

**PREOPERATIVE DETECTION OF LYMPH NODES METASTASIS IN PATIENTS WITH
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ABSTRACT

Background: Thyroid cancer is the most common endocrine malignancy and there have been a steady increase in its incidence over the past 15-20 years, It accounts for approximately 1% of all malignancies in developed countries with an estimated annual incidence of 122,000 cases worldwide. **Aim:** The aim of this study is to assess the diagnostic efficiency of preoperative ultrasonography and FNAC to detect lymph node metastasis in patients with PTC. **Patients and methods:-** In randomized descriptive study, A total of 30 unselected patients suffering from papillary thyroid cancer were treated in Al-Azhar University hospital from 2013 to 2016; all were treated for curative intent. For all patients were subjected to proper history taking including age, sex, occupation, associated other medical illness and then proper general and local examination. Then thyroidectomy and central neck dissection in addition to ipsilateral neck dissection for all patients and proceed to contralateral neck dissection if ipsilateral lymph nodes are positive in ultrasound. **Results:** Of 30 patients, With known thyroid cancer, neck metastases are often not detectable on routine physical examination. Both the central and lateral neck compartments can harbor nonpalpable, occult metastases. Postoperative anatomic changes add to the challenge of detecting disease by physical examination alone. Various imaging modalities can assist in detecting occult metastases. Preoperative neck US is recommended to assess the thyroid lobes and cervical lymph nodes for all patients undergoing thyroidectomy for malignant cytological findings on biopsy. **Conclusion:** Preoperative Ultrasound can detect cervical node metastasis with high sensitivity and specificity. Central lymph node dissection prevents nodal recurrence in the central compartment which carries a high incidence of morbidity during surgery for this recurrence.

KEYWORDS: total thyroidectomy, central lymph node dissection, lateral lymph nodes dissection.**INTRODUCTION**

Papillary thyroid carcinoma (PTC) frequently spreads to regional lymph nodes. Cervical lymph node metastases are common, affecting approximately 30–80 per cent of patients (*Mazzaferrri EL, Jhiang SM, 2014*). In addition to preoperative ultrasound evaluation, the presence of lymph nodes metastasis may also be predicted by clinical variables and histopathology. The aim of the present study was to assess the diagnostic value of preoperative ultrasonography for detecting metastatic lymph nodes at different cervical levels in patients with PTC. The histopathology of the neck dissection specimens was analysed and factors that may be predictive of lymph nodes metastases. (*Lim YC, Choi EC, Yoon YH, Koo BS, 2010*).

Therapeutic neck dissection is recommended for patients who present with palpable or biopsyproven metastatic lymph nodes. However, there is no clear consensus regarding the optimal extent of lateral neck dissection.

Most surgeons recommend therapeutic compartmental dissection for patients with metastatic lateral lymph nodes, with sparing of the spinal accessory nerve, internal jugular vein and sternocleidomastoid muscle (*Doyle VC et al, 2007*).

This strategy is based on previous reports showing that levels II–IV (jugular nodes) and VI (central cervical lymph nodes) are often involved in patients with PTC.

Patients and methods

This randomized descriptive study was conducted on 30 patients with papillary thyroid carcinoma in Al-Azhar University Hospitals during the period from September 2013 to October 2016.

All patients underwent total thyroidectomy, pretracheal, prelaryngeal (Delphian) and bilateral paratracheal lymph node dissection and lateral lymph nodes dissection if ipsilateral group are positive in neck ultrasound. The

central compartment was limited by the hyoid bone superiorly, the innominate vein inferiorly, the carotid sheaths in both sides laterally and the prevertebral fascia dorsally and was divided into three node sites: pretracheal and prelaryngeal (Delphian), ipsilateral paratracheal and contralateral paratracheal lymph nodes.

We defined the pretracheal, prelaryngeal (Delphian) and ipsilateral paratracheal lymph nodes as ipsilateral central compartment, and contralateral paratracheal lymph nodes as contralateral central compartment.

