



Performing Central Neck Dissection in Patients with Papillary Thyroid Carcinoma with Clinically Node Negative, Benefits and Drawbacks: A Comparative Study

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Abstract: Context: central neck dissection in addition to total thyroidectomy as a management procedure of patients with papillary carcinoma of the thyroid [PTC] was previously found to decrease the incidence of lymph node recurrence and allow and accurate PTC surgical staging that allow making a better decision regarding adjuvant radioactive iodine (RAI) ablation. But recently, central neck dissection in patients with clinical and radiological evidences of negative cervical lymph nodes was found to have many post-operative complications. Aim: to assess benefits, complications and drawbacks of performing central neck dissection by in PTC patients. Patients and methods: This is a prospective randomized study which included 70 PTC patients who was subjected to total thyroidectomy with or without neck dissection; all included patients have clinically negative cervical lymph nodes, 40 (60%) underwent total thyroidectomy in addition to central neck dissection and 30 (40%) patients were subjected to only total thyroidectomy without central neck dissection. We followed our patients for five years to detect recurrence, RFS and OS rates. Results: We found that operative time was longer in patients underwent central block dissection ($p=0.049$). Recurrence free survival and overall survival rates were not significantly different among both included groups, which denoted that central block neck dissection has no survival benefits in PTC patients. Conclusions: We have concluded that performing central neck dissection in PTC with clinically and radiologically negative lymph nodes has no benefits in increasing patients' survival or decreasing recurrence rate and might lead to prolongation of operation time, increasing post-operative morbidity.

Keywords: Central Neck Dissection, Papillary Thyroid Carcinoma, Recurrence, Survival

1. Introduction

Recently differentiated thyroid carcinoma has experienced a sharp elevation in its rate all over the world, and it has become the most prevalent malignancy [1]. Papillary carcinoma of the thyroid gland [PTC] forms about 90% of all malignant thyroid tumors and it still has a favorable prognosis and better patients' survival rates [2]. But PTC has a higher incidence of spread to cervical lymph nodes that could be related to higher incidence of local recurrence and distant metastasis, which negatively affects the survival of

patients [3-6].

Performing central neck dissection in addition to thyroidectomy as a prophylactic surgical management of PTC was previously found to decrease the incidence of lymph node recurrence and allow and accurate PTC surgical staging that allow making a better decision regarding adjuvant radioactive iodine (RAI) ablation [3, 7-9]. But recently, central neck dissection in clinically node negative was found to have many post-operative complications with uncertain evidences of improving PTC patients' survival or decreasing its recurrence [3, 10-13]. So, the benefits of

central neck dissection remain a controversial issue in PTC patients with clinically node-negative.

In the current study we aimed to assess benefits, complications and drawbacks of performing central neck dissection by comparing 2 cohorts of PTC patients the first cohort underwent total thyroidectomy with central neck dissection while the second cohort underwent total thyroidectomy without central neck dissection.

2. Materials and Methods

This is a prospective randomized study which included 70 PTC patients who underwent total thyroidectomy with or without central neck dissection through conventional trans-cervical approach; all included patients have clinically negative cervical lymph nodes from October 2014 to November 2019 in department of General surgery, Faculty of Medicine Zagazig University hospitals. Of included 70 PTC patients, 40 (60%) underwent total thyroidectomy in addition to central neck dissection and 30 (40%) patients underwent only total thyroidectomy without central neck dissection.

The decision of performing central neck dissection has been dependent on the status of PTC and on surgeon's opinion and on patient's acceptance. In case of performing bilateral central neck dissection we removed; pre-laryngeal, pre-tracheal in addition to para-tracheal groups of lymph nodes bilaterally, while in case of unilateral central neck dissection we removed the same lymph nodes in the ipsilateral site of PTC. We followed our patients for five years to detect recurrence, RFS and OS rates.

2.1. Inclusion Criteria

Patients aged from 20-50 years old, Patients accepted to be included in the study.

Operable PTC patients no extrathyroidal extension, less than 4 cm in size and with clinical and radiological evidence of absence of cervical lymph node metastases were included in the study.

2.2. Exclusion Criteria

Patients with PTC of more than 4 cm in size; presence of extra-thyroidal extension; pre-operative presence of clinical or radiological evidence of cervical lymph node metastasis, recurrent disease, distant metastasis or concomitant cancer were excluded from the study.

