

Evaluation of Benefits & Risks of Prophylactic Central Compartment Lymph Node Dissection in Papillary Thyroid Cancer

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Abstract: ***Objective:** Prospective case controlled study to evaluate benefits & risks of prophylactic central compartment lymph node dissection in papillary thyroid cancer. **Methods:** The Prospective study was undertaken from February 2013 to February 2015 on PTC patients. 133 patients were enrolled in the study in two groups. Group 1 – underwent total thyroidectomy with prophylactic central compartment lymph node dissection (TT + PCCLND). Group 2 –underwent only total thyroidectomy (TT) for benign thyroid disease. **Results:** A PCCLND was done in all group 1 patients comprising bilateral CCLND in n=20(60.6%) and ipsilateral CCLND in n=13(39.4%). 81.8% underwent parathyroid auto-transplantation in group 1 compared to 39.3% in group 2. Transient hypocalcaemia was seen in n=15(45.5%) in group 1 & n=42(42.4%) in group 2. Transient RLN Palsy occurred in n=7 (21%) in group 1 compared to n=13 (13%) in group 2. Permanent hypoparathyroidism was seen in n=3(0.09%) in group 1 and n=5(0.05%) in group 2. Right vocal cord palsy was seen in n=2(6.1%) in group 1 and n=3 (3 %) in group 2. **Conclusion:** In conclusion, this study demonstrates the technical feasibility and safety of PCCLND; that it is a better way to determine lymph node status for a more accurate staging of disease and risk stratification.*

Keywords: papillary thyroid carcinoma, prophylactic central compartment lymph node dissection, transient & permanent complications

1. Introduction

Carcinomas of thyroid are from thyroid follicular cells. Papillary thyroid cancer and its variants and follicular cancer thyroid are classified as well-differentiated. The papillary cancer thyroid has an excellent prognosis because of its indolent growth.

Around 80-85% cases of cancer thyroid are Papillary Thyroid Carcinoma (PTC). Around 50% can present with regional lymph node metastases and Micro metastases too are common in up to 90% of examined nodes.

The recurrence rate of preoperatively negative central lymph node metastases is high on postop review and is around 10-15% in the next 10 yrs.

A prophylactic central lymph node dissection (PCCLND) in papillary thyroid cancer done on patients with no evidence of nodal metastasis (clinically N0; cN0) is controversial. This controversy is due to the un-proven role of PCCLND in reducing the recurrence rates which is not proven by many prospective randomized controlled studies in a huge number of cohorts. But they may possibly increase morbidity because of transient and permanent hypoparathyroidism and recurrent laryngeal nerve injury rates that are higher in less experienced hands.

A PCCLND permits accurate staging, facilitates post-op treatment with Radio Active Iodine (RAI), Surveillance for recurrence long term, Minimize recurrence & Metastatic spread.

This is a prospective case controlled study to analyze the feasibility of a prophylactic neck nodal dissection in the central compartment in proven cases of papillary thyroid cancer patients with no evidence of cervical nodes clinically

or radiologically. The risks & the benefits of a PCCLND were evaluated and compared against benign thyroid disorder patients who underwent only total thyroidectomy which is the standard procedure for any case of cancer thyroid.

Aim of the Study

Prospective case controlled study to evaluate benefits & risks of prophylactic central compartment lymph node dissection in papillary thyroid cancer

2. Materials and Methods

A prospective case controlled study to evaluate benefits & risks of PCCLND in papillary thyroid cancer (PTC) was undertaken in Department of Endocrine Surgery, Madras Medical College.

The study period was from February 2013 to February 2015- a total of 2 years. Informed written consent was obtained from all participants. Approval from the ethics committee was obtained 133 patients were counselled to enrol in the study and divided in to two groups

Group 1 – comprising 33 patients with proven PTC with no clinical or radiological central compartment lymph nodes who underwent TT with prophylactic central compartment lymph node dissection (TT + PCCLND).

Group 2 – comprising of 99 consecutive patients who underwent only TT (TT).

In the initial assessment the following were documented

Demographic information

Age

Sex

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History of radiation exposure
History of thyroid disease
History of previous neck surgeries
Any family history of thyroid disorders
Past and current use of thyroid hormone treatment
Known or suspected familial PTC.

Study period

18 months with a follow-up period of 6 months.

