

*Research Article*

## Indications and Complications of Prophylactic Central Neck Dissection in Comparison with Therapeutic Central Neck Dissection in Management of Papillary Thyroid Cancer.

Abu Bakr Mohiey El-Deen MD\*, Elsherbiny M MD\*\*, Ashraf Wagdy MD\*, Hatem A MD\* and Mohamed S. Farahat Msc\*

\* Departments of Surgery, Minia University

\*\* National cancer institute -Cairo University

### Abstract

**Objective:** The aim of the study is to evaluate the proper surgical intervention with the lymphatic metastases in PTC. **Methods:** 50 patients were arranged into two groups according to their clinical presentations. **Group I** included patients who presented with suspicious thyroid swellings that were proved by fine needle aspiration cytology (FNAC) to be PTC; however, their clinical, ultrasonography, and computed tomography (CT) neck examination showed no evidence of macroscopic lymph node invasion (cN0). They underwent total thyroidectomy (TT) plus bilateral prophylactic central neck dissection (PCND). **Group II** included patients who presented with thyroid swellings had ascertained or suspected cervical lymph node metastases detected by clinical and/or neck ultrasonography. These were proved by FNAC to be PTC. They were treated with TT + bilateral CND. **Results:** The histopathological findings show some predictable differences among the two groups. Group 1 had the highest incidence of extracapsular spread, multifocality and tumor bilaterality but less incidence of microcarcinoma (Nodule size <1cm).as regard extracapsular spread, multifocality and microcarcinoma there is significant relation between two groups.for central compartment lymph node metastasis. Histological examination showed the presence of metastatic nodes in 40% of group 1 patients (therapeutic CND) and 20% of group 2 patients (prophylactic CND). Transient LRN paralysis occurred in one patient in group 1 (2%) and in two patients in group 2 (10%). Transient postoperative hypoparathyroidism occurred in four patient in group 1 (20%) and in five patients in group 2 (30%). **Conclusion:** tumor characteristics including extracapsular spread (ECS), multifocality and tumor size more than 1 cm were predictive factors for CLN metastases and incidence of occult metastases reached 20% so prophylactic CND is highly recommended in patients with these risk factors.

**Keywords:** central lymph node dissection (CLND). Papillary thyroid cancer (PTC)

### Introduction

Papillary thyroid cancer (PTC) is the most common type of thyroid cancer, representing about 90% of all thyroid malignancies and more than 90% of differentiated thyroid cancer (Viola, D et al., 2010). There are two different surgical approaches in the management of PTC specifically regarding the role of CLND. Worldwide, the vast majority of surgeons (mainly in Western countries) perform selective (elective or therapeutic) CLND (i.e., CLND in the presence of cervical lymphadenopathy).

However, other surgeons (mainly from East countries, such as Japan) support routine prophylactic CLND (Qu, H., et al., 2010). The predictive factors for central compartment LNM in patients with PTC were not well defined.

However, it is generally accepted that prognosis depends on sex, tumour multifocality, capsular invasion and tumour size. As a result, male gender, tumour size, extracapsular spread (ECS), lateral LNM and BRAF V600E mutation were suggested to be independent predictors of central compartment LNM (Yang, Y. et al., 2014).

Although surgical resection of all gross disease in well differentiated thyroid cancer (WDTC) is associated with excellent outcomes in terms of both survival and recurrence, the role of elective surgery for presumed microscopic nodal metastases is less clear. Patients selected for observation enjoy similar rates of recurrence, which has led to controversy over the role of elective node dissection (Siddiqui, S., et al., 2016). Recent reports indicate thyroidectomy plus nodal neck dissection resulted in 3% to 6% of PTC patients suffering permanent hypoparathyroidism and transient vocal cord paralysis. (De Carvalho, A. Y et al., 2015). These considerations generated a strong interest in a more comprehensive preoperative evaluation of the neck and renewed the controversy about the role and the extent of lymphadenectomy at the time of thyroidectomy. Moreover; many questions remain unanswered regarding the optimal management of patients with cervical lymph node metastases (Stack BC et al., 2012).

