Total endoscopic thyroidectomy versus conventional open thyroidectomy in thyroid cancer: a systematic review and meta-analysis

Background: Despite the considerable experience gained thus far using endoscopic technologies, the role of total endoscopic thyroidectomy (ET) for papillary thyroid cancer (PTC) remains controversial. We conducted a systematic review and meta-analysis to investigate the safety and effectiveness of total ET compared with conventional open thyroidectomy (OT) in PTC.

Methods: A systematic search was conducted using the PubMed, Embase and Cochrane Library electronic databases up to March 2018. The quality of included studies was evaluated using the Newcastle–Ottawa Scale. Review Manager software version 5.3 was used for the meta-analysis.

Results: Twelve studies including 2,672 patients were ultimately included in the systematic review and meta-analysis. ET was associated with longer operative time (P<0.0001), drainage time (P<0.00001) and hospital stay (P=0.03), higher transient recurrent laryngeal nerve (RLN) palsy rate (P=0.004) and a greater amount of drainage fluid (P<0.0001) compared with OT. Furthermore, no significant differences were detected between ET and OT in terms of retrieved lymph nodes (P=0.17), blood loss (P=0.22), transient hypocalcemia (P=0.84), permanent hypocalcemia (P=0.58), permanent RLN palsy (P=0.14), hematoma or bleeding (P=0.15) and seroma (P=0.54). In addition, the rates of tumor recurrence were comparable (P=0.18), whereas the proportions of stimulated thyroglobulin levels <1 ng/mL measured after completion of thyroidectomy and radioactive iodine therapy were less (P=0.02) in the ET than in the OT group.

Conclusion: ET is not superior to OT in terms of operation and drainage time, amount of drainage fluid, hospital stay or transient RLN palsy, but is comparable to OT in terms of retrieved lymph nodes and permanent complications. Despite the similar tumor recurrence rates between the two approaches, the level of surgical completeness in ET may not be as good as that for OT.

Keywords: endoscopic thyroidectomy, conventional open thyroidectomy, papillary thyroid carcinoma, meta-analysis

**Background**

Thyroid cancer is considered the most prevalent endocrine cancer, especially in women. Papillary thyroid cancer (PTC), the major histological subtype, constitutes approximately 85% of all thyroid malignancies. Although conventional open thyroidectomy (OT) is a standard surgery with low morbidity and minimal mortality for PTC, it requires a cervical incision in the neck. Nevertheless, the cosmetic outcome may be a particular concern, especially in young women.

The popularity of endoscopic technologies has allowed surgeons to complete resection and simultaneously deliver cosmetic results. In 1997, Hüscher et al first...
performed endoscopic thyroidectomy (ET).\textsuperscript{5} Since then, various ET approaches have evolved, such as breast,\textsuperscript{6} axillary,\textsuperscript{7} axillobreast,\textsuperscript{8} submental\textsuperscript{9} and oral cavity approaches.\textsuperscript{10} However, endoscopic techniques present some difficulties in obtaining adequate surgical views because of the small working space and two-dimensional operative views.\textsuperscript{11} In addition, surgical indications for ET remain ambiguous, and the benefits of ET are considered marginal for PTC.\textsuperscript{12,13} Some studies have even questioned the safety of ET for PTC and proposed that this method should be critically evaluated.\textsuperscript{14,15} Thus, it remains unsettled whether ET is effective and safe compared with OT.

To our knowledge, only one meta-analysis comparing outcomes between ET and OT has been published.\textsuperscript{16} However, the previous meta-analysis was conducted on five studies and focused on patients with papillary thyroid microcarcinoma (PTMC). Given the growing number of publications on this debatable subject and the extended indications for ET,\textsuperscript{7} it is necessary to perform a systematic meta-analysis to compare the effectiveness and safety of ET with OT in PTC patients.

**Materials and methods**

This systematic review and meta-analysis was conducted in accordance with the PRISMA statement.\textsuperscript{17}

**Search strategy**

A systematic search was conducted using the PubMed, Embase and Cochrane Library electronic databases on 15 March 2018. We used the following keywords and Medical Subject Headings (MeSH) terms: “laparoscopy” or “endoscopy” or “minimally invasive surgery” or “video-assisted surgery” and “thyroidectomy” and “thyroid cancer”. We also reviewed the reference lists from the retrieved articles.

