

Extent of Neck Dissection in Cases of Differentiated Thyroid Carcinoma

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Papillary thyroid carcinoma (PTC) is the commonest histopathological type of differentiated thyroid carcinoma (DTC). It was found that cervical LNs were affected in 20–50% of patients having PTC. Cervical metastases frequently takes place first in the central compartment and subsequently in the lateral one. The aim of this study is to detect the impact of the different neck surgeries for DTC on the local control of the disease.

Patients and methods: *This study was done between 2012 and 2015, on 30 patients with proved DTC either by fine needle aspiration biopsy done preoperatively or by histopathological examination of paraffin section of the excised thyroid glands postoperatively. Those patients were divided into three equal groups: one group underwent total thyroidectomy with ipsi-lateral LN dissection, the second one underwent total thyroidectomy with central LN dissection (CLND) and the last group only underwent total thyroidectomy. Histopathological examination of all resected tissues was done. Patients underwent whole body scan (WBS) and accordingly they received the appropriate therapy of radioactive iodine. Measuring serum thyroglobulin and thyroglobulin antibodies, and neck ultrasound were employed in the follow up.*

Results: *In the group that underwent CLND, three patients were shown to have positive LNs (30%), whereas in the group that underwent ipsi-lateral neck dissection, all patients showed malignant LNs (100%). In the whole study, seventeen patients (56.6%) received RAI once, 10 patients (33.3%) received RAI twice and 2 patients received a third dose of RAI. About 90% of the patients that received a second RAI therapy were from the groups that underwent ipsi-lateral LN dissection and CLND which indicate that those patients deserved these types of operations and thyroidectomy alone would not be enough to ensure a better outcome for those patients.*

Conclusion: *In patients with DTC, at least CLND should be performed together with total thyroidectomy if preoperative diagnosis is done. If LNs by US show criteria of malignancy, even in the absence of histological proof, total thyroidectomy and ipsi-lateral neck LN dissection is recommended.*

Key words: *Total thyroidectomy, papillary thyroid carcinoma, central lymph node dissection, lateral neck dissection.*

Introduction:

Papillary thyroid carcinoma (PTC) is the commonest histopathological type of differentiated thyroid carcinoma (DTC), with frequent spread to cervical lymph nodes (LNs).¹ It was found that cervical LNs were affected in 20–50% of patients having PTC.² Cervical metastases frequently takes place first in the central compartment and subsequently in the lateral one.^{3,4} The American Thyroid Association (ATA) recommends the

classification of the American Head and Neck Society, to distinctly identify neck levels from I to VII. Of these, levels I to V are included in lateral neck dissection, while levels VI and VII make up central neck dissection.⁵

The aim of this study is to detect the impact of the different neck surgeries for DTC on local control of the disease.

Patients and methods:

This study was done between 2012 and

2015, on 30 patients with proved DTC either by fine needle aspiration biopsy (FNAB) done preoperatively or by histopathological examination of paraffin section of the excised thyroid glands postoperatively.

Neck ultrasonography (US) was done for all patients with thyroid swellings to assess for malignancy criteria such as having a solid lesion with irregular margins, microcalcifications, local invasion, infiltration of the surrounding thyroid tissue, capsular interruption, high intranodular flow by Doppler or having suspicious regional lymph nodes (LNs) accompanying a thyroid nodule. However, patients with suspicious nodules <1cm were excluded from the study. Thyroid function tests were done (Free T3, Free T4 and TSH) to make sure that the patient is euthyroid before any intervention. All patients with suspicious thyroid swellings by US underwent FNAB. Cases with positive FNAB that were found by US to have suspicious or enlarged LNs were subjected to total thyroidectomy with ipsi-lateral neck dissection (dissection of level I to V with preservation of the internal jugular vein and sternomastoid if possible), whereas those with positive FNAB with no suspicious LNs by US were subjected to total thyroidectomy with central lymph nodes dissection (CLND) (dissection of level VI and VII). On the other hand, patients with negative FNAB with suspicious LNs in the US underwent LN biopsy. Patients with positive LN biopsy were subjected to total thyroidectomy with lateral neck dissection, however, others with negative LN biopsy were subjected to total thyroidectomy with CLND. As for patients with negative FNAB and neck US showing reactionary enlarged LNs, total thyroidectomy with CLND was done, whereas patients with no LN enlargement on US and negative FNAB, only total thyroidectomy was done.

