

A Clinical Study on Morbidity of Primary and Completion Thyroidectomy in Patients with Differentiated Thyroid Carcinoma

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ABSTRACT

BACKGROUND

Total Thyroidectomy is the surgical choice of therapy for patients with differentiated thyroid cancer (DTC) with > 4 cm or with specific risk factors. This is followed by radioiodine therapy (when indicated) and thyroid hormone suppression therapy. Patients with DTC with less than 1 cm growth without risk factors are recommended for lobectomy alone. For tumours measuring 1 – 4 cms, the choice of aggressive surgery is usually personalized decision. We wanted to evaluate the post-operative morbidity in relation to the surgical extent of primary and completion thyroidectomy in patients with DTC.

METHODS

64 adult patients who underwent thyroid gland surgery after a histopathological diagnosis of differentiated thyroid cancer between February 2016 and January 2018 in the Department of General Surgery at our institution were included. Length of hospital stay, post-operative hypocalcaemia, recurrent laryngeal nerve injury and number of recurrences were used as primary outcome measures for comparison between the two groups. Pre-operative staging to evaluate the extent of the primary thyroid gland disease was done with ultrasound neck, CT scan and MRI Neck. Immediate follow up of for 4 – 8 weeks followed by follow up with nuclear Medicine department for 16 to 19 months was done. All the surgeries were conducted by the same surgeon-duo, and whenever necessary an experienced surgical oncologist's expertise was used.

RESULTS

Among the 64 patients, 36 patients (56.25%) underwent primary total thyroidectomy (Group 'A'); and 28 patients (43.75%), (Group 'B') underwent lobectomy for DTC initially followed by completion thyroidectomy. Unilateral or Bilateral selective neck dissections were performed in 16/36 (44.44%) patients of Group A and 12/28 (42.85%) of Group B patients. There were 24 (66.66%) females and 12 (33.33%) males in group A. In Group B there were 18 (64.28%) females and 10 (35.71%) males. Statistical analysis showed that the opposite side only completion thyroidectomy surgery is associated with a statistically significant shorter hospital stay and had persistent hypocalcaemia lesser than those of primary total thyroidectomy and same side completion thyroidectomy group. Higher initial N stage has a higher likelihood of development of locoregional and metastatic recurrence while T stage independently has no statistically significant impact on any of the outcomes.

CONCLUSIONS

There is no statistically significant difference in post-operative morbidity or oncologic outcome between the primary total Thyroidectomy and completion thyroidectomy. However, less extensive surgery or staged surgery is associated with a better peri-operative outcome.

KEYWORDS

Thyroid, Malignancy, Total Thyroidectomy, Completion Thyroidectomy, Differentiated Carcinoma Thyroid

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BACKGROUND

Total Thyroidectomy has become the oncologic procedure of choice for differentiated thyroid cancers (DTC).⁽¹⁾ DTC is the most common endocrine malignancy and accounts for 90-95 per cent of all thyroid cancers.⁽²⁾ The subtypes of DTC include papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC) and Hurthle cell carcinoma. Over the last few decades, the incidence of thyroid cancer has been increasing worldwide.⁽³⁾ The increase in the incidence of thyroid cancer worldwide, especially in high income countries may be due to over-diagnosis.⁽⁴⁾ The over-diagnosis of thyroid cancer was reported among the young and middle-aged women (age < 60 years).⁽⁵⁾ Similarly developing countries may not be immune according to a recent report of doubling of thyroid cancer incidence in Kerala state in Southern India.⁽⁶⁾ Several studies have identified risk factors that are predictors of poor overall survival which include age greater than 45 yrs., male gender, familial disease, size greater than 4 cm, multifocal disease, bilateral disease, extra thyroidal extension (ETE), and distant metastases. Review of literature shows that a 10 year recurrence rate was 7.7 per cent following total thyroidectomy compared to 9.8 per cent in lobectomy for differentiated carcinoma Thyroid.⁽⁷⁾ However, for patients with micro carcinoma no difference in outcome was observed between lobectomy and total thyroidectomy.⁽⁸⁾ Ideally the decision of treating a patient with DTC should be taken by a multidisciplinary team prior to surgery. The team should aim at the type of surgery for the surgical clearance, minimize the chance of recurrence with minimal morbidity. But the controversy exists about the need for total thyroidectomy versus thyroid lobectomy in managing DTC. completion thyroidectomy surgery was warranted to remove the thyroid remnant when a thyroid cancer is identified in the initially removed thyroid tissue, for recurrent thyroid cancer, for occurrence of cancer in the thyroid remnant after an operation for benign thyroid disease and for symptomatic recurrent disease. Completion thyroidectomy has been associated with a higher morbidity rate in some studies when compared to the primary total thyroidectomy.^(9,10,11) However most studies do not precisely take into account the stage of local disease, when comparing the outcomes and also the extent, of Completion thyroidectomy performed, i.e. one side neck exploration versus both sides and a performance of simultaneous neck dissection in completion surgeries.^(2,12) These factors can independently have a significant impact on the outcome related to second surgery. In this present context this study was conducted to evaluate the post-operative morbidity rates, in relation to the surgical extent of primary and completion thyroidectomy in patients with DTC.

