

# Clinical Examination and Ultrasonography as Predictors of Lateral Neck Lymph Nodes Metastasis in Primary Well Differentiated Thyroid Cancer

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## Abstract

**Background:** Lateral neck dissection is risky and should be performed only as a therapeutic intervention for known disease. **Aim of the Study:** This study aims at finding predictors which help in selecting patients who have high risk of lymph node metastasis. **Methods:** All the patients with well differentiated thyroid cancer underwent thyroidectomy with lateral lymph nodes (LNs) dissection with available pathology report and sufficient data have been included in the study. **Results:** Sixty nine patients have been included in this study. In multivariate analysis, the most reliable and significant factors for detecting L.N. involvement were the clinical picture and the U/S appearance of the Neck with P value of (0.008) and (0.001) respectively. **Conclusion:** Clinical and U/S examinations are the most independent and reliable factors to detect lateral neck lymph nodes involvement.

## Keywords

Thyroid, Cervical Lymphadenectomy, Thyroid Carcinoma, Neck Ultrasonography

## 1. Introduction

According to American Thyroid Association (ATA), for optimal management of patients with thyroid cancer to be achieved, removal of cervical lymph nodes involved with metastases at the time of primary surgery is required. Lateral neck dissection should be performed only as a therapeutic intervention for known

disease [1]. A prophylactic lateral neck dissection alone for thyroid cancer has not been proven effective to improve survival [2]. Lateral neck dissection is risky and could be associated with significant morbidity. A lateral neck dissection usually involves levels II, III, and IV lymph nodes which may endanger the spinal accessory, phrenic, vagus, cervical sensory, sympathetic trunk, hypoglossal, greater auricular, and the marginal mandibular branch of the facial nerves. In addition to nerve injury, chyle leak is another complication of performing a lateral neck dissection [3] [4] [5].

For lateral neck to be evaluated for metastatic disease, Physical examination, imaging studies such as ultrasonography (US) with or without FNAB which allows for mapping of central and bilateral neck compartments, iodine scans, CT, hybrid imaging modalities such as single photon emission computed tomography/CT and positron emission tomography/CT, technetium 99 m scintigraphy and magnetic resonance imaging can each be important in this regard. US performed by experienced hands is considered by most clinicians, and by the ATA, as the screening and surveillance imaging tool of choice for detection of lateral neck metastases [1].

Timing of lateral neck dissection for well-DTC is less critical than the central neck dissection for thyroid cancer or lateral neck dissection for squamous cell carcinoma of head and neck. Omitting of routine prophylactic central neck dissection may result in a revision surgery being necessary which could be challenging due to manipulating the same operative field of thyroidectomy with its resultant scar tissue [6].

As recommended by the ATA thyroid cancer guidelines, negative neck US findings in DTC imply that the lateral neck be managed expectantly [1]. In cases when a lateral neck node is enlarged (>1.5 cm in levels I and IIa or >1.0 cm in levels IIb-Vb) or has sonographic features suggesting disease, an US-guided fine-needle aspiration should be attempted to confirm disease. Testing the aspirate for thyroglobulin in a pauci-cellular specimen may be considered [3] [7] [8]. Those nodes that have suspicious US characteristics and are not accessible to FNAB may be observed for progress with serial US at intervals recommended by the ATA before intervention.

Nodes less than 5 - 8 mm, especially without worrisome features, might be observed rather than attempting an FNAB. The expected risks of lateral neck dissection should always be weighed against the possible benefits [1].

Lateral neck dissection performed for macroscopic DTC metastases should be the selective neck dissection of levels IIa, III, IV, and Vb. "Berry picking" is not recommended. As metastatic thyroid disease to levels I is infrequent; dissection of level I is usually not indicated as it put the marginal mandibular branch of the facial nerve at risk, which might result in lower lip weakness [9]. Unless there are suspicious lymph nodes at level IIb or in the high jugular region (IIa); dissection above the accessory nerve (IIb) is generally not necessary. This could help to minimize postoperative morbidity associated with "shoulder syndrome", a condition of shoulder girdle weakness, stiffness and chronic pain that can arise when

CN XI function is impaired [10]. In cases in which metastases were found at level V, they occurred almost exclusively at sublevel Vb. Sublevel Va was rarely, if ever, involved with metastatic lymph nodes therefore routine elective dissection of level Va may also be unnecessary. This further reduces the risk of injury to the accessory nerve [11].

This study aims at finding predictors which will help in selecting patients who have high risk of lymph node metastasis and need lateral neck dissection and to avoid unnecessary neck dissection.

