Original Research Article

DOI: https://dx.doi.org/10.18203/2349-2902.isj20214084

Surgical management of papillary thyroid carcinoma

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Received: 26 September 2021 Revised: 10 October 2021 Accepted: 11 October 2021

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ABSTRACT

Background: Papillary thyroid carcinoma (PTC) is the most prevailing thyroid cancer but remains of a favorable prognosis. Thyroidectomy with excision of all positive cervical nodes remains the cornerstone of the management PTC. The role for prophylactic central neck dissection (PCND) remains controversial.

Methods: A prospective non randomised open label study of 20 PTC patients, 8 of them underwent total thyroidectomy with PCND and 12 underwent total thyroidectomy with modified radical neck dissection type III in El Zahraa hospital, Azhar university, and Damanhour oncology center, Egypt starting from September 2019 to August 2021. The incidence of central lymph node metastasis in N0 cases underwent PCND were reported, the relationship between lymph node metastasis with lympho-vascular permeation and capsular invasion, were analysed and sensitivity of fine needle aspiration cytology in diagnosis of PTC was reported.

Results: Occult central lymph node metastasis was observed in 62.5% of PTC lesions. The FNAC showed a sensitivity of 85%. Lympho-vascular permeation and capsular invasion showed a sensitivity of 94.12% and 58.82%, respectively for lymph nodes metastasis. Thyroiditis is detected in 50% of cases with PTC. Postoperative ablative dose of radioactive iodine 131 (RAI-131) ranged from 80 to 100 millicurie.

Conclusions: R0 resection is mandatory to cure PTC. PCND remains a debatable issue, that needs a large multicentre study with large sample of patients with long term follow up to ascertain the efficacy of PCND in reducing rate of local recurrence, morbidity and mortality.

Keywords: Papillary thyroid carcinoma, Thyroidectomy, Prophylactic neck dissection

INTRODUCTION

Papillary thyroid carcinoma (PTC), the most prevailing thyroid cancer, has the highest increase in incidence of any cancer and is postulated to soon become the third most common cancer among women. Despite this incremental increase in its incidence rate, PTC largely remains of a favorable prognosis, with most patients having a 5-year overall survival rate well above 90%. Thyroid cancers account for about 1.5% of adulthood carcinomas and 3% of all cancers in children. In females, however, thyroid cancers are the fifth most common cancer, comprising 6% of all cases; In addition, the

incidence of the new cases has been increasing recently. Furthermore, papillary cancer account for 74-80% of all thyroid cancers. Additionally, thyroid cancer's incidence in females compared to males is about 3-1.²

In contrast to many other cancers, thyroid cancer is almost always curable. Most thyroid cancers grow slowly and are associated with a very favorable prognosis. The mean survival rate after 10 years is higher than 90%, and is 100% in very young patients with minimal non-metastatic disease. Distant spread (i.e., to lungs or bones) is rare.³ For the diagnosis of this cancer the following investigations should be considered thyroid function

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studies, neck ultrasound, ultrasound guided fine-needle aspiration cytology (FNAC); moreover, for staging purpose computerized tomography scans can be requested. Afterwards, theses relevant workup should be discussed in the head and neck multidisciplinary team (MDT) for the decision about the treatment plan.⁴

In terms of the management, adequate surgery remain the mainstay of treatment with lymph node dissection in clinically and radiologically node positive cases; nevertheless, there is a debate about the survival benefit of prophylactic central compartment lymph node dissection.⁵ Given the fact that lymph node metastases are commonly observed, additionally in about 90% of the cases micro-metastases are reported; therefore, careful preoperative and intraoperative assessment of the central and ipsilateral cervical lymph nodes compartments is crucial.⁶ Thereafter, the patient should be subjected to further evaluation to decide the need for further treatment using radioactive iodine with/without thyroid stimulating hormone (TSH) suppression according to the American thyroid association (ATA) guidelines; furthermore, active surveillance and follow-up is highly recommended.

Aim of the study

The aim was to identify best surgical management of different types of PTC including total thyroidectomy with/without cervical lymph nodes dissection.

