

THE ROLE OF CENTRAL NECK DISSECTION IN DIFFERENTIATED THYROID CANCER

By

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ABSTRACT

Background: Thyroid cancer is the most common endocrine malignancy and differentiated thyroid cancer has a 10-year survival rate of \approx 90%. Cervical lymph node metastases are a common feature of papillary thyroid cancer while follicular thyroid cancer often spreads hematogenously.

Objective: To evaluate the role of central neck dissection in the management of differentiated thyroid cancer as regards its impact on both morbidity and overall outcome.

Patients and Methods: This was a prospective cross sectional study conducted on 30 patients diagnosed as differentiated thyroid cancer (DTC) and admitted at the Surgical Oncology Department of Al-Azhar University Hospitals and Damanhour Oncology Centre. All patients of the study subjected to clinical assessment by complete history taking, complete laboratory investigations, imaging studies and tissue diagnosis by fine needle aspiration cytology.

Results: the relation between positive LNs and tumor of 2-4 cm size which was central group which commonly diagnosed clinically and the absence commonly diagnosed radio logically and also associated with capsular invasion of thyroid. The most common type of the tumor was papillary type with a little percentage of follicular type and I131 was used as appellatives therapy for some of these cases.

Conclusion: central neck dissection is still beneficial especially in high risk group of cases where there was capsular invasion.

Key words: central neck dissection, differentiated thyroid cancer.

INTRODUCTION

Thyroid cancer is the most common endocrine malignancy, and its incidence is increasing at the highest rate among cancers in both the US and worldwide (*Pellegriti et al., 2013*). Differentiated thyroid cancer (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 (*Friedman et al., 2011*). Cervical lymph node metastases are a common feature of papillary thyroid cancer (PTC), with an incidence between 20-90% (*Haugen et al., 2016*). Conversely, follicular thyroid cancer (FTC) often spreads hematogenously, and rarely metastasizes to the cervical lymph nodes. Hurthle cell thyroid cancer (HTC) is a rare and aggressive form of differentiated thyroid cancer of follicular cell origin; HTC displays a lower rate of

cervical lymph node metastasis compared to PTC (*Goffredo et al., 2013*).

The prognostic value of nodal metastases is controversial: some Authors consider their presence predictive of local disease recurrence, but overall disease-specific survival does not seem to be adversely affected. Loco-regional metastasis to the cervical lymph node network can take place in one or more of the levels originally described by Robbins. Cervical lymph node levels VI and the upper part of VII, most commonly known as the central compartment, are often involved in thyroid malignancy. This anatomical district is considered to be the first echelon of nodal metastases in all thyroid carcinomas (*Giugliano et al., 2014*).

The central compartment is bounded by the hyoid bone (superior), carotid artery (lateral), and sternal notch or innominate artery (inferior). The American Thyroid Association (ATA) defines central compartment neck dissection as “comprehensive, compartment-oriented removal of the prelaryngeal and pretracheal nodes and at least one paratracheal lymph node basin.” The regional metastases to the cervical lymph nodes were traditionally believed to have an effect only on recurrence rate, but not mortality (*Hennessey and Goldenberg, 2016*).

Some authors recommend routine central neck dissection (CND) in order to prevent a future recurrence, citing the high risk of positive lymph nodes, better outcomes, and a lower morbidity rate associated with this initial operation, whereas others maintain that this procedure increases the risk of injury to

the parathyroid glands and recurrent laryngeal nerves, without any demonstrable benefits in terms of long-term survival (*Barczyński et al., 2013*). Central neck dissection allows for accurate pathologic staging of the lymph nodes and treatment of the micrometastases that may be responsible for the recurrence or persistence of the disease (*Giordano et al., 2012*). In addition, recurrence in this compartment is difficult to treat surgically and may become complicated, while central lymph node dissection during the initial thyroid surgery can be performed without extending the wound (*Pietro et al., 2013*).