### Aim of this work

The aim of the study is to evaluate the proper surgical intervention with the lymphatic metastases in PTC as regard predictive factors and pattern of central lymph node metastases plus assessment of prophylactic central neck dissection by comparing it with therapeutic central neck dissection as regard the surgical morbidity.

### Patients and methods

This is a prospective study at surgery department in Minia University Hospital and national cancer institute. 40 patients diagnosed as papillary thyroid cancer admitted in the period from March 2013 to March 2015.

### Inclusion criteria:

- (1) Age above 10 years and below 80 years.
- (2) Histopathologically proven presence of PTC.
- (3) Being fit for and willing to undergo surgery.

All patients consented to undergo surgery and join this study. For patients below 18 years of age, consent was given by their parents.

### Exclusion criteria:

- (1) Age below 10 years or above 80 years.
- (2) Recurrent or metastatic cases.
- (3) Histopathological report of any type of malignancy other than PTC, even the mixed papillary and follicular type.
- (4) Being unfit for or refusal to undergo surgery.
- (5) Being lost to postoperative evaluation or follow-up.

### The plan:

Patients were arranged into two groups according to their clinical presentations.

**Group I** included patients who presented with suspicious thyroid swellings that were proved by fine needle aspiration cytology (FNAC) to be PTC; however, their clinical, ultrasonography, and computed tomography (CT) neck examination showed no evidence of macroscopic lymph node invasion (cN0). They underwent total thyroidectomy (TT) plus bilateral PCND.

**Group II** included patients who presented with thyroid swellings had ascertained or suspected cervical lymph node metastases detected by clinical and/or neck ultrasonography. These were proved by FNAC to be PTC. They were treated with TT + bilateral CND.

In patients presenting with evident lymph node metastases to the lateral neck compartments, depending on the extent of metastases, selective ipsilateral or bilateral levels II–V dissection according to the classification of the Committee for Head and Neck Surgery and Oncology-American Academy of Otolaryngology-Head and Neck Surgery. Patients with palpable LNs on contralateral lateral compartment underwent LND after 2 weeks.

All operations were performed following the same surgical principles and using a conventional technique.

**TT** indicates removal of the whole thyroid gland aiming at leaving no thyroid tissue but making every effort to preserve the recurrent and external laryngeal nerves and the parathyroid glands. This is achieved through adequate identification and careful dissection of these structures.

CND (bilateral) entails removable of LNs at levels VI that include the prelaryngeal, the perithyroid LNs including those around the recurrent and external laryngeal nerves, the pretracheal, bilateral paratracheal LNs and the whole fibrofatty tissues from the level of the hyoid bone above to the innominate veins below and from the medial side of the carotid artery on one side to the contralateral one through a cervical incision.

In group two patients with clinically evident metastases LND entails removal of the whole LNs at levels II, III, IV and V in the ipsilateral side (the other side after 3 weeks in bilateral cases) sparing the sternomastoid muscle, accessory nerve, and internal jugular vein from the base of the skull above to the level of the clavicle below and posteriorly to edge of trapezius muscle.

The thyroid gland specimens were evaluated pathologically for tumor characters including tumor size multifocality, bilaterality, and extracapsular spread.

Lymph node specimens were evaluated pathologically for the frequency, number and bilaterality of metastasis in the central and lateral compartment were analyzed and interpreted.

Postoperative hypocalcaemia was defined as at least one event of hypocalcemia symptoms or at least one event of

biochemical hypocalcemia (ionized Ca level <1.0 mmol/l or total Ca level <8.0 mg/dl). Ionized Ca level and/or total Ca level were checked at follow-up. permanent hypocalcemia was defined as persistent symptoms or persistent biochemical hypocalcemia for more than 3 months.

