



The Role of Prophylactic Cervical Lymph Node Dissection with Total Thyroidectomy in Prevention Recurrence of Papillary Thyroid Carcinoma

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Abstract

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AIM: It is assess benefit prophylactic selective unilateral cervical lymph node (LN) dissection with total thyroidectomy for patients who have papillary thyroid carcinoma (PTC) and negative cervical lymph nodes metastasis and determination recommended risk factors for such surgery.

METHODS: This was a prospective study, 60 patients with PTC investigated by Fine needle aspiration, ultrasonography to support diagnosis patients with PTC, and negative lymph node metastasis. Nineteen patients are excluded from the entire 60 patients; remaining 41 patients are submitted to a total thyroidectomy and prophylactic selective one side ipsilateral lateral and central lymph nodes dissection (level II, III, IV, and V). Then, follow-up 2 years for all patients, postoperatively, for detection PTC recurrence.

RESULTS: The result shows that from the total 41 patients, two groups are positive and negative lymph nodes metastasis 24.4% (10) and 75.6% (31), respectively, positive lymph nodes metastasis is presented more in male 7 (70%) with significant difference ($p = 0.03$) and age groups <55 years old 6 (60%) with insignificant association ($p = 0.413$). Thyroid nodular size (>1 cm) and multiple nodules presented more in positive lymph nodes metastasis with significant difference in both. Multivariate binary logistic regression, sex, thyroid multinodularity, and thyroid nodule size were insignificant relationship of prediction of lymph nodes metastasis.

CONCLUSION: Prophylactic cervical LN dissection with total thyroidectomy for patients with PTC and negative cervical lymph nodes metastasis has beneficial role in preventing recurrence of PTC. Risk factors such as male gender, thyroid multinodularity (multiple nodule), and their size (>1 cm) have role in increasing chance of occurrence of cervical LN metastasis.

Introduction

Papillary thyroid carcinoma (PTC) is presented as more frequent cancer type (> 80%) from total thyroid gland cancer types [1], [2], with better prognosis in 10-year survival (more than 90%) [3], [4]. Papillary thyroid carcinoma has elevated level of cancer recurrence [5] and mortality [6] with lateral lymph node metastasis, consequently, this needs therapy as advanced surgical resection of thyroid gland and related cervical lymph nodes [7] and radioactive iodine [8]. Finally, resection of lateral lymph nodes (LLN) is controversy but resection the entire lymph nodes metastasis are associated with the low level of cancer recurrence and mortality [9], [10]. The recurrence of papillary thyroid carcinoma may reach to 28% [11] that depending on aggressive behavior of cancer, metastasis whether local or vascular or to distant sites, elevated concentration of thyroglobulin after thyroid cancer surgery [8]. Fine needle aspiration (FNA) with ultrasound guided has great role in identify papillary thyroid carcinoma, consequently, this incidence cancer has greatly increase through the world [12]. Pre-operative diagnosis or determination of the central lymph nodes

cancer invasion may be not easy for diagnosis the LLN metastasis due to the central lymph nodes that have small size and attach to organs such as trachea or thyroid gland [13], and LLN metastasis may associated with short-range time to cancer recurrence or death [14], [15], [16]. ATA (American Thyroid Association) instructions mention that surgical removal of central/LLN is done only when there are clinical or radiological signs, but it is not suggested for prophylactic lateral cervical lymph node dissection [17]. The purposes of study is assess benefit prophylactic selective unilateral cervical lymph node dissection with total thyroidectomy for patients who have PTC and negative cervical lymph nodes metastasis and determination recommended risk factors for such surgery.

Methods

Research principle

A prospective study was done between February/2019 and September/2021 in Al-Hilla Surgical

Teaching Hospital, 60 patients with PTC investigated pre-operative physical examination, ultrasonography-guided FNA, and ultrasonography (High-resolution ultrasound scanners (HD11 xe, Phillips Medical Systems, Bothell, WA, USA) to support diagnosis those patients with PTC and negative lymph node metastasis.

Criteria of patients

Medical data include age, gender, family history of thyroid cancer, and previous history of thyroidectomy or thyroid cancer. Complete investigation set was done for all patients preoperatively, including complete blood count, function tests for thyroid, renal, and liver, chest X-rays, neck CT, and neck MRI. Pre-operative consent was taken from all patients with explaining all post-operation complications that might result from such surgical operation. Inclusion criteria preoperatively are positive ultrasonography (TIRADS (thyroid imaging reporting and data system) Grade 3 and 4) with ultrasonography-guided FNA of thyroid gland indicated probable or confirm diagnosis of PTC; and neck examination and ultrasonography of negative cervical lymph nodes. Exclusion criteria are patients with cervical lymph nodes metastasis; previous history of thyroidectomy or thyroid cancer; and patients had thyroid cancer types other than PTC.

