, we cannot depend on it in determining the type of neck dissection performed. Selective neck dissection is an effective method in management of N0 neck.

Keywords: Elective Neck Dissection, Clinically Negative Neck Nodes, Head and Neck Malignancies

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Introduction

Squamous cell carcinoma represents more than 90 % of all head and neck cancers. A malignant tumour of epithelial origin, squamous cell carcinoma has regional distribution involved in the biological activity of the neoplasm. Behaviour of squamous cell cancer depends on its site of origin. Each anatomic site has its own particular spread pattern and prognosis. The status of the cervical lymph node is one of the most important factors in influencing therapeutic management and outcome for patients with squamous cell carcinoma of the upper aero digestive tract. For patients with head and neck squamous cell carcinoma, the presence of cervical lymph node metastases at the time of initial presentation and treatment reduces the 5-year survival rate by approximately 50 %. Moreover, the presence of contra-lateral or bilateral cervical metastases reduces prognosis by an additional 50 %. [1] Squamous cell carcinoma of the upper aero digestive tract is characterized by high frequency of lymphatic metastatic spread and patients with cervical metastases seem to be more likely to develop both distant metastases and regional recurrence at the primary site. The negative neck has several meanings. The neck may be negative to physical examination (palpation), to radiological evaluation, to pathological interpretation, negative contra-lateral to positive (N+) neck or negative after treatment (surgery, radiation or chemotherapy). Pre-operative clinical and radiological assessment determines the selection of the subsequent

operative procedure. Clinical palpation has an accuracy of approximately 70 %, computerised tomography (CT) and magnetic resonance (MR) imaging provide additional information regarding those that are inaccessible to palpation and may also show nodal necrosis, which is equated with tumour involvement in the appropriate clinical setting. Metabolic imaging with F-fluorodeoxy glucose positron emission tomography offers alternative but is not widely available into nodal physiology. Sonography-based methods [Colour Doppler ultrasonography and ultrasonography (USG) guided fine needle aspiration] have been used to assess intra-nodal amigo architecture and provide direct tissue assessment for the presence of metastases. During selective neck dissection, lymph nodes can be assessed intra-operatively by direct palpation and inspection and suspicious nodes may be sent for intra-operative histological assessment by frozen section and if found positive, the operation can be converted to more conventional modified radical or radical neck dissection. This is based on the premise that selective neck dissection may not be adequate treatment for macroscopic metastatic neck disease. Management of the clinically negative (cN0) neck includes watchful waiting and treating the neck when clinical metastases develop, prophylactic irradiation, and elective neck dissection. Because a considerable number of cN0 neck has occult lymph node metastases, expectant treatment of the neck may result in

development of neck recurrence, which is not always easily curable.

Aims and Objectives

- To define the degree of correlation between clinical preoperative assessment and histopathological examination in patients with head and neck cancer.
- To determine whether the use of a selective neck dissection used electively on all patients presenting with head and neck cancer and clinically N0 necks improves survival, disease-free survival and loco-regional disease control rates.

Materials and Methods

This was a hospital-based study conducted among 50 patients who presented with head and neck malignancy to the Department of Government, tertiary care hospital, from August 2012 to August 2014 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Inclusion Criteria

- All patients having head and neck cancer.
- The patient's neck must be staged as clinically N0 (cN0) according to physical (palpation) and radiological (CT scan) examination.

Exclusion Criteria

- Patients having malignancies other than head and neck.

- Patients having clinically palpable and radiologically positive nodes.
- Patients having distant metastasis.

Statistical Methods

Data was entered in MS Excel and analyzed using Statistical Package for Social Sciences (SPSS) software. Results were presented as tables.

Results

All patients included in our study were head and neck cancer patients. The site of primary tumour was different for each group of patients, but the necks of all patients included were staged as clinically N0. The patients were 35 patients with oral cavity carcinoma and 15 patients with laryngeal carcinoma. In the cases included in our study, the primary tumour had different T stage for each case.

Histopathological examination was done for the 70 selective neck dissection specimens obtained in our study. The results of histopathological examination revealed the following:

Lymph nodes were positive for malignant metastases in 30 (43 %) of 70 sides of neck in 18 patients. The positive sides of neck were distributed as follows: 24 sides of neck in cases of oral cavity carcinoma. 6 sides of neck in cases of laryngeal carcinoma. Lymph nodes were negative for malignant metastasis in 40 (57 %) of 70 sides of neck in 32 patients.