Postoperative management

Patients make a rapid recovery following surgery and are able to eat and drink on the day of surgery and are self-caring. They can usually be discharged to home on the first postoperative day.

Cord palsy was uncommon in our cases but we watched for stridor immediately postoperative as there may be a need for urgent tracheostomy to secure the airway if it is severely affected.

Also, postoperative bleeding was uncommon in our cases but we watched for it postoperatively to prevent suffocation of the patient if it occurred as the neck must be reopened immediately to allow relief of laryngeal edema and tracheal compression by blood clots.

Early symptoms of hypoparathyroidism (tingling around the mouth, toes and fingers) had been watched for as it must be promptly treated otherwise muscle cramps will occur. 10% calcium gluconate is injected slowly intravenous to avoid cardiac standstill and repeated till disappearance of tingling or muscle cramps. Then serum calcium level is checked within 12 hours.

After radioiodine treatment, or if the patient is not in need for radioiodine, we give the patient exogenous thyroxine to suppress TSH release and to make its serum level less than 1 ng/ml because it is recognized that TSH suppression is important to minimize the risk of

recurrence of papillary thyroid carcinoma. The patients were subjected to do periodic serum thyroglobulin level every 6 months to ensure that there is no recurrence occurred.

Post operative complications

Postoperative hypocalcaemia and recurrent laryngeal nerve injury were evaluated. Postoperative hypocalcaemia was defined as at least one event of hypocalcaemia symptoms (perioral numbness, or paresthesia of hands and feet) or at least one event of biochemical hypocalcaemia (ionized Ca level < 1.0 mmol/L or total Ca level < 8.0 mg/dl).

Statistical measures

Continuous data are expressed as median (range). The sensitivity, specificity, accuracy and positive and negative predictive values (PPV and NPV respectively). of ultrasonography for predicting metastatic lymph nodes at different neck levels were determined by comparing the ultrasound results with histopathological findings. P values were calculated and statistical analyses performed using SPSS version 18.0 software

RESULTS

The study involved 30 patients with thyroid cancer. The mean age of the studied group was 52.87±11.00 years. Age ranged from 25 to 68 years. The majority of the studied group was females (21 cases, 70.0%). **table (1).**

Table: 1 Distribution of age and sex

		No.= 30
Age (yrs)	Mean ± SD	52.87 ± 11.00
	Range	25 – 68
Sex	Female	21 (70.0%)
	Male	9 (30.0%)

30 cases (100%) presented with thyroid swellings and only 15 cases (50%) was presented with palpable lymph nodes. FNAC from thyroid gland or lymph node if palpable proved PTC. **table (2)**

Table (2): Clinical presentation, ultrasound and FNAC in studied patients

		No.	%
Swelling	Thyroid	30	100.0%
	Absent	15	50.0%
Palpable lymph nodes	Present	15	50.0%
	SMNG	30	100.0%
Neck US thyroid	PTC	30	100.0%
FNAC from thyroid or palpable LN			

There is 29 cases with positive central lymph nodes metastasis and 4 cases with positive lateral lymph nodes metastasis. **Table (3).**

Table (3): preoperative ultrasound for central and lateral lymph nodes

		No.	%
Neck US for central LNS	Positive	29	96.7%
	Negative	1	3.3%
Neck US for lateral LNs	Negative	26	86.7%
	Positive	4	13.3%

Table 4 shows tumor characteristics. Bilateral tumors were found in 5 cases (16.7%) and 5 patients (16.7%)

had multiple masses. 63.3% of the tumors were of grade II. Extra-capsular invasion was found in 5 cases (16.7%).

