



## TOTAL VERSUS SUBTOTAL THYROIDECTOMY IN GRAVES' DISEASE: A RANDOMIZED CONTROLLED TRIAL

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Article History: Received: 20.02.2023

Revised: 28.03.2023

Accepted: 27.04.2023

### Abstract

**Background:** Surgery is offered to patients with Graves' disease (GD) refractory to medical or radio-iodine therapy. Total thyroidectomy (TT) has been shown to lower recurrence rates of hyperthyroidism because the whole thyroid tissue is removed but subtotal thyroidectomy (ST) is thought to be associated with lower risk of postoperative complications.

**Aim and objectives:** To compare between the two techniques regarding postoperative recurrence of hyperthyroidism, hypocalcemia and hypoparathyroidism.

**Subjects and methods:** This was prospective controlled clinical trial, was carried out at Department of General Surgery, Assiut University Hospital, Assiut, Egypt on 80 patients were allocated randomly to one of the treatment groups Group TT And Group ST With a 1: 1 ratio, during two years duration (2020-2021),

**Result:** There were significant difference between both groups as regard recurrent hyperthyroidism.

**Conclusion:** With our findings demonstrating lesser relapse of hyperthyroidism and similar safety profiles of TT in tandem with a high proportion of patients eventually needing thyroxin replacement after ST, we believe that TT should be the surgical procedure of choice for patients with GD. We find little reason to continue to offer ST as an alternative.

**Keywords:** Graves' disease, Total thyroidectomy, Subtotal thyroidectomy, Outcome

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DOI:10.31838/ecb/2023.12.s1-B.199

### 1. INTRODUCTION

**Graves' disease** is an autoimmune disease that affects the thyroid gland (1) and it's the most common cause of hyperthyroidism. (2) Treatment of Graves' disease includes anti-thyroid drugs; radioiodine; and thyroidectomy. Patients with Graves' hyperthyroidism can be treated with any of these treatment options. There is a wide geographic variation in the choice of therapy. (3) Medical treatment with anti-thyroid drugs is often accepted as first-choice modality in Europe, followed by radioiodine in case of recurrence. Although surgery offers the advantage of quick control and low morbidity in experienced hands, it is infrequently recommended as initial treatment. Therapy with radioiodine is the most common treatment in the United States, while anti-thyroid drugs and/or thyroidectomy are used more often in Europe, Japan, and most of the rest of the world. Recent literature shows that the relapse rate was the highest among patients who received anti-thyroid

drugs (40%) as compared to those who received radioiodine (21%) or Surgery (5). (4)

Two different surgical techniques are used for the treatment of Graves' hyperthyroidism: a total thyroidectomy (TT) in which the entire gland is removed and a subtotal thyroidectomy (STT), in which most of the gland is removed leaving a small unilateral or bilateral remnant in situ about 4-5 grams. Although thyroidectomy has been broadly considered as a viable alternative therapy for patients with **Graves' disease**, the resection extent and remnant size of thyroid gland remains controversial. (6).

Aim of the work was to compare between the two techniques regarding postoperative recurrence of hyperthyroidism, hypocalcaemia and hypoparathyroidism within the studied patients (total number is 80 patients).

## 2. PATIENTS AND METHODS

This study was prospective controlled clinical trial was conducted in General Surgery Department at Assiut university hospital, including All patients diagnosed clinically, biochemically and immunologically with Graves' disease who underwent thyroidectomy at general surgery department in AUH for two years duration (2020-2021).The number of studied patients is 80(40 in each group).

Patients were allocated randomly to one of the treatment groups: Group TT and Group ST with a 1: 1 ratio using block randomization.

**Inclusion Criteria for study group:** All patients diagnosed clinically, biochemically and immunologically with Graves' disease who will undergo thyroidectomy at general surgery department in AUH.

**Exclusion Criteria for groups:** Previous thyroid or parathyroid surgery, recurrent hyperthyroidism after radioiodine therapy, preoperative recurrent laryngeal nerve palsy, patients unfit for operation, inability to comply with the follow-up protocol and suspicious thyroid nodules.

### Methods

The eligible subjects included in this study will be subjected to the following: Informed consent was obtained from each participant. Full history including: Patient personal data: Age, sex, smoking, occupation, and residence, History of present illness: onset, course, duration of symptoms and indication for surgery.

