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Clinical Investigation

Evaluation of central compartment lymph nodes in well differentiated thyroid malignancies for metastasis.

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Abstract

Background: In papillary carcinomas occult nodal metastasis in central compartment is common. Central Compartment Neck Dissection (CCND) routinely in all cases of thyroid malignancies is controversial. Recurrence and revision surgery in the central compartment is associated with high risk of vocal cord paralysis and hypocalcaemia. ***Methods:*** A prospective study of 30 patients with well differentiated thyroid malignancy underwent total thyroidectomy with Central Compartment Neck Dissection. On histopathological examination the number of lymph nodes showing metastasis and extracapsular spread was documented. ***Results:*** A total of 30 patients (27 females and 3 males) with the age group ranging from 6 to 62 years with a mean ±standard deviation of 40.49 ±12.29 years. 18 (63%) patients with age < 45 years and 12 (37%) patients with age >45 years . 19 patients in Stage I, 3 in Stage II, 7 in Stage III and 1 in Stage IV. TT+CCND [Total Thyroidectomy+ Central Compartment Neck Dissection] was done in 26 patients (86.6%) and Total Thyroidectomy+ Central Compartment Neck Dissection and Functional Neck Dissection (ipsilateral) [TT+CCND+FND] in 4 patients (13.3%). Metastasis in the Central Compartment was seen in 7 (23.3%) and transient hypocalcemia was seen in 8 patients (26.6%). There was no incidence of permanent hypocalcemia or vocal cord palsy. ***Conclusion:*** Total Thyroidectomy with Central Compartment Neck Dissection remains the treatment of choice in well differentiated thyroid cancer with an intermediate/ high risk score. An ipsilateral paratracheal clearance in N_0 neck prevents chances of regional recurrence in early stages of well differentiated thyroid malignancies (T_1 and T_2). Transient hypocalcemia is relatively common. However permanent hypocalcemia and Vocal cord paralysis is rare.

Key words: Central compartment neck dissection, Metastasis, Total thyroidectomy.

Introduction

Thyroid malignancies are common in our country, papillary carcinoma being the most common. Thyroid carcinoma occurs 2 to 3 times more often in women than in men. Although thyroid cancer can occur at any age, peak incidence is around 49 years of age. Lymph node metastasis is present in the central compartment in 39% of the patients.[2] Central compartment lymph nodes are the first to be involved in thyroid carcinoma. Even microcarcinomas can metastazise regionally[(1)].

In papillary carcinomas occult nodal metastasis in central compartment is common. However this does not have any impact on prognosis but is associated with higher chances of recurrence. Recurrence and revision surgery in the central compartment can be associated with high risk of vocal cord paralysis and hypocalcemia[(1)]. However the need for central compartment lymph nodes dissection routinely in all cases of thyroid malignancies is controversial considering the risk to recurrent laryngeal nerve and parathyroids.

The need for this study is to evaluate the ipsilateral central compartment lymph nodes histologically for metastasis in thyroid malignancies and thereby come to an inference whether elective central compartment dissection is mandatory in well differentiated thyroid malignancies with N_0 neck (no palpable lymph nodes).

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Materials and Methods

A prospective study which included 30 patients of well differentiated thyroid malignancy who underwent surgery in Sri RL Jalappa Hospital from December 2010 to September 2012. Preoperative workup included medical history and physical examination , thyroid function tests, fine needle aspiration cytology (FNAC), chest x-ray, ultrasound (USG) neck, Computerised Tomography (CT) scan- neck and thorax(suspected retrosternal extension). All patients had pre and postoperative evaluation of vocal cord movements by means of indirect laryngoscopy or fibre optic laryngoscopy. Informed consent was taken preoperatively for central compartment neck dissection explaining the risk to recurrent laryngeal nerve and parathyroids. Elective central compartment neck dissection was done along with Total thyroidectomy in all cases of thyroid malignancies with N_0 neck.

