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Accuracy of Ultrasound in Detection of Cervical Lymph Node Metastasis from Thyroid Cancer

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ABSTRACT

Background: Thyroid cancer is often associated with regional lymph node metastasis, necessitating accurate detection pre-operatively. Ultrasound [U/S] is a widely used imaging modality for evaluating cervical lymph nodes, but its reliability for detecting metastatic lymph nodes in thyroid cancer remains to be elucidated.

Aim of the work: This study aimed to assess the accuracy of pre-operative neck ultrasound in detecting cervical lymph node metastasis in patients with thyroid nodules undergoing total thyroidectomy.

Patients and Methods: A total of 30 patients diagnosed with thyroid nodules were included in this study. All patients underwent comprehensive pre-operative neck ultrasound followed by total thyroidectomy. The histopathological examination of excised tissue served as the gold standard for comparison. The study particularly focused on analyzing the sensitivity, specificity, and overall accuracy of U/S in detecting both central and lateral lymph node metastasis.

Results: Among the 30 patients, 14 exhibited metastatic lateral lymph nodes [46.7%], and 5 presented with metastatic central lymph nodes [16.7%]. The sensitivity of U/S for central lymph node metastasis was found to be 58%, with a specificity of 97%, resulting in an overall accuracy of 81.3%. For lateral lymph node metastasis, the sensitivity was 70%, specificity 93%, and accuracy 83.6%.

Conclusion: This study highlights that while ultrasound demonstrates high specificity for detecting metastatic lymph nodes in thyroid cancer, its sensitivity remains moderate. Therefore, while U/S is a valuable tool in pre-operative evaluation, it should be complemented with other diagnostic modalities to enhance detection rates of lymph node metastasis.

Keywords: Ultrasonography; Lymph Nodes; Papillary Thyroid Cancer.

INTRODUCTION

Thyroid carcinoma is the most frequent malignant head and neck tumor, and its incidence has increased globally in recent decades. This rise is almost exclusively attributed to papillary thyroid cancer [PTC] [1]. As of 2020, thyroid carcinoma ranked ninth among the most common cancers, with 586,000 cases reported worldwide [2]. In recent years, advancements in ultrasound instruments and technologies have led to a gradual increase in the number of people diagnosed with early-stage thyroid cancer [3].

Despite the majority of patients with PTC having better prognoses than those with other cancers, cervical lymph node metastasis [CLNM] is frequently observed in PTC patients. CLNM is a common form of metastasis in thyroid cancer [TC] and is associated with lower survival rates, highlighting the importance of rigorous nodal metastasis screening before surgery [1].

Early detection of lymph node metastasis [LNM] plays a significant role in shaping treatment strategies, including the surgical approach, the extent of surgery, postoperative adjuvant therapy, and prognosis. Furthermore, several studies have indicated that LNM is a risk factor for local tumor recurrence and cancer-specific mortality [4].

Cervical lymph nodes [CLN] are categorized into two groups: the lateral compartment [level IV] and the central neck compartment [levels VI or VII]. In patients with clinically involved central nodes in PTC, therapeutic central cervical lymph node dissection [CLND] is well established. However, the American Thyroid Association [ATA] guidelines indicate a debate regarding whether preventive central CLND should be performed in PTC patients with clinically negative nodes [cN0] [5].

Ultrasound is the first-line imaging method used to evaluate CLNM in PTC before surgery. While numerous studies have assessed the effectiveness of preoperative ultrasonography in diagnosing CLNM, the outcomes have been inconsistent. To better understand the diagnostic effectiveness of preoperative ultrasonography, we summarized the published data stratified by central and lateral neck levels [6].

Accurate detection of CLNM in PTC is essential for intervention and prognostic assessment, potentially enhancing surgical techniques, aiding patients undergoing radioiodine residual ablation, and reducing mortality and recurrence rates [6]. Ultrasound serves as a non-invasive and low-cost tool for distinguishing between benign and metastatic nodes [7]. Nonetheless, the gold standard for evaluating LNM remains lymph node biopsy or pathological investigation following surgical dissection [8].

The aim of this work is to evaluate the diagnostic accuracy of preoperative neck ultrasound in detecting cervical lymph node metastases from thyroid carcinoma and to determine its value in decision-making regarding cervical lymph node dissection.

PATIENTS AND METHODS

This prospective study included 30 participants with thyroid carcinoma who underwent total thyroidectomy and neck dissection at Al-Azhar University Hospitals. The study compared the preoperative neck ultrasound findings with the postoperative pathological results.