## 2. Patients and Methods

This is a retrospective study in which all patients who had undergone thyroidectomy with lateral neck lymph nodes dissection for well differentiated thyroid cancer at South Egypt Cancer institute in the period from 2008 to 2012 have been reviewed. According to the definitions of the American Head and Neck Society and the American Academy of Otolaryngology—Head and Neck Surgery, lateral neck compartment extends from the carotid arteries to the medial border of the trapezius muscle and involves levels II, III, IV and V [12] [13] [14].

In this study, data about the primary tumor size, age, sex, thyroid capsular invasion; multi-focality of primary disease and histological type have been collected. The clinical evidences (palpable  $\pm$  hard LNs) as well as US evidences of lymph node involvement, have been evaluated as potential predictors of lateral lymph node metastasis. The US evidences of LN involvement was based mainly on loss of hilar echogenicity (fat center), poorly defined irregular borders, size  $>$  5 mm in its shortest diameter and round shape [15] [16]. In this study, a node was considered suspicious if one or more of these criteria was met. Lateral LN dissection has been also done based on intraoperative evidences of metastasis even with negative clinical and ultra-sonographic data (probability of false negative clinical and US examination).

Included in this study were all patients with well differentiated thyroid cancer underwent thyroidectomy with lateral lymph nodes dissection that have available pathology reports and sufficient data. Excluded from this study were all patients with thyroid cancer other than well differentiated ones or patients with well differentiated thyroid cancer underwent thyroidectomy without lateral lymph nodes dissection or with no available pathology reports and no sufficient data.

Data have been collected from patient files and computerized data base at south Egypt cancer institute, Assiut University. Statistical analysis has been performed using STATA intercooled version 9.2. Quantitative data has been analyzed using Student t test or Mann-Whitney test when appropriate. Qualitative data has been compared using Chi square test. Univariate and multivariate logistic regression analysis has been done to detect factors that predict LNs involvement. P value has been considered significant if it was less than 0.05. The study was accepted by the ethical committee at south Egypt cancer institute.

### 3. Results

Sixty nine patients who had undergone thyroidectomy with lateral neck lymph nodes dissection for well differentiated thyroid cancer at South Egypt Cancer institute in the period from 2008 to 2012 have been included in this study (**Table 1**).

In univariate analysis, lateral neck metastasis was more frequent in patients with papillary thyroid cancer, capsular invasion, positive clinical examination and positive U/S examination. No relationship could be detected for gender, age, tumor size or multi-focality.

All factors that were associated with lateral neck LN metastases were included in the multivariate regression analysis. In the multivariate analysis, the most reliable and significant factors for detecting L.N. involvement were the clinical picture and the U/S appearance of the Neck with P value of (0.008) and (0.001) respectively (**Table 2**).

Clinical examination could significantly detect involved LNs ( $P \leq 0.008$ ) with sensitivity and specificity rate of 86.4% and 80.4% respectively.

Ultra-sonic examination could significantly detect involved LNs ( $P \leq 0.001$ ) with sensitivity and specificity rate of 86.4% and 85.1% respectively.

Combined clinical and ultra-sonic examination could improve sensitivity to 95% but decrease specificity to 74%.

Negative predictive value in combination of clinical examination and ultrasonography was 98% that is only 2% with truly positive lymph nodes will miss

**Table 1.** Clinico-pathological and US characteristics.

Variable	Value (%)
Total patient number	69
Male/Female	16/53
Median age [range]	41 [19 - 78]
Pathology	
Papillary	44 (63.7%)
Follicular variant papillary	15 (21.7%)
Follicular	10 (14.6%)
Tumor size (cm)	2 (0.1 - 11)
Capsular invasion	29 (45.3%)
No capsular invasion	40 (54.7%)
Tumor multifocality	19 (27.5%)
Tumor non multifocality	50 (72.5%)
Clinically detected LNs	28 (40.6%)
Clinically non detected LNs	41 (59.4%)
U/S significant LNs	26 (37.7%)
U/S non-significant LNs	43 (63.3%)
Pathologically positive LNs	22 (32%)
Pathologically negative LNs	47 (68%)

LN: Lymph nodes.