All cases with well differentiated thyroid malignancy with N_0 neck (no clinically palpable lymph nodes) are included in the present study. Benign thyroid lesions, thyroid cancers with palpable neck node (N+), thyroid cancers which are not well differentiated on histopathological examination, thyroid carcinomas previously treated by radio iodine or surgery, thyroid malignancies with N_0 neck physically unfit for surgery, pre-existing recurrent laryngeal nerve paralysis are excluded from the present study. The specimen was subjected for histopathological examination to look for any metastasis in central compartment lymph nodes and the number of lymph nodes showing metastasis and extra capsular spread was documented. Data was evaluated by descriptive statistical studies using Mean, Standard Deviation and Proportion. The serum total calcium concentration was measured on the morning after surgery, 3 days postoperatively and 3 months of follow up. The presence of immobility or decreased movements of vocal cords is considered as Postoperative palsy or paresis. Any persistent vocal cord dysfunction even after six months postoperatively was considered permanent. The normal reference range of total calcium was 8.5 to 10.5 mg/dl. Hypocalcemia is considered as corrected serum calcium level <8mg/dl with or without clinical features of hypocalcemia (perioral tingling, numbness, positive Trousseau`s or Chovstek`s sign, carpopedal spasm and tetany). Oral administration of calcium and Vitamin D during postoperative periods was done to prevent occurrence of severe postoperative hypocalcemia in patients with sign and symptoms of hypocalcemia. Hypocalcemia is considered permanent, when calcium replacement was necessary even after six months postoperatively.

Post operative radioiodine treatment (after 6 weeks) with standard doses of 100 to 150 mCi was given for patients classified as high risk for recurrence (age >45 years , tumour size >2cm, capsule invasion , extrathyroidal extension ,and/or positive lymph node findings). Patients were followed up every month for 3 months and subsequently every 3 months with Serum calcium, Thyroid function tests , and USG neck. Serum Thyroglobulin level was estimated every 6 months.

Results

Majority of patients between the age group of 31 to 50 years (56.5%) with a mean ±standard deviation of 40.49 ±12.29 years. Majority of the cases in our study group were females (90%). The most common presenting symptom was swelling in the anterior aspect of neck (100%) followed by pain in the swelling (33.3%) and sudden increase in the size by swelling (26.6%) . Twenty seven patients had papillary thyroid carcinoma and 3 had follicular variant of papillary thyroid carcinoma. Among 30 patients, 19 patients were under 45 years of age all had TNM stage I disease(according to the present TNM staging all cases irrespective of the size of tumour and nodes without distant metastasis with age <45 years) . Of the remaining 11 patients who were above 45 years age , 3 cases had stage II ,7 cases had stage III and 1 case with stage IV .

Total thyroidectomy with Central compartment neck dissection was done in 27 patients and an additional ipsilateral Functional neck dissection was done for 3 patients who had subclinical nodes found on table .The specimens were sent separately and subjected to histopathological examination for metastasis. Of the 30 patients, 12 patients had lymph nodes in the central compartment ranging between to 5 in number. Among these 12 patients, 5 patients had reactive changes and 7 had metastasis (which included 3 patients who had lymph nodes in the lateral compartment). The metastatic nodes were less than 3 each in 6 patients and 5 nodes in 1 patient. Among the patients who were > 45 years of age , 3 out 11 patients (36.6%) had metastasis in central compartment whereas , among patients who were < 45 years of age , 4 out 19 patients (21%) had metastasis in central compartment. There was a slightly higher incidence of metastasis in patients more than 45 years of age (57.1%).Transient hypocalcemia was noted in 8 patients (26.6%). Recurrent laryngeal nerve palsy was nil. The incidence of transient hypocalcemia subsided in 7 cases (87.5%) by the end of 3 months and the remaining 1 case (12.5%) by months. There was no incidence of permanent hypocalcemia.

All our patients were subjected to Radio Active Iodine (RAI) scan 3 to 4 weeks after surgery. Only

12 patients underwent RAI ablation, as they had higher T stages (T_3, T_4), extrathyroidal spread, multiple metastatic lymph nodes (subclinical), and higher grade of tumour. Six patients (20%) were advised RAI[Radio Active Iodine] ablation but defaulted, another 12 patients (40%) were in the younger age group and did not have significant RAI uptake in the postoperative scan and were not advised RAI scan .