Surgical operation

Nineteen patients are excluded from the entire 60 patients due to incompatible with inclusion criteria, remaining 41 patients are submitted to a total thyroidectomy and prophylactic selective one side ipsilateral lateral and central lymph nodes dissection (neck side affected by thyroid cancer), and this lymph nodes dissection began with Level II, III, IV, and V. Post-operation, all patients confirmed histopathological analysis for confirm diagnosis PTC with negative or positive cervical lymph nodes metastasis.

Surgery procedure begin with patients is laid in operational bench with lifting 15° upward, putting pillow below back of patients (inter-scapular area). Curved skin incision in lower neck is done 3–4 cm over level of sternum and continue to lateral side to sternocleidomastoid muscles. This incision is continue deep to platysma, then upper and lower skin flaps are done, The strap muscles are splitting, resection of the unilateral thyroid lobe is completed after ligation and dissection of the superior thyroid vessels at the superior pole. The parathyroid glands and recurrent laryngeal nerve should be recognized. Finally, the thyroid gland is now whole dissection with isthmus and pyramidal lobe. The contralateral thyroid lobe must be entire dissection in a same way to that described. For lymph nodes dissections, the neck moved upward and rotated to the opposite side. The modified McFee incision is done, sub-platysmal flaps are elevated with attention

Table 1: General descriptive of the present data

Parameters	% Values
Age (years)	
Mean ± SD	47.24 ± 7.27
Median	48
Range	32–63
≤55/N (%)	30 (73.2%)
>55/N (%)	11 (26.8%)
Sex	
Male/N (%)	16 (39%)
Female/N (%)	25 (61%)
Thyroid nodule size (cm)	
≤1/N (%)	12 (29.3%)
>1/N (%)	29 (70.7%)
Thyroid multinodularity	
Single nodule/N (%)	21 (51.2%)
Multiple nodules/N (%)	20 (48.8%)

to save the greater auricular and marginal mandibular nerves, this lymph nodes dissection involved with level II, III, IV, and V.

Follow-up all patients postoperatively to diagnose recurrence rate of PTC including eight visits beginning from 1st week post-operation to end of 2nd year post-operation. A clinicopathologic findings, serum thyroglobulin level, ultrasonography-guided FNA, and ultrasonography for follow-up and diagnosis recurrence of cervical LN metastasis if it occurs post-operation.

Statistical study was analyzed with SPSS version 26. Continuous and categorical variables represented as means ± SD and numbers (percentages), respectively. Kolmogorov–Smirnov test was for determination the normality of continuous data. Significant difference level was determined by Independent Samples T Test. Multivariate logistic regression was applied to predict independent risk factors (preoperatively). Fisher's exact test was used for categorical data. $p \leq 0.05$ was meaning significant difference.

Results

In the present analysis, two groups are positive and negative lymph nodes metastasis (10 (24.4%) and 31 (75.6%), respectively) were result, and all patients with total thyroidectomy and ipsilateral lateral and central LN dissection. From the total 41 patients, 39% [16] and 25 (61%) are male and female, respectively, and the most cases of positive lymph nodes metastasis are presented in male 7 (70%) with significant difference ($p = 0.03$), and age groups ≤55 years old 6 (60%) with insignificant association ($p = 0.413$). Thyroid nodular size (>1 cm) and multiple nodules were presented more in positive lymph nodes metastasis with significant difference in both ($p = 0.047$ and 0.032 , respectively) as in Tables 1 and 2.

As shown in Table 3, in applying multivariate binary logistic regression, sex (male) and thyroid multinodularity (Single nodule) were insignificant relationship of prediction of cervical lymph nodes

Table 2: Association of baseline data between positive and negative lymph nodes metastasis

Parameters	Positive lymph nodes metastasis (n=10)/N (%)	Negative lymph nodes metastasis (n=31)/N (%)	*p value
Age (years)			
≤55	6 (60)	24 (77.4)	0.413
>55	4 (40)	7 (22.6)	
Sex			
Male	7 (70)	9 (29)	0.03
Female	3 (30)	22 (71)	
Thyroid nodule size (cm)			
≤1	4 (40)	23 (74.2)	0.047
>1	6 (60)	8 (25.8)	
Thyroid multinodularity			
Single nodule	2 (20)	19 (61.3)	0.032
Multiple nodules	8 (80)	12 (38.7)	