Indirect laryngoscopy was repeated on the second postoperative day to check for recurrent laryngeal nerve injury (RLNI), and patients with RLN injury were submitted to regular additional examinations every 3 months until vocal cord mobility was regained. If the mobility remained impaired for more than 1 year postoperatively it was regarded as permanent RLNI.

**Results**

Group I included 20 patients with papillary thyroid cancer (PTC) diagnosed pre-operatively as negative lymph node metastases (cN0). They underwent total thyroidectomy (TT) plus bilateral prophylactic central neck dissection (PCND).

Group II included 20 patients with PTC with positive cervical LN metastasis (clinically and/or radiologically). All cases underwent total thyroidectomy (TT) + bilateral therapeutic central neck dissection (TCND). Some cases underwent lateral neck dissection including group 2-0 (LND) according to clinical and radiological finding.

**Table (1): Patient demographics.**

	<b>Group I (n=20)</b>	<b>Group II (n=20)</b>	<b>P value</b>
<b>Age</b>			
Range	(10-70)	(20-70)	0.383
Mean ± SD	36.30±10.27	40±10.39	
<b>Sex</b>			
Male	9(45%)	7(35%)	0.027
Female	11(55%)	13(65%)	

The mean age was slightly older in group 2 (36.30 vs 40). the majority of patients was females especially in group 2 (55% vs 65%).

**Table (2): Comparison between 2 groups in histopathology of the tumors studied.**

	<b>Group I (n=20)</b>	<b>Group II (n=20)</b>
<b>Nodule size &lt; 1 cm (microcarcinoma)</b>		
Positive	0(0%)	2(10%)
<b>Extracapsular spread</b>		
Positive	1(5%)	8(40%)
<b>Multifocality</b>		
Positive	7(35%)	9(45%)
<b>Laterality</b>		
Bilateral	4(20%)	7(35%)

**Table (3): Comparison between 2 groups in Relationship of histopathologic factors for central compartment lymph node metastasis (pN1a)**

	<b>pN1a</b>		<b>P value</b>
	<b>Group I (n=8)</b>	<b>Group II (n=10)</b>	
<b>Nodule size &lt; 1 cm</b>			
Negative	3(37.5%)	10(100%)	< .001*
Positive	0(0%)	0(0%)	
<b>Extracapsular spread</b>			
Negative	7(87.5%)	6(60%)	.027*
Positive	1(12.5%)	4(40%)	
<b>Multifocality</b>			
Negative	7(87.5%)	0(0%)	.013*
Positive	1(12.5%)	10(100%)	
<b>Laterality</b>			
Unilateral	0(0%)	10(100%)	.842
Bilateral	8(100%)	0(0%)	

As regard Extra capsular spread, multifocality and microcarcinoma: There are significant relation between two groups **Bilaterality:** There are insignificant relations between two groups.

**Table (4): Comparison between 2 groups in Central lymph node dissection findings:**

	<b>Group I (n=20)</b>	<b>Group II (n=20)</b>	<b>P value</b>
<b>+Ve LN in Ipsilateral central compartment</b>			
Negative	12(60%)	0(0%)	.020*
Positive	8(40%)	20(100%)	
<b>Central LN total number</b>			
Range	(0-10)	(0-20)	.060
Mean ± SD	1.0 ± 2.71	12.0 ± 4.00	

Histological examination showed the presence of metastatic nodes in 100% of group 2 patients (therapeutic CND) and 40% of group 1 patients (prophylactic CND).