The inclusion criteria for the study comprised participants aged 18 years or older, individuals with suspicious cervical lymph nodes and thyroid carcinoma, and those who consented to participate. Conversely, the exclusion criteria included patients who were unable to undergo surgery, those who had previously undergone neck surgeries, and individuals with confirmed pathological metastatic cervical lymph nodes.

Data collection

The study involves a comprehensive approach to patient evaluation, beginning with complete history taking. This includes gathering personal information such as age, name, and sex, along with any specific complaints the patient may have. A thorough review of past medical and surgical histories is conducted, in addition to assessing the family history for any occurrences of thyroid cancer.

Following the initial history, a physical examination is performed. After a general assessment of the patient's overall condition, a focused head and neck examination is conducted. This includes assessing the size and firmness of the thyroid gland and checking for any enlarged lymph nodes in the neck. Indirect laryngoscopy is also utilized to evaluate the mobility of the vocal cords, providing further insight into the patient's condition.

Laboratory investigations are critical to the assessment, including a complete blood count [CBC], thyroid profile comprising TSH, FT3, and FT4 levels, and tests for kidney and liver functions. Additionally, a coagulation profile and serum calcium level are measured to ensure a comprehensive evaluation of the patient's health.

Neck Ultrasound [U/S]

Increased size, a rounded form, no apparent hilum, an irregular reflection pattern, irregular boundaries, cystic changes, and microcalcifications are some ultrasound features of metastatic lymph nodes. The ultrasound evaluation of lymph nodes that might be suspicious employed a size cutoff value of 1 cm.

Thyroidectomy

During the surgical procedure, the patient should be positioned supine with their head supported and extended using a shoulder roll or gel pad at the scapula level. Care must be taken to avoid hyperextension of the neck, and the arms should be gently tucked at the sides. After intubation, the operating bed may be rotated 180 degrees for optimal workspace. A curvilinear collar incision, approximately 2 cm above the sternal notch and clavicle edge, is traditionally used, ideally measuring between 6-8 cm to ensure proper exposure without excessive stretching of the skin.

Once the thyroid gland is located, a capsular dissection is performed on the lateral aspect, followed by careful dissection of the overlaying strap muscles. The surgeon identifies the crico-thyroid space, providing visibility to the thyroid's superior pole. The superior pedicle is divided using a harmonic scalpel or clips, taking care to avoid damage to the superior thyroid nerve and recurrent laryngeal nerve. Finally, after removing the thyroid gland, a suction drain is inserted, and hemostasis is achieved before closure in layers.

Neck dissection

The amount of tissue and the number of lymph nodes depend on how far the cancer has spread. Incisions begin at the lateral edge of the collar incision from the thyroidectomy and run in a J-shaped manner [J-shaped incision]. Flaps are raised below the platysma. After that, the lymph nodes are removed while preserving the nerves and blood vessels. The wound is closed over the suction drain at the conclusion of the surgery.

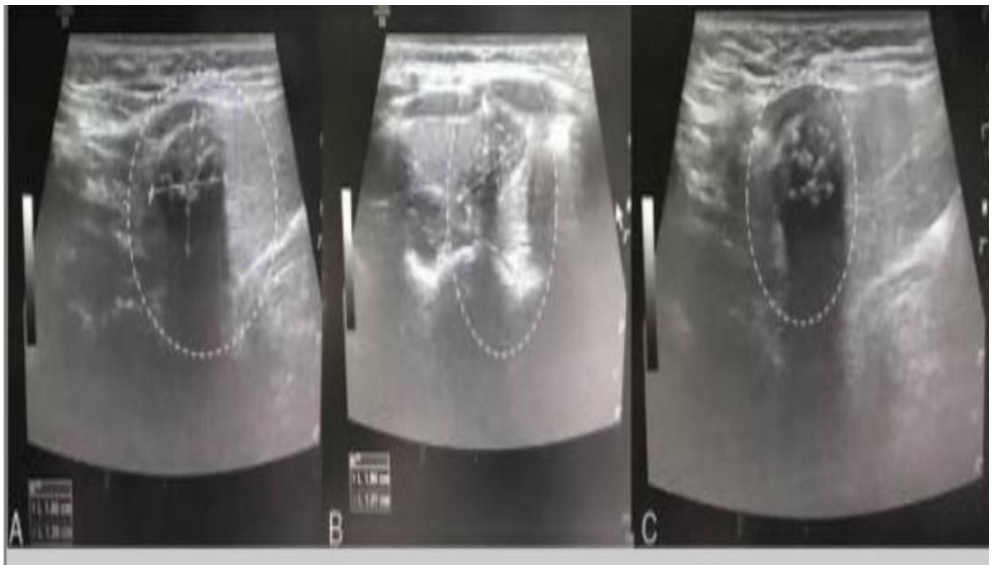

Figure [1]: Enlarged lymph node A: shows that white circle around lymph mode, B: Hypoechogemicity, and C: shows the microcalcifications