Table: (4) Characteristics of the studied tumors

		No.	%
Laterality	Bilateral	5	16.7%
	Unilateral	25	83.3%
Numbers of tumors	Multiple	5	16.7%
	Single	25	83.3%
Tumor grade	I	6	20.0%
	II	19	63.3%
	III	5	16.7%
Extra-capsular invasion	No	25	83.3%
	Yes	5	16.7%

In 30 patients (100%), clinically or radiologically positive lymph nodes were detected. Central and ipsilateral lymph nodes dissection for 30 patients (100%). And

contralateral lymph nodes dissection in 5 cases (16.7%) with positive lymph nodes in ipsilateral group in preoperative ultra-sound. **table (5).**

Table (5): Proportion of lymph nodes dissection

		No.	%
Central lymph Node dissection	Yes	30	100.0%
Ipsilateral lymph Node dissection	Yes	30	100.0%
Contralateral lymph Node dissection	No	25	83.3%
	Yes	5	16.7%

Histopathology report post-operative proved PTC in thyroid gland and positive central lymph nodes in 27 cases (90.0%) and positive ipsilateral nodes in 4 cases (13.3%). **Table (6).**

Table (6): Post-operative histopathological report for thyroid, central and lateral lymph nodes

		No.	%
Histopathological findings in thyroid	PTC	30	100.0%
Histopathological findings in central LNs	Negative	3	10.0%
	Positive	27	90.0%
Histopathological findings in ipsilateral LNs	Negative	26	86.7%
	Positive	4	13.3%

The accuracy of US for central lymph nodes is 85.6% while sensitivity was 96.7% and specificity is 90.0% and

positive predictive value 96.7% and negative predictive value NPV is 90.0%. **table (7).**

Table (7): Diagnostic accuracy of US in central LN

NECK US for central LN	Histopathological findings in central LNs				Total	
	Negative by Histopathology		Positive by Histopathology			
	No.	%	No.	%	No.	%
Positive by US	3	10.0%	26	86.7%	29	96.7%
Negative by US	0	0.0%	1	3.3%	1	3.3%
Total	3	10.0%	27	90.0%	30	100.0%

The accuracy of US for ipsilateral lymph nodes is 85.6% while sensitivity was 75.0% and specificity is 96.2% and

positive predictive value (PPV) 75.0% and negative predictive value (NPV) is 96.2%. **table (8).**

Table (8): Diagnostic accuracy of US in lateral LN

Neck US for lateral LNs	Histopathological findings in ipsilateral LNs		Total	Chi-square test	
	Negative by	Positive by		X ²	P-value

	Histopathology		Histopathology		No.	%		
	No.	%	No.	%				
Negative by US	25	96.2%	1	25.0%	26	86.7%	15.189	0.000
Positive by US	1	3.8%	3	75.0%	4	33.3%		
Total	26	100.0%	4	100.0%	30	100.0%		

We found that 3 cases (10.0%) had temporary hypocalcemia, 2 cases (6.7%) had seroma post operative and only two cases (6.7%) had permanent hypocalcemia.

Also, temporary vocal cord dysfunction was found in only one cases (6.7%) and one case 3.3% with permanent loss of voice. **Table (9).**

Table: (9) Relation between associated complications and lymph node involvement.

		No.	%
Intra operative complications	Injury of IJV	1	3.3%
	No	29	96.7%
Early post operative complications	No	25	83.3%
	Seroma	2	6.7%
	Hoarsness of voice	1	3.3%
	Permenant loss of voice	1	3.3%
	Temporary hypocalcemia	1	3.3%
Late post operative complications	No	23	76.7%
	Temporary hypocalcemia	3	10.0%
	Permenant hypocalcemia	2	6.7%
	Permenant loss of voice	1	3.3%
	Hoarsness of voice	1	3.3%

DISCUSSION

Thyroid cancer is the most common endocrine malignancy and there have been a steady increase in its incidence over the past 15-20 years. Cervical lymph node metastases in papillary thyroid cancer are frequent; occurring in 30-80% of patients with the central compartment of the neck is the most frequently involved.

