



OUTCOMES AND EFFECTIVENESS OF SURGICAL MANAGEMENT FOR PAPILLARY THYROID CANCER: A PROSPECTIVE STUDY

Muhammad Aijaz^{1*}, Jetha Yogal Kumar², Simran³, Shafein Jatoi⁴, Muhammad Wassam⁵, Hafiz Waqas Ahmed⁶, Neha Kumari⁷, Yokta Mukhi⁸

^{1*,2,4} House Officer, Abbasi Shaheed Hospital, Karachi, Pakistan.

³House Officer, Dow University Hospital, Karachi, Pakistan.

⁵Year MBBS Student, Al Tibri Medical College, Isra University, Karachi, Pakistan.

⁶Consultant General Surgery, Al Tibri Medical College and Hospital, Karachi, Pakistan.

⁷MBBS Student, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan

⁸MBBS Student, Al Tibri Medical College, Isra University, Karachi, Pakistan

***Corresponding Author:** Muhammad Aijaz,

* Email: muhammd.aijaz8799@gmail.com

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 of papillary thyroid carcinoma (PTC). The role for prophylactic central neck dissection (PCND) remains controversial.

Objectives: The aim of this study is to determine the optimal surgical approach for managing papillary thyroid carcinoma (PTC), specifically evaluating the effectiveness of total thyroidectomy with or without cervical lymph node dissection and investigating the role of prophylactic central neck dissection in improving patient outcomes.

Study place and duration: The study was conducted at Abbasi Shaheed hospital between August 2023 and June 2024.

Methodology: A prospective non randomised open label study of 20 papillary thyroid carcinoma patients, 8 of them underwent total thyroidectomy with prophylactic central neck dissection (PCND) and 12 underwent total thyroidectomy with modified radical neck dissection. This study reported on the incidence of central lymph node metastasis in clinically node-negative (N0) patients who underwent prophylactic central neck dissection (PCND). It also analyzed the correlation between lymph node metastasis and factors such as lymphovascular invasion and capsular invasion. Additionally, the sensitivity of fine-needle aspiration cytology in diagnosing papillary thyroid carcinoma (PTC) was evaluated.

Results: Occult central lymph node metastasis was observed in 62.5% of papillary thyroid carcinoma (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 papillary thyroid carcinoma (PTC). **Conclusions:** The study concluded that resection is mandatory to cure papillary thyroid carcinoma. Prophylactic central neck dissection 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 (PTC), Thyroidectomy, Prophylactic neck dissection (PCND), metastasis.

INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer, with a rapidly rising incidence rate that's expected to make it the third most common cancer among women. Despite its increasing prevalence, papillary thyroid carcinoma generally has a favorable prognosis, with a 5-year survival rate exceeding 90% for most patients [1]. Thyroid cancers account for a relatively small percentage of adult cancers (1.5%) and childhood cancers (3%), but they're more common in women, ranking as the fifth most common cancer type among females, making up around 6% of all cases. The incidence of new cases of thyroid cancer has been on the rise in recent times. Notably, papillary cancer accounts for approximately 74-80% of all thyroid cancer cases. Moreover, thyroid cancer exhibits a significant gender disparity, with females being roughly three times more likely to be diagnosed than males [2].

In contrast to many other cancers, thyroid cancer is typically highly treatable and often curable. These cancers usually grow slowly and have a very positive outlook. Patients often have a high survival rate exceeding 90% over a 10-year period. For young patients with early-stage disease that hasn't spread, the survival rate is often 100%. Fortunately, distant metastasis to organs like the lungs or bones is uncommon [3,4]. To diagnose thyroid cancer, the following tests are typically considered, thyroid function tests, neck ultrasound, and ultrasound-guided fine-needle aspiration cytology (FNAC). Additionally, CT scans may be used for staging purposes. Once the diagnostic workup is complete, the case should be reviewed by a multidisciplinary team (MDT) specializing in head and neck cancers to determine the best course of treatment. Effective management of thyroid cancer primarily involves surgery, which may include lymph node dissection for patients with clinically or radiologically evident lymph node involvement [5]. However, the benefits of prophylactic central compartment lymph node dissection (PCND) are still debated. Given the high incidence of lymph node metastases and micrometastases (reported in approximately 90% of cases) thorough preoperative and intraoperative evaluation of central and ipsilateral cervical lymph node compartments is essential [6]. Following surgery, patients should undergo further assessment to determine the need for additional treatments, such as radioactive iodine therapy and thyroid-stimulating hormone (TSH) suppression, in accordance with American Thyroid Association (ATA) guidelines. Ongoing surveillance and follow-up are also crucial components of care [7].