**Pre-operative preparation:** Routine laboratory investigations and Thyroid function tests included measurement of serum free triiodothyronine (fT3; reference range 2 – 6.78 pmol/l), free thyroxin (fT4; reference range 12–30 pmol/l) and thyroid-stimulating hormone (TSH, thyrotropin; reference range 0.4-4.5 mIU/ml. Imaging studies such as Neck U/S and CT Neck. High-resolution Doppler ultrasonography of the neck with both 7.5- and 12-MHz linear-array transducers (Logiq®7; GE, Solingen, Germany), indirect laryngoscopy to assess mobility of vocal cords, patients rendered Euthyroid before operation using antithyroid drugs, patients were instructed to stop medical treatment and start administration of Lugol's iodine three times daily for 10 days preoperatively.

**Post-operative Follow-up:** Clinical, biochemical, ophthalmological and ultrasonographic follow-up was undertaken at 1, 3, 6, 9 and 12 months after surgery. Biochemical evaluation consisted of measurement of serum concentrations of TSH, T3 and T4 at each visit. Ophthalmological examination was carried out with assessment of the severity of ophthalmopathy and the activity of the eye disease. All patients received postoperative levothyroxine treatment. The levothyroxine dose was adjusted to keep the serum TSH concentration within the reference range of 0.4–4.2 munits/l. Recurrent hyperthyroidism was diagnosed if a low serum TSH concentration was found with raised levels of fT3 and fT4 after 4 weeks of levothyroxine substitution withdrawal. Indirect laryngoscopy was performed within one-week post-operative.

**Outcome measures:** Primary (main): Prevalence of recurrent hyperthyroidism, postoperative hypocalcaemia and hypoparathyroidism. Secondary (subsidiary): Operation time and technical difficulties, temporary or permanent recurrent laryngeal nerve injury, impact of operation on hyperthyroidism associated ophthalmopathy.

**Ethical Consideration:** Study protocol had been submitted for approval by Institutional Review Board, Assuit University. Informed verbal consent had been obtained from each participant sharing in the study. Confidentiality and personal privacy had been respected in all levels of the study.

**Data management and Statistical Analysis:** Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. Statistical tests using parametric tests ( T-test ) and chi-square test to detect significant difference between two groups . determine of P value which  $P < 0.05$  will be significant.

## 3. RESULTS

**Table (1)** shows that there was insignificant difference between both groups as regard age or sex.

**Table (1):** Comparison between the studied groups as regard demographic data

	Group TT (n=40)	Group ST (n=40)	Test	P
<b>Age</b>			T=1.05	0.85
<b>Mean± SD</b>	35.12±3.54	36.3±3.44		
<b>Sex</b>			$\chi^2=0.05$	0.81
<b>Male</b>	15	16		
<b>Female</b>	25	24		

T: Two-Sample Independent t Test  $\chi^2$ : Chi-square test

**Table (2):** Comparison between the studied groups regarding general complications

	Group TT	Group ST	Test	P
<b>Hematoma</b>				
Yes	1	0	$\chi^2=1.013$	0.316
No	39	40		
<b>Wound site infection:</b>				
Yes	0	0	-	1
No	100	100		

$\chi^2$ : Chi-square test

**Table (2)** shows that there was insignificant difference between both groups as regard Hematoma and Wound site infection.

**Table (3):** Comparison between the studied groups as regard specific complications

	Group TT	Group ST	Test	P
<b>RLN palsy:</b>				
<b>Transient</b>				
Yes	1	0	$\chi^2=1.013$	0.316
No	39	40		
<b>Permanent</b>				
Yes	0	0	-	1
No	40	40		
<b>Hypocalcaemia</b>				
<b>Transient</b>				
Yes	1	0	$\chi^2=1.013$	0.316
No	39	40		
<b>Permanent</b>				
Yes	1	0	$\chi^2=1.013$	0.316
No	39	40		

$\chi^2$ : Chi-square test

**Table (3)** shows that there was insignificant difference between both groups as regard specific complications.

**Table (4):** Comparison between the studied groups regarding results of surgery

	Group TT	Group ST	Test	P
<b>Recurrent hyperthyroidism</b>	0	5	5.333	0.02*
<b>Ophthalmopathy</b>				
<b>Improvement</b>	29	26	0.5247	0.72
<b>No change</b>	4	5		
<b>Progression</b>	7	9		

$\chi^2$ : Chi-square test

p: p value for comparing between different categories

\*: Statistically significant at  $p \leq 0.05$

**Table (4)** shows that there was significant difference between both groups as regard recurrent hyperthyroidism

#### 4. DISCUSSION

Over the years, subtotal thyroidectomy (ST) has become the mainstay of treatment for toxic goiter; however, total and near total thyroidectomy (TT & NTT) is increasingly being considered. Near-total (NTT) thyroidectomy in which less than 1 g of thyroid tissue remains and Total thyroidectomy

(TT) have been utilized in the treatment of Graves' disease for long time (7).