**Study selection**

Two independent authors (CC and SMH) reviewed study titles and abstracts to exclude irrelevant articles, and studies meeting the inclusion criteria were selected for full-text assessment. Any discrepancy was resolved by consensus. The inclusion criteria were as follows: 1) English language; 2) comparative studies between ET and OT for patients with PTC; 3) studies comparing at least one outcome of surgery; and 4) multiple studies from the same institution were assessed and the highest quality and most up-to-date of these was retained. The exclusion criteria were as follows: 1) studies that were reviews, case reports, letters, conferences, editorials, or expert opinions; 2) studies that focused on patients with thyroid cancer other than PTC; and 3) studies reporting on the pediatric population.

**Data extraction and quality assessment**

Data were extracted into prepared standardized forms by two independent reviewers.

The primary data extracted from each study included the first author, year of publication, geographical region, study type, number of patients, patient demographics, pathological characteristics of PTC, operative details (extent of thyroidectomy, surgical approach), intraoperative outcomes, postoperative outcomes and oncological outcomes (stimulated thyroglobulin [sTg], tumor recurrences). Intraoperative outcomes included operative time, blood loss and the number of retrieved lymph nodes. Postoperative outcomes included hospitalization period after the operation, volume and duration of drainage, postoperative complications (transient hypocalcemia, permanent hypocalcemia, transient recurrent laryngeal nerve [RLN] palsy, permanent RLN palsy, hematoma or bleeding, and seroma). Total thyroidectomy (TT) included near-TT and TT, whereas less than total thyroidectomy (LTT) included hemithyroidectomy and subtotal thyroidectomy. The sTg level was measured after total completion of thyroidectomy and radioactive iodine therapy and defined as <1.0 ng/mL as an indicator of surgical completeness. Any disagreement was resolved by discussion and consensus.

The quality assessment of nonrandomized studies was also performed by two independent reviewers using the Newcastle–Ottawa Scale, with some modifications to match the requirements of this study.\textsuperscript{18,19} The quality was assessed based on three aspects: patient selection, comparability of groups and outcome assessment. Only studies awarded six or more stars were considered as high-quality studies.

**Statistical analysis**

Review Manager software version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014) was used for data analysis. For continuous outcomes, the weighted mean differences (WMDs) with corresponding 95% CIs were calculated. For dichotomous outcomes, the ORs with corresponding 95% CIs were examined. The quality was assessed by the Cochran $Q$ test and evaluated the extent of inconsistency by the $I^2$ statistic, which was divided into three degrees including low (25%–49%), moderate (50%–74%) and high (≥75%) levels.\textsuperscript{20} When $P>0.1$
and $I^2<50\%$, a fixed-effects model was used; otherwise, a random-effects model was applied. We used the following methods to explore sources of heterogeneity: 1) subgroup analysis (TT and LTT) and 2) sensitivity analysis conducted by excluding each of the included studies to identify which studies influenced the degree of heterogeneity. The possible presence of publication bias was estimated by Egger’s test and Begg’s test, investigated using STATA version 12.0 (Stata Corporation, College Station, TX, USA). $P$-values <0.05 were considered statistically significant.

**Results**

**Study selection**

The initial search yielded 2,633 potentially relevant articles. Seventeen potential articles were identified after screening titles and abstracts. After full-text review, an additional five articles were excluded for the following reasons: including cases of follicular thyroid cancer ($n=1$), $21$ cohorts may have overlapped ($n=2$) $22,23$ and some conflicts in articles ($n=2$). $24,25$ Finally, 12 observational articles were obtained for final analysis (Figure 1). $7,26–36$

**Study and patient characteristics**

Table 1 shows the total number of 2,672 PTC patients included, of whom 799 underwent ET and 1,873 underwent OT. Eight studies $26–30,32–34$ were performed in the Republic of Korea and four studies $7,31,35,36$ in China. All 12 studies were retrospective. In terms of surgical approach, in six studies the axillobreast approach (ABA) was performed, $26–28,32–34$ in three studies the bilateral breast approach (BBA) was performed, $31,35,36$ in two studies the transaxillary approach (TAA) was performed, $30$ and in the remaining study either ABA or TAA was performed for thyroidectomy. $29$

The pathological details of each study are summarized in Table 2.

