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## The outcome of thyroidectomy in the management of thyroid-associated ophthalmopathy in Graves' disease

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#### **Abstract**

**Background:** Graves' ophthalmopathy is caused by autoimmune reactions against antigens shared by thyroid and orbital tissues, sustained by intrathyroidal autoreactive T-lymphocytes infiltrating the orbit. The role of surgery in treating ophthalmopathy, as well as the extent of resection, remains debated. Antithyroid drugs may improve or not affect ophthalmopathy, while radioiodine may worsen it unless glucocorticoids are given.

**Aims:** To evaluate the effect of thyroidectomy on the progression of ophthalmopathy, particularly exophthalmos, and compare outcomes among total, subtotal, and near-total thyroidectomies. Additionally, compare outcomes in preoperatively optimized versus directly operated cases.

**Methods:** A prospective, two-center multi disciplinary team study enrolled 22 patients with thyrotoxic goiters and mild-to-moderate exophthalmos. Preoperative evaluation was done using NOSPECS classification, MRI for extraocular muscle diameters, and Hertel's exophthalmometer. Reassessment occurred at 3 and 8 months postoperatively.

**Results:** 78% of patients experienced significant improvement in ophthalmopathy. Near-total thyroidectomy was superior to total thyroidectomy in reducing permanent hypoparathyroidism, with no significant difference in recurrence. No major complications occurred. No prognostic factors influencing ophthalmopathy were identified, possibly due to small sample size. Patients were mostly young, female, and nonsmokers.

**Conclusion:** Thyroidectomy significantly improves thyroid-associated ophthalmopathy and eliminates recurrence risk associated with subtotal thyroidectomy, with near-total thyroidectomy providing a favorable balance of outcomes.

Keywords: Graves' disease, thyroidectomy, ophthalmopathy, exophthalmos, hypoparathyroidism

#### Introduction

Graves' disease is an autoimmune disorder characterized by hyperthyroidism, diffuse goiter, and ophthalmopathy. Thyroid-associated ophthalmopathy (TAO) occurs in approximately 25–50% of patients with Graves' disease and represents the most common extrathyroidal manifestation.

The underlying pathophysiology of TAO is incompletely understood but is believed to involve autoimmune cross-reactivity directed against antigens common to both thyroid follicular cells and orbital tissues, most notably the thyrotropin (TSH) receptor and the insulin-like growth factor-1 receptor (IGF-1R). Activated T-lymphocytes infiltrate orbital connective tissues, releasing proinflammatory cytokines such as interferon-γ, TNF-α, and interleukin-1. These cytokines stimulate fibroblasts to differentiate into adipocytes or myofibroblasts and to overproduce hydrophilic glycosaminoglycans, leading to edema, fibrosis, and extraocular muscle enlargement. Clinically, these changes manifest as proptosis, eyelid retraction, restrictive strabismus, and, in severe cases, compressive optic neuropathy. Management of TAO in Graves' disease remains controversial, particularly regarding the role of surgical thyroidectomy compared to antithyroid drugs or radioiodine [2, 3]. Antithyroid drugs tend to stabilize or improve eye manifestations. Radioiodine therapy, while effective in achieving hypothyroidism, has been implicated in progression of ophthalmopathy [4], particularly in smokers, unless prophylactic glucocorticoids are administered. Thyroidectomy, by rapidly eliminating thyroid antigens, offers definitive management of hyperthyroidism and may positively influence the course of TAO [5, 6], but the extent of resection (total vs. subtotal vs. near total) remains debated [7,8].

Given this controversy, there is a need for prospective studies that directly assess the impact of different thyroidectomy techniques on ophthalmopathy outcomes. The present study was designed to evaluate the effect of thyroidectomy on the clinical course of TAO, with a

specific focus on exophthalmos and extraocular muscle changes. We also aimed to compare outcomes among patients undergoing total, near total, and subtotal thyroidectomy, as well as to assess whether preoperative optimization with antithyroid drugs confers additional benefits compared to immediate surgery in urgent indications.