METHODS

The present study was conducted prospectively using an analytic study design. A total of 64 adult patients who underwent thyroid gland surgeries after a histopathological

diagnosis of differentiated thyroid cancer between February 2016 and January 2018 in the Department of General Surgery at our institution were included. An ethical committee clearance was obtained before commencement of the study. An ethical committee approved consent letter was used for the study.

Inclusion Criteria

1. Patients of all age groups were included.
2. Patients of both the genders were included.
3. Patients who underwent lobectomy, for DTC was included under the completion thyroidectomy group (Group B).
4. Patients undergoing primary Total Thyroidectomy were included as Primary surgery group (Group A).

Exclusion Criteria

Patients undergoing surgery other than primary or completion thyroidectomy (neck dissection/excision biopsies), second unsuccessful exploration, and patients with carcinoma of Thyroglossal cyst were not included in the study.

Outcome Parameters Observed

Length of hospital stay, post-operative hypocalcaemia, recurrent laryngeal nerve injury and number of recurrences were used as primary outcome measures for comparison between the two groups. Hypocalcaemia was further differentiated as transient or persistent using cut off intervals of 3 months. The standard protocol followed in the present study was to collect the data regarding patients who underwent Total thyroidectomy for DTC as the primary surgery. There were 36 patients who underwent Primary thyroid surgery were grouped as Group 'A' patients. Group 'B' patients were those who underwent lobectomy for DTC but were subjected to completion thyroidectomy due to final diagnosis reported by the pathologist. Both the group patients were subjected to radioactive iodine ablation therapy and a lifelong TSH suppression. All the patients were subjected to Pre-operative staging for local extent of the disease with neck MRI. CT scan or ultrasounds of neck were done wherever necessary. All the Patients followed up for 4–8 weeks in the department of General Surgery and for 16 to 19 months in the department of Nuclear Medicine at 3 monthly intervals. Serum Thyroglobulin, TSH and a whole body radio iodine scan were undertaken at the end of 1st year and 2nd year. Management of hypoparathyroidism, if detected was undertaken at regular intervals. All the surgeries were conducted by the same surgeon duo and whenever necessary an experienced surgical oncologist's expertise was used. In patients where uni/bilateral selective lateral neck dissections were required, they were undertaken by the same team. The occurrence of recurrent laryngeal nerve injury was considered as positive if there was voice change on two occasions, confirmed by video laryngoscopy by the ENT surgeon. Hypocalcaemia was considered when ionized serum calcium level falls below 1 mmol/L and a continued prescription of calcium supplements at three months requiring further workup for hypoparathyroidism was undertaken. Length of hospital stay was calculated in number of days from the date of admission

to the date of discharge. Radioiodine whole body scan at the end of 1st year was considered as a minimum follow-up requirement for documentation of recurrent disease. Other investigations for evidence of recurrence were undertaken such as MRI or PET-CT in the presence of a rising Thyroglobulin level and the absence of iodine avid disease was undertaken. All the data was analyzed using standard statistical methods using standard statistical methods using online social science statistics calculators (https://www.socscistatistics.com/tests/what_stats_test_wizard.aspx). P value of less than 0.05 was used as a threshold for statistical significance.

