

# Surgical Outcomes in Thyroidectomy for Patients with Graves' Disease: A Randomized Controlled Trial

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## ABSTRACT

**Background:** Thyroidectomy is a preferred protocol for patients with Graves' disease. However, it may be a challenging option in post-surgical management of various factors. There, this study aims to compare the surgical outcomes of total thyroidectomy and subtotal thyroidectomy in patients with Graves' disease to provide evidence-based surgical decision-making.

**Methods:** This randomized controlled trial was conducted at Sheikh Zaid Hospital, Rahim Yar Khan, October 2023 to April 2024; enrolled 120 patients diagnosed with Graves' disease using a simple random sampling technique were assigned to Group A (n=60) and B (n=60) who underwent total thyroidectomy, and subtotal thyroidectomy respectively. Preoperative assessments and surgeries were performed while postoperative outcomes, complications, and thyroid function tests were also monitored and represented using independent t-tests while a  $p < 0.05$  was considered significant.

**Results:** It was revealed that operative time was significantly higher for total thyroidectomy than subtotal thyroidectomy  $125.60 \pm 14.56$  and  $97.54 \pm 12.56$  respectively, suggesting significantly lower time consumption in subtotal thyroidectomy procedure ( $p = 0.001$ ). Patients who underwent subtotal thyroidectomy had a significantly shorter hospital stay compared to those who underwent total thyroidectomy ( $p = 0.02$ ). Moreover, levels of triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) were significantly different between the two groups. Patients who underwent subtotal thyroidectomy had significantly lower T3 and T4 levels and higher TSH levels compared to those who underwent total thyroidectomy ( $p < 0.05$ ).

**Conclusion:** Subtotal thyroidectomy demonstrated favorable outcomes, including shorter operative time, lower rates of postoperative complications, and thyroid function tests compared to total thyroidectomy. These findings help and support the consideration of subtotal thyroidectomy as a viable surgical approach for patients with Graves' disease.

**Keywords:** Grave Disease, Thyroidectomy, Thyroxine, Triiodothyronine.

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## INTRODUCTION

Graves' disease (GD), hallmarked by hyperthyroidism, is a challenge that cannot be overlooked in the surgical world<sup>1</sup>. It leads to gland hypertrophy, increased vascularity, and many associated complications<sup>2</sup>. Though there are many advancements in the medical field, thyroidectomy remains a preferred protocol despite the ongoing debate within the medical community<sup>3-4</sup>. Depending on the procedure details, thyroidectomy focuses on considerations that demand carefulness<sup>5</sup>. Total thyroidectomy (TT) involves complete removal of the thyroid gland, while subtotal thyroidectomy (ST) entails partial removal, leaving behind a remnant of thyroid tissue<sup>6</sup>. Both procedures have their benefits, limitations, and disadvantages<sup>7-8</sup>. Both procedures have their proponents and critics, with varying opinions regarding their efficacy, safety, and impact on long-term outcomes<sup>9-10</sup>.

The lack of consensus regarding the preferred surgical approach for Graves' disease created a critical need for rigorous comparative studies to elucidate the optimal strategy<sup>11</sup>. This randomized controlled trial (RCT) seeks to address this gap by systematically comparing surgical outcomes in patients undergoing either total or subtotal thyroidectomy for Graves' disease<sup>8</sup>. Disclosing this evidence will be helpful for decision-making aiming to enhance the quality of care and improve patient outcomes in the management of Graves' disease<sup>12-13</sup>. In-depth evaluation offers insights as well. Ultimately, the findings of this study hold the potential to inform clinical practice, empower healthcare providers with evidence-based recommendations, and ultimately optimize the surgical management of patients with Graves' disease. Therefore, this study aimed to compare the post-surgical outcomes of TT and ST in patients with Graves' disease to provide evidence-based surgical decision-making.

## METHODS

This randomized controlled trial was used to compare the outcomes of TT vs ST in patients with GD. The patients were randomized into two groups using a simple random sampling technique: Group A (n=60), which underwent TT, and Group B (n=60), which underwent ST. The participants were recruited from October 2023 to April 2024 at Sheikh Zaid Hospital, Rahim Yar Khan. Ethical approval was taken from Sheikh Zaid Medical College (567/IRB/SZMC/SZH). Patients aged between 20-50 years diagnosed with

GD were selected. Participants were deemed suitable candidates for surgical intervention based on clinical evaluation. Exclusion criteria included subjects bearing any contraindications for surgery. Inclusion criteria included the subjects diagnosed with GD, their willingness to participate in the study, and their fitness for surgical intervention based on clinical assessment. The exclusion included severe comorbidities that pose significant surgical risks, inability or unwillingness to comply with study protocols, and any contraindications for thyroid surgery.