Table 1: Demographic Distribution

	Gender	N	%	
Sex Distribution	Female	16	32 %	
	Male	34	68 %	
	Total	50	100 %	
	Age Group (Years)	Female	Male	Total
Age Distribution	< 40	4	5	9
	41 - 50	3	7	10
	51 - 60	5	9	14
	> 60	4	13	17
	Total	16	34	50
p-value - 0.72				

Table 2

T Stage	N			%
T2	12			24 %
T3	23			46 %
T4	15			30 %
Total	50			100 %
T Stage	Site		Total	
	Oral Cavity	Larynx		
T2	12	0	12	
T3	19	4	23	
T4	4	11	15	
Total	35	15	50	
p-value < 0.05				
Intra-op Findings	Site		Total	
	Oral Cavity	Larynx		
Malignant/ Suspect	22	6	28	
Negative	23	19	42	
Total	45	25	70	
p-value - 0.047				
Intra-operative Findings of Lymph Nodes According to Site				
Post-op Findings	Site		Total	
	Oral cavity	Larynx		
Malignant/ Suspect	24	6	30	
Negative	21	19	40	
Total	45	25	70	
p-value - 0.024				
Post-operative Histopathological Examination of Neck Dissection Specimens				

Table 3

	Type of Neck Dissection	N	%
Number and Type of Neck Dissection	I-III	33	47 %
	II-IV	25	36 %
	I-V	12	17 %
	Total	70	100 %
Intra-operative Findings of Lymph Node Examination	Intra-op Findings	N	%
	Malignant/ Suspect	16	32%
	Negative	34	68%
	Total	50	100%
	Intra-op Findings	N	%
	Malignant/ Suspect	28	40%
	Negative	42	60%
Total	70	100%	

Fifty patients with head and neck carcinoma were staged pre-operatively as clinically N0 neck. All patients were subjected to selective neck dissection (SND). 20 patients underwent bilateral neck dissection. So, 70 selective neck

dissections were performed. The type of SND performed was determined according to the site of primary lesion: 45 neck dissections were performed in 35 cases of oral cavity carcinoma as supra-omohyoid neck dissection (level I-III) was done in 33

cases, functional neck dissection (level I-V) was done in 12 cases with 10 cases undergoing bilateral neck dissections. 25 lateral neck dissections were performed in 15 cases of laryngeal carcinoma as bilateral neck dissection was done in 10 cases. While performing selective neck dissection in the 70 necks (50 patients) included in our study, intra-operative assessment of lymph nodes was done according to predetermined criteria by which we were able to justify whether the

examined node is negative for malignant metastases, positive or suspected for metastases.

Following the previous criteria shown in our study, following results were revealed: 42 (60 %) of 70 sides of neck in 30 patients were negative for lymph node metastases.

28 (40 %) of 70 sides of neck in 20 patients were positive (or suspect) for lymph node metastases.

Table 4

Overall	%
Sensitivity	90.0 %
Specificity	97.5 %
PPV	96.4 %
NPV	92.9 %
Accuracy	94.3 %
Oral cavity	%
Sensitivity	87.5 %
Specificity	95.2 %
PPV	95.5 %
NPV	87.0 %
Accuracy	91.1 %
Larynx	%
Sensitivity	100.0 %
Specificity	100.0 %
PPV	100.0 %
NPV	100.0 %
Accuracy	100.0 %

Table 5

T-Stage	Post-op Findings		Total
	Negative	Malignant/ Suspect	
T2	9	3	12
T3	15	8	23
T4	8	7	15
Total	32	18	50

Incidence of Nodal Metastasis versus T Stage

The incidence of metastatic cervical lymph nodes according to the tumour stage: Stage III and IV patients had a higher incidence of lymph node metastases compared to stage I and II patients. Post-operative histopathological examination of selective

neck dissection specimens revealed cervical lymph node metastasis in 18 patients. Of these 18 patients, 3 patients were stage T2, 8 patients were of stage T3, and 7 patients were of stage T4.

Table 6

Radiotherapy	No	Percentage
Yes	38	76 %
No	12	24 %
Total	50	100 %
Indication for Postoperative Radiation		
	No	Percentage
Positive for Metastasis	18	47 %
Advanced Primary Lesion[T3 or T4]	20	52 %
Total	38	100 %

38 patients (60 %) received post-operative radiotherapy, 18 patients received post-operative radiation because post-operative histopathological examination was positive for metastasis in these patients and the other 20 patients received post-operative radiation because their primary lesions were advanced (T3 or T4).