The most important morbidities associated with CND consist of recurrent laryngeal nerve damage and hypocalcemia related to parathyroid hypo-function or to accidental parathyroidectomy. The incidence of surgical complications is variable, surgeon and centre-dependent, and correlates with pathological features of the tumor. It is important to keep in mind the data available in the most current scientific literature: transient hypocalcaemia has been reported with an incidence of up to 30%, while recurrent laryngeal nerve injury has been observed with an incidence of in 1-3%. Complications are an unpleasant, and sometimes unavoidable, which are a reality of intense surgical activity. Minimization of their incidence can only come from accurate knowledge of the relevant surgical anatomy, standardized and careful surgical techniques and clear therapeutic indications (*Giugliano et al., 2014*).

The use of routine prophylactic central neck dissection for the treatment of

differentiated thyroid cancer has been an area of debate over the past few decades. The decision of when to perform a prophylactic central neck dissection must be based on retrospective studies and expert opinion. The American Thyroid Association recommended that prophylactic central neck dissection should be reserved only for the use in invasive or advanced (T3 and T4) papillary thyroid cancers. When planning the initial treatment of a patient with differentiated thyroid cancer one must determine the efficacy of central neck dissection. In conclusion, the benefits of prophylactic central neck dissection are too meager to outweigh its associated risks, and thus the use of central neck dissection should be reserved for high-risk patients in the hands of an experienced surgeon (*Hennessey et al., 2016*).

AIM OF THE WORK

The aim of the present work is to evaluate the role of central neck dissection in the management of differentiated thyroid cancer as regard its impact on both morbidity and overall outcome.

PATIENTS AND METHODS

This was a prospective cross-sectional study conducted on 30 patients diagnosed as differentiated thyroid cancer (DTC) and admitted at the Surgical Oncology Department of Al-Azhar University Hospitals and Damansour Oncology Centre.

This prospective study included the patients with the following criteria: presence of clinically positive or radiologically suggestive LN enlargement in any patients undergoing thyroidectomy, all cases diagnosed as DTC by biopsy at

the preoperative workup and planned to be operated and cases with high suspicion of malignancy as: rapid increase of size in short time, local signs of infiltration to the surrounding structures like change of voice, dysphagia, ear pain, blackout,...etc. The study was submitted for approval of the Hospital Ethics Committee.

All patients in the present study were subjected to the following:

Preoperative assessment: A. Clinical evaluation: complete history-taking, thorough clinical examination, laboratory investigations: preoperative laboratory work up of the patients will include the following: Complete blood picture, blood glucose level. - Renal function tests. - Liver function tests. - Thyroid profile (T3, T4, TSH) and thyroid antibodies, serum calcium level. C. Imaging: ultrasound neck, CT neck in selective cases, fiberoptic laryngoscopy; Pathology: Fine needle aspiration cytology (FNAC) with or without US guidance from any suspicious nodule.

Operative procedure: Under general anesthesia with intubation while the patient in the supine position with neck extension thyroidectomy then central neck dissection will be performed. Routine identification of recurrent laryngeal nerve and the parathyroid gland will be identified and preserved. Hemostasis will be ensured throughout the surgery. Suction drain will be inserted.

We follow the surgical technique discussed by *Prescott and Udelsman (2012)*, for detailed steps of central neck dissection.

Postoperative assessment including Clinical assessment: voice changes,

manifestations of hypocalcemia, and amount of drainage. Laboratory assessment of serum calcium level, Full histopathological examination of both thyroid gland and central compartment obtained lymph node specimens.

Statistical analysis:

The collected data were tabulated and analyzed using SPSS version 16 software

(SPSS Inc, Chicago, ILL Company). Categorical data were presented as number and percentages while quantitative data were expressed as mean \pm standard deviation (S.D) and range. Chi square test (X²), or Fisher's exact test (FET) were used to analyze categorical variables.

RESULTS

Demographic Data:

The age of patients ranged between 18-66 years with a mean age of 44.5 \pm 18.7 years. Seven of the patients were males

(7/30, 23.33%) while 23 were females (23/30, 76.66%) with a male to female ratio of 1:3.3 (**Table 1**).