**Assessment of postoperative complications:**

**Table (5): Comparison between 2 groups in the incidence of the postoperative complications among the two groups**

	<b>Group I (n=20)</b>	<b>Group II (n=20)</b>	<b>P value</b>
<b>Temporary RLN injury</b>			
Negative	19(95%)	18(90%)	.048
Positive	1(5%)	2(10%)	
<b>Permanent RLN injury</b>			
Negative	20(100%)	20(100%)	-----
Positive	0(0%)	0(0%)	
<b>Temporary hypoparathyroidism</b>			
Negative	16(80%)	10(50%)	.700
Positive	4(20%)	10(50%)	
<b>Permanenthypoparathyroidism</b>			
Negative	20(100%)	19(95%)	.311
Positive	0(0%)	1(5%)	

- No deaths were recorded.
- Transient LRN paralysis occurred in one patient in group 1(5%) and in two patients in group 2(10%), Paralysis rate was slightly higher ingroup 2 with insignificant relation between two groups.
- No cases recorded with Permanent paralysis in the two groups
- Transient postoperative hypoparathyroidism occurred in four patient in group 1(20%) and in five patients in group 2(25%). the incidence was slightly higher in group 2 with insignificant relation between two groups.
- Permanent hypoparathyroidism developed in one patient (5%) in group 2 with insignificant relation between two groups.

**Discussion**

The benefits of prophylactic central compartment lymph node dissection (PCND) in papillary thyroid cancer (PTC) are still under investigation. This treatment seems to reduce PTC recurrence/mortality rates but has a higher risk of surgical complications. The lack of prospective randomized trials does not allow definitive recommendations (Viola, D. et al., 2015).

In our study, extracapsular spread (ECS), multifocality and tumor size more than 1 cm were associated with more CLN metastases with significant relation between two groups.

In a study by (Bae KH et al., 2015) they concluded that Central neck metastasis is associated with younger age, larger tumor, lymphovascular invasion, and lateral lymph node metastasis in small (T1/T2) PTC patients. They recommended prophylactic

central lymph node dissection in patients with these risk factors.

In our study histological examination showed the presence of central compartment metastatic nodes in 40% of group 2 patients (therapeutic CND) and 20% of group 1 patients (prophylactic CND). This result is consistent with previous data that 21% of patients with an apparently healthy central compartment tested positive at histology (Palestini, N. et al., 2008). And in other studies, the rates ranged from 38% to 71% (Lee YS et al., 2007).

Also a study by (Ducoudray, R. et al., 2013) have found that prophylactic CND modified the indication for radio-iodine therapy and confirmed the feasibility and relatively acceptable safety of prophylactic LN dissection. The overall complication rate of permanent hypoparathyroidism was (2%) and RLN injury (0.5%).

Advantage of PCND is a reduced necessity to repeat  $^{131}\text{I}$  treatments and that only histological study of the lymph nodes most commonly affected by metastases will permit an accurate staging of the disease that will be useful for planning therapeutic strategy and follow-up. Lastly, surgical management of recurrences of disease in the central compartment is problematic owing to cicatricial fusion of tissues but the disadvantage was a higher prevalence of permanent hypoparathyroidism. (Roh J-L et al., 2007).

An analysis of our data shows that transient LRN paralysis rate was slightly higher in group 2 (9% versus 10%) with insignificant relation between two groups. no cases recorded with permanent paralysis in the two groups

Transient postoperative hypoparathyroidism was slightly higher in group 2 (20% versus 20%). with insignificant relation between two groups. permanent hypoparathyroidism developed only in one patient (9%) in group 2 with insignificant relation between two groups.

This finding agrees with data from study by (Palestini, N et al., 2008) which reported that none of the patients in either group A (therapeutic CND) or group B (prophylactic CND) reported permanent laryngeal recurrent nerve paralysis. Transient laryngeal recurrent nerve paralysis occurred most often in group A patients (5.8% versus 0.8%). None of the patients in either group A or group B developed permanent hypoparathyroidism. Transient hypoparathyroidism was highest in group A patients (31% versus 27%).

### Conclusion

Finally we can conclude that therapeutic and prophylactic modalities CND are an important adjunct to total thyroidectomy for the treatment of PTC. CND helps in reducing local recurrence (occult metastases reached 40%) and probably the need for radioiodine ablation. Also there is no significant difference in the complication rate when performed by trained surgeons.

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