The aim of this study was to compare between the two techniques regarding postoperative recurrence of hyperthyroidism, hypocalcaemia and hypoparathyroidism.

This study showed that there was insignificant difference between both groups as regard age or sex.

**Osama et al. (8)** did prospective study was done at Ain Shams University Hospitals and Banha teaching hospital during the period between March and September 2019. This study included 40 cases of SMNG. They showed that there is statistically non-significant difference between both groups regarding age, gender, hormonal status or operative time.

**Abdel-Latif et al. (9)** did prospective randomized controlled study included a total of 84 patients with toxic goiter, attending at Endocrine Surgery Unit, General Surgery Department, Mansoura University Hospitals. This study was conducted between February 2018 and January 2019. The included subjects were randomly divided into two groups; Group 1 (TT) consisted of 42 patients underwent total thyroidectomy, Group 2 (NTT) consisted of 42 patients underwent near total thyroidectomy. Age: The mean age was  $41.43 \pm 9.27$  years with 32 (38%) patients within age of (51-75) and 52 (62%) patients within age of (25-50). Sex: Males represented 12 patients (14%) while females represented 72 patients (86%). There was insignificant difference between both groups as regard age or sex.

This study illustrated that there were insignificant difference between both groups as regard Hematoma and Wound site infection.

**Osama et al. (8)** showed that there is statistically non-significant difference between the studied surgical techniques regarding hematoma and wound site infection. Only one patient (5%) from those underwent total thyroidectomy had hematoma. No one of patients within both techniques had wound site infection. Only one case was complicated by postoperative hematoma 1 hour after surgery in group A (TT Group).

**Abdel-Latif et al. (9)** showed that in their study 5 patients (6%) of all 84 cases experienced a post-operative hematoma. Only 2 of the whole study group (2.3%) needed to be re-explored intra operatively, and 4 patients (4.7%) of all 84 cases experienced a post-operative bleeding.

**Efremidou et al. (10)** reported that hemostasis can be better achieved with total thyroidectomy. Postoperative hemorrhage requiring reoperation occurred in 2 patients (0.2%).

This study demonstrated that there was highly significant difference between both groups as regard specific complications.

**Osama et al. (8)** showed that there is statistically non-significant difference between the studied surgical techniques regarding occurrence of RLN palsy, postoperative hypocalcaemia and postoperative hypoparathyroidism. Only one patient (5%) from those underwent total

thyroidectomy had transient RLN palsy. No one of patients within both techniques had permanent RLN palsy. One patient (5%) had transient and another one (5%) had permanent hypocalcaemia underwent total thyroidectomy.

**Abdel-Latif et al. (9)** showed that among all patients 6 patient showing post-operative temporal recurrent laryngeal nerve injury (7%), only one patient showed signs of RLN injury at long term period in total thyroidectomy group.

**Liu ZW et al. (11)** show that Total thyroidectomy was more effective than subtotal thyroidectomy techniques (both bilateral subtotal thyroidectomy and the Dunhill procedure) at preventing recurrent hyperthyroidism in 0/150 versus 11/200 participants (OR 0.14 (95% CI 0.04 to 0.46);  $P = 0.001$ ; 2 trials; moderate quality evidence).

**Karamanakos et al., (12)** who reported higher incidence of temporary and permanent RLN palsy in total thyroidectomy than subtotal thyroidectomy group, but it was statistically non-significant.

This study showed that there was significant difference between both groups as regard recurrent hyperthyroidism.

**Abdel-Latif et al. (9)** showed that serum TSH levels post-operatively at the 1st month showed no significant change in TSH values, After 6 months the follow up TSH levels showed lowered levels in 2 cases (4.8%) in the Near total thyroidectomy (NTT) group and the toxic manifestations began to be presented on patients, On follow up of the two group of cases for TSH levels after 1 year 6 patients (14.3%) from the (NTT) group showed lowered TSH levels and re-presentation of the toxic manifestations on patients.

**Barczyński et al. (13)**. Showed that Two hundred patients were included, of whom 95 underwent Bilateral subtotal thyroidectomy and 96 underwent total thyroidectomy completed the 5-year follow-up. Recurrent hyperthyroidism occurred in nine patients after BST and in none after TT ( $P = 0.002$ ).

## 5. CONCLUSION

Total thyroidectomy is superior to subtotal thyroidectomy for patients with GD as it includes adequate eradication of the disease, prevention of recurrent goiter and avoidance of the need for completion surgery in case of occult malignancy, but it is associated with Some morbidity (postoperative thyroidectomy complications: RLN palsy and hypoparathyroidism).

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