The rationale for introducing central lymph node dissection in papillary thyroid carcinoma was similar to that emphasized for treating medullary carcinoma of the thyroid gland: preventing local recurrences in the central compartment where reoperation is difficult (*Sakorafas et al, 2015*).

Most of the literature has reported the pattern of cervical lymph nodal metastasis without separation of the ipsilateral or contralateral central compartment in PTC patients (*Koo et al, 2010*).

The current study demonstrated that sensitivity and specificity of preoperative ultra-sound for prediction of lymph nodes metastasis in central group were 96.7 % and specificity is 90.0 % respectively and for lateral group were 75.0 % and specificity is 96.2 %.and PPV and NPV were 96.7% and 90.0% respectively.

This is different from a study by **Harry S., 2011** who reported in his study that the The sensitivity, specificity, PPV, and NPV were 90.3%, 80.9%, 68.3%, and 94.8%, respectively

The current study demonstrated that 100% of patients have lymph node metastasis; the central compartment is

involved in 29/30 of them.

This is similar to a study by **Moo and Fahey, 2011** who reported that the central compartment lymph node metastases are found in 40%-90% of cases. Even in papillary microcarcinoma the rate of lymph node metastases has been reported in 25%-45% of cases. The ipsilateral central compartment was involved in all of them.

This is different from a study by **Pereira et al, 2014** who reported in there study that the prevalence of nodal metastasis in the central compartment was 60%.

These results support a study by **Wada and colleagues, 2013** who found ipsilateral central compartment nodal involvement in 36.3% of a larger series (n = 259).

In our study, the lateral compartment of the ipsilateral neck was dissected in 30 cases in which they had positive central lymph nodes. we found that positive lateral nodes were found in only 4 cases (13.3%). the median number of dissected nodes was 22 (range: 18-28), no skip metastases were found in our study. This means that in clinically or radiologically negative lateral LN metastasis we do not need to do lateral lymph node dissection even if CLNs were positive for metastases.

Our results are different from a study by **Vergez et al, 2010** who found that 31% had metastatic invasion of the central and lateral compartment lymph nodes and 14.5% had metastatic invasion to the central nodal compartment only with no skip metastases. They also found that the average number of central lymph nodes harvested to be

4.7 ± 0.4 (range 0-21) and 25 ± 1.1 lymph nodes for the lateral neck dissection (average 6-54).

In our study, we found that all patients with metastatic contralateral central lymph nodes have metastatic ipsilateral central lymph node metastases (no skip metastases).

This is different from the study by **Sadowski and colleagues, 2015** who found that 5% of all patients undergoing bilateral CLND have positive contralateral lymph node metastases without evidence of spread to the ipsilateral central lymph nodes.

The significances lie in: In patients with known thyroid cancer, neck metastases are often not detectable on routine physical examination. Both the central and lateral neck compartments can harbor nonpalpable, occult metastases. Posttreatment anatomic changes add to the challenge of detecting disease by physical examination alone. Various imaging modalities can assist in detecting occult metastases to best direct treatment strategies.

As previously mentioned, preoperative neck US is recommended to assess the contralateral thyroid lobe and cervical lymph nodes for all patients undergoing thyroidectomy for malignant cytological findings on biopsy.

CONCLUSION

1. In primary papillary thyroid cancer, we propose that total thyroidectomy and bilateral central lymph node dissection is the least surgical treatment recommended.
2. Preoperative neck US for patients with thyroid cancer is more sensitive and specific in the evaluation of cervical compartment lymph nodes.
3. Ultra-sound can detect cervical node metastasis with sensitivity and specificity of 96.7 % and 90.0 % respectively.
4. Central lymph node dissection prevents nodal recurrence in the central compartment which carries a high incidence of morbidity during surgery for this recurrence.
5. Central lymph node dissection in good hands does not add to the morbidity of total thyroidectomy (hypoparathyroidism and recurrent laryngeal nerve injury).

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