Inclusion criteria for the study

Proven cases of papillary thyroid cancer, with no nodes clinically or radiologically (cN0)

Exclusion criteria

Hyperthyroidism
Previous neck surgeries involving thyroid and adjacent areas
Clinically T (1-4) N1 Mx case
Concomitant primary hyperparathyroidism
Inability to give informed consent
Cannot meet follow-up requirements
All the patients were comparable with age, diagnosis, demographics.
The specialized investigation done were
Preop-Serum Calcium: to rule out hypocalcaemia
Ultrasonography (USG): for features of PTC in the thyroid nodule & to rule out central/lateral compartment nodes.
Fine needle aspiration and Cytology (FNAC): for confirmation of benign or malignancy in a nodule

Video Laryngo- Scopy (VLS): this is done in our department for both preoperative & postoperative patients to assess vocal cord (VC) status. Any patients having a diminished movement of vocal cords or palsy of vocal cords were followed up regularly after 3 & 6 months.

All the patients in our study fulfilled our criteria & underwent TT. The patients in group 1 underwent a PCCLND in addition to a TT.

3. Procedure

By a skin crease collar incision after or during thyroidectomy, an “en bloc” dissection is performed that includes the Delphian lymph nodes, pre-tracheal nodes & para-tracheal nodes.

“The superior margin is at the level of the hyoid bone, the inferior margin is at the level of the brachiocephalic vessels, the lateral margin at the medial aspect of the common carotid artery, and the contra lateral margin is past the midline of the trachea but not encompassing the contra lateral inferior parathyroid gland”.

Patients with solitary nodule of thyroid underwent a unilateral/ipsilateral paratracheal lymph nodal dissection on the side the nodule. Attempts were made to remove all the fibro-fatty tissue in the lymph nodal basin. At no time was a “berry-picking” done. The RLN was identified and all fibro-adipose tissue above & below the plane of the nerve removed.

All the parathyroid glands with their blood supply were meticulously preserved. Their colour noted with care. On Inadvertent removal of a parathyroid gland it was auto-transplanted in to the sternocleidomastoid muscle. Any parathyroid gland which looked discoloured due to venous congestion the capsule was slightly opened to let out the stasis. If the gland still looked discoloured or blackish blue then the gland was excised and auto-transplanted.

The specimens were labelled separately and sent for histopathology examination in separate containers by clearly marking the side of the lobe, the number of nodules and the side of the nodal fibro fatty tissue from the lymph nodal dissection.

Postoperatively the patient is closely monitored for signs and symptoms of hypocalcaemia. Serum calcium is done for the patients postop or at the first symptom or sign of hypocalcaemia and a clinical or biochemical hypocalcaemia recorded.

A calcium concentration in the serum that was below 8mg/dl was taken as postop hypocalcaemia. The hypocalcaemia was treated with oral &/or Intravenous calcium & Vitamin D. The same treatment continued till the patient became symptomatically better & normocalcaemic.

Prior to discharge a VLS was done & the vocal cord status recorded. Any patient with a mild hoarseness of voice or diminished movement of vocal cords or palsy was advised voice therapy. At 6 months follow-up a repeat VLS done for the symptomatic or cord palsy patient & the same recorded.

At the time of follow-up with the histopathology report the patients were duly advised Radio-Active Iodine (RAI) ablation & lifelong thyroxine suppression therapy.

At 6 months postop a serum thyroglobulin (Tg) & thyroglobulin antibody (ATg) measured.

With the staging of the tumor & post therapy whole body scan (WBS) finding & the serum Tg & ATg values the patients were risk stratified & followed up regularly.

4. Results

From February 2013 to August 2014 33 patients (group1) underwent TT with PCCLND for Papillary Carcinoma Thyroid at Department of Endocrine Surgery, Madras Medical College. They were compared with consecutive 99 benign patients (group2) who underwent TT alone.

Age is taken as a criterion in all types of staging for PTC. The patients in group1 n= 25 were <45 thereby coming under lower risk as far as age are concerned. (Table 1)

Sex ratio was more females than males in both groups. A diagnosis of Multi-Nodular Goitre was made in 78 patients and Solitary Nodule Thyroid in 54 patients. The values of parathyroid auto transplantation are significant. More cases in group 1 81.8% underwent auto transplantation compared to 39.3% in group 2. The inferior parathyroid glands were transplanted more in group 1. (Table 1)

In group 1 11 patients (33%) had the surgery done in 120-150 minutes, 8 patients (24.2%) had the duration of 150-180 minutes, 8 patients (24.2%) in 180-210 minutes & 4 in 210-240 minutes. The longest duration was 240-270 minutes seen in 1 patient (3%)

Comparatively in group 2 26 had in 60-90 mins, 44 in 90-120 mins, 28 in 120-150 mins & 1 in 150-180 mins. None of the patients in group 2 exceeded 180 mins. (Table 2)