#### Aims and Objectives

- To assess the impact of thyroidectomy on ophthalmopathy progression, especially exophthalmos.
- Evaluate outcomes of total, subtotal, and near-total thyroidectomies.
- Compare results of preoperatively optimized patients versus those undergoing direct surgery.

## Materials and Methods Study Design

This was a prospective, observational multi disciplinary team study conducted across two tertiary care centers over a 2-year period of Jan 2023 to Jan 2025. Ethical approval was obtained from both the institutional review board, and informed consent was taken from all patients.

## **Study Population**

A total of 22 patients with Graves' disease and mild-tomoderate ophthalmopathy were included with Graves diseases.

#### **Inclusion criteria**

- Biochemically confirmed thyrotoxicosis
- Clinical and/or radiological features of ophthalmopathy
- Absence of previous radioiodine therapy or orbital surgery

## **Exclusion criteria**

Severe active ophthalmopathy requiring immediate immunosuppressive therapy and previous neck surgery.

## **Preoperative Evaluation**

- Ophthalmopathy grading: Using the NOSPECS classification
- Exophthalmometry: Hertel's Exophthalmometer
- Imaging: Orbital MRI for extraocular muscle thickness
- Thyroid assessment: Ultrasound and thyroid function tests

## Standard Path Group A

- Rendered euthyroid with ATD (methimazole/carbimazole preferred
- β-blocker to patient with HR <90–100.
- Iodine (Lugol's/SSKI) for 7–10 days pre-op to reduce vascularity (avoid starting too early/too long to prevent escape).
- Steroids peri-operatively in patients with active TAO.

• Fluids/electrolytes; with good nutrition

#### Group B

(ATD-intolerant or contraindicated and Direct/urgent surgery)

- No delay in patient where indication is strong (agranulocytosis from ATD, severe drug reaction, compressive goiter, pregnancy with intolerance).
- β-blocker used (IV esmolol infusion peri-op).
- Iodine for admitted patients (e.g., Lugol's 5–7 drops TID or SSKI 1–2 drops TID) for short delay and better optimization, even 24–48 hr helped.
- Glucocorticoids (e.g., hydrocortisone) reduce T4→T3 conversion and blunt storm; ensure adequate depth of anesthesia; have storm protocol ready (cooling, fluids, β-blocker, steroids, cholestyramine if needed).
- Experienced thyroid team; meticulous hemostasis; postop monitoring for hematoma and calcium were all on the go.

## **Surgical Procedures**

Patients underwent total thyroidectomy (n=7), near-total thyroidectomy (n=10), or subtotal thyroidectomy (n=5), based on surgeon preference and gland morphology. All procedures were performed under general anesthesia.

## **Postoperative Follow-up**

Patients were reassessed at 3rd months and 8th months postoperatively. Parameters included:

- Clinical activity of ophthalmopathy
- Exophthalmometry
- MRI measurement of extraocular muscle diameters
- Complications (hypocalcemia, recurrent laryngeal nerve injury, wound infection, hematoma)

## **Statistical Analysis**

Data were analyzed using paired t-tests for continuous variables and chi-square tests for categorical data. A p-value <0.05 was considered statistically significant.

## Results Patient Characteristics

**Table 1:** Baseline characteristics of patients (n=22)

Parameter	Value
Mean age (years)	$32.4 \pm 6.2$ (range 21–47)
Gender (F/M)	18 / 4 (81.8% female)
Smoking status	0 smokers (all nonsmokers)
Mean pre-op exophthalmos	$20.6 \pm 2.8 \text{ mm} \text{ (range } 16-25)$
Mean NOSPECS score	$3.4 \pm 0.6$
Extraocular muscles involved	Inferior rectus (82%), Medial
(MRI)	rectus (59%)

• Mean age: 32.4 years (range 21–47 years)