**Meta-analysis of intraoperative outcomes**

Eleven studies calculated operative times for ET vs OT, $7,26–32,34–36$ and the operation time in the ET group was significantly longer than that in the OT group ($WMD=50.46$, $95\% CI$ 40.50 to 60.42, $P<0.00001$). However, there was a high level of heterogeneity among the studies ($I^2=87\%$, $P<0.00001$). The meta-analysis results remained unaffected when each individual study was removed from the data set.

Ten studies presented the number of retrieved lymph nodes, $7,27–35$ and the pooled data showed no significant differences between groups ($WMD=0.53$, $95\% CI$ –1.29 to 0.22, $P=0.17$). Furthermore, there was a high level of heterogeneity among the studies ($I^2=80\%$, $P<0.00001$). After excluding the study by Lee et al, $33$ there were still no significant differences between groups ($WMD=0.14$, $95\% CI$ –0.47 to 0.20, $P=0.42$), but no heterogeneity was observed among the studies ($I^2=0\%$).

Four studies $7,31,34,36$ compared intraoperative blood loss and the pooled data showed no significant differences between groups ($WMD=4.37$, $95\% CI$ –2.62 to 11.36, $P=0.22$). In addition, there was a moderate level of heterogeneity.

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**Figure 1** Flow diagram for study selection.

**Abbreviation:** FTC, follicular thyroid cancer.
Table I: General characteristics of studies included in the meta-analysis

| Study (first author, year) | Region | Study type | No of patients | Age (years), mean ± SD | Gender, M/F | Extent of thyroidectomy, TT/LTT | Surgical approach | Matching² | Quality score |
|---------------------------|--------|------------|----------------|------------------------|-------------|--------------------------------|------------------|----------|--------------|
| Chung 2007²⁶              | Korea  | RS         | 103 (16–44)    | 38.0 ± 2.2             | 1/102       | 88/15                          | BABA             | 4, 9     | 6            |
| Hong 2011²⁷              | Korea  | RS         | 57             | 39.0 ± 2.2             | 11/49       | 0/57                           | BABA/UABA        | 1, 2, 4, 7, 9 | 7            |
| Kim 2011²⁸               | Korea  | RS         | 95             | 39.0 ± 2.2             | 2/93        | 95/0                           | BABA             | 6         | 7            |
| Tae 2011²⁹               | Korea  | RS         | 31             | 36.2 ± 2.2             | 1/102       | 88/15                          | BABA             | 6         | 7            |
| Lee 2012³⁰               | Korea  | RS         | 37             | 42.3 ± 2.2             | 11/49       | 0/57                           | BABA             | 6         | 7            |
| Tan 2015³¹               | China  | RS         | 34             | 30 (16–44)             | 11/49       | 0/57                           | BABA             | 6         | 7            |
| Huang 2016³²             | China  | RS         | 75             | 38.0 ± 2.2             | 11/49       | 0/57                           | BABA             | 6         | 7            |
| Kim 2016³³               | Korea  | RS         | 173            | 38.9 (17–57)           | 11/49       | 0/57                           | BABA             | 6         | 7            |
| Lee 2016³⁴               | Korea  | RS         | 75             | 42.2 ± 2.2             | 11/49       | 0/57                           | BABA             | 6         | 7            |
| Park 2016³⁵              | Korea  | RS         | 50             | 38.0 ± 2.2             | 11/49       | 0/57                           | BABA             | 6         | 7            |
| Xiang 2016³⁶             | China  | RS         | 49             | 34.2 ± 2.2             | 11/49       | 0/57                           | BABA             | 6         | 7            |
| Ren 2017³⁷               | China  | RS         | 20             | 36.0 ± 2.2             | 11/49       | 0/57                           | BABA             | 6         | 7            |

Notes: ¹Features matching ET and OT: 1 = age; 2 = gender; 3 = body mass index; 4 = tumor size; 5 = multiplicity; 6 = bilaterality; 7 = extrathyroidal extension; 8 = tumor stage; 9 = extent of thyroidectomy. ²Median (range).