*Fisher's exact test.

metastasis ($p = 0.277$ and 0.063 , respectively), but thyroid nodule size (≤ 1) was significant relationship of prediction of cervical lymph nodes metastasis (p value= 0.03)

Table 3: Multivariate logistic regression of risk factors associated with lymph nodes metastasis

Parameters	Odds ratio	95% CI	p value
Sex			
Male	0.372	0.063–2.213	0.277
Thyroid nodule size (cm)			
≤1	0.122	0.018–0.816	0.03
Thyroid nodules number			
Single nodule	7.269	0.901–58.62	0.063

As shown in Table 4, follow-up of patients with PTC was done postoperatively for detection of recurrence rate.

Discussion

In the present study, all 41 patients with papillary thyroid carcinoma and negative lymph node metastasis undergo total thyroidectomy with prophylactic lymph nodes resection from Stage II to Stage V (surgical removal of ipsilateral lateral and central cervical lymph nodes) to reduce risk of recurrence of thyroid cancer metastasis, this procedure is supported by Lang *et al.* study [18] and Jungbin Kim *et al.* study [19]. In existing study, lymph nodes metastasis is 24.4% which is near or slightly difference from result of Qiang Lui *et al.* study [20] 13.4%, Sippel *et al.* [21] 27.6%, and Viola *et al.* [22] 46.2%. In general, distribution of PTC is more in female gender 25 (61%) and age group <55 years old, 30 (73.2%) in this study as compared to other study are predominant female gender and younger age group from 20–55 years [23]. However, ATA instructions, patients who have tumor stage T3 or T4 with negative cervical lymph nodes metastasis, need prophylactic central cervical lymph node dissection [17] and FNA is indicated when size of thyroid nodules ≥ 1 cm to diagnosis the thyroid cancer or can used when size of thyroid nodules <1 cm in association with extrathyroid invasion or probability LLN metastasis [24] as involves in the present study. Furthermore, surgical removal of central lymph nodes is obligatory in patient with PTC who has lateral LN metastasis to preclude cancer

recurrence and skip metastasis [13]. In this study, age groups (≤ 55 and >55 years old) are insignificant difference in association with cervical LN metastasis but sex (male), thyroid multinodularity (multiple nodule), and their size (>1 cm) have significant association for detection of cervical LN metastasis.

Table 4: Follow-up of patients with PTC postoperatively for detection of recurrence rate

Visits Tests	Thyroglobulin levels	Ultrasonography-guided FNA	Ultrasonography	Clinicopathologic findings
First visit (1 st week)	Undetected	Normal	Normal	Normal
Second visit (1 st month)	Undetected	Normal	Normal	Normal
Third visit (6 months)	Undetected	Normal	Normal	Normal
Fourth visit (12 months)	Undetected	Normal	2 cases diagnosis	Normal
Fifth visit (15 months)	Undetected	Normal	Normal	Normal
Six visit (18 months)	Undetected	Normal	Normal	Normal
Seventh visit (21 months)	Undetected	Normal	Normal	Normal
Eight visit (24 months)	Undetected	Normal	Normal	Normal

PTC: Papillary thyroid carcinoma, FNA: Fine needle aspiration.

Many studies show that lateral LN metastasis is more risky in male gender, bigger size of cancer, youthful age group, and multiple cancer sites in thyroid gland [25], [26], [27], [28]. Lateral LN metastasis in thyroid papillary cancer is significantly associated with cancer size (> 2 cm) and recorded by Qiang Lui *et al.* study [20]. During period of follow-up in this study for diagnose the recurrence of cervical LN metastasis, two cases from 10 cases (positive cervical LN metastasis) are detected and this represent 20% of PTC recurrence, in comparing Roh *et al.* [29] and Zuniga *et al.* [30] studies showed 4.1% and 20% recurrence rate, respectively. In this represented research, some disadvantages found during course of preparing the study, including non-randomized, and do not follow-up for long period to determine result of recurrence or mortality of PTC.

Conclusion

Prophylactic cervical LN dissection with total thyroidectomy for patients with PTC and negative cervical lymph nodes metastasis has beneficial role in preventing recurrence of PTC. Risk factors such as male gender, thyroid multinodularity (multiple nodule), and their size (>1 cm) have role in increasing chance of occurrence of cervical LN metastasis.

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