Table (1): Demographic data of the studied patients

Parameters Patients	No.	%	P
Sex:			
Male	7	23.33%	0.01
Female	23	76.66%	
Age:			
Range	18-66		
Mean \pm S.D	44.5 \pm 18.7		

During physical examination 27 cases (90%) were firm in consistency while three cases (10%) had hard consistency and the statistical analysis revealed that firm consistency is the most common in our cases (P = 0.001) (Table 3). A

retrosternal extension of the swelling present in two cases (2/30, 6.7%) while the common presenting symptom was an evident neck swelling present in 28 cases (93.3%) (P = 0.01) (**Table 2**).

Table (2): Clinical examination of patients of the study

Clinical finding	No.	%	P
Consistency:			
Firm	27	90%	< 0.001
Hard	3	10%	
Retrosternal extension:			
No	28	93.3%	< 0.001
Yes	2	6.7%	

By ultrasonographic and CT examination of the neck; 17 cases (17/30, 56.7%) had single nodule, 8 cases (26.7%) had unilateral multiple nodules while 5 cases had bilateral multiple nodules. The statistical analysis revealed that the single nodule was the most common finding in

cases of our study (P = 0.021). Twenty-seven (90%) cases had microcalcifications while only 3 cases (10%) had no calcification. The diameter of the nodules ranged between 5-28 mm with a mean diameter of 14.3±6.7 mm (Table 3).

Table (3): Imaging of the swelling in patients of the study

Variable	No.	%	P
Number of nodules:			
Unilateral multifocal	8	26.7%	0.021
Bilateral multifocal	5	16.7%	
Single nodule	17	56.7%	
Microcalcification:			
Yes	27	90%	0.001
No	3	10%	
Diameter			
Range	5-28		
Mean±S.D	14.3±6.7		

Ten cases (33.3%) had tumor size belonged to T1, 6(20%) cases belonged to T3, and no case (0.0%) belonged to T4 while 14 cases (46.7%) belonged to T2 which was the statistically significant type

in our cases. In addition 18 cases (60%) had no LN metastasis and 12 cases (40%) belonged to N1 stage of lymph nodes. Also, all cases had no distant metastasis (100%) (Table 4).

Table (4): TNM staging of the swelling in patients of the study

Variable	No.	%	P
Tumor size:			
T ₁	10	33.3%	< 0.01
T ₂	14	46.7%	
T ₃	6	20%	
T ₄	0	0.0%	
L.N status:			
N ₀	18	60%	>0.05
N ₁	12	40%	
Distant metastasis:			
M ₀	30	100%	0.001
M ₁	0	0.0%	

Post-operatively, vocal cord immobility was present in 2 cases (6.7%), temporary hypocalcemia in 4 cases (13.3%), and hematoma was present in another two cases (6.7%). Of our patients

only one needed to be admitted to ICU (3.3%) and the total hospital stay ranged between 1-4 days with a mean of 1.3±0.65 day (Table 5).

Table (5): Postoperative complications in patients of the study.

Variable	No.	%	P
Vocal cord mobility:			
Mobile	28	93.3%	0.001
Immobile	2	6.7%	
Temporary hypocalcemia:			
Yes	4	13.3%	0.001
No	26	86.7%	
Presence of hematoma:			
Yes	2	6.7%	0.001
No	28	93.3%	
I.C.U admission:			
Yes	1	3.3%	0.001
No	29	96.7%	
Total hospital stay (day):			
Range	1-4		
Mean±S.D	1.3±0.65		

By microscopic examination of the dissected central LNs, +ve LN were found in 18 cases (60%) with combined contralateral in 8 cases (26.6%), and the number was ranging from 4-12 in

ipsilateral and from 1-3 in contralateral LNs. In the lateral LNs, +ve LNs were found in 7 cases (23.3%), and the number was ranging from 3-7 (**Table 6**).