Histopathological examination of all excised tissues was done and only positive cases of DTC were included in the study. Those patients were further divided into three equal groups of 10 patients each according to the type of surgery performed. One group underwent total thyroidectomy with

ipsi-lateral LN dissection, the second one underwent total thyroidectomy with CLND and the last group only underwent total thyroidectomy.

Post-operatively, no replacement therapy was given till the first whole body scan (WBS) I^{131} was done, about 4 weeks later, when serum TSH was found to be above 40 mU/L. WBS was used to assess the complete resection of all functioning thyroid tissue in the neck either in the operative bed or in LN metastasis. Positive cases received ablative dose of radioactive iodine (RAI) according to their body weight. On the fifth day after the scan, replacement therapy was started with suppressive dose levo thyroxin (LT4) (1.6-1.8 $\mu\text{g}/\text{Kg}$). The 2nd WBS was done after 6 months (after stoppage of thyroxin therapy for 3 weeks). This was followed by giving therapeutic dose of RAI for positive cases. Then a 3rd WBS was done after 6 months for those patients that received the therapeutic dose, where positive patients received another therapeutic dose of I^{131} .

Evaluation of Eltroxin therapy by serum TSH was done after a month, 3 months and 6 months from starting therapy. Serum thyroglobulin Tg (non suppressed) and serum thyroglobulin antibody Tg-Ab were measured with the TSH before the first WBS was done and were repeated after therapy. Neck US was done for patients with positive 2nd WBS then repeated after 6 months.

Results:

Neck US that was done for all the 30 patients included in the study showed suspicious criteria of malignancy, whereas FNAB was positive for malignancy in 12 patients (40%) and was inconclusive in 18 patients (60%) that were proved later to be malignant in paraffin section. Histopathological examination of the resected tissues showed that 13 patients (43.3%) had PTC, 10 patients (33.3%) had follicular thyroid carcinoma (FTC) and 7 patients (23.4%) had follicular variant papillary thyroid carcinoma (FVPTC).

The tumor was present in one lobe in 21 patients (70%) while the other lobe was involved in 9 patients (30%). Patients with

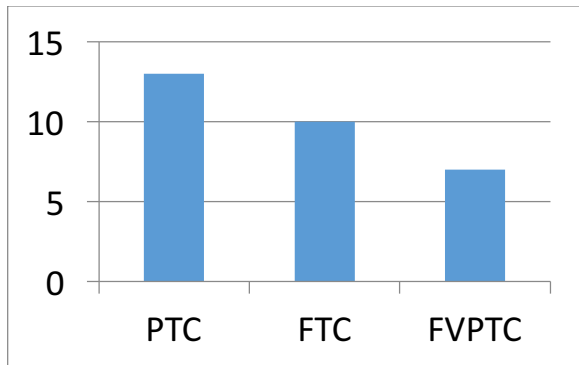


Figure (1): Histopathological types of DTC.

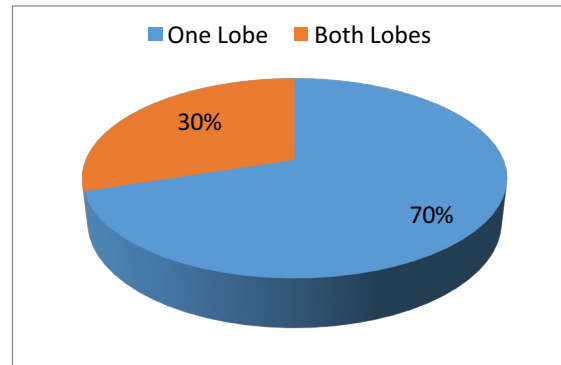


Figure (2): Bilateralism.

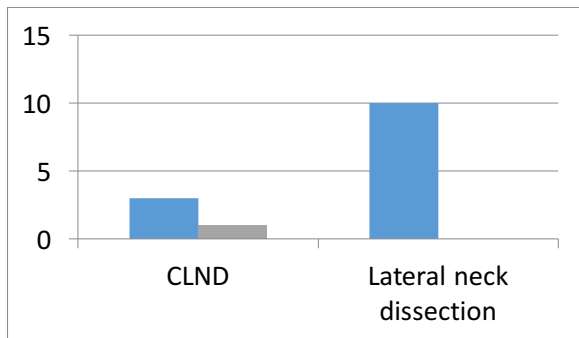


Figure (3): Patients with positive LNs.



Figure (4): Total thyroidectomy specimen with left side lateral neck dissection.