RESULTS

Among the 64 patients included in the present study 36 patients (56.25%) underwent Primary total thyroidectomy (Group 'A'); and 28 patients (43.75%), (Group 'B') underwent lobectomy for DTC initially and later completion thyroidectomy, due to final diagnosis reported by the pathologist. Among the Group B patients 18/28(64.28%) had surgery on the contra lateral previously unexplored side of neck, while 10 (35.71%) had undergone lobectomy on the same side of the neck. Unilateral or Bilateral selective neck dissections were performed in 16/36 (44.44%) patients of Group A and 12/28 (42.85%) patients of Group B. There were 24 (66.66%) females and 12 (33.33%) males in group A. In Group B there were 18 (64.28%) females and 10 (35.71%) males. The youngest patient was aged 31 years and the eldest patient was aged 54 years with a mean age of 42.5 ±2.45 years in group A. The youngest patient was aged 33 years and the eldest patient was aged 51 years with a mean age of 40.65 ±3.05 years in group B. The socio- economic status in group A was observed and found that 17/36 (47.22%) patients belonged to lower group, 10/36 (27.77%) belonged to middle group and 09 (25%) belonged to higher economic status group. In group B it was found that the incidence was 11/28 (39.28%), 09 (32.14%) and 08/28 (28.57%) in lower middle and higher groups respectively. In group A 11/36 (30.55%) of patients belonged to Urban areas and 25 (69.44%) of patients belonged to Rural areas. In group B, 09/28 (32.14%) patients belonged to Urban areas and 19 (67.85%) of patients belonged to Rural areas (Table 1).

The post-operative outcomes in both groups were observed and analysed. The parameters studied were length of hospital stay, post-operative hypocalcaemia, recurrent laryngeal nerve injury and recurrence. The mean hospital stay in group A was 07.3 days with standard deviation 02.60. In group B, the mean hospital stay was 06.7 days with standard deviation 01.35. The incidences of recurrent laryngeal nerve Injury (RL nerve) in group A was 01/36 (02.77%) and in group B it was 4/28 (14.28%). It was found that there was no statistically significant difference between the primary (A group) and completion thyroidectomy group in terms of, multivariate analysis was performed. In group A, there was no incidence of post-operative hypocalcaemia in 22/36 (61.11%) of patients, Transient hypocalcaemia in 13/36 (36.11%) and persistent hypocalcaemia in 01/36

(02.77%) patients were observed. In group B, there was no incidence of post-operative hypocalcaemia in 14/28 (50%) of patients, Transient hypocalcaemia in 10/28 (39.28%) and persistent hypocalcaemia in 03/28 (10.71%) patients were observed. In group A, there were no cases of recurrence in 33/36 (91.66%). Local recurrences in 02/36 (05.55%) and metastases in 01/36 (02.77%) of patients were observed. In group B, there were no cases of recurrence in 23/28 (82.14%). Local recurrences in 03/28 (10.71%) and metastases in 02/28 (07.14%) of patients were observed. (Table 2). Higher initial N stage has a higher likelihood of development of loco regional and metastatic recurrence while T stage independently has no statistically significant impact on any of the outcomes (Table 2).

Observation	Group A - 36	Group B - 28
Mean Age		
Mean	42.75	40.65
SD	2.45	3.05
Males	12	18
Females	24	10
Socio economic status		
Low	17	11
Middle	10	09
High	09	08
Urban	11	09
Rural	25	19

Table 1. Demographic Data (n-64)

Observation	Primary Total Thyroidectomy- 36	Completion Thyroidectomy- 28	P Value
Hospital stay			
Mean	07.3	06.7	0.686
SD	02.60	01.35	
R L nerve Injury- n (%)			
Yes	01 (02.77)	04 (14.28)	--
No			
Post-operative hypocalcaemia			
No	22 (61.11)	14 (50.0)	0.792
Transient	13 (36.11)	11 (39.28)	
Persistent	01 (02.77)	03 (10.71)	
Recurrence			
No Recurrence	33 (91.66)	23 (82.14)	0.536
Local/ Regional	02 (05.55)	03 (10.71)	
Metastases	01 (02.77)	02 (07.14)	