All included PTC patients gave a written consent to be included in the study after detailed explanation of the surgical procedures and aim of the study, and the study protocol was approved by "the local ethical institutional review board of Faculty of medicine, Zagazig University".

All patients underwent ultrasonography and computed tomography to evaluate the cervical lymph nodes status preoperatively. We defined clinically, node-negative state by the absence of suspicious cervical lymph nodes on ultrasonography and computed tomography images.

We performed staging of PTC according to the 7th edition

of "American Joint Committee on Cancer/International Union for Cancer Control (AJCC/UICC)". All included PTC patients underwent flexible laryngoscopy pre-operatively and after surgery. We considered persisting paralysis of the vocal cord for more than six months as a permanent paralysis. We defined permanent hypoparathyroidism when the levels of serum parathyroid hormone were less than 15 pg/ml continuously for >6 months. We considered the occurrence of abnormal masses during physical evaluation, neck ultrasonography, or computed tomography and confirmed by FNAC as development of recurrence.

We assessed resected lymph nodes number, occurrence of postoperative complications, the need for RAI ablation, recurrence free survival rate and overall survival rates and compared between the two included cohorts regarding these parameters.

2.3. Surgery

All operations were done by the same 3 surgeons so techniques of thyroidectomy and lymph node dissection techniques were similar for all included patients. Identification and exposure of the recurrent laryngeal nerves has been done till their points of insertion in the larynx, and we have identified and preserved the parathyroid glands.

We assessed levels of serum calcium and parathyroid hormones on the 1st postoperative day, and later on according to subsequent clinical evaluation.

For statistical analysis we used "Statistical Package for the Social Sciences version 20.0 (SPSS Inc, Chicago, IL, USA)". We have used Chi-square or Fisher's exact tests to compare between categorical variables whenever appropriate, and used T-test, Mann-Whitney U-test and Wilcoxon signed rank test for comparison between continuous variables. We calculated survival rates using the Kaplan-Meier survival curves and considered $p < 0.05$ as statistically significant.

3. Results

Patients' demographics and clinic-pathological data of all included PTC patients were detailed in Table 1.

We found that size of the tumor was larger in the group of patients underwent central block neck dissection than patients underwent only thyroidectomy ($p=0.006$), incidence of multifocal tumor ($p=0.005$), extra-thyroid extension ($p=0.002$), higher T stage, presence of lympho-vascular and peri-neural invasion ($p=0.003$), were higher in the group of patients underwent central block neck dissection than patients underwent only thyroidectomy.

We found that number of removed lymph nodes in central block neck dissection group was 7 ± 4 (range 3–30). We found no significant correlations between both included group of patients regarding age or sex of the patients, grade of tumors or dose of radioactive iodine ablation.

Operative results

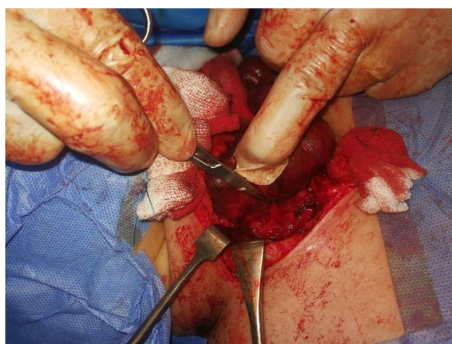
We found that operative time was longer in patients underwent central block dissection ($p=0.049$).

Postoperative findings: Table 2; Figure 1.

Transient hypo-calcemia and recurrent laryngeal nerve injury was higher in the group of patients underwent central block dissection than in the other group underwent only thyroidectomy ($p=0.039$ and 0.029 respectively).

Recurrence and follow-up results: Table 2; Figure 2.

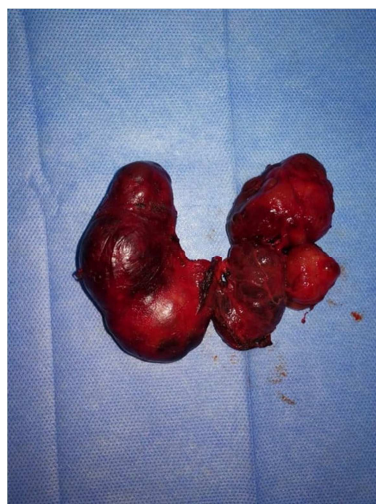
We assessed the recurrence of the tumor; clinically, radiologically and by assessment of serum thyroglobulin. We found no statistically significant differences in PTC recurrence between both included groups. Recurrence free survival and overall survival rates were not significantly different among both included groups, which denoted that central block neck dissection has no survival benefits in PTC patients.



