



## Original Research

# Comparison of endoscopic and conventional open thyroidectomy for Graves' disease: A meta-analysis



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## HIGHLIGHTS

- Endoscopic thyroidectomy (ET) appeared to be a better cosmetic satisfaction, lesser amount of blood loss.
- Conventional open thyroidectomy (OT) with a shorter operation time and lower hospital cost compared with ET for patients with Graves' disease.
- ET was associated with an equivalent adverse event and complication rates compared with OT.
- Endoscopic thyroidectomy appeared to be a safe and feasible operation for patients with Graves' disease.

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## ABSTRACT

**Background:** Despite experience with the use of endoscopic surgical technology, there is controversy over the role of endoscopic thyroidectomy (ET) for Graves' disease (GD). This study aimed to conduct a meta-analysis to evaluate the cosmetic and safety outcomes of ET versus conventional open thyroidectomy (OT) for GD with respect to short-term consequences.

**Methods:** We searched the following English language databases (Ovid MEDLINE, ISI Web of Science, and the Cochrane Library), and Chinese language databases (CNKI, CBMdisc, and SinoMed) between January 1996 and November 2015. The quality of the included studies was determined by the Newcastle-Ottawa Scale. A meta-analysis was conducted using RevMan 5.3 software. Pooled mean differences (MD) or odds ratios (OR) with  $I^2$  were calculated using either fixed or random-effect models.

**Results:** Six trials including 846 total cases were ultimately selected for meta-analysis. ET was associated with reduced blood loss (MD = -32.02; 95%CI: -36.92 to -27.12;  $P < 0.00001$ ) and better cosmetic satisfaction (OR = 38.92; 95%CI: 17.40–87.06;  $P < 0.00001$ ) than OT. However, OT was associated with reduced operation time (MD = 19.70; 95%CI: 2.04–37.35;  $P = 0.03$ ) and lower hospital costs (MD = 303.21; 95%CI: 123.07, 483.36;  $P = 0.0010$ ). Furthermore, ET and OT were not significantly different in terms of drainage volume, and they had an equivalent complication rate, including for transient recurrent laryngeal nerve palsy, transient hypocalcemia, postoperative hypothyroidism, and recurrent-hyperthyroidism.

**Conclusions:** ET appeared to provide better cosmetic satisfaction and a reduction in blood loss, whereas OT had a shorter operation time and lower hospital costs. Randomized clinical trials with large samples that include long-term follow-up data are necessary to confirm our findings.

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## 1. Introduction

Primary hyperthyroidism is considered an autoimmune disease that afflicts approximately 12 in one-thousand people, 90 percent of whom have GD [1]. High metabolic syndrome is a manifestation of GD due to the excessive production of thyroid hormone, and complications may include marasmus, cardiopathy, osteoporosis and even death [2]. Therapeutic options include pharmacotherapy

Abbreviation: SE, standard error; SMD, standardized mean difference; OR, standardized odds ratio.

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(anti-thyroid drugs, ATDs), radiotherapy (radioactive iodine therapy, RAI), and surgery. In Asia and Europe, ATDs are recommended as the first-line treatment. RAI or surgery becomes second-line in patients with recurrence. In the US, before RAI or surgery, ATDs are used as adjuncts [3]. ATDs only own display 50–60 percent remission rates. Although RAI can effectively attain hypothyroidism, it cannot avoid the side-effects of radiation [4]. Encouragingly, OT has a cure rate of 92 percent for GD [5]. However, OT requires a cervical collar incision, which looks similar to a “suicide scar” on the anterior neck. This is a concern for patients who take a keen interest in their personal appearance.

In 1997, Hüsche performed the first ET and achieved a workable approach to gain an improved cosmetic result [6]. ET had good outcomes in cases of thyroid goiter [7], and an estimated ten-thousand thyroid operations have been performed using an endoscopic surgical approach in approximately two-hundred Chinese hospitals [8]. The first endoscopic subtotal thyroidectomy for a GD patient was performed using a precordial approach by Yamamoto in 2001 [9]. In 2002, the first total endoscopic thyroidectomy (TET), via a breast areola approach, for GD was conducted by Wang in China and was first reported in 2004 [10,11]. Despite the increased recognition of successful experiences, surgical indications remain ambiguous. Due to GD's marked gland enlargement, with a rich vasculature and therefore difficult hemostasis, there still exists a controversy wherein several studies claim that ET may cause excessive bleeding in GD patients, and it is therefore considered to be an absolute or relative contraindication for them [12–14].

