Original Research Article

The role of prophylactic central compartment lymph node dissection in differentiated thyroid carcinoma

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Abstract

Background: Differentiated thyroid carcinoma, arising from thyroid follicular epithelial cells, accounts for the vast majority of thyroid carcinomas. Of the differentiated cancers, papillary cancer comprises about 85% of cases compared to about 12% that have follicular histology, including conventional and oncocytic (Hurthle cell) carcinomas, and <3% that are poorly differentiated tumors. In general, stage for stage, the prognoses of PTC and follicular cancer are similar. The aim of this study is to evaluate the benefit of central compartment lymph node dissection in accurate staging of the disease and plan radioiodine treatment and dosing. And also to assess the morbidity associated with central neck dissection.

Materials and methods: This was a prospective clinical study conducted at MNJIO and RCC, Hyderabad. 20 patients with carcinoma thyroid who underwent total thyroidectomy and prophylactic central compartment lymph node dissection from December 2015 to December 2017 were included. The protocol was submitted to the ethics committee at Osmania Medical College and was approved.

Results: We analyzed the number of patients of that age in whom the disease stage changed due to the presence of central nodal dissection. Prophylactic CND resulted in upstaging of tumour in 2/20 (10%) patients from stage I to stage II. Also in 4/20 (20%) patients, the evidence of node metastases influenced also the therapeutic strategy because these patients would not have been treated with 131-I if the prophylactic central neck dissection had not been performed. Thus a prophylactic CLND may play an even larger role in determining RAI use. A prophylactic CLND that demonstrates a lack of lymph node metastasis would strengthen the case not to use RAI treatment in a low-risk patient.

Conclusion: With the available evidence, we advocate a selective approach to performing prophylactic CND and to be done in high volume centres. Routine prophylactic central lymph node dissection should be avoided in the absence of involved lymph nodes, reserving the procedure to "high-risk" patients as defined by ATA and European Society of Endocrine Surgeons, which include extremes of ages, large primary tumor size, and male gender, which were similar to high risk cases seen in our study.

Key words

Papillary Thyroid Cancer, Dissection in differentiated thyroid carcinoma, Radioiodine treatment and dosing.

Introduction

Thyroid carcinoma is the most common endocrine malignancy, and its incidence is increasing at the highest rate among cancers in both the US and worldwide. The National Cancer Institute's annual Surveillance Epidemiology and End Results (SEER) database estimates that there will be 62,450 new cases of thyroid cancer in the US in 2015, with an incidence of 13.5 per 100,000 [1].

The absolute increase in the incidence of thyroid cancer is estimated to be 9.4 per 100,000 individuals, with papillary thyroid cancer (PTC) accounting for the majority of these cases. The nationwide relative frequency of thyroid cancer in India among all the cancer cases was 0.1%–0.2%. The age-adjusted incidence rates of thyroid cancer per 100,000 are about 1 for males and 1.8 for females as per the Mumbai Cancer Registry, which covered a population of 9.81 million subjects [2].
Overall, differentiated thyroid carcinoma (DTC) has a 10-year survival rate of greater than 90%. However, despite its promising survival rate, local recurrence occurs in 20%–30% of papillary thyroid cancer patients due to clinically undetectable metastasis to cervical lymph nodes [3].

PTC is the most common type of differentiated thyroid carcinoma. It is well known as a lymphotropic type of cancer and thus has high tendency to metastasize to regional lymph nodes (LNs). Clinically evident nodal disease is present in approximately 5 to 10 percent of patients with PTC and a preoperative neck ultrasound can detect LN disease in up to 30 percent of patients [4].

In contrast, less than five percent of patients with FTC develop nodal metastatic disease; the hematogenous rather than the lymphatic route is the primary pathway for metastasis [5]. The prognosis of FTC is related to the age on presentation and the degree of capsular with or without vascular invasion. The diagnosis of FTC cannot always be made at the time of initial surgery. Prophylactic central neck dissection (pCND) during the first operation is of no value in FTC because the diagnosis of cancer is not established at that moment and also it tends not to spread via the lymphatic route [4].

Considering the high rate of lymph node metastases, routine or so-called prophylactic central compartment lymph node dissection (CLND) in clinically no patients is a matter of intensive research and is still debated [6].

Arguing that the procedure is associated with higher morbidity, especially injury to the parathyroid glands (most frequently the lower) [7], with rates of transient hypoparathyroidism of 14 to 60%, permanent hypoparathyroidism of 3 to 11%, transient vocal cord paralysis of 3 to 7%, and permanent recurrent laryngeal nerve injury of 0 to 4% [8].