About 29 (96.7%) cases were disease free at the end of mean follow up of 1 year and 1 (3.3%) case was lost for follow up 6 months after surgery. There were no deaths and no local, regional or distant metastasis.

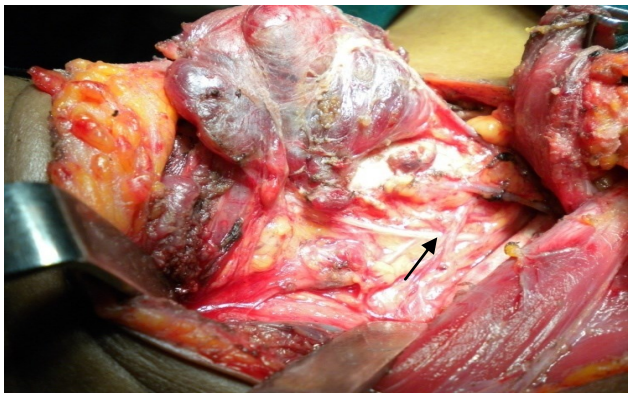

Fig :1- Showing Recurrent Laryngeal Nerve.

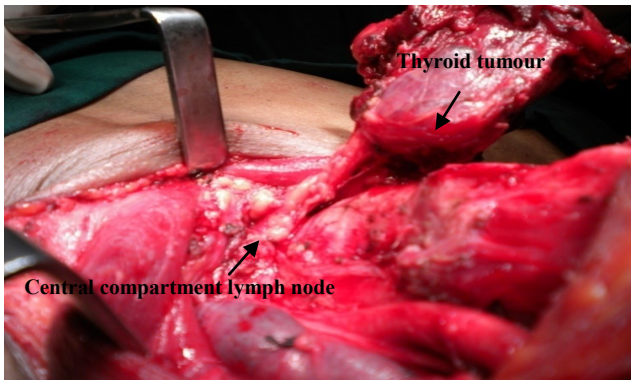

Fig : 2-Showing thyroid tumour with central compartment lymph nodes

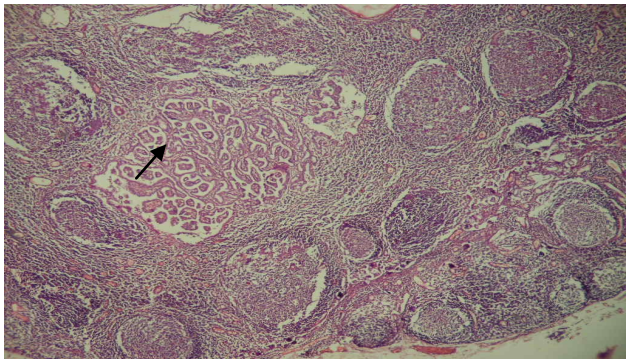

Fig : 3-lymphnode with metastasis from PTC

Discussion

In the present study majority of the patients between the age group of 31 to 50 years (56.5%) and range was 6 to 62 years. We classified the patients in two groups – less than 45 years of age (63%) and more than 45 years of age (37%) as the risk of recurrence increases in patients above 45 years of age [4,7,14,16]. This was in contrast to studies by Tissel and Kukkonen who found higher incidence of malignancy in older age group[4,7,5,14,16].

In the present study 90% of patients were females and 10% males with female to male ratio of 9:1. This gender ratio was similar to the study by Zuniga[19]. Various other studies also show a higher prevalence of well differentiated thyroid cancer in female patients ranging from 55% to 70% of the patients in the respective studies[11,14,18,26]. All the patients presented with swelling in the thyroid region. 33% of the patients presented with pain in the swelling and 26.6% of patients presented with sudden increase in the size of swelling which was due to haemorrhage within the nodule. 3 patients (10%) had dysphagia due to large node in the trachea-oesophageal groove and extension of nodule into the retropharyngeal space. 1 patient had dyspnoea on exertion due to compression of trachea laterally and retrosternal extension and 4 patients had significant weight loss. Out of 30 patients in our study 19 patients were less than 45 years of age and therefore belonged to Stage I. Among 11 patients who were more than 45 years of age, 3 patients were in Stage II (27.2%) 7 in Stage III (63.6%) and 1 in Stage IVa(9.1%).This was similar to a study by Lim who had more number of thyroid malignancies in stage I and stage II[26].