Patients went through a series of clinical evaluations before surgery. General anesthesia was used with careful incision afterward made in the front of the neck to access the thyroid gland. Subsequently, meticulous dissection techniques were adopted to specify important structures following complete removal using suture. In the same way, precise incisions are limited to the side of the thyroid lobe being removed. One lobe of the thyroid gland and a portion of the isthmus was meticulously excised, leaving the contralateral lobe intact. Post-operative care included close monitoring for complications such as bleeding, infection, and damage to parallel structures, with appropriate management strategies implemented as inclusion needed.

The sample size was estimated using the open-source calculator, Open EPI, using a reference study of Sun et al.<sup>14</sup>. Thus, a total sample of 120 was determined on a 95% confidence level, 80% power of the test, and 8% bound of error using the following formula:  

$$n = [DEFF * Np(1-p)] / [(d^2/Z^2(1-\alpha)/2 * (N-1) + p * (1-p))]$$

Evaluating intra-operative variables involved a detailed assessment of operative duration and expected blood loss factors. The operational time was measured from the incision's beginning to the surgical wound's closing<sup>15</sup>. The surgical team took minutes and documented them. The blood loss was calculated using standard procedures such as suction volume measurement and surgical sponge counting. The anesthesia team and surgical personnel measured milliliter blood loss and reported it in the intraoperative record.

In post-operative complications, the length of hospital stay until discharge was estimated in days between the two groups. This was ensured by the nursing staff

and confirmed by the attending physician. Discharge was consistent among participating centers, based on the specified criteria of recovery status, wound healing, and care of any post-operative problems<sup>16</sup>. Thyroid function post-surgery had been evaluated during follow-up by assessing the thyroid hormone levels. These exams were performed at preset intervals after surgery, often one week, one month, three months, and six months after that. Blood samples were also taken using standardized laboratory procedures. Endocrinologists were hired to analyze the healthcare specialists who are knowledgeable about testing. Monitoring and treatment were done to maintain accuracy. Indications were considered to evaluate thyroid dysfunction.

The demographic characteristics of participants were represented through frequencies, percentages, mean and standard deviations. Further, an independent test was used to compare the mean values of post-surgi-

cal complication i.e., length of hospital stays and thyroid function tests between the two groups while a  $p < 0.05$  was considered significant.

## RESULTS

The demographical descriptions box shows the mean age of the participants i.e., Group A:  $48.98 \pm 2.63$  years and Group B:  $48.63 \pm 2.89$  years while the female population is reported to be more than males. Furthermore, the BMI and disease duration are found to be varying among these groups. The interpretation of the outcome measures had listed operative time calculated in minutes was notably raised for the TT procedure than ST with a mean value of  $125.60 \pm 14.56$  and  $97.54 \pm 12.56$  respectively  $p < 0.005$  showing significantly lower time consumption in the ST procedure. Moreover, the amount of blood loss as estimated in milliliters was also significantly lower ( $p < 0.005$ ) in the ST procedure than in the TT procedure (Table 1).

**Table 1: Demographic description of study participants**

Variables	Total Thyroidectomy	Sub-Total Thyroidectomy	p-value
	Group A	Group B	
Age (Years)	$48.98 \pm 2.63$	$48.63 \pm 2.89$	0.78
Gender			
Males	23 (38.33)	22 (36.66)	0.85
Females	37 (61.66)	38 (63.33)	0.85
Mean BMI (Kg/m <sup>2</sup> )	$25.3 \pm 3.1$	$24.8 \pm 2.9$	0.65
Duration of Graves' Disease (Years)	$5.2 \pm 1.4$	$5.0 \pm 1.6$	0.75
Operative time	$125.60 \pm 14.56$	$97.54 \pm 12.56$	0.001
Blood loss in milliliters	$53.58 \pm 2.56$	$32.56 \pm 3.21$	0.001

The patients who underwent ST had a shorter average length of stay of 3.56 days compared to patients who underwent TT with 5.54 days. The difference in the

length of hospital stay between the two groups was statistically significant ( $p = 0.02$ ). The details are depicted in Table 2, Figure 1.