Endocrine surgeons, head and neck surgeons and otolaryngologists are divided between

supporters and detractors of its use. In the last decade, in order to reduce locoregional relapse (LR) rate and thyroglobulin (Tg) serum levels, a trend toward routine dissection, avoiding radioactive iodine (RAI), has been generally reported. Nevertheless, lastly, considering evidence-based medicine (EBM) data, several authors suggested its avoidance in clinical practice reserving prophylactic dissection in high-risk patients [7, 9, 10].

The most recent ATA and UEC guidelines stated that prophylactic LND could be considered in high-risk patients with advanced primary tumors and should be performed by high-volume surgeons to avoid definitive complications. A reduced local recurrence rate and a lower Tg serum level may be expected. The procedure allows a better staging too, but a prospective randomized study on RCLND role could be very expensive and not readily feasible.

Aim and objectives

- To evaluate the benefit of central compartment lymph node dissection in accurate staging of the disease.
- To plan radioiodine treatment and dosing.
- To assess the morbidity associated with central neck dissection.

Materials and methods

A prospective clinical study was conducted on 20 patients with thyroid carcinoma operated at MNJ Institute of Oncology and Regional Cancer Centre from December 2015 till December 2017, to evaluate the benefit of central compartment lymph node dissection in accurate staging of the disease, to plan radioiodine treatment and dosing, to assess the morbidity associated with central lymph node dissection.

Inclusion criteria

All patients with differentiated thyroid carcinoma with clinically negative cervical nodal status were included in the study.

Exclusion criteria

Patients with thyroid carcinoma with cervical nodal metastasis are excluded from the study.

All patients with carcinoma thyroid were evaluated by clinical examination, ultrasonography of the neck, Fine needle aspiration biopsy of the thyroid swelling. All patients with differentiated thyroid carcinomas on Fine needle aspiration biopsy and who are clinically and radiologically negative for cervical lymph nodes are treated with thyroidectomy and prophylactic central compartment lymph node dissection. Patients were followed up in the post-operative period and monitored for symptoms and signs of hypocalcemia and hoarseness of voice. Patients were started on prophylactic oral calcium supplementation on post-operative day 1. Serum calcium levels were estimated on postoperative day 3 and calcium supplementation is adjusted. After the serum calcium levels were in the normal range and patient is symptom free, patients were discharged and followed up in the outpatient of the hospital.

Patients were kept on regular follow up after surgery by clinical examination. During clinical examination patients were being examined for any local recurrence/regional recurrence and for any symptoms or signs of hypocalcemia. Symptomatic patients were subjected to imaging such as ultrasonography of the neck and estimation of serum calcium levels. The maximum period of follow up was 24 months and the mean period of follow up was 12 months.

Results and Discussion

Results were depicted as per **Table – 1 to 9**. Operative photographs were as per **Figure – 1 to 4**. Thyroid carcinoma is the most common endocrine malignancy with increased incidence in the last several decades. Papillary thyroid carcinoma (PTC) is the most common histological subtype, accounting for more than 80% of all cases. The prognosis of PTC is generally good, with 10-year survival rate exceeds 95% and 20-year survival rate exceeds

93% [11]. Despite its excellent outcomes, studies have showed that recurrence is an important factor increasing its morbidity and mortality, and cervical lymph node metastasis is most important variable known to increase the risk of local recurrence. It has been shown that cervical lymph node metastasis was found in 20–90% of patients who underwent cervical lymph node dissection. Of these, central lymph node metastasis is the most common [12].

Table – 1: Age distribution.

Age in years	No of patients	%
<20	1	5.0
21-30	3	15.0
31-40	3	15.0
41-50	1	5.0
51-60	7	35.0
>60	5	25.0

Table – 2: Sex distribution.

Gender	No. of patients	%
Male	7	35.0
Female	13	65.0

Table – 3: Post-operative histology of the tumor.

Histology	No. of patients	%
Papillary carcinoma	16	80.0
Follicular variant of papillary carcinoma	4	20.0
Follicular carcinoma	0	0

Table – 4: Incidence of central lymph nodes in clinically diagnosed patients.

	No. of patients	%
Central nodes Positive	8	40.0
Central nodes Negative	12	60.0

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Table – 5: Correlation of central nodes with preoperative radiological tumor size.

USG size	No. of patients	No. of patients with CN +
<2 cm	3	1 (33.3%)
2-4 cm	10	3 (30.0%)
4-6 cm	3	2 (66.6%)
6-8 cm	2	2 (100%)
>8 cm	2	0

Table – 6: Central lymph nodes with age.