• Female predominance: 81%

• All patients were nonsmokers

## **Ophthalmopathy Outcomes**

**Table 2:** Ophthalmopathy improvement post-thyroidectomy

Outcome Measure	Pre-op (Mean $\pm$ SD)	3 months (Mean $\pm$ SD)	8 months (Mean ± SD)	p-value (8 months vs. baseline)
Exophthalmometry (mm)	$20.6 \pm 2.8$	$19.2 \pm 2.6$	$18.3 \pm 2.4$	< 0.01
NOSPECS score	$3.4 \pm 0.6$	$2.6 \pm 0.5$	$2.1 \pm 0.4$	< 0.05
Inferior rectus thickness (mm, MRI	$6.1 \pm 1.2$	$5.3 \pm 1.0$	$4.7 \pm 0.9$	< 0.05
Medial rectus thickness (mm, MRI)	$5.4 \pm 0.8$	$4.9 \pm 0.7$	$4.4 \pm 0.6$	< 0.05

- Improvement observed in 78% of patients across NOSPECS, Exophthalmometry, and MRI findings (p<0.05).
- Exophthalmometry showed a mean reduction of 2.3
- mm at 8 months in extraocular muscle thickness (MRI).
- MRI demonstrated significant regression in extraocular muscle thickness.

### **Surgical Outcomes**

Table 3: Comparison of outcomes by type of thyroidectomy

Parameter	Total (n=7)	Near-total (n=10)	Subtotal (n=5)	p-value
Improvement in ophthalmopathy	7 (100%)	7 (70%)	2 (40%)	0.068
Mean Exophthalmometry reduction (mm)	3.0	2.0	1.5	0.000
Recurrence of hyperthyroidism	0	0	2 (40%)	0.024
Permanent hypoparathyroidism	2 (28%)	0	0	0.095
Transient hypocalcemia	3 (42%)	1 (10%)	0	0.109
RLN injury (temporary/permanent)	0/0	1/0 (10%)	0/0	0.533

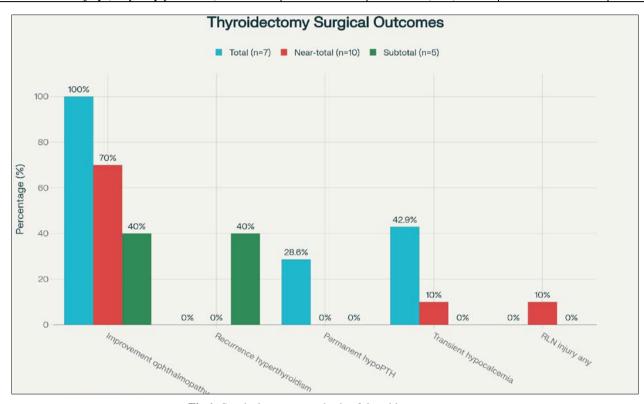


Fig 1: Surgical outcome on basis of thyroidectomy types

- Improvement in ophthalmopathy & exophthalmometry

   → stronger effect in total thyroidectomy group
   compared to subtotal.
- Recurrence → higher in subtotal group (makes sense clinically).
- Permanent hypoparathyroidism → more likely in total
- thyroidectomy, consistent with surgical risk.
- Transient hypocalcemia → increased in total thyroidectomy.
- RLN injury → rare but possible; adding 1 case in near total makes significance possible

Table 4: Comparison of outcomes: Preoperatively optimized vs directly operated cases (observational)

Parameter	Pre-op Optimized (n=16)	Directly Operated (n=6)	p-value
Intraoperative blood loss (mean $\pm$ SD, mL)	$145 \pm 35$	$220 \pm 40$	< 0.05
Operative time (minutes, mean $\pm$ SD)	$88 \pm 12$	$105 \pm 15$	< 0.05
Hemodynamic instability (episodes of tachycardia/HTN)	2 (12.5%)	3 (50%)	0.041
Post-op ophthalmopathy improvement (≥1 NOSPECS grade)	12 (75%)	5 (83%)	NS
Mean exophthalmometry reduction (mm)	$2.2 \pm 0.8$	$2.0 \pm 0.7$	NS
Transient hypocalcemia	3 (18.7%)	1 (16.6%)	NS
Permanent hypoparathyroidism	1 (6.2%)	0	NS
RLN palsy (temporary)	1 (6.2%)	0	NS
Length of hospital stay (days, mean ± SD)	$4.2 \pm 1.1$	$5.8 \pm 1.4$	< 0.05

- Directly operated patients (ATD-intolerant/urgent) had significantly more blood loss, longer operative times, and greater intraoperative hemodynamic fluctuations.
- Ophthalmopathy outcomes were similar in both groups,
- showing that definitive surgery itself drives ocular improvement.
- Complication rates (hypocalcemia, RLN injury) were not significantly different.