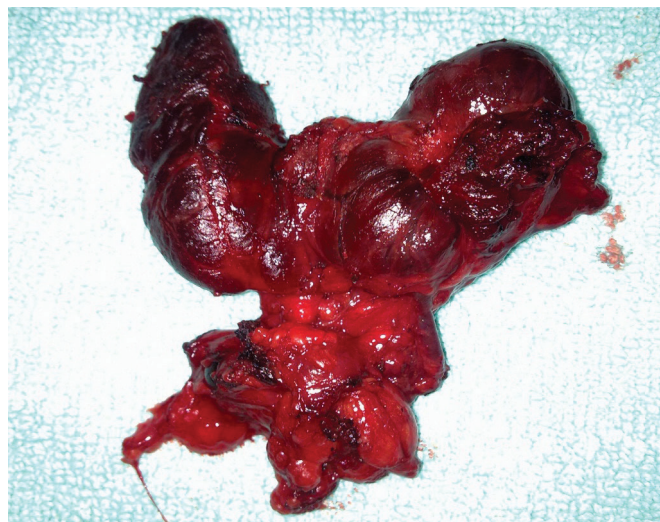


Figure (5): Total thyroidectomy specimen with CLND.

follicular carcinomas had the tumor only in one lobe.

Multi focal tumors were found in 10 patients (33.3%) with papillary carcinoma, while in the other 20 patients (66.7%) it was uni-focal.

In the group that underwent CLND, three patients from the 10 were shown to have positive LNs (30%), whereas in the group that underwent lateral neck dissection, all 10

patients showed malignant LNs (100%).

Complications: There were 2 patients (6.6%) with temporary unilateral recurrent laryngeal nerve (RLN) neurapraxia (in the group of lateral neck dissection) that resolved completely after 3 months. Three patients (10%) developed temporary hypoparathyroidism, also in the group that underwent lateral neck dissection. Two of them recovered after 4 months, whereas

one patient remained to have permanent hypoparathyroidism. No mortalities were recorded by the end of the follow up period.

Post-operative management: In the group that underwent only total thyroidectomy, WBS was positive in 5 patient (50%) that received ablative dose of RAI and when WBS was repeated, it showed a successful ablative dose in 4 patients, whilst one patient received a therapeutic dose. Patients with negative WBS, did not receive any further therapy.

As for the group that underwent CLND, five patients (50%) showed positive first WBS and on doing the second WBS (after receiving the ablative dose of the RAI), two patients showed complete response (20%) and 3 patients (30%) required to have the therapeutic dose of RAI. On doing the 3rd WBS, those patients showed successful therapy with the RAI.

However, in the group of lateral neck dissection, seven patients (70%) showed positive first WBS that was followed by giving ablative dose of RAI. The second WBS was positive in 6 patients (60%) that received therapeutic dose of RAI, whereas one patient (10%) showed complete response. When the 3rd WBS was done after giving the therapeutic dose of RAI, three patients (30%) showed successful therapy, whilst 2 patients (20%) were still positive and received RAI again.

In the whole study, seventeen patients (56.6%) received RAI once, 10 patients (33.3%) received RAI twice and 2 patients received a third dose of RAI. Sixty % of the patients with a second RAI therapy were from the group that underwent lateral neck dissection, 30% were from the group that underwent CLND and 10% were from the group that underwent only total thyroidectomy. Thus, about 90% of the patients that received a second RAI therapy were from the groups that underwent ipsi-lateral LN dissection and CLND which indicate that those patients deserved these types of operations and thyroidectomy alone would not be enough to ensure a better outcome for those patients.

Ninety percent of the patients that had a positive 1st WBS showed high Tg level that

was suppressed by therapy. Four patients from the 5 that had positive 1st WBS after only total thyroidectomy, showed an elevated level of Tg that was suppressed by therapy. The same was for those who underwent CLND, whereas the whole 7 patients with positive 1st WBS after lateral neck dissection showed elevation of its level that was further suppressed by therapy.

Neck US that was done for patients with positive 2nd WBS and its repetition after 6 months, did not show any residual tissues.