The study aimed to show that prophylactic central neck dissection may be beneficial in reducing local recurrence and improving outcomes in papillary thyroid carcinoma patients, particularly those with high-risk features such as lymphovascular invasion and capsular invasion. The study also identified predictive factors for lymph node metastasis and evaluate the effectiveness of fine-needle aspiration cytology (FNAC) in diagnosing papillary thyroid carcinoma (PTC).

OBJECTIVE OF STUDY

The objective of the study is to determine the optimal surgical approach for managing various types of papillary thyroid carcinoma (PTC), specifically total thyroidectomy with or without cervical lymph node dissection.

METHODOLOGY

This study included 20 patients with papillary thyroid carcinoma (PTC) treated at Abbasi Shaheed Hospital between August 2023 and June 2024. All patients had a confirmed pathological diagnosis of papillary thyroid carcinoma (PTC). They were divided into two groups: one with 8 patients who had no clinical evidence of lymph node involvement and another with 12 patients who had clinically apparent lymph node involvement. The patient group consisted of 11 males and 9 females, with ages ranging from 19 to 71 years and an average age of 36.05 years.

Preoperative laboratory tests included T3, T4, TSH, complete blood count, prothrombin time, INR, serum urea, creatinine, random blood sugar and chest X-ray. Diabetic patients underwent HbA1c assessment and those with abnormal results were referred to an endocrinologist for blood sugar management. Patients' performance status was evaluated before anesthesia consultation. For patients with node-positive status, total thyroidectomy was performed along with central compartment node dissection and modified radical neck dissection (MRND). Following surgery, patients underwent evaluation for radioactive iodine (RAI-131) ablation. None of the patients received post-operative levothyroxine, instead being kept in a hypothyroid state to facilitate a whole-body scan for detecting residual malignant disease. The scan was performed 21-28 days postoperatively, once TSH levels were suitable.

Inclusion & Exclusion Criteria

The study included patients with resectable papillary thyroid carcinoma (PTC). Patients were excluded if they had other types of thyroid cancer, previous neck radiation or surgery, significant neck scarring, morbid obesity or any physical /psychiatric condition that would hinder their ability to participate in postoperative follow-up.

Ethical Approval

The study was approved by Institute of review board of Abbasi shaheed Hospital. 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.

Statistical Analysis

Data was analyzed by using IBM SPSS software package version 20.0. Qualitative data were described using number and percentage. Quantitative data were described using range (minimum and maximum), mean, standard deviation, 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 (Thyroid Imaging Reporting and Data System) ranged from 3 to 5 (Table 1).

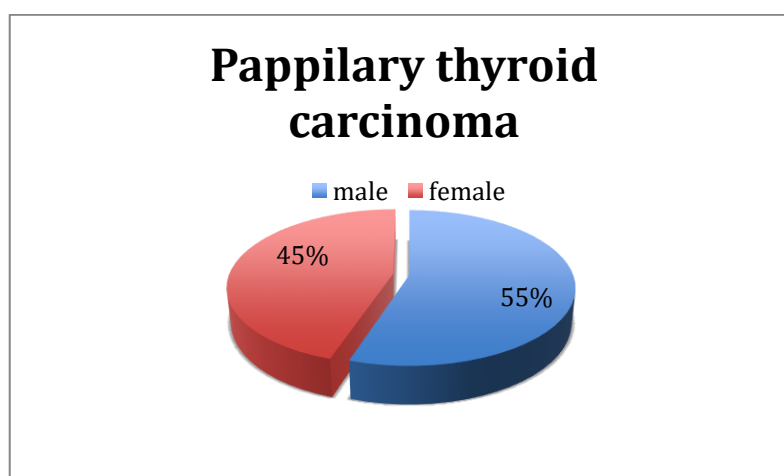


Fig 1 showed the gender distribution of papillary thyroid carcinoma

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 nodule	6	30
Multinodular goitre	14	70
TI-RADS category		
3 (Mild Suspicious)	2	10
4 (Mod Suspicious)	5	25
5 (Highly Suspicious)	13	65
Procedure		
Total thyroidectomy with PCND	8	40
Total thyroidectomy with CLND and MRND type III	12	60
Complications	Procedure	
Mild transient hypocalcaemia	Total thyroidectomy with PCND	5
Neck and left shoulder paresthesia	Total thyroidectomy with CLND and MRND	5

Fine-needle aspiration cytology (FNAC) results were consistent with papillary thyroid carcinoma (PTC) in 17 patients, suspicious for malignancy in 2 patients and atypical follicular neoplasm suggestive of PTC in 1 patient. When compared to postoperative pathology, which confirmed PTC in all patients, the FNAC demonstrated 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