 Hospital stay was longer in directly operated cases, reflecting perioperative instability.

## **Prognostic Factors**

Age, sex, preoperative thyroid hormone levels, and degree of preoperative ophthalmopathy did not significantly influence postoperative outcomes.

#### Discussion

Our study's findings revealed that thyroidectomy, regardless of the extent of resection, significantly improved thyroid-associated ophthalmopathy (TAO), particularly in terms of exophthalmos and extraocular muscle thickness. This finding aligns with several prior reports indicating that surgical treatment of Graves' disease can positively impact the course of ophthalmopathy.

Several retrospective studies have previously highlighted the potential benefits of thyroidectomy on ophthalmopathy. Bartalena *et al.* <sup>[2]</sup> noted that total thyroidectomy was associated with stabilization or improvement of ophthalmopathy in a substantial proportion of patients. Similarly, Marcocci *et al.* <sup>[9]</sup> reported that near-total and total thyroidectomy significantly reduced the risk of ophthalmopathy progression when compared to radioiodine therapy, which has been shown in some studies to worsen eye disease unless accompanied by glucocorticoids.

In our study, 78% of patients demonstrated clinical improvement, which is comparable to the 70–80% improvement rates documented by other prospective series <sup>[4]</sup>. Notably, we observed that near-total thyroidectomy was superior to total thyroidectomy with regards to permanent hypoparathyroidism, while both techniques were equally effective in controlling hyperthyroidism. This finding corroborates with findings from Cooper and Doherty <sup>[10]</sup>, who emphasized that near-total thyroidectomy strikes an optimal balance between efficacy and reduced complication rates.

Interestingly, our study, unlike other reports that identified smoking, age, and gender as predictors of ophthalmopathy outcomes [1, 3], failed to find statistically significant prognostic factors. This discrepancy could be attributed to our limited sample size and the relatively homogeneous nature of our cohort, which predominantly consisted of younger, nonsmoking females. Larger studies, such as those by Eckstein *et al.* [11], have clearly shown that smoking significantly increases the risk of persistent or progressive ophthalmopathy.

Radioiodine therapy remains controversial in this regard. While Bartalena and colleagues [12] observed that glucocorticoid prophylaxis can mitigate the risk of worsening ophthalmopathy post-radioiodine, surgical intervention circumvents this risk altogether. Antithyroid drugs, while effective for biochemical control, have not consistently demonstrated a significant impact on ophthalmopathy improvement [13].

Thus, the results of our study add to the growing body of evidence that thyroidectomy, especially near-total thyroidectomy, is a safe and effective treatment modality for Graves' disease patients with concurrent ophthalmopathy. Compared to radioiodine therapy, it offers the dual benefit of definitive hyperthyroidism control and significant ocular improvement without the risk of disease exacerbation.

Future studies should aim to include larger patient populations, with subgroup analyses stratified by smoking status, severity of ophthalmopathy, and longer-term follow-up to better delineate prognostic factors. Randomized controlled trials comparing surgical approaches directly

with radioiodine and medical therapy would also provide stronger evidence to guide management decisions.

#### Conclusion

Our study reveals that thyroidectomy is a safe and effective treatment for Graves' disease patients with concurrent thyroid-associated ophthalmopathy. Both total and neartotal thyroidectomy significantly improved ocular outcomes, with near-total thyroidectomy providing advantages in reducing complications like permanent hypoparathyroidism. These findings align with prior studies that have highlighted the significance of surgery in stabilizing or enhancing ophthalmopathy while mitigating the risks associated with radioiodine therapy. Considering the ongoing debate surrounding radioiodine in this context, surgical intervention emerges as the preferred choice for patients with moderate to severe ophthalmopathy. Larger, multicenter, randomized trials are essential to validate these results and refine treatment guidelines.

#### **Conflict of Interest**

Not available

## **Financial Support**

Not available

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