Discussion:

In my study on 30 patients, neck US was done pre-operatively for all patients and showed suspicious criteria for malignancy. In 2006, Cooper et al. agreed that thyroid US is the imaging investigation of choice for suspicious thyroid nodules.⁶ It was reported by the ATA that the high-resolution neck US can detect thyroid nodules in 19–68% of randomly selected cases.⁵

In my series, FNAB showed a positive result of thyroid cancer in 12 patients (40%) while it was inconclusive in the remaining 18 (60%). According to Yeh and co-workers in 2004, although FNAB is a very sensitive test for PTC, sometimes false-negative results are detected; therefore, a negative FNAB should not negate concerns in the presence of worrying clinical findings.⁷

FNAB of thyroid nodules has become the primary diagnostic modality in the evaluation of thyroid nodules. However, the role of thyroid cytology in diagnosis could be limited by the presence of atypical cytological patterns, in this case, we should consider surgery, especially if it was shown to be PP (possible papillary carcinoma).⁸

Nodules that have a lot of follicular cells with little or no colloid are almost impossible to classify into benign or malignant depending on FNAB. Thus, surgical biopsy is recommended as nearly 20% of these lesions are follicular carcinomas.⁹

According to Hu and co-workers in a 2008 publication, PTC was found to be the most common type of thyroid cancers, representing from 75 to 85% of all thyroid

cancer patients¹⁰ and this is consistent with my results.

In my study, thirty % of patients had the tumor in both lobes and it was found to be PTC, multi focal tumors were found in 10 patients (33.3%) with PTC, while in the other 20 patients (66.7%) it was uni-focal, whereas in a study done by Passler et al, they found bilateral tumors in the form of FVPTC in 19% of his patients, PTC in 10% and follicular thyroid carcinoma (FTC) in 5%; unilateral multifocal tumors were found in the form of FVPTC in 14%, PTC in 4% and FTC in 5%. Uni-focal tumors were found in the form of FVPTC in 68%, PTC in 85%, and FTC in 90%.¹¹

Multifocal and contra-lateral lesions are common in PTC and their prevalence is not related to the size of the tumor. Therefore, histopathological examination of the whole gland is highly advisable in order to estimate the rate of multifocal PTC (mPTC) properly.¹²

The extent of surgery for DTC, before the 2009 ATA guidelines, was a controversial issue, as there was no evidence that either lobectomy or total thyroidectomy is associated with a higher survival rate. Those who support total thyroidectomy state that complete resection of thyroid tissue helps use radioactive iodine for detection of residual or metastatic disease postoperatively, and for treatment as well.^{13,14} Moreover, total thyroidectomy could also exclude the probability of undetected multifocal disease in the contra-lateral lobe.¹⁵ On the other hand, those who support lobectomy indicate that PTC is an indolent disease having an excellent prognosis, so patients should not be exposed to complications related to total thyroidectomy, such as hypo-parathyroidism and RLN injury without a clear survival benefit.¹⁶

However, from the recent recommendations of the ATA is that patients having thyroid cancer greater than 4 cm, or those with gross extra-thyroidal extension should be operated upon by total thyroidectomy, whereas for patients with thyroid cancer more than 1 cm and less than 4 cm without extra-thyroidal extension, and without clinical

evidence of any lymph node metastases, the primary surgical intervention could be either total thyroidectomy or lobectomy. Thyroid lobectomy alone may be a sufficient surgical management for low-risk papillary and follicular carcinomas; however, the management team may prefer to perform total thyroidectomy to enable RAI therapy or to enhance follow-up depending on disease features and/or patient preferences. As for patients with thyroid cancer less than 1 cm without extra-thyroidal extension, the initial surgery should be thyroid lobectomy unless there are obvious indications to excise the other lobe.⁵

The results of Adam et al. in 2014¹⁷ were consistent with a report from the SEER (Surveillance, Epidemiology and End Results) database by Mendelsohn et al. in which they studied data of 22,724 patients with PTC from 1988 to 2001. They illustrated that there was no difference in survival between patients operated upon by lobectomy and those operated upon by total thyroidectomy.¹⁸

Nixon et al. in their publication in 2010 reported isthmusectomy as a surgical treatment for thyroid carcinoma. Their results suggest that isthmusectomy alone could be a sufficient surgery for patients having small DTC confined to the isthmus. The advantage of this procedure is that it decreases the risks of postoperative complications by avoiding dissection of the RLN and parathyroid glands.¹⁹ However, ATA guidelines did not mention isthmusectomy as an appropriate surgical procedure for thyroid cancer.

The site of the LNs could also be useful for decision-making. Malignant LNs are much more likely to arise in levels III, IV, and VI than in level II. However, this may not be true for PTC tumors arising in the upper thyroid pole, where they have more tendency to show skip metastases to levels III and II.⁵

The extent of LN dissection is an another controversial issue. A study done by Bhattacharyya indicated that limited positive nodal lymphadenectomy in patients with PTC showed similar survival rates to those undergoing more extensive neck dissections.