Abbreviations: BABA, bilateral axillobreast approach; BBa, bilateral breast approach; ET, endoscopic thyroidectomy; F, female; LTT, less than total thyroidectomy; M, male; OT, open thyroidectomy; RS, retrospective study; TAA, transaxillary approach; TT, total thyroidectomy; UABA, unilateral axillobreast approach.

Meta-analysis of postoperative outcomes

Eleven studies reported the transient postoperative RLN palsy rate. The cumulative transient postoperative RLN palsy rate, 7.3% (95% CI 1.46 to 15.11, P = 0.004), was significantly lower in the ET group (6.48, 95% CI 1.46 to 11.15, P = 0.004) compared to the OT group. The proportion of transient RLN palsy in the ET group (7.3%) was significantly lower than that in the OT group (9.9%, P = 0.04). The cumulative permanent postoperative RLN palsy rate, 2.8% (95% CI 0.15 to 0.51, P = 0.0003) (Table 3 and Figure 3A–C).

Eight studies described the duration of drainage and reported a larger amount of drainage in the ET group (WMD 11.16, 95% CI 1.09 to 21.26, P = 0.0001). In addition, the duration of drainage after removal of drainage was analyzed (WMD 0.65, 95% CI 0.06 to 1.24, P = 0.03) and the result was associated with significant heterogeneity (94.9%, P = 0.00001). After removing the study by Kim et al., the previously high heterogeneity drastically declined (57.3%, P = 0.19), but the significance of the result was unchanged (WMD 0.65, 95% CI 0.06 to 1.24, P = 0.03). After removing the study by Kong et al., the significance of the result was unaltered (WMD 0.65, 95% CI 0.06 to 1.24, P = 0.03). In addition, the duration of drainage was also analyzed (WMD 1.16, 95% CI 1.09 to 21.26, P = 0.0001). After removing the study by Park et al., the significance of the result was unchanged (WMD 1.16, 95% CI 1.09 to 21.26, P = 0.0001). Furthermore, this study by Huang et al. showed a higher level of heterogeneity as well (74.9%, P = 0.0001). After removing the study by Kong et al., the significance of the result was unaltered (WMD 1.16, 95% CI 1.09 to 21.26, P = 0.0001). In addition, the duration of drainage was also analyzed (WMD 1.16, 95% CI 1.09 to 21.26, P = 0.0001). After removing the study by Park et al., the significance of the result was unchanged (WMD 1.16, 95% CI 1.09 to 21.26, P = 0.0001). Furthermore, this study by Huang et al. showed a higher level of heterogeneity as well (74.9%, P = 0.0001). After removing the study by Kong et al., the significance of the result was unaltered (WMD 1.16, 95% CI 1.09 to 21.26, P = 0.0001).
Table 2 Pathological characteristics of studies included in the meta-analysis

| Study (first author, year) | Tumor size (mm) | Multiplicity (n/N) | Bilaterality (n/N) | Extrathyroidal extension (n/N) | Positive LNs (n/N) | No of metastatic LNs |
|---------------------------|-----------------|-------------------|-------------------|-----------------------------|-------------------|---------------------|
| Chung 2007<sup>26</sup>   | <10             | NR                | NR                | NR                          | NR                | NR                  |
| Hong 2011<sup>27</sup>    | 7.2±±2.30       | NR                | NR                | 10/57                       | NR                | NR                  |
| Kim 2011<sup>28</sup>     | 6.0±±2.0        | NR                | NR                | NR                          | NR                | NR                  |
| Tan 2011<sup>29</sup>     | 7.6±±4.9        | 6.4±±2.3          | 2/31              | 0/31                        | 2/31              | NR                  |
| Lee 2012<sup>30</sup>     | 5.0±±2.31       | 4.1±±2.64         | 3/37              | 5/41                        | NR                | NR                  |
| Tan 2015<sup>31</sup>     | 7.0±±3.0        | 8.0±±4.0          | NR                | NR                          | NR                | NR                  |
| Huang 2017<sup>32</sup>   | 4.8±±1.9        | 4.9±±2.3          | 5/75              | 9/123                       | NR                | NR                  |
| Kim 2016<sup>33</sup>     | NR              | NR                | NR                | NR                          | NR                | NR                  |
| Lee 2016<sup>34</sup>     | 5.8±±3.5        | 6.2±±3.7          | 12/75             | 30/233                      | NR                | NR                  |
| Park 2016<sup>35</sup>    | 8.0±±3.7        | 7.6±±1.9          | 7/50              | 19/102                      | 10/50             | NR                  |
| Xiang 2016<sup>36</sup>   | 7.7±±4.2        | 12.4±±7.9         | 26/49             | 37/47                       | 4/173             | 8/47                |
| Ren 2017<sup>37</sup>     | <10             | <10               | NR                | NR                          | NR                | NR                  |
| Overall                   | 6.4±±3.2        | 6.7±±3.7          | 55/317            | 102/582                     | 10/81             | 18/138              |