On histopathology examination all the 30 patients showed Papillary carcinoma. However 3 patients(10%) were follicular variant of Papillary carcinoma thyroid in whom preoperative FNAC had showed follicular neoplasm. Few studies have shown predominance of papillary carcinoma[7, 26]. All patients in the present study underwent Total thyroidectomy with central compartment neck dissection (TT+CCND) in order to evaluate the prevalence of micro metastasis in central compartment lymph nodes in well differentiated thyroid malignancies with N_0 neck. However 4 of these patients also underwent an ipsilateral functional neck dissection in the same sitting as multiple small lymph nodes (subclinical and also missed on Ultrasound) were found along the middle third of jugular vein during surgery. There are various studies which advocate elective clearance of central compartment lymph nodes during the initial surgery for papillary thyroid

The reasons for this are relatively higher incidence of lymph node metastasis in the central compartment which is the first echelon of lymphatic drainage in thyroid[9,17] . Clearance of central compartment is easier and safer when performed during initial surgery compared to revision surgery[15,17]. Though the cure rates were not affected , the morbidity and regional distant metastasis is less when elective clearance of central compartment is done and post- operative radio iodine ablation is more effective and Thyroglobulin assay and ^{131}I scan more reliable[1]. Higher T stage of primary tumour is associated with higher metastasis and higher risk of recurrence [4, 7, 9, 12,15, 19,26]. However studies by Zuniga, Doherty and Shindo ,Mithra do not advocate elective central compartment clearance in well differentiated thyroid malignancies with N_0 neck ,as it does not affect survival ,has higher risk of complications like hypocalcemia and recurrent laryngeal nerve injury and small lymph nodes can be treated by radio iodine[2, 14, 19,26].

In our study no lymph nodes were found in central compartment in 18 out of 30 patients and only 12 patients (40%) had central compartment lymph nodes, ranging from 3 to 5 in number in these patients. Among the 12 patients who had lymph nodes in the central compartment , only 7 had metastasis and 5 patients had reactive lymph nodes .Among 4 patients who were found to have lymph nodes in the lateral neck , 3 had metastasis in central compartment .Therefore the prevalence of metastasis in the central compartment in our study was 23.3%. The number of metastatic nodes retrieved in various patients in our study were less than 3 nodes each in 6 out of 7 patients and 5 nodes in 1 patient. Therefore the number of metastatic nodes is not related to the number of nodes retrieved. However presence of subclinical nodes in the lateral nodes is associated with high incidence of metastasis in central compartment.

Among the patients who were more than 45 years of age , 3 out of 11 patients(27.2%) had metastasis in central compartment where as among patients who were less than 45 years of age , 4 out of 19 patients (21%) had metastasis in central compartment. This incidence of metastasis in central compartment (23.3%) is similar to studies done by Tissel who quoted 25% . Studies by Noguchi and Qubain have shown significant difference in metastasis from tumour which were less than 1 cm and more than 1 cm in diameter[15]. However our study had no microcarcinomas (<1 cm). Therefore significant difference was not seen on the size of tumour in T_1. However, among patients more than 45 years of age metastasis was higher in T_3 than in T[2.4,14, 19].

In one series transient hypocalcemia was seen in 8 patients (26.6%) which lasted less than 3 months in 7 patients and 4 months in 1 patient. There was no permanent hypocalcemia (duration more than 6 months). All these patients were managed by oral supplements of calcium and vitamin D. However in literature, transient hypocalcemia after central compartment neck dissection has been reported to range between 13 % to 50%[22,23].