In addition, there is no meta-analysis that has systematically reviewed the differences between ET and OT for GD. Therefore, it is necessary to perform a comparative study between ET and OT for adult GD patients based on systematic and comprehensive analysis with data that meet specific criteria.

## 2. Materials and methods

### 2.1. Search strategy

MEDLINE via PubMed, ISI web of Science, the Cochrane Library, and Chinese biomedical databases (CNKI, CBMdisc, and SinoMed) were searched using a combination of the following medical subject heading (MeSH) terms: “endoscopic” or “laparoscopy” or “minimally invasive”, and “thyroidectomy”, and “hyperthyroidism”, “graves' disease” with limits of “human” and published in English or Chinese literature between January 1996 and November 2015. The final inclusion of articles was determined by consensus from two reviewers, and a third reviewer rendered a deciding verdict.

### 2.2. Eligibility criteria

Two reviewers independently screened all of the retrieved abstracts and titles to determine the eligible studies using the following inclusion criteria: (a) studies that focused on patients only with GD; (b) comparative studies between ET and OT; (c) age > 18 years, with no restrictions on gender or nationality; and (d) identification of redundant publications, of which only the highest quality and most recent studies were retained.

Studies were excluded based on the following criteria: (a) oral presentations as well as poster presentations, case reports, expert comments, abstracts, letters, and literature reviews and published without manuscripts; (b) studies that used robot surgical procedure, because there are differences in operation mode; (c) no clearly reported outcomes, or lacking control groups or not compared with OT; and (d) studies reporting on pediatric patients.

### 2.3. Data extraction and quality assessment

Reviewers independently used standardized forms to extract data and confirm them. The quality of the nonrandomized study was assessed using the Newcastle-Ottawa Scale with some modifications for compliance with the requirements of this study. The quality was evaluated by using the following items: patient selection, comparability, and assessment of outcome. The quality test was applied for assessing methodological quality as ‘higher’ (estimated 6 or more stars) [15].

### 2.4. Baseline characteristics of the study participants

Age, gender ratio, number of patients, and gland size were recorded as demographic and general clinical characteristics.

### 2.5. Information about interventions and postoperative complications

Complete information was collected about prescribing Lugol's iodine preoperatively and the ET surgical approach. Complications included conversion to OT, transient recurrent laryngeal nerve (RLN) palsy, permanent RLN palsy, transient hypocalcemia, recurrent-hyperthyroidism, hypothyroidism, and surgical injury.

### 2.6. Outcomes for effectiveness

The following factors were abstracted to compare the effectiveness of ET and OT: operative time, blood loss, cosmetic satisfaction, drainage volume, hospital costs, and complications.

### 2.7. Statistical analysis

Review Manager software version 5.3 (RevMan, Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014) was used to perform the meta-analysis. The Mantel-Haenszel method was used to calculate the odds ratio (OR) with a corresponding 95% confidence interval (CI) for dichotomous outcomes. Mean differences (MD) with a corresponding 95% CI were calculated for continuous outcomes using the inverse-variance method [16]. A meta-analysis was performed using fixed- or random-effects models, depending on the heterogeneity. Heterogeneity was measured using the  $\chi^2$  and  $I^2$ , with  $P < 0.05$  considered significant. Random-effects analysis was performed if the  $I^2$  statistic was greater than 50%. Sensitivity analysis was also conducted by excluding individual studies from the data set and analyzing the effect on the overall results to identify statistical heterogeneity [16]. Furthermore, potential publication bias was estimated by Begg's funnel plot as well as Egger's linear regression test [17]. STATA statistical software version 12.0 (Stata corporation, College Station, TX, USA) was used to perform data analyses. All  $P$ -values were two-sided and were considered significant if  $< 0.05$ .

## 3. Results

### 3.1. Description of included studies in the meta-analysis

One hundred eighty-one ( $n = 181/410$ ) articles were identified as being potentially relevant for the search strategy. After full-text review, twenty-five ( $n = 25/181$ ) articles were screened as being potentially relevant to this study. In addition, two articles were excluded because the cohorts may have overlapped. Six studies were ultimately determined to be up-to-standard and were selected for the meta-analysis [18–23] (Fig. 1).

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