Meanwhile, postoperatively one patient, after total thyroidectomy with PCND suffered from mild transient hypocalcaemia and one more patient after total thyroidectomy with central lymph nodes dissection (CLND) and Modified Radical Neck Dissection (MRND) has suffered from neck and left

shoulder numbness , paresthesia (Table 1).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)

Lymphovascular permeation was positive in 94.1% of cases with positive nodal metastasis and 66.7% of cases with negative nodal metastasis. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of lymphovascular permeation for nodal metastasis were 94.12%, 33.33%, 88.89%, 50%, and 85%, respectively(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 \pm 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 grp			
Total no. of cases	8		
Presence of positive nodes	5/8 (62.5%)		
No. of positive nodes	0-7	2.25 ± 2.49	
Total nodes	3-13	6.38 ± 3.2	

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

Variables	Positive nodes or nodal metastasis				Sensitivity	Specificity	PPV	NPV	Accuracy
	Negative, (n=3)		Positive, (n=17)						
	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 (FE, p)	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 (FE, p)	0.065 (1.000)								

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.

DISCUSSION

Complete resection (RO) is widely accepted as the primary treatment for differentiated thyroid cancer. In our study of 20 patients, 55% were male and 45% were female, contrasting with findings by Lorenz et al that suggest a higher incidence in females. We found PTC prevalence to be 30% in thyroid glands with solitary nodules and 70% in multinodular goiters. However, Brito et al suggest that thyroid cancer may be less common in multinodular goiter compared to solitary nodules. According to Li et al, the prevalence of multifocal PTC has been reported to range from 18% to 87%[9,10].

In our study, fine-needle aspiration cytology (FNAC) had a sensitivity of 85% in diagnosing

malignancy, whereas Hajmanoochehri et al reported a higher sensitivity of 95.2% [11]. We also found that 50% of PTC cases were associated with thyroiditis, compared to a reported mean rate of 40.11% among patients with Hashimoto thyroiditis (HT) [12].

In our study, the total number of cervical lymph nodes removed ranged from 3 to 42, with a median of 16. In comparison, Albuja-Cruz reported a median of 21 lymph nodes removed during modified radical neck dissection (MRND), with a range of 2 to 86 [13]. In our study, 62.5% of clinically node-negative (N0) patients who underwent prophylactic central neck dissection (PCND) had positive central lymph node metastases, with a mean of 2.25 positive nodes[14].

According to Sun et al, central lymph node metastasis occurs in 20-90% of patients and the American Thyroid Association recommends routine PCND only for patients with advanced tumors (T3 and T4). Similarly, Liu et al found positive central lymph node metastases in 53.7% of clinically node-negative (N0) patients who underwent PCND[15,16]. According to Albuja-Cruz et al, lymphovascular invasion was observed in 62% of cases. In contrast, Atakan et al reported that a lower incidence of lymphovascular invasion, affecting 18.79% of cases. Notably, when examining the correlation between lymphovascular invasion and nodal metastasis, Atakan et al found that lymphovascular invasion was present in 69.8% of cases with positive nodal metastasis and 30.2% of cases with negative nodal metastasis[12]. Atakan et al also found that lymph node metastasis was significantly more common in the lymphovascular permeation (LVP) positive group compared to the LVP negative group, with a 30.61 times higher risk in the LVP positive group. Similarly, Mao et al reported that vascular invasion increases the relative percentage of lymph node metastasis in patients with papillary thyroid carcinoma (PTC) [13].

In our study, capsular invasion was present in 60% of cases and absent in 40%. Among cases with positive nodal metastasis, 58.8% had capsular invasion and 41.2% did not. In contrast, among cases with negative nodal metastasis, 66.7% had capsular invasion and 33.3% did not. Atakan et al reported a lower incidence of capsular invasion at 32%. According to Sun et al and Mao et al, capsular invasion is associated with an increased risk of central lymph node metastasis and is a significant risk factor for nodal metastasis[17].

CONCLUSIONS

The study concluded that surgical management offers the best chance for a cure in papillary thyroid cancer (PTC), with complete (R0) resection being essential for effective treatment. The role of prophylactic central neck dissection (PCND) remains a topic of debate, necessitating large-scale, multicenter studies with long-term follow-up to determine its impact on local recurrence, morbidity and mortality rates. Analyzing the relationship between factors such as tumor size, location, lymphovascular invasion, capsular invasion and central lymph node metastasis can provide valuable insights. Ultimately, surgeon expertise and thorough understanding of anatomy and potential variations are critical in minimizing complications following thyroidectomy and neck dissection.