**Table 2: Evaluation of hospital stay time and thyroid function test.**

Variables	Total Thyroidectomy $\pm$ SD	Subtotal Thyroidectomy $\pm$ SD	t-stat	p-value
Length of Hospital Stay (in days)	$5.54 \pm 1.25$	$3.56 \pm 2.1$	1.25	0.02
Triiodothyronine (pg/ml)	$122.95 \pm 5.58$	$112.55 \pm 1.25$	3.44	0.01

Tetraiodothyronine ( $\mu\text{g/dL}$ )	7.98 $\pm$ 1.1	6.52 $\pm$ 0.9	1.09	0.04
TSH (mIU/L)	1.59 $\pm$ 0.91	2.34 $\pm$ 1.2	0.96	0.04
Hypocalcemia (mmol/L)	1.85 $\pm$ 0.5	1.22 $\pm$ 0.4	2.73	0.008

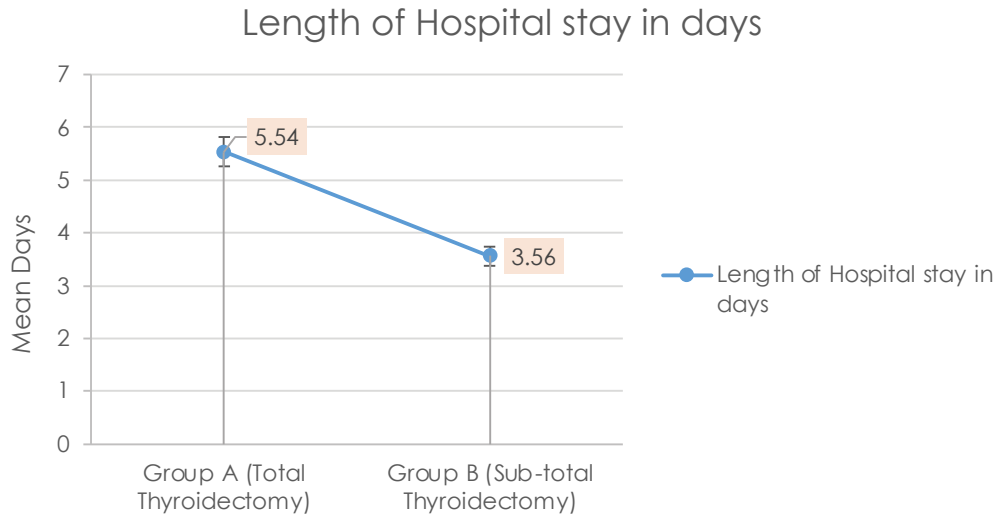


Figure 1: Length of hospital stay in days among Groups A and B.

The ST group revealed a lower mean at T3 (112.55 pg/ml,  $p=0.01$ ), T4 levels (6.52  $\mu\text{g/dL}$ ,  $p=0.04$ ), and hypocalcemia (1.22 mmol/L,  $p=0.008$ ) in comparison to TT group. However, TSH levels were higher in the TT

group (1.59 mIU/L,  $p=0.04$ ) in comparison to the ST group. Whereas, both groups revealed significant differences as depicted in Table 2, Figure 2.

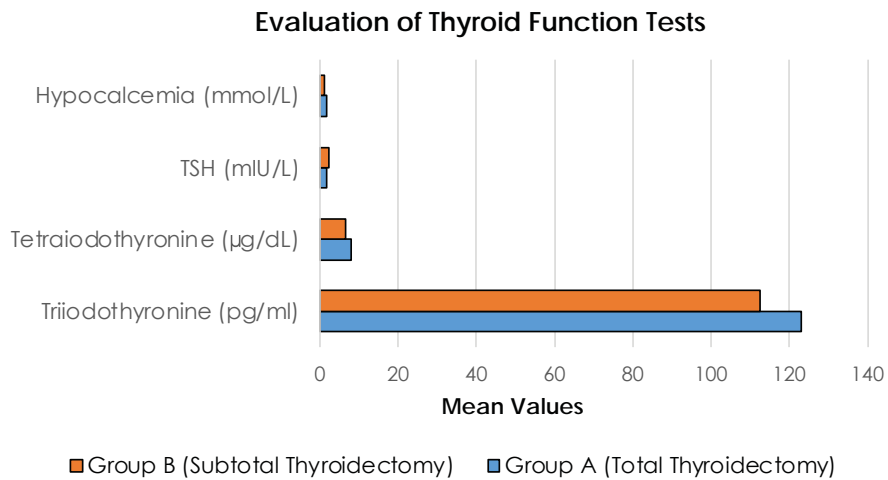


Figure 2: Evaluation of thyroid function tests among Groups A and B.