Age in years	No. of patients	No. of patients with central node + (%)
<20	1	0
21-30	3	1 (33.3%)
31-40	3	1 (33.3%)
41-50	1	0
51-60	7	2 (28.5 %)
>60	5	4 (80.0%)

Table – 7: Central lymph nodes with gender.

Gender	No. of patients	No. of patients with central node +
Male	7	5 (71.4%)
Female	13	3 (23.0%)

Table – 8: Central lymph nodes with histology of tumor.

Histology	No. of patients	No. of patients with central nodes + (%)
Papillary carcinoma	16	7 (43.7 %)
Follicular variant of papillary	4	1 (25.0%)
Follicular carcinoma	0	0

In our study, out of the 20 cases, there was 7 males (35%) and 13 females (65%) with mean age of 48.95 years (range from 10 to 70 years). These results are similar to study by Viola, et al. (2015) where the number of females 74.6% and

males were 25.4% and the mean age of the patients at the time of diagnosis was 44.5 years (range, 18–80 y) [13]. The incidence of thyroid carcinomas is significantly more in females than in males. The incidence of this disease peaks in the third and fourth decades of life.

Table – 9: Comparison of post-operative morbidity and mortality after CLND.

	No. of patients	**%**
Temporary Hypocalcemia	6	30.0
Permanent Hypocalcemia	0	0
Temporary RLN Injury	2	10.0
Permanent RLN Injury	0	0
Chyle leak	2	10.0

Figure - 1: Thyroid lobes being mobilized with bluish lymph nodes in central compartment.

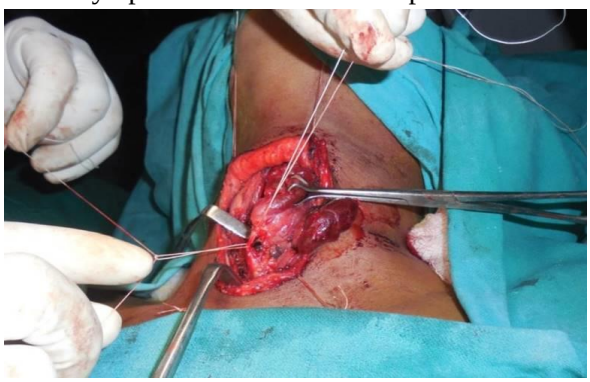

Figure - 2: Total thyroidectomy specimen.

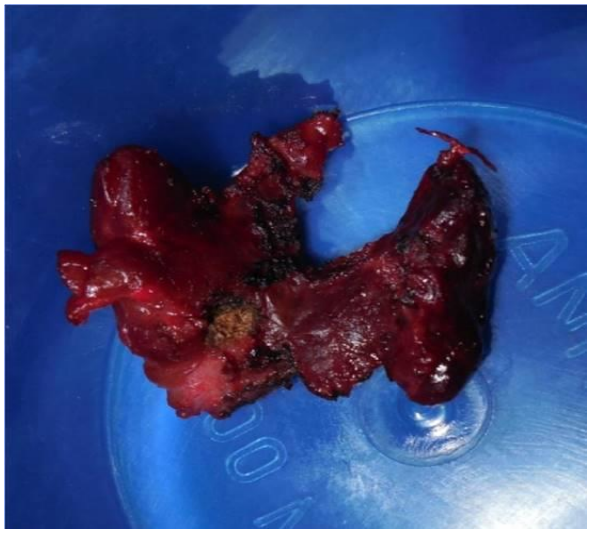

Figure - 3: Enlarged right lobe being mobilized with bluish central lymph nodes.

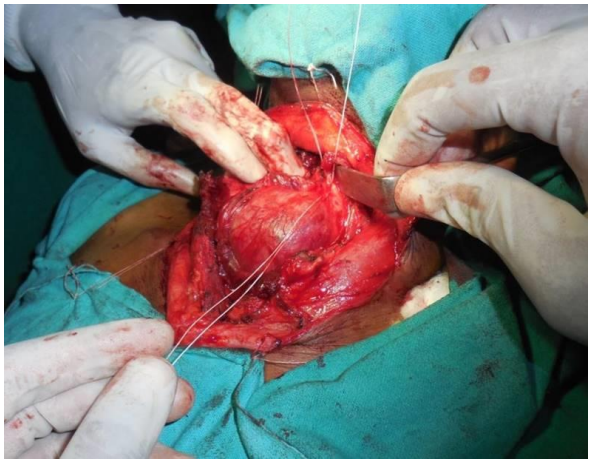

Figure - 4: Total thyroidectomy with central nodes specimen.