Discussion

The status of regional lymph nodes is the most important prognostic indicator in patients with head and neck squamous cell carcinoma (HNSCC). With the exception of distant metastasis, the presence of cervical lymph node metastasis is the single most adverse independent prognostic factor in HNSCC. For patients with HNSCC, the presence of cervical lymph node metastasis at the time of initial presentation and treatment reduces the 5-year survival rate by approximately 50%, irrespective of the primary site. Moreover, the presence of contra-lateral or bilateral cervical metastasis reduces prognosis by an additional 50 % (Rinaldo et al., 2004). [2]

In cases of cytologically proven nodal metastases, there is no debate about the necessity of treating the neck. Questions arise on regional treatment when no metastasis can be detected, knowing that the accuracy of diagnostic techniques to assess the neck is still limited. This keeps the basic discussion on elective treatment of the neck ongoing (Robert, 2004). [3]

Recently, new techniques have been explored like radioimmunosciintigraphy (RIS), positron emission tomography (PET) and sentinel node procedures.

Twenty-five percent of tumour positive elective neck dissections of clinically N0 necks contain micro metastases smaller than 3 mm. Many of these metastatic nodes contain tumour cells not even seen on histological slides prepared with conventional haematoxylin and eosin staining, although they may be detected by immunohistochemistry and molecular analysis. Immunohistochemically investigations have found additional micro metastases in 15 % of patients who had no evidence of metastatic disease on routine pathological assessment. [4] Sentinel lymph node biopsy (SLNB) is an attempt to identify the presence of metastatic disease in the lymphatic drainage area of the primary tumour. A high accuracy rate has been reported when identification of the sentinel node was performed with pre-operative lymphoscintigraphy with isosulfan blue and radio colloid injection followed by intra-operative use of a gamma probe (Hart et al. 2005).

Most reports on results of SLNB have been described in patients with oral cavity or oropharyngeal squamous cell carcinoma. In a series of 61 clinically N0 patients undergoing surgical resection of T1-T2 oral cavity or oropharyngeal squamous cell carcinoma, SLNB upstaged the clinically N0 neck in 44 % of patients, when combined with serial pathological

sectioning and immunohistochemistry (Ross et al. 2004). [5]

There is still controversy about the issue of appropriate management for the clinically N0 neck, as well as a debate over the issue whether selective neck dissection is merely a staging procedure, or a fully-fledged therapeutic operation (MacLennan et al. 2003).

Patients undergoing elective treatment of the N0 neck appear to have a survival advantage over patients who are simply observed. A review of 156 patients with T1 and T2 carcinoma of the tongue staged N0 demonstrated that when elective neck dissection was carried out together with glossectomy, the survival rate was 55 % compared with 33 % when the neck was observed

Proponents of the elective treatment of the neck accept the morbidity of such treatment and argue that delay of detection of metastatic cervical disease until it is clinically evident is associated with significant decrease in survival rates.

Successful surgical salvage in such cases ranges only from 30 % to 50 % (Kowalski et al. 2000). [6] The regional control rate has also been shown to correlate with the amount of radiation delivered to the neck. Nodal levels with a high risk of harbouring occult metastasis vary according to the site of primary tumour. The lymph nodes in these regions should be electively removed whenever appropriate as the morbidity is much less than that associated with radical neck dissection and the efficacy is comparable. For patients with oral cavity cancer, selective neck dissection of levels I - III should be carried out. It has been reported that level IV lymph nodes are involved in 16 % of patients with carcinoma of the tongue, and it is recommended that level IV lymph nodes should be included in selective neck dissection as the additional morbidity is minimal (William et al. 2006). [7]

The issue of the use of elective surgery versus elective radiation ends not at which treatment modality is more beneficial, but which one is less harmful. The patient's age, general health, family support, reliability and patient's own wishes are important.

Out of the 50 patients included in our study, 38 patients (76 %) received post-operative radiotherapy, 18 patients received post-operative radiation therapy as they showed occult metastases in histopathological examination of post-operative lymph node specimens and 20 patients received post-operative radiation because of their advanced primary tumour (T3 or T4).

The sex distribution in our study was in favour of males who constituted 74 % of the cases (37 cases) as compared to females who constituted 26 % of the cases (13 cases). The age of the patients included in our study ranged from 33 to 76 years with a mean age of 54.5 and standard deviation was 9.96.

The probability of lymphatic spread, whether subclinical or obvious is dictated by a number of factors. Shah (1990) [8] reported that larger tumour has a greater likelihood of cervical spread, and pharyngeal lesions metastasize more frequently than those in the larynx or oral cavity. He also stated that ipsilateral metastatic disease occurs in approximately 50 % of patients with carcinoma of the oral cavity, oropharynx, hypopharynx or supraglottis. Bilateral and/or contra-lateral metastatic disease occurs in 20 - 35% of these patients.

Meyers (1997) [9] also reported that tumours localized in the oral cavity, oral mucosa, oropharynx, hypopharynx and supraglottis have a higher frequency of metastasis compared to areas such as superior gingiva, hard palate and glottis.