METHODS

A prospective non randomised open label study of a total of 20 patients who were diagnosed with PTC were treated in El Zahraa university hospital, Azhar university, and Damanhour oncology center between September 2019 and August 2021. All the patients were pathologically diagnosed as PTC. Patients were divided into two groups, group one of 8 patients with clinically node negative status, and group two of 12 patients with clinically positive lymph node status. There were 11 male patients and 9 female patients. Their age ranged from 19 to 71 years with a mean age of 36.05±14.05 years (Table 1).

Inclusion criteria

Patients with resectable PTC were included in the study.

Exclusion criteria

Patients with other types of thyroid carcinomas, previously irradiated neck, previous neck surgeries or scaring, morbidly obese patients and patients with any physical or psychiatric condition that could impair patient's ability to cooperate with postoperative data collection were excluded from the study.

Ethical consideration

An informed consent was obtained from the patient concerning the complication of the procedure, the complication of the radioactive material, and the acceptance to be enrolled in the study.

Preoperative Ultrasonography was performed in all 20 patients to determine the lymph node status and tumor characteristics and using the American college of radiology-thyroid imaging reporting and data system (ACR TI-RADS) to identify candidates for FNAC; afterwards we used the Bethesda system to plan for the surgical procedures.

Regarding surgery, 8 patients with N0 status were surgically managed with total thyroidectomy with PCND and 12 patients with N1b status were surgically managed with total thyroidectomy with central compartment nodes dissection and modified radical neck dissection type III.

Patient preparation (pre-operative preparation)

Laboratory investigations were requested including T3, T4, T.S.H, complete blood count, prothrombin time and INR, serum urea, serum creatinine, random blood sugar, and chest X-Ray. Additionally, HBA 1 C was assessed in diabetic patients and patients with abnormal results were referred to endocrinologist for proper control of blood sugar. Besides an assessment of patients' performance status were conducted prior to anesthesia consultation.

Intra-operative preparation and operative procedure

All the procedures were done under general anesthesia with patient in supine position with neck extension. Total thyroidectomy with bilateral PCND was performed for clinically and radiologically node negative PTC patients.

Key steps in the procedure are: Identification and ligation of the upper pole after saving the external laryngeal nerve, identification of and saving of superior and inferior parathyroid glands after ligation of the tertiary branches of inferior thyroid artery to prevent compromising the blood supply of the parathyroid and identification of the recurrent laryngeal nerve (RLN) prior ligation of the branches of the inferior thyroid artery; therefore, we have used some anatomic landmarks to assist us in identification of the RLN. The tubercle of Zuckerkandl marks the posterolateral aspect of the thyroid lobe and is most often we found it lateral to the recurrent laryngeal nerve (Figure 1).

Afterwards, we proceed to bilateral PCND through following and clearing the whole course of the RLN and trachea till the suprasternal notch, excising the group VI cervical lymph nodes (Figure 2).



Figure 1: Right recurrent laryngeal nerve.

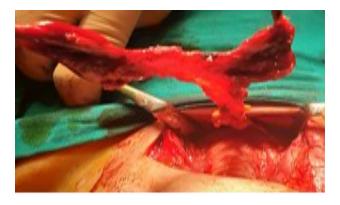


Figure 2: The whole thyroid gland excised with the level 6 group of lymph nodes.

Total thyroidectomy with central compartment nodes dissection and modified radical neck dissection type III was performed for patients with node positive status. We start with MRND first using extended thyroid incision using the usual curvilinear incision of thyroidectomy till the tip of the ipsilateral mastoid process along the anterior border of the sternocleidomastoid muscle.

Key steps in MRND type III are: Raising the skin flaps in sub-platysemal plane to save the marginal mandibular nerve in the upper flap; additionally, extra care is used when elevating the lower flap in close proximity of the accessory spinal nerve where we use a blade along its course on dissecting the lower flap.

Proper exposure of the four areas of special attention, Lower end of internal jugular vein, Upper end of internal jugular vein, Junction of lateral border of clavicle with lower edge of trapezius and Submandibular triangle where the malignant disease can lurk.

Identification of the accessory spinal nerve at two points, the first one at its origin deep to the upper end of the sternocleidomastoid muscle and close to the upper end of the internal jugular vein. The second point 1 cm below the Erb's point, the point where the great auricular nerve winds from behind the muscle on its route to supply the skin over the parotid gland at the junction of the upper third and lower two-thirds of the sternocleidomastoid, the accessory nerve is identified as it runs in a caudo-lateral

direction to the anterior border of the trapezius using dissecting scissor and bipolar cautery (Figure 3).