The mean size of the thyroid nodule in our study was 4.42 cm (range from 1.3 to 12 cm). Out of the 20 cases that underwent prophylactic central compartment lymph node dissection, 8 (40%) cases showed involvement of central nodes. This is similar to the study by Dobringa, et al. 2017, which has shown central nodal involvement of pCND in about 43.2% of patients [14]. This is in concurrence with the incidence of clinically non-palpable central nodal disease which is reported to be 40 to 70% [8, 15, 16].

When the histological assessment was done of the 20 thyroid specimens, 7/16 (43%) patients with papillary carcinoma showed central node metastasis and 1/4 (25%) patients with follicular variant of PCT had central nodes. These results

are similar to a study by David Hughes, et al. (2011) [17] and Cooper, et al. (2006) [18, 19] who reported that papillary thyroid cancer and the follicular variant of papillary thyroid cancer have a propensity for central lymphatic spread that occurs in 20% to 50% of patients and another study by Ahn, et al., (2013) who reported an incidence of 64.3% central lymph node metastases in patients with PTC [20].

In our study, the risk of central lymph nodes involvement was higher in patients with higher age (>60 years) with 4/5 (80%) patients showing central lymph nodal metastasis. Male patients showed high risk of central node metastasis 5/7 (71.0%) and also patients with large primary tumour size (>4cm). These results are similar to study by Shirley, et al. (2017), Dobringa, et al. (2017) and also similar to guidelines proposed by ATA and European Society of Endocrine Surgeons [14, 21, 22] while ATA states that prophylactic CLND for patients with T3 and T4 primary tumors or if the information gained will guide further steps in therapy. The European Society of Endocrine Surgeons state that prophylactic CLND should be considered in those with high-risk features, including T3-4 tumors, age <15 or >45, male gender, bilateral or multifocal disease.

As regard procedure related complications in CND group in our study; transient hypocalcemia was observed in 6 (30.0%) patients, temporary recurrent laryngeal nerve injury in 2 (10.0%) patients, chyle leak in 2 (10.0%) patients. None of the 8 patients had permanent hypocalcemia and permanent recurrent laryngeal nerve injury. The 2 chyle leak patients were managed conservatively. The study by Roh, et al. (2007) reported transient hypocalcemia in 30.5% patients, permanent hypocalcemia in 4.9% and permanent RLN injury in 3.6% patients, which are comparable to our study [23]. Another study by Palestini, et al. (2008), showed transient hypocalcemia in 27% of patients and permanent hypocalcemia and permanent RLN injury in 0 patients, which again are comparable to results in our study [24].

Considering that prophylactic central lymph nodal dissection could change American Joint Committee on Cancer (AJCC) stage in patients >55 years of age, we analyzed the number of patients of that age in whom the disease stage changed due to the presence of central nodal dissection. Prophylactic CND resulted in upstaging of tumour in 2/20 (10%) patients from stage I to stage II. Also in 4/20 (20%) patients, the evidence of node metastases influenced also the therapeutic strategy because these patients would not have been treated with 131-I if the prophylactic central neck dissection had not been performed. Thus a prophylactic CLND may play an even larger role in determining RAI use. A prophylactic CLND that demonstrates a lack of lymph node metastasis would strengthen the case not to use RAI treatment in a low-risk patient.

Conclusion

Papillary thyroid cancer is the most common thyroid malignancy, and metastatic spread involving lymph nodes of the central neck is common.

Prophylactic central compartment lymph node dissection helps in accurate staging of the disease that will be useful for planning therapeutic strategy and follow-up. This was seen in our study, where 40% (8/20) of patients with radiologically normal central compartment were tested positive after central nodal dissection and of the 20 patients, 2 (10%) patients were upstaged from stage I to II following prophylactic CND.

With the current ATA guidelines recommending assessing the size and number of lymph nodes involved before deciding on RAI treatment, prophylactic CLND may play an even larger role in determining RAI use. This was demonstrated in our study where 4 (20%) patients who after prophylactic CND, were candidates for adjuvant RAI treatment. Indeed, prophylactic central neck dissection was found to result in an increased use of radioactive iodine and, ultimately, in more favourable outcomes.