Tumour of any size but with invasion to adjacent structures like trachea, oesophagus was seen in 4 (12.1%) patients. The presentation was varied in that a T1 or T2 tumour was node positive in 6 (18.2%) patients totally and a tumour of size >4cm with invasion to adjacent skeletal muscle was seen in 5 patients (15.2%). (Table 3)

Hypocalcaemia is transient if the patient is symptom free or normocalcaemic by 6 months. The P value of 0.458 was not statistically significant

Transient RLN Palsy occurred in 7 patients (21%) in group 1 compared to 13 (13%) patients in group 2. The P value is 0.669 which is not statistically significant. (Table 1)

At 6 months follow-up some showed an improvement. Transient hypocalcaemia was seen in n=15 patients in group 1 whereas the Sr.Calcium was in the range of 7-7.9 in n=3 in Group 1 and in n=5 in Group 2.

The serum Parathormone was 15-65pg/ml in n= 31 patients group 1 whereas it was low in the range of 10-14 pg/ml in n=3 in group 1 and n= 4 in group 2

Patients with Sr.PTH in the range of 10-14 pg/ml after 6 months of surgery were considered as permanent hypoparathyroidism. Patients with the PTH value in the range of 15-65 pg/ml which was the normal cut off value had low Sr.Calcium values n=3 in group 1 and n=2 in group 2. However the values of PTH were taken in to account to denote hypoparathyroidism. There was no vocal cord palsy in 93.9% in group 1 and 97% in group 2. Right vocal cord palsy documented in 6.1% in Group 1 and 3 % in Group 2.

5. Discussion

PTC carries an excellent prognosis but metastasis to regional lymph nodes occurs frequently. Micro metastasis is more frequent than overt clinically enlarged nodes.

The topic of PCCLND in a clinically node negative cN0 patient is still a controversy & debatable. But a therapeutic node dissection is a must. (22) In favour of PCCLND, it can be done in the same setting through the same incision as for a thyroidectomy. There is no investigation to definitely rule out central compartment node metastases definitely. In our patients 13 (39.4%) had an apparently healthy central compartment preop and intraop were upstaged by histopathology due to the presence of nodes which was not diagnosed preop

In this study on comparing the PCCLND patients with the benign thyroid disease patients who underwent only thyroidectomy there was no difference as to the age, sex or

presentation. The size of the tumour was significant in that 17 (51.5%) patients had a tumour size of 2-4cm.

Studies show that a maximal tumour diameter larger than 3 cm carries a worse prognosis (23). Though an N0 staging was found in 18 (54.5%) patients who had a tumour size ranging from 2-4 & >4cm a high number of N1 was seen in tumours >4cm in 5 (15.2%) patients & most of the tumours with N1 showed extra thyroidal invasion to the muscles. 4 (12.1%) patients showed invasion to the trachea, oesophagus & 1 to the subcutaneous tissue. All these patients had cN0 clinically. The size of the tumour & extra capsular invasion independently predicts lymph node metastases (24, 25)

The complications of TT are hypoparathyroidism & RLN Palsy. The rate of transient hypocalcaemia was 45.5% in group 1 (TT+PCCND) as against 42% in group 2 (TT alone) (26, 27) To till date there is no definite consensus regarding the complications of CCLND. Though numerous case series abound & many groups still attempt to study it. (28, 29, 30)

In TT done in an endocrine centre, the rate of hypoparathyroidism that is permanent is 1%– 2% and the permanent RLN injury is 1%–2% of patients. (31, 32). As stated earlier the data on recurrence or mortality after a PCCLND in PTC from prospective randomized studies is lacking. Studies show that the risk of permanent complications that are parathyroid-related increases with this procedure and the rates are as high as 4 to 11% (32, 33, and 34) But analysis of data in our study shows that our transient hypocalcaemia was not different from the rate of hypocalcaemia in the TT alone group. The percentage of permanent hypoparathyroidism in our study in group 1 was 3% & in comparison group 2 was 5.1%. This finding was consistent with other studies also which showed low rates of permanent hypoparathyroidism (0–1.8%) & permanent RLN paralysis (0–0.3%) (36, 37 38 39)

In our study the rate of permanent RLN injury is 3% after TT & 6.1% after TT + CCLND consistent with other studies with the following rates after TT is between 0% to 5.5% & 0%–5.7% after TT + CCLND. (42).

One patient was a 39 yr old female a case of MNG with a T3N1Mx tumour who underwent TT+B/L CCND. The right RLN was accidentally transected while attempting to remove a paratracheal lymph node. The nerve was immediately sutured and though the patient had only mild hoarseness of voice right vocal cord palsy was diagnosed immediate postop and which did not improve even after 6 months.