Table (6): Microscopic examination of the removed L.N in patients of the study

Variable	No.	%
Central L.N:		
No. of dissected L.Ns	8-21	
+ve L.N (cases)	18	60%
+ve L.Ns (No.)	4-12	
+ve ipsilateral L.Ns	18	60%
Combined ipsilateral + contralateral L.N	8	26.6%
+ve contralateral L.N	1-3	
Lateral L.N:		
No. of dissected L.Ns	17-30	
+ve L.Ns (cases)	7	23.3%
+ve L.Ns (No.)	3-7	

According to the presence or absence of LNs in relation to the size of the tumor; the most common tumor size that didn't have LNs was the T1 group (6/10, 60%) (P = 0.031) while the most common tumor size that have LNs was T2 (10/20, 50%) (P = 0.021) (**Table 6**).

In T1 group of cases LNs most commonly present in the central group

(4/4, 100%) (P = 0.021); in addition in T2 group of cases LNs most commonly present in the central group (6/10, 60%) (P = 0.023) while in T3 group of cases also LNs most commonly present in central group (3/6, 50%) (P = 0.000) (Table 6). Positive central and positive lateral LNs was more commonly in T3 group without significant relation to the tumor size (P =

0.235). while positive central with negative lateral LNs was significantly present in group of T1 tumor size (P = 0.034) and finally negative central lymph

nodes with positive lateral nodes was commonly present in T3 group of cases without any significant relation to the tumor size (P = 0.326) (Table 7).

Table (7): Relation between the size of tumor and positive L.Ns (central and lateral)

Variable	T1 (n = 10)	T2 (n = 14)	T3 (n = 6)	P
No. L.Ns	6 (60%)	4 (40%)	0 (0.0%)	>0.05
Presence of L.Ns:	4 (20%)	10 (50%)	6 (30%)	>0.05
+ve central + +ve lat	0 (0%)	3 (30%)	2 (33.3%)	
+ve central + -ve lat	4 (100%)	6 (60%)	3 (50%)	
-ve central + +ve lat	0 (0%)	1 (10%)	1 (16.7%)	
P	>0.05*	>0.05*	>0.05*	

In the group of single nodule (17/30, 56.7%); nine (52.9%) had positive LNs and 8 (47.1%) had negative LNs without significance between both groups (P = 0.231); in addition unilateral multifocal group (8/30, 26.7%); 6 of them (75%) had positive LNs and two (25%) has negative LNs with significance correlation between

unilateral multifocal cases and positive LNs (P = 0.01). finally, bilateral multifocal cases (5/30, 16.7%); three of them (60%) had positive LNs and two (40%) had negative LNs without significance between both groups of LNs (0.321) (Table 8).

Table (8): Relation between nature of the swelling and +ve L.Ns.

Nature of detection	+ve L.Ns		-ve L.Ns		P
	No.	%	No.	%	
Single nodule	9	52.9%	8	47.1%	>0.05
Unilateral multifocal	6	75%	2	25%	
Bilateral multifocal	3	60%	2	40%	

Positive LNs were present in all cases of capsular invasion (7/7, 100%) with highly significance correlation between capsular invasion and positive LNs (P = 0.000) while absence of capsular invasion associated with positive LNs in 11 cases

(11/27, 47.8%) and negative LNs were present in 12 cases (12/27, 52.2%) in this group without significance between the presence or absence of LNs in absence of capsular invasion (P = 0.365) (Table 9).

Table (9): Relation between capsular invasion and +ve L.Ns.

Capsular invasion	+ve L.Ns		-ve L.Ns		P
	No.	%	No.	%	
Present	7	100%	0	0.0%	<0.02
Absent	11	47.8%	12	52.2%	>0.05
P	>0.05		<0.001		

Twenty-six of our cases were papillary carcinoma (26/30, 86.7%) while 4 cases (4/30, 13.3%) with a significance of

predominance of papillary carcinoma in our group of cases ($P < 0.001$) (**Table 10**).