## DISCUSSION

The study compared TT to ST in Graves' disease patients, with demographic data indicating equal mean ages and a more significant number of females in both groups. Intraoperative results favor the inclusion of subtotal thyroidectomy procedures to avail a short period for surgery, which in turn will lead to less loss of blood and easiness for the surgeon. It has also been seen that such patients had to spend less time in their wards, and the individuals also had low levels of triiodothyronine and thyroxine. However, thyroid-stimulating hormone levels were more significant. Thus, this paper necessitates the efficacy and need for such procedures to improve Graves' disease results. One other research comparing TT and ST for the treatment of multinodular goiter included data from 23 trials and 11,601 individuals, seeking to assess outcomes such as recurrent laryngeal nerve (RLN) damage, recurrence rates, and hypocalcemia incidence. The calculated data documented a Lower incidence of RLN following ST but a greater recurrence rate than TT<sup>32</sup>.

In contrast, TT provided advantages such as complete disease elimination and a decrement in the requirement for reoperation in situations of latent malignancy<sup>17-19</sup>. However, TT is also connected with a high rate of morbidity due to surgical sequelae such as RLN palsy and hypoparathyroidism, which require lifetime L-thyroxine replacement<sup>19,20</sup>. Thyroidectomy, a popular treatment for a variety of thyroid disorders, is associated with hazards such as recurrent laryngeal nerve (RLN) damage, hypocalcemia, and hematoma development, according to the literature<sup>15</sup>. Because problems can be life-threatening, they must be identified and managed immediately after thyroidectomy. Age over 45, male gender, Graves' disease, increased systolic blood pressure, and usage of certain drugs all increase the risk of hematoma development. Intraoperative identification of the RLN is critical for reducing the risk of damage<sup>21</sup>. The most common consequence is hypocalcemia, which occurs more frequently after complete thyroidectomy than after partial thyroidectomy, increasing the risk of hypoparathyroidism. Overall, post-thyroidectomy problems highlight the significance of close postoperative monitoring, with incidence rates and risk-mitigation measures varying depending on the kind of thyroidectomy performed<sup>22-24</sup>. A randomized controlled experiment comparing complete thyroidectomy versus partial thyroidectomy for Graves' disease (GD) patients found substantial differences in postoperative hyperthyroidism recurrence<sup>25-27</sup>. Over two years, 80 patients were randomly assigned to either Group TT or Group ST at a 1:1 ratio. Results revealed a drop in the frequency of occurrence of hyperthyroidism in the TT group compared to the ST group. The safety profiles were also found to be approachable and comparable<sup>17</sup>. However, it cannot be neglected that a large group of individuals in the ST group subsequently needed

thyroxine replacement<sup>28-32</sup>. Based on the following data, this paper recommends that TT should be the recommended surgical treatment for patients with GD since it decreases hyperthyroidism recurrence while not significantly raising postoperative morbidity.

## CONCLUSION

Summarizing the results, there is enough evidence regarding the effectiveness and favorable outcomes of partial thyroidectomy vs complete thyroidectomy as a surgical care aspect of Graves' disease patients. Subtotal thyroidectomy is effective in operations that take less time, thus causing less blood loss, making it notable as an efficient and less invasive procedure. Additionally, reduced hospital stay was seen, followed by lower levels of triiodothyronine and thyroxine following surgery. However, it is also worth noting that partial thyroidectomy is also linked with the increased thyroid-stimulating hormone, which may have consequences for thyroid function management.

## ACKNOWLEDGMENTS

None.

## CONFLICT OF INTEREST

There is nothing to declare.

## ETHICAL APPROVAL

Ethical approval was taken from Sheikh Zaid Medical College (567/IRB/SZMC/SZH).

## AUTHORS CONTRIBUTION

All authors equally contributed to the manuscript.

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