**Table 2.** Significance of clinical picture and neck U/S in predicting lateral neck metastasis.

Characteristics	Pathologic lymph nodes status		Predictive Value (PV)	P value
	-ve LNs = 47 cases	+ve LNs = 22 cases		
Clinical Examination (C/E)				
-ve LNs	38 cases (True negative)	3 cases (False positive)	-ve PV: 93%	<0.008
+ve LNs	9 cases (False negative)	19 cases (True positive)	+ve PV: 68%	
Ultrasonography (U/S)				
-ve L.N.	40 cases (True negative)	3 cases (False positive)	-ve PV: 93%	<0.001
+ve L.N.	7 cases (False negative)	19 cases (True positive)	+ve PV: 73%	
Combined (C/E&U/S)				
-ve L.N.	40 (True negative)	1 (False positive)	-ve PV: 98%	
+ve L.N.	7 (False negative)	21 (True positive)	+ve PV: 75%	

lateral lymph node dissection. Also positive predictive value in combination of clinical examination and ultrasonography was 75% that is 75% of the patients with truly negative lymph nodes will avoid unnecessary lateral neck dissection (**Table 2**).

#### 4. Discussion

From all included parameters in this study, only clinical examination and Neck U/S were independent predictors of metastasis to lateral neck lymph nodes in well differentiated thyroid cancer.

Age, sex, capsular invasion and multi-focality as well as papillary thyroid cancer and tumor size were not predictive of lymph node metastasis in this research.

Several studies have described clinico-pathological factors associated with lymph node metastasis. But results from those studies were inconsistent [17] [18].

It's important to know whether or not tumor size is predictor of lymph node metastasis. Some studies have showed that L.N. metastasis is associated with large tumor size [19] [20] [21] [22]. However, our study and other studies reported that tumor size was not an independent predictor of lymph node metastasis in multivariate analysis [23] [24]. Also in the present study there is no correlation between age and LNs metastasis which is inconsistency with other earlier studies [23] [24]. Although a previous review has found an association between gender and lymph nodes metastasis [25] [26], we and Roh *et al.* have found that there was no association between gender and lymph nodes metastasis [24]. Moreover, we and Roh *et al.* found no relation between tumor multi-focality and lymph node metastasis [24].

In this study capsular invasion is not associated with lymph node involvement which is shown also by By *et al.* [20]. However, Moon *et al.* showed that minimal extra-thyroidal extension was significantly associated with lymph nodes metastasis [27].

We compared the preoperative clinical and imaging findings with the histopathological diagnosis. This study shows that, there is a strong association of lymph node metastasis with reported positive lymph nodes detected by clinical examination and neck US.

Negative predictive value for either clinical examination or ultrasonography examination of the neck was 93% for each. Positive predictive value for either of clinical examination or ultrasonography was 68% and 73% respectively. However, negative predictive value in combination of clinical examination and ultrasonography was 98% that is only 2% with truly positive lymph nodes will miss lateral lymph node dissection. Also positive predictive value in combination of clinical examination and ultrasonography was 75% that is 75% of the patients with truly negative lymph nodes will avoid unnecessary lateral neck dissection (Table 2).

Clinical examination has sensitivity of (86.36%) and specificity of (80.85%). The main advantage of accurate preoperative ultrasonography is that suspicious, yet non-palpable lymph nodes can be surgically considered. Neck US examination has sensitivity of (86.36%) and specificity of (85.11%).

By combining both clinical and Neck US examination, they had have sensitivity of (95%) and specificity of (74%).

This study has included only the cases with lateral neck dissection that have positive clinical and ultrasonography evidences of LNs metastasis, or negative clinical and US evidences with suspicious intraoperative evidences, therefore sensitivity and specificity could be estimated. However, prospective, large study could be more powerful in this regard.

Previously published studies also have shown substantially high values for sensitivity and specificity of ultrasound [3] [28] [29]. Stulak *et al.* showed sensitivity of 83.5 and specificity of 97.5 for primary well-differentiated thyroid cancer [3]. In cases of subsequent operations, sensitivity rose to 90.4% and specificity was 78.9% [3]. In recurrent well-differentiated thyroid cancer, 92.1% ultrasound sensitivity has been reported [29].

So both clinical examination and US examination could be reliable and effective tools to be used as preoperative predictors of lateral lymph nodes involvement in well differentiated thyroid cancer to avoid unnecessary lateral lymph node dissection.

This study has several limitations. First, this study is a retrospective; however, prospective study could be more powerful in this regard.

Second, since this study was retrospective analysis, the prognostic significance of lymph nodes metastasis such as the relation to tumor recurrence could not be investigated. Long-term follow up studies are needed to confirm the prognostic

significance of lymph node metastasis. Third, our study population was a cohort of patients for a single center. Therefore, it is unlikely that this small cohort could provide reliable statements and a much larger number of cases in multi-center will be needed to generalize these results.

## 5. Conclusion

Clinical and US examinations are the most independent and reliable factors to detect metastasis in lateral neck lymph nodes. These two tools may be enough and efficient in detecting lateral lymph node involvement which could help in decision making for lateral lymph node dissection in well differentiated thyroid cancer.

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