Table (10): Relation between different types of differentiated thyroid cancer.

Histopathologic variants	No.	%
Papillary thyroid carcinoma:	26	86.7%%
Well differentiated papillary carcinoma	20	76.9%
Papillary Microcarcinoma	3	11.5%
Follicular variant of papillary carcinoma	3	11.5%
Follicular carcinoma	4	13.3%
P	<0.001	

DISCUSSION

Enlargement of thyroid gland is a common occurrence in most parts of the world especially in the iodine deficient goiter belt areas, where the prevalence may be as high as 40%. The development of goiter is a concern to both the patient and the clinician because of the fear that the swelling may be malignant. Most goiters are benign and even in solitary nodules selected for surgery or clinical grounds malignancy is found in only around 10% (*Hirachand et al., 2013*).

This was a prospective study conducted on 30 cases of thyroid swelling diagnosed as thyroid cancer admitted to the Surgical Oncology Department of Al-Azhar University Hospital and Damanhour Oncology Center.

Our study revealed that the age of patients was in the fifth decade of life.

Santosh and his Colleagues (2014) found in their study that the patients were in the second and third decades of life which disagree with our results.

This study revealed that females more commonly affected than males with a male to female ratio of 1:2.7.

Santosh and his Colleagues (2014) revealed in their study that females were more commonly affected than males with a male to female ratio of 1:9 which coincides with our study results.

Borsaikia and Patar (2016) revealed in their study that females were more commonly affected (83.5%) by thyroid swelling than males (16.5%) which was in agreement with our results.

Halbhavi and his Coworkers (2018) found in their study that females were more commonly affected than males with a male to female ratio of 1:9 which was in agreement with our results.

The main presenting symptom in our cases was neck swelling mainly nodular with little cases of smooth swelling.

Santosh and his Colleagues (2014) revealed in their study that the main presenting feature was the presence of a swelling in front of the neck in 35% of patients which was in agreement with our study results.

Borsaikia and Patar (2016) revealed in their study that all cases of their study (100%) presented by swelling in the thyroid region of the neck which coincides with our results.

Halbhavi and his Coworkers (2018) found in their study that the main presenting symptom was swelling in the thyroid region of the neck (100%) which coincides with our results.

Remonti and his Coworkers (2015) revealed in their study that ultrasonographic examination of the thyroid swelling showed hypoechogenicity, irregular margins, microcalcifications, and absent halo suggesting malignant nature which was in agree with our results.

Brito and his Coworkers (2014) revealed in their study that by ultrasonography of the neck the swellings that showed cystic nature or spongiform appearance signifying benign nature which disagreed with our results.

That is because, pure cystic lesions are always thought to be benign; on the contrary, polyconcamerated cysts and complex nodules may harbor a risk of malignancy. Also, a spongiform nodule may relay the overall impression of iso- to hyperechogenicity, but it must be distinguished from iso- or hyperechoic complex nodules with isolated discrete cystic areas, because the first are benign and the latter may be malignant.

Kwak and his Colleagues (2011) document in their study the high specific features for thyroid cancer are microcalcifications, irregular margins which agreed with our results.

The swelling discovered either by clinical examination or accidentally during examination of the neck for other diseases.

Li and his Colleagues (2013) and *Davies with his coworkers (2014)* found in

their studies that the thyroid swelling were discovered either clinically on self-palpation by the patient, or during a physical examination by the clinician or incidentally during a radiologic procedure such as ultrasonography (US) imaging, computed tomography (CT) which was in agreement with our study.

The histopathologic examination of our cases revealed that the most common carcinoma was papillary carcinoma than follicular carcinoma.

Tamhane and Gharib (2016) revealed in their study that the most common malignant carcinoma was the papillary carcinoma (97-99%) and follicular carcinoma constitute about little percentage which agreed with our results.

Santosh and his Colleagues (2014) revealed in their study that only 10% of cases were malignant in nature while the remaining were benign which contradicts our results that found malignant swelling constitute nearly half the cases.