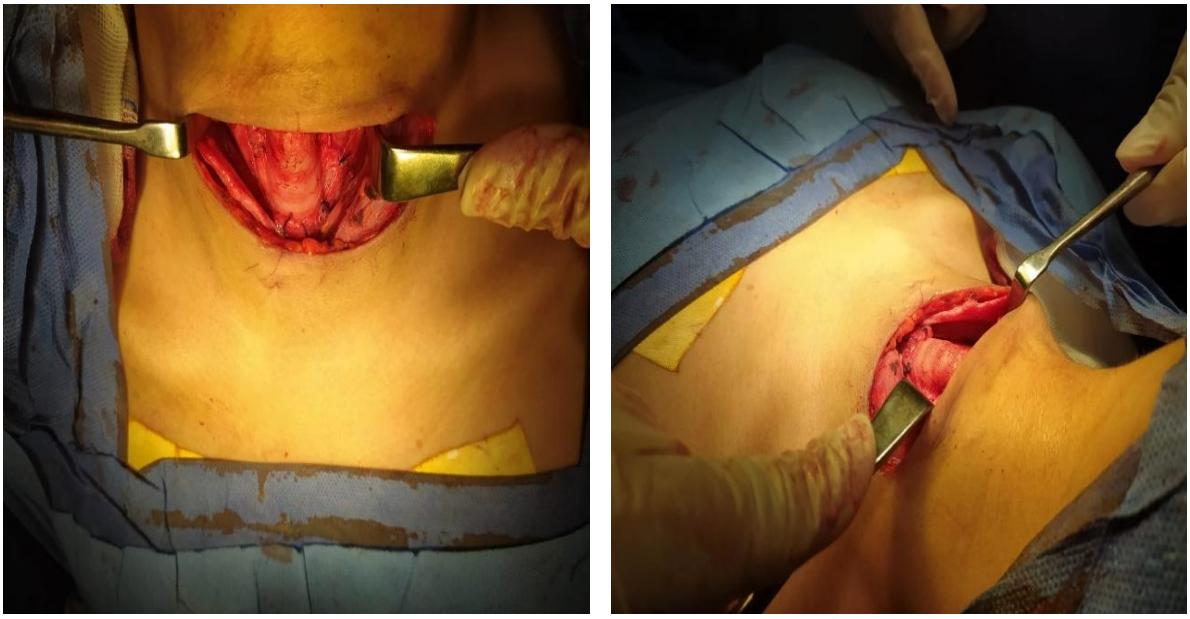

Figure [2]: Total thyroidectomy and central lymph node dissection

Statistical Analysis

Statistical analysis was conducted using SPSS [Statistical Package for the Social Sciences] software, which allowed for comprehensive data evaluation. Descriptive statistics were calculated to summarize the demographic data and key variables, including means, standard deviations, and frequencies. Inferential statistics were employed to assess relationships between variables, with significance determined using p-values. Also, receiver operating characteristic [ROC] curve analysis was performed to evaluate the diagnostic performance of the variables in predicting outcomes. various diagnostic statistics, including sensitivity and specificity were computed to assess the performance of the diagnostic tests used in the study. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The mean age was 41±10.5 with a range of about [18-50] years, and as regards sex, there were 25 females [83.3%] and 5 males [16.7%], respectively [Table 1].

Regarding the complaints of the studied cases, there were 14 cases with neck lumps [46.7%], 13 cases with pressure symptoms [43.3%], and 3 cases with toxic symptoms [10%] [Table 2].

Regarding metastatic lymph nodes, there were 14 cases with metastatic lateral lymph nodes [46.7%] and 5 cases with metastatic central lymph nodes [16.7%] [Table 3].

The mean TSH value was 2.18 ± 1.40, with a range of 1 to 4. The mean free T3 was 6.5 ± 0.9, with a range of 4 to 7. The mean free T4 was 1.5 ± 0.5, with a range of 0.95 to 1.9. There were 2 cases of hyperthyroidism [6.7%] and 28 cases in a euthyroid state [93.3%] [Table 4].