Therefore, he concluded that a formal neck dissection may not be needed for the efficient treatment of PTC patients with cervical nodal metastases.²⁰ Furthermore, in the study done by Zuniga and Sanabria in 2009, prophylactic CLND did not offer any changes in the rate of neck recurrence in patients without clinical stage disease.²¹

One of the latest recommendations of the ATA includes that therapeutic CLND should accompany total thyroidectomy for patients with clinically involved central LNs, whilst prophylactic CLND (ipsi-lateral or bilateral) should be considered in PTC patients with clinically unaffected central LNs (cN0) who have advanced primary tumors (T3 or T4), clinically affected lateral LNs (cN1b), or if the information will be required to plan further therapy. However, this is considered a weak recommendation with low-quality evidence.⁵

On the other hand, there is a strong recommendation by the ATA to perform thyroidectomy without prophylactic CLND for small (T1 or T2), noninvasive, clinically node-negative PTC (cN0) and for most follicular cancers. However, therapeutic lateral neck dissection should be performed for patients with biopsy-proven metastatic lateral cervical lymphadenopathy.⁵ This is consistent with our results.

A study done by Fama et al. revealed that CLND must always be done, lateral LN dissection may be either performed in cases having ipsi-lateral positive lymph nodes or in more advanced diseases without lymph node affection, whereas inspection and excision of the contra-lateral LNs should only be done if there is an evidence of gross node metastases.²²

Practically, the most adequate dose of thyroid hormone for most postoperative patients with DTC is the one that decreases the serum TSH level to just below the normal range. At a minimum, patients should not be allowed to have increased TSH levels, as this would represent an inadequate treatment of both postsurgical hypothyroidism and DTC⁶ and this is consistent with what was done with patients in my study.

In my study, two patients developed temporary RLN paralysis. In a study done by Pacin et al, it was found that the rate of permanent RLN paralysis is rare (<2%) when patients are operated upon by an experienced surgeon. However, transient vocal cord dysfunction is more common but resolves spontaneously in most cases within 1–6 months.²³ In expert's hands, the rate of RLN injury and hypoparathyroidism is insignificant in neck dissection.²⁴

In my series, seventeen patients (56.6%) received RAI once, 10 patients (33.3%) received RAI twice and 2 patients received a third dose of RAI. Rao et al. reported that 442 cases with cervical lymph node metastases were subjected to I131. Three hundred and seventy eight of these cases (85.5%) revealed complete response and 20 (4.5%) revealed partial response, whereas 44 cases (10%) did not respond to the radio-iodine therapy.²⁵

Serum thyroglobulin (Tg) is best measured just before I131 administration, if patients undergo L-T4 withdrawal. The presence of circulating thyroglobulin antibodies (Tg-Ab) may interfere with immunometric assays and result in falsely lower Tg levels. Around 25% of patients with thyroid carcinoma and 10% of the general population have Tg-Ab, thus direct measurement of Tg-Ab should be engaged instead of using the Tg recovery test to rule out the presence of those antibodies. Serial serum Tg-Ab measurements may act as an inaccurate substitute marker of residual normal thyroid tissue or tumor. Follow-up with serum Tg and Tg-Ab measurements during L-T4 treatment, in addition to performing neck US every 6 to 12 months is recommended for those patients.²⁶

Neck US is highly sensitive in detecting cervical metastases in patients with DTC, particularly when associated with a high Tg level. It is more sensitive than neck palpation and has the ability to detect small impalpable LNs. Lymph nodes with short axis smaller than or equal to 0.5 cm should be carefully followed up with periodical US monitoring. US should be performed initially at 3 to 6 months after total thyroidectomy and then, every 6 to 12 months, depending

on the patient's risk. Low-risk patients are considered free from the disease after 3 to 5 years of follow-up, then no more annual neck US is required.²⁷

Conclusion:

In patients with DTC, at least CLND should be performed together with total thyroidectomy if preoperative diagnosis is done. If LNs by US show criteria of malignancy, even in the absence of histological proof, total thyroidectomy and ipsi-lateral neck LN dissection is recommended. RAI has a golden rule for post-operative treatment of patients with DTC. Its use can be repeated several times according to the follow up WBS. Both Tg estimation and RAI¹³¹ scanning are used in detecting recurrent disease in the post-treatment monitoring of these patients.

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