Borsaikia and Patar (2016) revealed in their study that follicular carcinoma (4.24%) more commonly occurred than papillary carcinoma (1.41%) which contradicts our results.

Hirachand and his Colleagues (2013) found in their study that the most common malignant neoplasms were papillary carcinoma which coincides with our results.

Our results revealed increase in the serum level of TSH in malignant cases than in benign cases.

Tamhane and Gharib (2016) reported in their study that Haymart with *Coworkers (2008)* concluded in their

studies that increased serum TSH or TSH even in the upper limit of normal is associated with increased risk and an advanced stage of malignancy which disagree with our results.

Gharib and his Coworkers (2016) documented in their study that *Gerschpacher and coworkers, (2010)* concluded in his study that low levels of thyrotropin (TSH) are associated with a decreased probability of malignancy, whereas increased levels of serum TSH, even when the levels are still within reference limits, are statistically associated with an increased risk of cancer in thyroid nodular disease and this coincides with our results.

Randolph and his Colleagues (2012) found in their study that the impact of lymph node compromise on the prognosis is controversial and according to prevailing opinions, lymph node metastases that are macroscopic, present in large numbers or characterized by extracapsular extension increase the risk of relapse and mortality in patients older than 45 years old and this run in line with our results.

I131 was used as an apllative therapy for some of our cases *Rosario and his Colleagues (2013)* use I131 as a part of apllative therapy for malignant cases of their study which was in agreement with our study.

CONCLUSION

Based on the results obtained by this sudy, we can conclude that Central neck dissection is still beneficial especially in high risk group of cases where there was capsular invasion.

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دور تشريح الغدد الليمفاوية المركزية بالرقبة فى السرطان المتباين للغدة الدرقية

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خلفية البحث: يعتبر سرطان الغدة الدرقية أحد الأورام الخبيثة الأكثر شيوعاً فى الغدد الصماء، ويصل معدل الحياة لأكثر من 10 سنوات مع سرطانات الغدة الدرقية المتباينة فى نسبة تتجاوز 90%. ويُعد انبثاث العقدة الليمفاوية العنقية سمة شائعة من سرطان الغدة الدرقية الحليمي بينما ينتشر فى حالات سرطان الغدة الدرقية المسامي غالباً فى الدم.

الهدف من البحث: تهدف هذه الدراسة إلى تقييم دور الاستئصال المركزى للغدد الليمفاوية للرقبة فى حالات أورام الغدة الدرقية المتباينة مع توضيح بصمته على معدلات الإعتلال والنتائج العامة لهذا العلاج.

المرضى وطرق البحث: تم إجراء هذه الدراسة كدراسة مقطعية مرتقبة أجريت على 30 مريضاً تم تشخيصهم على أنهم سرطان غدة درقية متباين وتم قبولهم فى قسم الأورام الجراحية فى مستشفيات جامعة الأزهر ومركز دمنهور للأورام. جميع مرضى الدراسة خضعوا للتقييم السريري عن طريق أخذ التاريخ الكامل، والفحوصات المخبرية الكاملة، ودراسات التصوير وتشخيص الأنسجة بواسطة أخذ عينة بالإبر الدقيقة.

نتائج البحث: أظهرت الدراسة وجود علاقة بين الغدد الليمفاوية الإيجابية والورم بحجم 2-4 سم والتي كانت مجموعة مركزية والتي عادة ما يتم تشخيصها سريرياً والغياب يشخص عادةً إشعاعياً وبترافق أيضاً مع غزو غلاف الغدة الدرقية. وكان النوع الأكثر شيوعاً للورم هو النوع الحليمي بنسبة مئوية صغيرة من النوع المسامي، وقد استخدم I131 كعلاج ملحي لبعض هذه الحالات.

الإستنتاج: لا يزال تشريح العنق المركزى مفيداً خاصةً فى مجموعة الحالات الشديدة الخطورة حيث كان هناك غزو غلاف الغدة الدرقية.