The efficacy of thyroidectomy for Graves' disease: a meta-analysis
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Authors' objectives
The study had four objectives: (1) to review all modern clinical trials; (2) to use meta-analysis to determine the overall efficacy of both total and subtotal thyroidectomy (TT and ST respectively) for Graves' disease; (3) to compare thyroid function and complications rates of TT and ST; and (4) to determine if there is an optimum thyroid remnant size.

Searching
MEDLINE was searched over the last 35 years using the keywords 'Graves' disease', 'toxic goiter' and 'surgery'. The authors also manually searched the bibliographies of each retrieved article.

Study selection
Study designs of evaluations included in the review
Published studies with a mean follow-up of 5.6 years (range: 1 month to 32 years), and in which post-operative follow-up of thyroid function was provided, were included.

Specific interventions included in the review
The specific interventions included were TT and ST.

Participants included in the review
Patients diagnosed with Graves' disease (also known as diffuse toxic goiter). Patients with other causes of hyperthyroidism such as nodular or multi-nodular toxic goiter were excluded. Age was reported in 31 studies with 5,859 participants ranging in age from 4 to 78 years; the average age was 32.9 years. Gender was reported in 31 studies with 6,250 participants: 1,131 were male (18.1%) and 5,119 were female (81.9%).

Outcomes assessed in the review
Persistent or recurrent hyperthyroidism, post-operative hypothyroidism, and post-operative euthyroidism. Outcomes were measured using clinical signs and symptoms, or serum levels of T4 and/or thyroid-stimulating hormone (TSH).

The following adverse outcomes were calculated for ST and TT: temporary and permanent recurrent laryngeal nerve (RLN) injury, and temporary and permanent hypoparathyroidism. The overall mortality rate and rate of cancer found incidentally were also obtained. In patients who underwent ST, an attempt was made to determine the ideal amount of thyroid tissue to leave in the neck.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
No formal assessment of quality was undertaken.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The original studies did not distinguish between persistent or recurrent hyperthyroidism and hypothyroidism, so these two outcomes were grouped together. The incidence of persistent or recurrent hyperthyroidism was calculated for all thyroidectomy patients.
Data were extracted for the following categories: study identification and year of publication, number of participants, location of study, study period, percentage of male participants, average age in years, percentage follow-up, length of follow-up in years, and outcomes.

**Methods of synthesis**

How were the studies combined?

Meta-analysis was performed using a weighted least-squares linear regression. Significance testing was carried out using an unpaired Student's t-test. A P-value of less than 0.05 was considered to be statistically significant.

How were differences between studies investigated?

The authors did not report any tests for assessing heterogeneity, although it was stated that age, gender, percentage, and length of follow-up were examined to ensure that studies could be combined.

**Results of the review**

Thirty-five studies were included in the review with 7,241 participants.

Persistent or recurrent hyperthyroidism occurred in 7.2% of all patients.

TT was performed on 538 patients and hypothyroidism occurred in all cases.

ST was performed in 6,703 patients: 59.7% achieved euthyroidism, 25.6% became hypothyroid, and 7.9% had either persistent or recurrent hyperthyroidism.

Permanent RLN injury occurred in 0.9% of TT patients and 0.7% of ST patients (P was non significant).

Permanent hypoparathyroidism occurred in 0.9% of TT patients and 1.0% of ST patient (P was non significant).

There was an 8.9% decrease in hypothyroidism and a 6.9% increase in euthyroidism for each gram of thyroid remnant (P=0.0001 for both results).

There were no peri-operative mortalities reported in 4,470 operations.

Incidental carcinoma was found in the resected thyroid tissue in 84 (4.5%) of the 1,882 patients.

**Authors’ conclusions**

The authors state that overall, thyroidectomy successfully treated hyperthyroidism in 92% of patients with Graves’ disease. There were no cases of hyperthyroidism following TT. ST achieved a euthyroid state in almost 60% of patients with an 8% rate of persistent or recurrent hyperthyroidism. There was no statistically-significant difference in complication rates between TT and ST.

**CRD commentary**

The authors have stated the research question and the inclusion and exclusion criteria. The literature search was limited by searching only one database. It was not stated whether the search was restricted to English language publications or whether unpublished information was sought, so it is possible that additional relevant studies might have been missed. There were no further analyses to test for publication bias.

The quality of the included studies was not formally assessed, and the authors did not report how the articles were selected, or who performed the selection and data extraction.

The data extraction was reported in one table, whilst the results of the linear regression were reported in the text of the review. Heterogeneity was not formally assessed, although the authors did address some of the issues which may have led to heterogeneity, such as age, gender, percentage followed-up and length of follow-up.
The authors’ conclusions appear to follow from the results, but should be viewed with caution because of limitations in the quality of the review process.

**Implications of the review for practice and research**

Practice: The authors state that in patients with mild forms of Graves’ disease, ST can be performed in order to try to achieve a euthyroid state. TT, however, is probably the best operation for severe disease and large goiter in order to ensure that hyperthyroidism does not recur.

Research: The authors state that with the outcome of this review, the outcome of surgery for Graves’ disease can now be compared to radioactive iodine and anti-thyroid drugs.

**Bibliographic details**


**PubMedID**

10792958

**DOI**

10.1006/jsre.2000.5875

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Adolescent; Adult; Aged; Child; Child, Preschool; Female; Graves Disease/pathology/surgery; Humans; Male; Middle Aged; Organ Size; Postoperative Complications/mortality; Thyroid Neoplasms/pathology/surgery; Thyroidectomy; Treatment Outcome

**AccessionNumber**

12000001132

**Date bibliographic record published**

31/01/2002

**Date abstract record published**

31/01/2002

**Record Status**

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