Table 2. Postoperative Outcome and Hospital Stay of Patients (n-64)

DISCUSSION

Differentiated thyroid cancer (DTC) is usually not very common disease of the Thyroid; incidence is about 1 % of all cancers and women are more often affected than men. However, the incidences reported in many parts of South East Asia particularly in iodine deficient areas are higher. When compared to other solid tumours, DTC is potentially curable with documented survival rate of > 90 %. There exists controversy about the need for total thyroidectomy versus thyroid lobectomy in managing DTC. Total Thyroidectomy studies showed a lower recurrence rate in patients with DTC but in patients with micro carcinoma the recurrence rates were similar.^(13,14)

However, not all groups agreed with this aggressive approach to all patients with DTC. In a study at Memorial Sloan Kettering Cancer Center, New York, USA, they observed that there was no difference in local or regional

recurrence and on multivariate analysis. The factors like male gender and age above 45 years were independent predictors of poorer overall survival.⁽¹⁵⁾ These findings were supported by Japanese reports where, unlike Western countries, completion thyroidectomy was not generally available and thyroid lobectomy has been the mainstay of surgery for PTC.⁽¹⁶⁾ It is now recommended by most of the surgeons all over the world that the patients who are diagnosed with DTC, that initially patients who undergo less than total thyroidectomy should undergo less than total thyroidectomy should undergo a completion thyroidectomy to remove any residual or multifocal cancer tissue.^(17,13,14) Completion thyroidectomy surgery was supposedly more difficult to perform than the first surgery and hence associated with more complications.⁽¹³⁾ However tumour stage and the extent of surgery can act as possible risk factors, and therefore, the two groups need to be standardized against these factors before a comparison is made.

The standard policy in our Hospital was performance of a total thyroidectomy followed by Radioactive Iodine (RIA) therapy and TSH suppression in all patients with a diagnosis of DTC which is operable without distant metastases. In this prospective study analysis, it was observed that there was no statistical difference between post-operative complications of primary total thyroidectomy and completion thyroidectomy. However review of literature showed that few studies comparing the morbidity outcomes between primary total thyroidectomy and completion thyroidectomy and did not take the risk factors of surgical extent and tumour stage into account.^(16,17,18) In the present study statistical analysis showed that the opposite side only completion thyroidectomy is associated with a statistically significant shorter hospital stay and had persistent hypocalcaemia lesser than those of primary total thyroidectomy and same side completion thyroidectomy. Higher initial N stage has a higher likelihood of development of loco regional and metastatic recurrence while T stage independently has no statistically significant impact on any of the outcomes (Table 2). The factors playing their roles in the outcome parameters studied are the extent of surgery, surgery with or without neck dissections and completion thyroidectomy when performed on the unexplored side only. They were associated with shorter hospital stay and lesser risk of persistent hypocalcaemia. Shortcomings in this study are that 1. the effects can be attributed again to lesser degree of surgical trauma in these cases of staged surgeries as compared to the bilateral neck exploration in primary total thyroidectomy group or bilateral completion thyroidectomy. 2. However, although length of hospital stay is shorter for the contralateral completion thyroidectomy group, it does not take into account the time spent by the patient in the hospital at their first surgery. 3. The selective lateral neck dissections were performed when pre-operative imaging, clinical examination or FNAC confirms lateral neck nodal disease. 4. The two groups were not homogeneous groups on the basis of age with a significant P value. But both groups had similar mean age at the time of admission. 5. The length

of follow-up was considerably longer in the group A which with a mean of 19 months versus 16 months in case of group B patients. In both the groups the absence of recurrence was not statistically significant. The incidence of RL nerve injury was lower with Primary Total Thyroidectomy patients rather than completion thyroidectomy.

CONCLUSIONS

There is no statistically significant difference in post-operative morbidity or oncologic outcome between the primary total thyroidectomy and completion thyroidectomy. However, less extensive surgery is associated with a better peri-operative outcome.

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