Hosal et al. (2000) [10] performed a study on 210 patients with head and neck squamous cell carcinoma. All the patients

included in the study were pre-operatively staged as N0 neck. Three hundred SNDs were performed, and the type was determined according to the site of primary tumour. They were oral cavity in 91 (43 %), oropharynx in 30 (14 %), hypopharynx in 16 (8 %), and larynx in 73 (35 %) patients.

Our study was performed on 50 patients with head and neck squamous cell carcinoma. All the patients were staged as clinically N0 neck according to clinical examination (palpation) and CT scan. The site of primary tumour was oral cavity in 35 (70 %) and larynx in 15 (30 %) patients.

All patients were subjected to selective neck dissection (SND). We have performed 70 neck dissections in 50 patients as bilateral neck dissection was done in 20 patients in whom bilateral occult metastasis was suspected depending on the primary tumour site and size.

Selective neck dissection allows removal of subclinical and sub pathological metastases and thus allows accurate staging and treatment of occult disease and assists in patient counselling and prognostication. The information obtained from SND permits judicious use of adjuvant therapy such as radiation therapy. The combined goal of minimizing morbidity and avoiding over-treatment may be achieved by SND, which can optimize cure rates as well as functional and cosmetic results (Ferlito et al. 2006).

In our study, while performing SND in the 70 sides of neck (50 patients) included in our study, we have performed intra-operative assessment of lymph nodes by using inspection and palpation. This assessment was done according to predetermined criteria by which we were able to justify whether the examined node is negative for malignant metastases or positive (or suspected) for metastases.

By following the predetermined criteria, our study revealed that 42 of 70 sides of

neck (60 %) in 32 patients were negative for lymph node metastases and 28 of 70 sides of neck (40 %) in 18 patients were positive (or suspected) for lymph node metastases. The results of post-operative histopathological examination revealed that lymph nodes were positive for malignant metastases in 30 neck dissections of 70 (42.8 %) in 18 patients and negative for metastasis in the remaining 40 neck dissections (57.1 %) in 32 patients.

Our study also agrees with a study carried out by Finn et al. (2002) [11] who performed a prospective study determining the accuracy of clinical intra-operative lymph node assessment in the node negative neck. Forty-six neck dissections from 34 patients with head and neck cancer were prospectively examined intra-operatively by a single surgeon; all obvious nodes were clinically assessed, morphologically described, and subsequently correlated with pathological findings. Sixty palpable nodes were identified intra-operatively in 32 neck dissections, 22 were classified by the surgeon as clinically malignant or suspect, and 38 as clinically benign. Thirteen of the group of 22 lymph nodes the surgeon identified as positive or suspicious for malignancy were histologically shown to be benign (59 %) and nine malignant (41 %). Thirty-one of the group of 38 lymph nodes the surgeon identified as negative or benign were histologically benign (82 %) and seven malignant (18 %). In the 14 neck dissections with no obviously palpable lymph nodes, four (29 %) were positive for metastases.

Our study revealed the relation between the tumour size and the incidence of occult metastasis to regional lymph nodes, we detected that the more advanced the tumour, the more the incidence of occult lymph node metastasis. Post-operative histopathological examination of selective neck dissection specimens revealed positive lymph node metastasis in 18

patients. Of these 18 patients, 3 patients were staged as T2 tumour, 8 patients were T3, 7 patients were T4. Thus, the more advanced the tumour, the more the incidence of occult metastases. T3 and T4 patients showed a higher incidence of occult metastases. Value of chi-square test (χ^2) was 14.76 and p-value was 0.002 (< 0.05), this means that these results were statistically significant.

Recently, Ferlito et al. (2006) [12] concluded that SND continues to be an evolving surgical procedure. A better understanding of the pattern of nodal metastasis, the biology of the primary tumour, and prognostic indicators of metastatic disease in the neck should clarify some of the issues related to extent of neck dissection required. [13]

The author also concluded that prospective randomized trials comparing SND to comprehensive neck dissection and in particular the role of post-operative radiation therapy and indications for its use following SND will be required to resolve some of these controversial issues.

Conclusion

The management of N0 neck remains controversial. The incidence of occult lymph node metastases in cases of head and neck cancer is high (42.8 % in our study). So, the neck must be properly managed at the same time with the primary tumour. The decision to use elective neck dissection or elective neck irradiation is guided by the treatment of the primary tumour. Intra-operative lymph node assessment alone is not an effective method in clinical staging of the neck. So, we cannot depend on it in determining the type of neck dissection performed. Selective neck dissection is an effective method in management of N0 neck.

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