Dissection of the facial coverings of the internal jugular vein, carotid artery and saving the vagus nerve (Figure 4).

Identification and ligation of thoracic duct on the left side and right jugular lymph duct trunk on the right side. Which is identified at the angle between the internal jugular vein, subclavian vein and the clavicle. Mostly, it was found to pass medial to the jugular vein, then posterior to it and finally curves around to enter the junction of the internal jugular and subclavian vein. Once identified we transfix it with some surrounding fat using proline 3/0 stitch (Figure 5).



Figure 3: The right accessory spinal nerve.



Figure 4: The right vagus nerve posterior to the internal jugular vein and common carotid artery.



Figure 5: The thoracic duct transfixed.

Once thoracic duct transfixed, we continue dissection delivering the specimen, including the scalene nodes

situated in the Chaissaignac's triangle, which is defined as the triangle between where the longus coli and scalenus anterior attach to the carotid tubercle of C6 with the subclavian artery, through the tunnel under the sternomastoid to the posterior triangle where we proceed to further neck dissection for group V of neck nodes.

Clearing the posterior triangle from whole fatty content without breaching the prevertebral fascia to preserve the phrenic nerve, overlying the scalenus anterior muscle, and the brachial plexus, emerging between the scalenus anterior and scalenus Medius muscles (Figure 6).

Proper hemostasis and closure with suction drain in layers.



Figure 6: The left phrenic nerve deep to the prevertebral fascia running on scalenous anterior muscle.

Post-operative care

The patient was transferred to ward and vital signs obtained, normal diet allowed after complete recovery, post-operatively, the patient stays inpatient for one day in case of thyroidectomy only and two days in case of thyroidectomy with MRND. All the patients were positioned in semi setting position.

Patients were carefully observed in the postoperative period for the incidence of the following complications: Dyspnea and stridor, bleeding and hematoma formation, hypocalcemia, voice changes, seroma, surgical site infection, Chyle leak, limited shoulder mobility and neck, shoulder and arm paresthesia.

Post-operative corrected and ionized calcium was requested in case of postoperative tetany or numbness; no antibiotics were prescribed in the postoperative period for all patients. Post-operative analgesia was only paracetamol tablets. All patients were instructed to start feeding in the immediate postoperative period.

The suction drain was removed after 24 hours in thyroidectomy only patients and after an average of four days in case of thyroidectomy with MRND. Complete wound healing is expected one-week post-operative.

The next step in the management is determining patient need for RAI-131 ablation. All of the gentlemen and ladies that were recruited in the study were not prescribed post-operative levothyroxine, to keep the patient on the hypothyroid side to prepare him for the post-operative whole-body scan to detect any residual of the malignant disease. The whole-body scan was performed using RAI-131 in a dose of 5 mci in a period ranged from 21 to 28 days according the result of TSH. Afterwards; all of our patients received an ablative dose of RAI-131 according to the postoperative histopathological result.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, SD, median and interquartile range (IQR).

RESULTS

Radiologically, 6 patients were diagnosed as solitary nodule of thyroid, while 14 patients were diagnosed as multinodular goiter. Furthermore, their TI-RADS category ranged from 3 to 5 (Table 1).

Table 1: Demographic data and clinical features.

Variables	N	%
Gender		
Male	11	55
Female	9	45
Total	20	100
Age (years)		
Min-max	19-71	
Mean±SD	36.05±14.05	
Median (IQR)	34.5 (25-41.50)	
Multifocality		
Solitary thyroid	6	30
nodule	0	30
Multinodular goitre	14	70
TI-RADS category		
3	2	10
4	5	25
5	13	65
Procedure		
Total thyroidectomy	8	40
with PCND	o	40
Total thyroidectomy		
with CLND and	. 12	60
MRND type III		
Complications	Procedure	
Mild transient	Total thyroidectomy	5
hypocalcaemia	with PCND	3
Neck and left	Total thyroidectomy	
shoulder paresthesia	with CLND and	5
shoulder paresulesia	MRND	

The FNAC results were consistent with PTC in 17 patients, suspicious for malignancy (papillary carcinoma) in 2 patients and atypical follicular neoplasm (suspicious of papillary carcinoma) in only 1 patient. Consequently, on correlation with the postoperative pathology in which all the patient diagnosis was PTC, the FNAC showed a sensitivity of 85% (Table 2).