Permanent hypocacemia is rare and accounts for 1 to 10 %[12, 18 ,23]. This shows that with selective intracapsular ligation o f inferior thyroid artery and good dissection techniques and use of bipolar cautery can minimize morbidity due to parathyroid injury . In our series there was no Recurrent laryngeal nerve (RLN) injury. However literature quotes that RLN injury in thyroid malignancies to the tune of 1 to 7%[12, 14,18]. Recurrent laryngeal nerve injury incidence varies according to stage of tumour, extrathyroidal spread and surgeons experience. Total thyroidectomy with central compartment clearance can be a safe procedure in the hands of experienced surgeon with good bipolar cautery and proper selection of cases. The use of optical magnification (microscopes) and intraoperative nerve monitoring further reduces injury.

All our patients were sent for Radioiodine scan 3 to 4 weeks after surgery, 12 patients underwent Radioiodine ablation, as they had higher T stages (T_3, T_4) ,extrathyroidal spread, multiple metastatic lymph nodes (subclinical), and higher grade of tumour. 6 patients (20%) were advised RAI ablation but defaulted , another 12 patients (40%) were in the younger age group and did not have significant RAI uptake in the postoperative scan and were not advised RAI scan. Various studies in literature have quoted RAI ablation in 25 to 60 % of their patients depending on stage and aggressiveness of diease and complication of resection[7, 11,26]. After an average follow up of one year , none of our patients had local , regional or distant metastasis. 1 patient was lost to follow up 6 months following surgery. However this follow up is too short for well differentiated thyroid malignancies treated adequately.

Various studies in literature, quoted 20 years survival rates of 90% and above in PTC (Papillary Thyroid Carcinoma) stage I after total thyroidectomy with prophylactic central compartment clearance where as recurrence rates varied between 10 to 50% in high risk scores of primary tumour, locally advanced tumours where central compartment neck dissection was not done , and in patients who had gross extra thyroidal spread[1,7,8,12,14,17] Therefore considering the benefits and risk

(morbidity) in performing elective central compartment neck dissection in well differentiated thyroid malignancies it would be safer to perform elective central compartment neck dissection (at least ipsilateral paratracheal clearance) in all the cases if the surgeon is experienced. A complete elective central compartment clearance would be indicated in higher stages of primary tumours, higher grade tumours, large tumours and bad risk factors like extrathyroidal extensions.

Conclusion

Metastasis (occult) in central compartment in patients with clinically N_0 disease was 23.3 %.Total thyroidectomy with central compartment clearance remains the treatment of choice in well differentiated thyroid cancer with an intermediate/high risk score. At least an ipsilateral paratracheal clearance would be beneficial and prevents later chances of regional recurrence in early stages of well differentiated thyroid malignancies (T_1 and T_2). Transient hypocalcemia is relatively common following Central compartment clearance. However permanent hypocalcemia is rare if surgery is properly done. Vocal cord paralysis is rare. Post-operative RAI scan and ablation should be done in all intermediate/ high risk cases , particularly if they show radio iodine up take after thyroidectomy. The patients should be periodically followed up with USG, serum calcium, and serum Thyroglobulin.