References

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program (SEER) Cancer Statistics Review 1975-2012. Updated August 2015. Available at: http://1.usa.gov/1S3dLLn. Accessed October 12, 2015.
2. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian Journal of Endocrinology and Metabolism, 2011; 15 (Suppl2): S78-S81.
3. Friedman M, Kelley K, Maley A. Central neck dissection. Operative Techniques in Otolaryngology -Head and Neck Surgery, 2011; 22: 169–72.
4. Chan AC, Lang BH, Wong KP. The pros and cons of routine central compartment neck dissection for clinically nodal negative (cN0) papillary thyroid cancer. Gland Surg., 2013; 2(4): 186-195.
5. Gabriella Pellegriti, Francesco Frasca, Concetto Regalbuto, et al. Worldwide Increasing Incidence of Thyroid Cancer: Update on Epidemiology and Risk Factors. Journal of Cancer Epidemiology, vol. 2013, Article ID 965212, 10 pages, 2013.
6. Goddard JA, Steward DL. Prophylactic central lymph node dissection in differentiated thyroid cancer. Endocrine, 2013; 44(2): 275–7.
7. Conzo G, Avenia N, Bellastella G, et al. The role of surgery in the current management of differentiated thyroid cancer. Endocrine, 2014; 47(2): 380–8.
8. Calò, et al. Total thyroidectomy without prophylactic central neck dissection in clinically node-negative papillary thyroid cancer: is it an adequate treatment? World Journal of Surgical Oncology, 2014; 12: 152.
9. Mazzaferri EL, Doherty GM, Steward DL. The pros and cons of prophylactic central compartment lymph node dissection for papillary thyroid carcinoma. Thyroid, 2009; 19(7): 683–9.
10. Conzo G, Calo' PG, Sinisi AA, De Bellis A, Pasquali D, Iorio S, Tartaglia E, et al. Impact of prophylactic central compartment neck dissection on locoregional recurrence of diff rentiated thyroid cancer in clinically node-negative patients: a retrospective study of a large clinical series. Surgery, 2014; 155(6): 998–1005.
11. Brassard M, Borget I, Edet SA, Giraudet AL, Mundler O, Toubeau M. Long-term follow-up of patients with papillary and follicular thyroid cancer: a prospective study on 715 patients. J Clin Endocrinol Metab., 2011; 96: 1352–9.
12. Robbins KT, Shaha AR and Medina JE. Consensus statement on the classification and terminology of neck dissection. Arch Otolaryngol Head Neck Surg., 2008; 134: 536-538.
13. D. Viola G., et al. Prophylactic Central Compartment Lymph Node Dissection in Papillary Thyroid Carcinoma: Clinical Implications Derived From the First Prospective Randomized Controlled Single Institution Study. The Journal of Clinical Endocrinology & Metabolism, 2015; 100(4): 1316–1324.
14. Dobrinja C., et al. Rationality in prophylactic central neck dissection in clinically node-negative (cN0) papillary thyroid carcinoma: Is there anything more to say? A decade experience in a single-center. International Journal of Surgery, 2017; 41: S40-S47.
15. Pereira JA, Jimeno J, Miquel J, Iglesias M, Munné A, Sancho JJ, Sitges-Serra A. Nodal yield, morbidity, and recurrence after central neck dissection for papillary thyroid carcinoma. Surgery, 2005; 138: 1095–1101.
16. Lee YS, Kim SW, Kim SW, Kim SK, Kang HS, Lee ES, Chung KW. Extent of routine central lymph node dissection with small papillary thyroid carcinoma. World J Surg., 2007; 31: 1954–1959.
17. Hughes D.T., Doherty G.M. Central neck dissection for papillary thyroid

cancer. Cancer Control, 2011; 18(2): 83-88.
18. Cooper DS, Doherty GM, Haugen BR, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid, 2006; 16(2): 109-142.
19. Arturi F, Russo D, Giuffrida D, et al. Early diagnosis by genetic analysis of differentiated thyroid cancer metastases in small lymph nodes. J Clin Endocrinol Metab., 1997; 82(5): 1638-1641.
20. Ahn D, Sohn JH, Park JY. Surgical complications and recurrence after central neck dissection in N0 papillary thyroid carcinoma. Auris Nasus Larynx, 2013; 1000-16.
21. Shirley LA, Jones NB, Phay JE. The Role of Central Neck Lymph Node Dissection in the Management of Papillary Thyroid Cancer. Frontiers in Oncology, 2017; 7: 122.
22. Haugen B.R., Alexander E.K., Bible K.C., Schlumberger M., et al. 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: 1–133.
23. Roh JL, Park JY, Park CI. Total thyroidectomy plus neck dissection in differentiated papillary thyroid carcinoma patients. Pattern of nodal metastasis, morbidity, recurrence, and postoperative levels of serum parathyroid hormone. Ann Surg., 2007; 245: 604-610.
24. Palestini N, Borasi A, Cestino L, Freddi M, Odasso C, Robecchi A. Is central neck dissection a safe procedure in the treatment of papillary thyroid cancer? Our experience. Langenbecks Arch Surg., 2008; 393: 693–698.