Table 2: Distribution of the studied cases according to pre-operative FNAC and post-op pathology, (n=20).

Variables	Pre-op FNAC		Post-op pathology	
	No.	%	No.	%
Papillary carcinoma	17	85	20	10
Suspicious smear for malignancy (papillary carcinoma)	2	10	0	0
Atypical follicular lesion (suspicious of papillary carcinoma)	1	5	0	0
Total	20	100	20	100

Sensitivity: 17/20 (85.0%)

Meanwhile, postoperatively one patient, after total thyroidectomy with PCND, suffered from mild transient hypocalcaemia and one more patient, after total thyroidectomy, central lymph nodes dissection (CLND), and MRND, has suffered from neck and left shoulder numbness and paresthesia (Table 1).

Interestingly, the postoperative histopathological results in 10 patients showed thyroiditis in association of PTC; however, no histopathological signs of thyroiditis were detected in the other 10 patients.

The total number of cervical lymph nodes retrieved ranged from 3.0 to 42.0 with a mean of 16.90 ± 11.95 . Furthermore, the number of positive nodes ranged from 0.0 to 23.0 with a mean of 5.25 ± 5.41 (Table 3).

PCND was performed for 8 cases. Surprisingly, on review of the postoperative histopathological reports 5 specimens (62.5%) were positive for nodal metastasis. The no. of total nodes excised has ranged from 3-13 with

a mean of 6.38±3.20; furthermore, no. of positive nodes ranged from 0-7 with a mean of 2.25±2.49 (Table 3).

On review of the histopathological reports, Lymphovascular permeation was positive in 16 case (94.1%) with positive nodal metastasis and negative in 1 case (5.9%); however, it was positive in 2 cases (66.7%); with negative nodal metastasis and negative in 1 case (33.3%). Therefore, the lympho-vascular permeation showed sensitivity, specificity, positive predictive value and negative predictive value and accuracy of 94.12%, 33.33%, 88.89%, 50%, 85%, respectively for nodal metastasis (Table 4).

Table 3: Descriptive analysis of the studied cases according to number of total nodes retrieved and number of positive nodes (n=20), and results of PCND, (n=8).

Variables	Min- Max	Mean±SD	Median (IQR)			
Total nodes retrieved	3-42	16.90±11.95	16 (7-27)			
Positive nodes	0-23	5.25±5.41	3.50 (1.50-8)			
Central group nodal metastasis in N0 group						
Total no. of cases	8					
Presence of	5/8					
positive nodes	(62.5%)					
No. of positive nodes	0-7	2.25±2.49				
Total nodes	3-13	6.38±3.20				

On other hand, the capsular invasion was positive in 12 patients (60%) and negative 8 patients (40%). Capsular invasion was positive in 10 cases (58.8%) with positive nodal metastasis and negative 7 cases (41.2%); nevertheless, it was positive in 2 cases (66.7%); with negative nodal metastasis and negative in 1 case (33.3%). Therefore, it showed sensitivity, specificity, positive predictive and negative predictive value and accuracy of 58.82%, 33.33%, 83.33%, 12.50%, 55%, respectively for nodal metastasis (Table 4).

Table 4: Relation between positive nodes or nodal metastasis with lympho-vascular permeation and relation between positive nodes or nodal metastasis with capsular invasion.

	Positive nodes or nodal metastasis								
Variables	Negat	Negative, (n=3) Posit		ve, (n=17)	Sensitivity	Specificity	PPV	NPV	Accuracy
	N	%	N	%					
Lympho-vascular permeation									
Negative	1	33.3	1	5.9	94.12	33.33	88.89	50	85
Positive	2	66.7	16	94.1					
χ^2 (FEp)	2.135 (0.284)								
Capsular invasion									
Negative	1	33.3	7	41.2	58.82	33.33	83.33	12.50	55
Positive	2	66.7	10	58.8					
χ^2 (FEp)	0.065 (1.000)								
2									

 χ^2 : Chi square test, FE: Fisher exact, p: P value for comparing between the studied groups, PPV: Positive predictive value, NPV: Negative predictive value.

In this study all of the patients have received postoperative ablative dose of RAI-131. Three patients (15%), node negative, received 80 millicurie (mci) and seventeen patients (85%), node positive, received 100 mci.