A

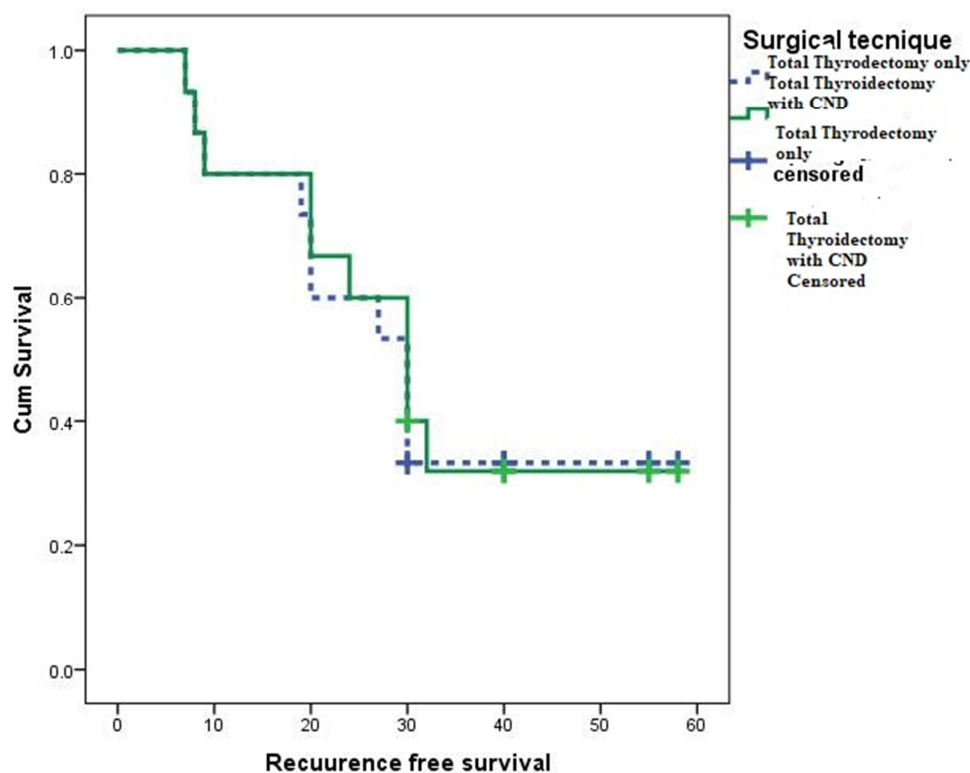


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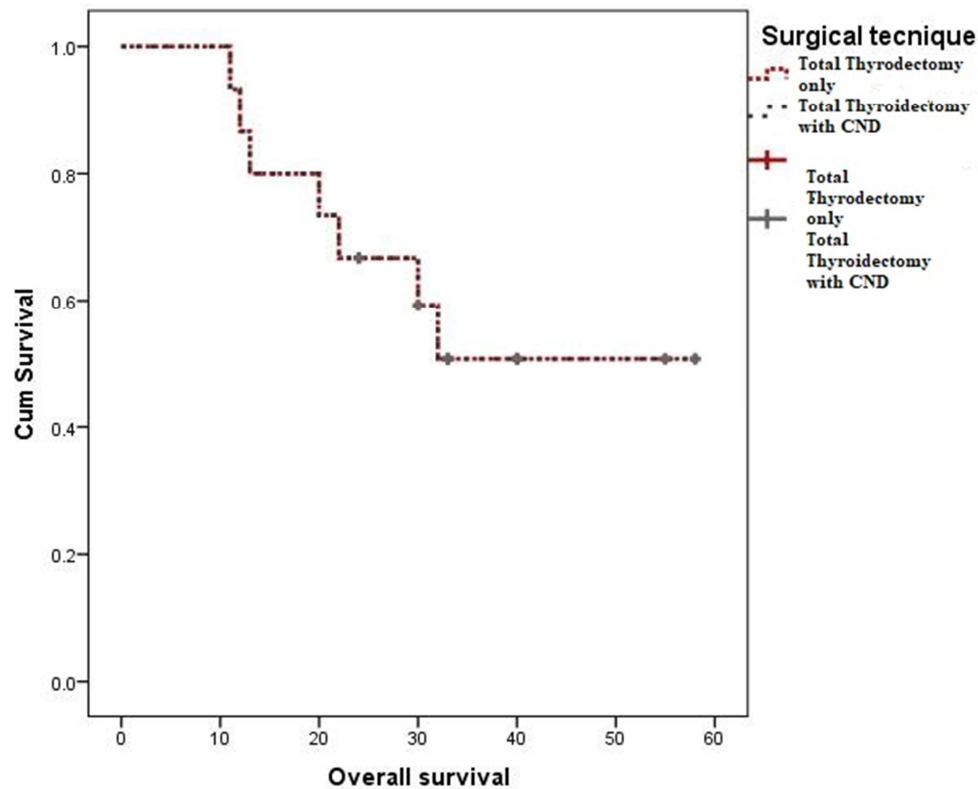