In central LNM, ultrasound has a sensitivity of 58% and a specificity of 97%, resulting in an accuracy of 81.3%. In lateral LNM, ultrasound has a sensitivity of 70% and a specificity of 93%, resulting in an accuracy of 83.6% [Table 5].

Table [1]: The studied cases' demographic data

Variables		
Age	Mean± SD	41±10.5
	Min.-Max.	18-50
Sex	Male	5 [16.7%]
	Female	25 [83.3%]

Table [2]: Complaint of studied cases

Complaint, n [%]	
Toxic symptoms	3 [10%]
Neck lump	14 [46.7%]
Pressure symptoms	13 [43.3%]

Table [3]: Metastatic lymph nodes of studied cases

Metastatic lymph node		
Lateral	**Yes**	14 [46.7%]
	No	16 [53.3%]
Central	**Yes**	5 [16.7%]
	No	25 [83.3%]

Table [4]: Thyroid status of studied cases

Variables		
TSH value	Mean± SD	2.18 ±1.40
	Min.-Max.	1-4
Free T3, pmol/L	Mean± SD	6.5±0.9
	Min.-Max.	4.0 - 7.0
Free T4	Mean± SD	1.5±0.5
	Min.-Max.	0.95 - 1.9
Thyroid status, n [%]	Hyperthyroidism	2 [6.7%]
	Euthyroid	28 [93.3%]

Table [5]: Ultrasound's sensitivity, specificity, and accuracy in diagnosing cervical lymph node metastasis

Diagnostic Method	Sensitivity	Specificity	Accuracy
Central LNM	58%	97%	81.30%
Lateral LNM	70%	93%	83.60%

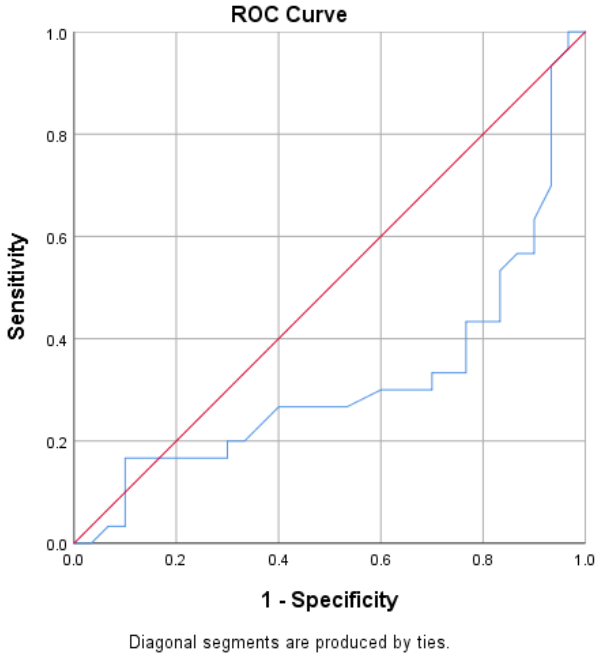

Figure [1]: Ultrasound's ROC curve in diagnosing cervical lymph node metastasis

DISCUSSION

The conventional ultrasound criteria for diagnosing malignant lymph nodes remain disputed, exhibiting low specificity and sensitivity. There is still a need for improvements in accuracy or for an efficient alternative imaging diagnostic tool. Additionally, retropharyngeal ultrasound and operator-dependent imaging may be particularly challenging for evaluating retrosternal and mediastinal regions [9].

The demographic data revealed an average age of participants at 41 ± 10.5 years, with 16.7% male and 83.3% female representation. The higher prevalence of thyroid cancer in females may stem from hormonal, genetic, and environmental factors, along with a greater prevalence of thyroid nodules in females, which can progress to cancer. Hormonal regulation by estrogen and progesterone could also play a role [10]. These findings align with **Al-Hilli *et al.*** [11], who found an average patient age of 44 years [± 16.8 SD] among 176 men and 285 women in their study on lymph node detection in papillary thyroid carcinoma.