DISCUSSION

There is no debate that R0 resection is the mainstay of treatment for differentiated thyroid cancer. The present study included 20 patients, 11 male patients (55%) and 9 female patients. Lorenz et al reported that female is more liable to differentiated thyroid carcinoma than male. The prevalence of PTC in a thyroid gland with solitary nodule was 30% and in multinodular goitre was 70%. According to Brito et al thyroid cancer may be less frequent in multinodular goiter (MNG) compared to solitary nodule (SN); additionally, Li et al noted that the reported prevalence of multifocal PTC ranges from 18% to 87%. 9,10

In the present study, the FNAC sensitivity to diagnose malignancy was found to be 85%. On the other hand, Hajmanoochehr et al reported that the FNAC sensitivity was found to be 95.2%. ¹¹ The incidence of PTC with thyroiditis was 50% in our study; nonetheless, Lai et al reported that the mean rate of PTC among patients with Hashimoto thyroiditis (HT) was 40.11%. ¹²

In our study the total number of cervical lymph nodes retrieved has ranged from 3 to 42 with a median of 16 (7-27); nevertheless, Albuja-Cruz reported that the median number of lymph nodes removed during MRND for the entire cohort was 21 (range, 2-86).¹³

In the current study, PCND showed positive central lymph nodes metastasis in 62.5% of the N0 group, and the mean of the number of positive nodes was 2.25±2.49. Sun et al noted that central lymph node metastasis (CLNM) is observed in 20-90% of patient; moreover, he reported that the American thyroid association guidelines recommend that routine PCND should be performed only in patients with advanced T3 and T4 primary tumors. Furthermore, Lie et al noted positive CLNM in 53.7% of N0 patients underwent PCND. ^{16,17}

The histopathological reports showed that the lymphovascular permeation (LVP) was positive in 90% and was negative in 10% of patients, and it was positive in 94.1% and 66.7% in cases with positive nodal metastasis and cases with negative nodal metastasis respectively.

Albuja-Cruz et al reported that lympho-vascular invasion was 62%; however, Atakan et al reported lympho-vascular invasion in 18.79% of cases and it was positive in 69.8% and 30.2% in cases with positive nodal metastasis and cases with negative nodal metastasis respectively. Moreover, he noted that the lymph node metastasis was significantly more common in LVP (+) group compared to LVP (-) group and the risk was 30.61

times greater in LVI (+). Additionally, Mao et al noted that vascular invasion has been reported to increase in the relative percentage of lymph node metastasis in patients with PTC. ¹⁵

Furthermore, in our study the capsular invasion was positive in 60% and negative 40% of cases, and it was positive and negative in 58.8% and 41.2% of cases with positive nodal metastasis respectively; nevertheless, it was positive and negative in 66.7% and 33.3% in cases with negative nodal metastasis respectively. Atakan et al reported capsular invasions in 32% of cases. ¹⁴ According to Sun et al capsular invasion carries an increased risk of central lymph nodes metastasis; on the other hand, Mao et al reported that capsular invasion is a significant risk factor for nodal metastasis. ^{15,16}

All of the patients included in this study have received post-operative ablative dose of RAI-131, 15% received 80 mci and 85% received 100 mci. Notably, Andresen et al reported that the effective ablative doe of RAI-131 ranges from 30 mci to 100 mci with equivalent ablation rates (85-90%). 18

Limitations

A limitation of this study was that it was of relatively small sample size. It would be beneficial to conduct another study on larger number of patients.

CONCLUSION

Surgical management of PTC is the best chance for cure of the disease; however, R0 resection is mandatory to cure PTC. PCND remains a debatable issue that needs a large multicenter study with large sample of patients with long term follow up to ascertain the efficacy of PCND in reducing rate of local recurrence, morbidity and mortality. Additionally, correlation between different parameter like tumor size, tumor location, lymphovascular and capsular invasion, and incidence of central nodal metastasis. Finally, surgical experience and proper knowledge of the anatomy and its anomalies is crucial to reduce the rate of post thyroidectomy and neck dissection complications.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

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Cite this article as: Elgamal WM, Ragheb RA, Elsharkawy A. Surgical management of papillary thyroid carcinoma. Int Surg J 2021;8:3231-7.