C

Figure 1. Total thyroidectomy (A and B) and post-operative appearance of the thyroid gland (C).



A



B

Figure 2. Kaplan Meier survival curves of RFS rate (A) and OS rate (B) of included PTC patients.

Table 1. Associations between both included two groups of PTC patients regarding demographic, pathological, and operative data.

Variables	Total N=70	Surgical techniques		p
		Total Thyroidectomy with block neck dissection N=40 (57%)	Total Thyroidectomy N=30 (43%)	
Age groups:				
<40 years old	45 (64.3)	25 (62.5)	20 (66.7)	0.099
>40 years old	25 (35.7)	15 (37.5)	10 (33.3)	
Gender:				
Female	55 (78.5)	33 (82.5)	22 (73.3)	1
Male	15 (21.5)	7 (27.5)	8 (23.7)	
Multifocality:				
Present	38 (54.2)	28 (66.7)	10 (33.3)	0.005
Absent	32 (45.8)	12 (33.3)	20 (66.7)	
Size:	1-4 cm	2-4 cm	1-2.5 cm	0.006
Extra-capsular invasion				
Present	28 (40)	22 (66.7)	6 (33.3)	0.002
Absent	42 (60)	18 (33.3)	24 (66.7)	
Histopathological subtype:				
Classical PTC	50 (13.4)	25 (71.4)	25 (50)	0.005
Follicular PTC	15 (20)	12 (17.4)	3 (50)	
Other subtypes	5 (23.3)	3 (7.2)	2 (42.9)	
Locoregional infiltration:				
present	28 (40)	22 (66.7)	6 (33.3)	0.003
Absent	42 (60)	18 (33.3)	24 (66.7)	

*p<0.05 is statistically significant **p≤0.001 is statistically highly significant.

Table 2. Associations between both included two groups of PTC patients regarding post-operative and patient outcome.

Variables	Total N=70 (%)	Surgical techniques		p
		Total Thyroidectomy with block neck dissection N=40 (57%)	Total Thyroidectomy N=30 (43%)	
Postoperative hypocalcaemia:				
Absent	60 (85.7)	33 (82.5)	27 (90)	0.039
Present	10 (14.3)	7 (17.5)	3 (10)	
Postoperative recurrent laryngeal nerve paralysis:				
Absent	63 (90)	35 (87.5)	28 (92)	0.029
Present	7 (10)	5 (12.5)	2 (8)	
Recurrence:				
Absent	48 (68.6)	26 (65)	22 (73.3)	0.075
Present	22 (31.4)	14 (35)	8 (26.7)	
Death				
No	45 (64.3)	23 (57.5)	22 (73.3)	0.085
Yes	25 (35.7)	17 (42.5)	8 (26.7)	
Recurrence free survival:				
Median	44.5	35	39	0.073
Range	20 - 60	18 - 49	20 - 60	
Overall survival:				
Median	51	49	45	0.098
Range	30 - 60	29 - 56	26 - 50	

*p<0.05 is statistically significant **p≤0.001 is statistically highly significant.