References

1. Kristein Boelaert. Thyroid gland: Revised Guidelines for the Management of Thyroid Cancer. N R Endo.April 2010; 6:185-86.
2. Wada N, Duh QY, Sugino K, Iwasaki H, Kameyama K, Mimura T et al, Lymph node metastasis from 259 papillary thyroid microcarcinomas. Annals of surg.2003;237(3):399-07.
3. Tisell LE. Role of lymphadenectomy in the treatment of thyroid differentiated thyroid carcinomas, British J Surg.1998;85:1025-26.
4. Hughes DT, Gerard M, Doherty. Central neck dissection in papillary thyroid cancer. cancer control.2011;18(2):83-88.
5. Shaha A R. Thyroid cancer: Extent of thyroidectomy Cancer Control. Cancer 2000;7(3):240-45.
6. Scheumann FW, Gimm O,Wegener G,Hudeshagen H, Dralle H. Prognostic significance and surgical management of locoregional lymph node metastasis in papillary thyroid cancer. World J. Surg. 1994; 18:559-68.
7. Salter K D,Andersen P E, Cohen J , Schuff K G,Lester L, Shindo M, Sauer D, Gross N D. Central nodal metastasis in papillary thyroid carcinoma based on tumour histologic type and focality. Arch Otolaryngol Head Neck 2010; 136 (7): 692-96.
8. Slough CM, Randolph GW. Workup of Well differentiated Thyroid Carcinoma. Cancer Control 2006;13(2):99-05.
9. Carter WB, Tourlot JB, Savell JG, Lilienfeld H. New treatments and shifting paradigms in differentiated thyroid cancer management. Cancer Control 2011; 18(2):96-03.
10. Guerrere MA, Clark OH. Controversies in the Management of Papillary Thyroid Cancer Revisited. ISRN Oncol 2011;30(3):128.
11. Sivanandan R, Soo KC. Pattern of cervical lymph node metastases from papillary carcinoma of thyroid. British J Surg 2001;88:,1241-44.
12. Shindo M ,Stern A .Total thyroidectomy with and without selective central compartment dissection-A comparison complication rates. Arch Otolaryngol Head Neck 2010; 136 (6): 584-87.
13. Carty S, Cooper DS, Doherty GM, Duh Q Y,Kloos RT,Mandel SJ, et al. Consensus statement on terminology and classification of central neck dissection for thyroid cancer. Thyroid 2009;19:1153-58.
14. Tisell LE, Nilsson B, Molne J, Hansson G, Fjalling M, Jansson S, Wingren U et al. Improved survival of patients with papillary thyroid cancer after surgical micodissection. World J Surg 1996;20:854-59.
15. Cranshaw, Carnaille B. Micrometastasis in thyroid cancer. An important finding? Surg Oncol. 2008;17:253-58.
16. Shindo M, Wu JC, Park EE, Tanzella F. The importance of central compartment elective lymph node excision in the staging and treatment of papillary thyroid cancer. Arch otolaryngol Head Neck Surg 2006;32(6):650-54.
17. Qubain SM, Nakano S, Baba M, Takao S, Aikou T. Distribution of lymph node micrometastasis in pNO well differentiated thyroid carcinoma. Surgery 2002;131(3):249-56.
18. Gimm O, Rath WF, Dralle H. Pattern of lymph node metastases in papillary thyroid carcinoma . British J Surg 1998;85:252-54.
19. Zuniga S, Sanabria A. Prophylactic central neck dissection in stage No papillary thyroid carcinoma. Arch otolaryngol Head Neck Surg 2009;135 (11):1087-91.
20. Chung Y S, Suh Y J. Is central lymph node dissection mandatory in 2 cm or less sized papillary thyroid cancer ?.J Korean Surg Soc 2010;79:332-39.

21. Sarkofas GH, Sampanis D, Safioleas M. Cervical lymph node dissection in papillary thyroid cancer :Current trends, persisting controversies and unclarified uncertainties. Surg Oncol 2010;19:57-70.
22. Roh JL, Park JY, Park C. Prevention of postoperative hypocalcemia with routine oral calcium and vitamin D supplements in patients with differentiated papillary thyroid carcinoma undergoing total thyroidectomy plus central neck dissection. Cancer 2009;251-58.
23. Mithra I, Nichani JR, Yap B, Homer JJ. Effects of central compartment neck dissection on hypocalcemia incidence after total thyroidectomy for carcinoma. LO 2011;125:497-01.
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(5): 693-98.
25. Agarwal S, Chand G, Jaiswal S, Mishra A, Agarwal G, Agrawal A, et al. Pattern and risk factors of Central Compartment lymphnode metastasis in papillary Thyroid Cancer: A Prospective Study from an Endocrine Surgery Centre. Thyroid Res 2O12:1155-62.
26. Lim LHY, Chong YK, Hong GS, Lim TH. Well differentiated thyroid carcinoma: Factors predicting recurrence and survival Singapore Med J. 2002; 43(9):457-62.
27. Teixeira G, Teixeira T, Gubert F, Chi. kota H, Tufano R. The incidence of central neck micrometastasic disease in patients with papillary thyroid cancer staged preoperatively and intraoperatively as N0. Surgery 2011;1161-67.
28. Noguchi S, Murakami N. The value of lymph node dissection in patients with well differentiated thyroid cancer. Surg Clin North Am 1987;67:251.