The lymph nodes adjacent to the RLN above and below should be meticulously dissected and the nerve exposed in its entire course and kept in the field of vision during the entire time of dissection. The RLN may be a thick nerve without any branches or may have 2, 3 or up to 5 branches. Each branch of the RLN must be meticulously preserved. If any of the branches are injured the morbidity for the patient increases with symptoms of hoarseness or regurgitation manifesting. As regard to parathyroid auto transplantation usually the inferior parathyroids are auto transplanted because they usually are in the line of dissection.

In our study the parathyroids were immediately transplanted on removal during the procedure. The specimen too was checked thoroughly and if any parathyroids removed inadvertently it too was auto transplanted. At the end of the procedure the trachea is bared completely with the innominate vein exposed inferiorly and all the fibro-fatty tissue in the dissecting nodal basin removed in its entirety along with the thyroid gland. Perfect haemostasis is achieved and the wound closed with a suction drain for all patients because of the extensive nodal dissection.

The specimens were labelled in separate containers so that the pathology of the tumour regarding its multifocality, multicentricity and the nodal metastases to ipsilateral or contralateral compartment can be accurately documented in order to ideally stage the patient.

Our patients at 6 months follow-up did not show high thyroglobulin values >10 ng/ml but these values should be taken in conjunction with thyroglobulin antibody levels. In our study the mean Tg is 1.034 +/- SD 0.944(0.10-3.20) & the ATg is 44.70 +/- SD 108.27(1.50-558). Thyroglobulin antibody levels itself can be used as prognostic indicator in PTC follow up.

All our patients with PTC were subjected to RAI ablation range 51-100-150 mCi. By doing a complete procedure & definitely staging the patient & after RAI ablation the patients can be followed up with serial TG & same sample ATg.

None of our patients went for a respiratory complication requiring a tracheotomy or had haemorrhage in postop requiring re-exploration or severe wound infection or gaping.

The duration of surgery was higher in PCCLND group which is understandable considering the meticulous dissection necessary for complete clearance of the nodal basins. The hospital stay was longer in group1 (TT+PCCLND) due to longer necessity of drain & presence of wound in duration.

The small sample size and less period of study of two years is the limitation of this study.

6. Conclusion

A TT with PCCLND in PTC patients may reduce local recurrence of PTC and may improve survival. In the study at our centre a higher rate of transient complications was seen in TT+PCCLND than in TT alone but the rate of permanent complications was not different in either group.

So when performed by experienced endocrine surgeons a TT with prophylactic central compartment node dissection (TT+PCCLND) can be combined in the initial treatment of PTC. All the individuals in the study are in follow-up and no one has developed any recurrence or metastases In order to understand the efficacy of TT+PCCND in terms of risk reduction for recurrence and survival, longer and controlled randomized prospective studies with large numbers are needed.

Table 1

		Group 1 (n=33)	Group 2 (n=99) P-Value
Age	<45	25	86
	>45	8	13
Sex	female	28	92
	male	5	7
Diagnosis	MNG	23	55
	SNT	10	44
FNAC Diagnosis	PTC	30	
	MTC	3	
	Nodular Colloid Goitre		81
	Colloid GOITRE with Thyroiditis		18
Auto Transplantation of Parathyroids	Not Transplanted	6	60
	Right superior	0	20
	Left superior	0	3
	Right inferior	17	1
	Left inferior	10	12
Tumour Size	Irrelevant		99
	<2cm	9	
	2-4cm	17	
	>4cm	7	
Transient Hypocalcaemia	No Hypocalcaemia	18 (54.5%)	57 (57.6%)
	Transient Hypocalcaemia	15 (45.5%)	42 (42.4%)
Transient RLN Palsy	No Paresis	26 (78.8%)	86 (86.9%)
	Right VC Movement Diminished	5 (15.2%)	8 (8.1%)
	Left VC Movement Diminished	1 (3%)	2 (2%)
	Right VC Palsy	1 (3%)	3 (3%)
Follow-up Sr.Calcium Levels	8-10 mg/dl	30 (90.9%)	94 (94.9%)
	7-7.9mg/dl	3 (9.1%)	5 (5.1%)
Follow-up Sr.PTH Levels	15-65 pg/dl	30 (93.9%)	95 (96%)
	10-14 pg/dl	3 (6.1%)	4 (4%)
Hypopara- thyroidism	Nil	30	94
	Permanent hypoparathyroidism	3	5
Vocal Cord Palsy	Nil	31(93.9%)	96(97%)
	Permanent VC Palsy	2(6.1%)	3(3%)