4. Discussion

Performing central neck dissection in PTC patients who were found to be node negative as a prophylactic procedure against long term recurrence and its survival benefits remains a controversial issue [2].

Previous researchers who advised and supported such procedure as it supposed to decrease PTC recurrence risks and the need for reoperation in addition to more accurate staging through identification of occult metastases in the cervical lymph nodes that affects taking decisions about the need for postoperative RAI ablation [7-10, 14, 15]. But many previous researchers found a contradictory results regarding central neck dissection that it did not decrease rates of tumor recurrence, did not improve patients survival in addition to more risks of causing post-operative complications as vocal cord palsy and hypo-parathyroidism [15-18].

In the current comparative prospective study we found that performing central neck dissection was of no statistically significant values regarding reduction of rates of recurrence more than total thyroidectomy alone, additionally no differences in survival benefits in patients subjected to central neck dissection more than patients subjected to only total thyroidectomy, our results were similar to results of Yoo et al., [2], Kim et al., [13] and Zetoune et al., [18] who showed that central neck dissection has no advantage regarding decreasing recurrence of the disease or improving patients out come in comparison to thyroidectomy alone. In the 2006 American Thyroid Association (ATA) guidelines of PTC management performing central neck dissection was recommended routinely for PTC patients even with nodes negative and regardless of the tumor size [19]. But in year 2009 and year 2015 the ATA guidelines limit the need for central neck dissection to advanced PTC (T3 and T4) [19, 20]. Central block neck dissection was not recommended for PTC with clinically and radiologically negative cervical

lymph nodes as showed by the guidelines of “British Thyroid Association (BTA)” in case of young patients aged <45 years old, solitary tumor with a size less than 4 cm [21], that was in line with our results. Similarly the 2018 NCCN guidelines did not recommend preforming central neck dissection in case of clinically and radiologically negative lymph nodes [22, 23].

Conflicting results were found by Su et al., [24] and Calo et al., [25], Zhao et al. [8], who showed that central block neck dissection in addition to total thyroidectomy in PTC patients decreased risks of recurrence but increasing incidence of hypoparathyroidism and recurrent laryngeal nerve injury. Su et al., [24] stated that performing central neck dissection with thyroidectomy for PTC patients is a safe and efficient surgical procedure, as it not only removes occult central lymph node metastases, but also it leads to marked reduction in rate of PTC local recurrence [24]. Based on our recent report and other researches However, based on the results of the present study and results of former studies, central block neck dissection in addition to total thyroidectomy in PTC patients with clinically node-negative has no benefits regarding recurrence or survival. Su et al., [24] demonstrated different results that central neck dissection did not increase the incidence of damage to the parathyroid glands or increased the rates of recurrent laryngeal nerve injury [24]. Shen et al. revealed a marked reduction in PTC recurrence in patients underwent central neck dissection [26]. Su et al., [24] recommend performing central neck dissection in the same time of performing thyroidectomy as PTC has high incidence of cervical lymph node metastases that was in line with So et al., [27].

Su et al., [24] demonstrated results different from us that there was no increased morbidity and post-operative complications in patients underwent neck dissection.

However, the Su et al., [24], study has many limitations which make it less accurate than our current study. First, its

retrospective non-randomized nature while our study is a prospective randomized one. Additionally in their study the decision to perform a central neck dissection was related to surgeon's preference and was not individualized for every patient.

4.1. Strengths of Our Work

Prospective randomized nature of the study.

Long term follow-up of patients for recurrence and survival rates which were lacked in other reports.

The comparative nature of that study which allows detection of differences between studied groups.

4.2. Limitations of Our Work

First, the study included a relatively small number of PTC patients. Second, most studied tumors were less than 3 cm in size so it was difficult to determine benefits of central neck dissection in tumors sized more than 4 cm. Further studies that included with larger number of PTC patients and included larger tumors are needed to overcome these limitations and determine differences in recurrences between included groups.

5. Conclusion

We have concluded that performing central neck dissection in PTC with clinically and radiologically negative lymph nodes has no benefits in increasing patients' survival or decreasing recurrence rate and might lead to prolongation of operation time, increasing post-operative morbidity by increasing incidence of hypoparathyroidism and recurrent laryngeal nerve palsy.

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