Abboud *et al.* [12] assessed the diagnostic accuracy of neck ultrasonography for detecting lymph node metastasis from papillary thyroid carcinoma [PTC] in 206 patients aged 14 to 88, with a mean age of 56. An increased incidence of PTC in elderly patients is thought to result from factors like ionizing radiation exposure, genetic mutations, and immune influences. Similarly, **Zhou *et al.*** [13] examined the qualitative and quantitative properties of ultrasonography for evaluating cervical lymph node metastasis from PTC, studying 55 lymph nodes from 46 individuals, with an average participant age of 47.11 ± 13.87 years.

The study identified that the most common symptom of thyroid cancer is a neck lump [46.7%], followed by pressure symptoms [43.3%] and toxic symptoms [10%]. Additionally, 16.7% of patients had central metastatic lymph nodes, while 46.7% had lateral metastatic lymph nodes. Also, **Abboud *et al.*** [12] reported that the percentages of cases involving central and lateral metastatic lymph nodes were 68% [n = 141 cases; 141/206] and 60% [n = 34 cases; 34/57], respectively.

Moreover, for central lymph node metastasis [LNM], sensitivity was 20%, specificity was 97%, and accuracy was 58.3%; this indicates the low performance of ultrasound in detecting central cervical LNM. In lateral LNM, sensitivity was 70%, specificity was 93%, and accuracy was 81.6%, demonstrating that ultrasound shows high performance in the detection of lateral cervical LNM.

The results highlight a significant discrepancy in the performance of ultrasound for detecting central versus lateral lymph node metastasis [LNM] in cervical evaluations.

The ultrasound's performance in detecting central lymph node metastasis [LNM] is suboptimal, with a sensitivity of just 20%. This indicates a high rate of false negatives, meaning many positive cases of metastasis go undetected, leading to potential underdiagnosis. Although the specificity is high at 97%, which indicates accurate detection of disease absence, its clinical usefulness diminishes when positive cases are frequently missed. In contrast, ultrasound shows a much higher sensitivity for lateral LNM at 70%, along with a specificity of 93% and an accuracy of 81.6%. This suggests that ultrasound is a more reliable diagnostic tool for lateral cervical LNM, facilitating better clinical decision-making and timely interventions. Overall, while ultrasound has value for lateral LNM assessment, it falls short for central LNM, prompting the need for supplementary imaging techniques or more invasive diagnostics in patients with conditions like papillary thyroid cancer to ensure effective management.

Our findings align with **Zhao *et al.*** [9], who reported ultrasound sensitivity, specificity, and area under the curve [AUC] values of 0.33, 0.93, and 0.69, respectively, indicating high false negatives and poor accuracy for diagnosing central cervical lymph node metastasis [CLNM] in papillary thyroid cancer [PTC]. In contrast, ultrasound showed better effectiveness for lateral CLNM, with sensitivity, specificity, and AUC values of 0.70, 0.84, and 0.88, respectively. Additionally, **Schumm *et al.*** [2] highlighted that preoperative ultrasound is valuable for lymph node staging in PTC, showing the highest sensitivity [0.72] and specificity [0.97] for lateral compartment involvement [$p < 0.05$].

Abboud *et al.* [12] found that ultrasound's sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV] for predicting metastatic papillary thyroid cancer [PTC] in the central neck were 69%, 71%, 84%, and 51%, respectively, while in the lateral neck, these values were 85%, 65%, 78%, and 75%. **Feng *et al.*** [4] investigated the effectiveness of ultrasonography [US], computed tomography [CT], and their combination for detecting cervical lymph

node metastasis [CLNM] in PTC patients. They concluded that ultrasound outperformed CT, particularly in the lateral compartment, and that combining US and CT improved diagnostic effectiveness for lateral CLNM compared to central CLNM.

This study faces several limitations affecting its validity. The subjective nature of ultrasound examinations can introduce variability in interpreting lymph node characteristics. Additionally, the small sample size limits the generalizability of the results and reduces statistical power. The study also did not consider potential confounding factors, such as patients' diverse clinical backgrounds and the presence of other malignancies, which could influence lymph node metastasis detection rates. Future research should involve larger, more diverse populations and standardized protocols to enhance applicability.

In conclusion, presurgical neck ultrasound demonstrates higher sensitivity and specificity in detecting lateral cervical lymph node metastasis compared to central lymph node metastasis in patients with thyroid cancer. Given these findings, it is advisable to consider prophylactic central neck dissection in high-risk patients, even when ultrasound does not show obvious metastatic disease. This study highlights the importance of utilizing neck ultrasound to identify clinically impalpable lymph nodes, reinforcing its role in the preoperative assessment of thyroid cancer.

Disclosure: None to be disclosed.

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