REFERENCES

1. Spinelli C, Strambi S, Bakkar S, Nosiglia A, Elia GM, Bertocchini A et al. Surgical Management of Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma. Experience in 25 Patients. *World J Surg.* 2021;44(1):155-62. Uchino S, Ishikawa H, Miyauchi A, Hirokawa M, Noguchi S, Ushima M et al. Age- and Gender Specific Risk of Thyroid Cancer in Patients with Familial Adenomatous Polyposis. *J Clin Endocrinol Metab.* 2019;101(12):4611-7.
2. Ito Y, Miyauchi A, Kihara M, Fukushima M, Higashiyama T, Miya A. Overall Survival of Papillary Thyroid Carcinoma Patients: A Single- Institution Long-Term Follow-Up of 5897 Patients. *World J Surg.* 2018;42:615-22.
3. National comprehensive cancer network (NCCN) guidelines version 2, 2021. Thyroid carcinoma- papillary carcinoma. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed on 05 March 2021.
4. Conzo G, Tartaglia E, Avenia N, Calò PG, De Bellis A, Esposito K et al. Role of prophylactic central compartment lymph node dissection in clinically N0 differentiated thyroid cancer patients:

- analysis of risk factors and review of modern trends. *World J Surg Oncol*. 2016;14:149.
5. Attard A, Paladino NC, Lo Monte AI, Falco N, Melfa G, Rotolo G et al. Skip metastases to lateral cervical lymph nodes in differentiated thyroid cancer: a systematic review. *BMC Surg*. 2019;18(1):112.
6. Haugen BR, Alexander EK, Bible KC, Doherty GM. American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*. 2016;26(1):1-133.
7. Lorenz K, Schneider R, Elwerr M. Thyroid Carcinoma: Do We Need to Treat Men and Women Differently. *Visc Med*. 2020;36:10-3.
8. Brito JP, Yarur AJ, Prokop LJ, McIver B, Murad MH, Montori VM. Prevalence of Thyroid Cancer in Multinodular Goiter versus Single Nodule: A Systematic Review and Meta-Analysis. *THYROID*. 2013;23(4):449-55.
9. Li G, Lei J, You J, Jiang K, Li Z. Independent predictors and lymph node metastasis characteristics of multifocal papillary thyroid cancer. *Medicine*. 2018;97:5(e9619).
10. Hajmanoochehri F, Rabiee E. FNAC accuracy in diagnosis of thyroid neoplasms considering all diagnostic categories of the Bethesda reporting system: A single-institute experience. *J Cytol*. 2015;32(4):238-43.
11. Lai X, Xia Y, Zhang B, Li J, Jiang Y. A meta- analysis of Hashimoto's thyroiditis and papillary thyroid carcinoma risk. *Oncotarget*. 2017;8(37):62414-24.
12. Albuja-Cruz MB, Thorson CM, Allan BJ, Lew JJ, Rodgers SE. Number of lymph nodes removed during modified radical neck dissection for papillary thyroid cancer does not influence lateral neck recurrence. *Surgery*. 2012;152:1177-83.
13. Atakan A, Celik M, Bulbul BY, Can N, Tastekin E, Ayturk S et al. Relationship between lymphovascular invasion and clinicopathological features of papillary thyroid carcinoma. *Bosn J Basic Med Sci*. 2017;17(2):144-51.
14. Mao J, Zhang Q, Zhang H, Zheng K, Wang R, Wang G. Risk Factors for Lymph Node Metastasis in Papillary Thyroid Carcinoma: A Systematic Review and Meta-Analysis. *Frontiers in Endocrinol*. 2020;11:265.
15. Sun W, Lan X, Zhang H, Dong W, Wang Z, He L et al. Risk Factors for Central Lymph Node Metastasis in CN0 Papillary Thyroid Carcinoma: A Systematic Review and Meta-Analysis. *PLoS ONE*. 2015;10:e0139021.
16. Lie-Hao J, Chen C, Tan Z. Clinical Characteristics Related to Central Lymph Node Metastasis in cN0 Papillary Thyroid Carcinoma: A Retrospective Study of 916 Patients. *Int J Endocrinol*. 2014;385787:6.
17. Andresen NS, Buatti JM, Tewfik HH, Pagedar NA, Anderson CM, Watkins JM. Radioiodine Ablation following Thyroidectomy for Differentiated Thyroid Cancer: Literature Review of Utility, Dose, and Toxicity. *Eur Thyroid J*. 2017;6:187-96.