Abbreviations: ET, endoscopic thyroidectomy; LN, lymph node; NR, not reported; OT, open thyroidectomy.

95% CI 0.80 to 5.23, \( P = 0.14 \), and no heterogeneity existed \( I^2 = 0 \% \).

Eight studies reported the transient postoperative hypocalcemia rate \( 26,28,29,31,32,34–36 \) whereas seven reported permanent postoperative hypocalcemia rates \( 26,28,29,32,34–36 \). No significant differences were observed between the two groups in terms of transient hypocalcemia (OR 0.93, 95% CI 0.46 to 1.87, \( P = 0.84 \)), but high heterogeneity existed \( I^2 = 81\% , P = 0.0001 \). The meta-analysis results remained unchanged (OR 1.26, 95% CI 0.74 to 2.16, \( P = 0.40 \)) but a moderate decline in the heterogeneity \( I^2 = 53\% , P = 0.06 \) was observed when the study by Kim et al was removed. \( 32 \) In the case of permanent postoperative hypocalcemia, neither significant differences (OR 0.82, 95% CI 0.39 to 1.69, \( P = 0.58 \)) nor heterogeneity \( I^2 = 0\% \) were detected.

Regarding other complications, such as postoperative hematoma or bleeding (OR 1.76, 95% CI 0.81 to 3.81, \( P = 0.15 \)) and postoperative seroma (OR 1.33, 95% CI 0.53

Table 3 Outcomes of meta-analysis comparing ET vs OT

| Outcomes                  | No of studies | No of patients | OR/WMD | 95% CI      | P-value | \( I^2 \) (%) |
|---------------------------|---------------|----------------|--------|------------|---------|--------------|
| Intraoperative outcomes   |               |                |        |            |         |              |
| Operative time            | 11            | 724            | 1,640  | 50.46      | 40.50   | 60.42        | <0.00001     | 87          |
| No of retrieved LNs       | 10            | 676            | 1,640  | –0.53      | –1.29   | 0.22         | 0.17         | 80          |
| Blood loss                | 4             | 179            | 290    | 4.37       | –2.62   | 11.36        | 0.22         | 72          |
| Postoperative outcomes    |               |                |        |            |         |              |
| Duration of drainage      | 3             | 104            | 167    | 1.88       | 1.22    | 2.54         | <0.00001     | 76          |
| Volume of drainage        | 5             | 230            | 341    | 111.96     | 61.66   | 162.26       | <0.00001     | 95          |
| Hospitalization period    | 8             | 566            | 1,440  | 0.65       | 0.06    | 1.24         | 0.03         | 90          |
| Transient RLN palsy       | 11            | 762            | 1,832  | 2.64       | 1.36    | 5.11         | 0.004        | 48          |
| Permanent RLN palsy       | 9             | 653            | 1,679  | 2.04       | 0.80    | 5.23         | 0.14         | 0           |
| Transient hypocalcemia    | 8             | 555            | 1,416  | 0.93       | 0.46    | 1.87         | 0.84         | 81          |
| Permanent hypocalcemia    | 7             | 521            | 1,386  | 0.82       | 0.39    | 1.69         | 0.58         | 0           |
| Hematoma or bleeding      | 10            | 674            | 1,538  | 1.76       | 0.81    | 3.81         | 0.15         | 0           |
| Seroma                    | 4             | 258            | 357    | 1.33       | 0.53    | 3.34         | 0.54         | 0           |
| Oncological outcomes      |               |                |        |            |         |              |
| sTg < 1.0 ng/mL           | 2             | 29             | 343    | 0.33       | 0.13    | 0.81         | 0.02         | 0           |
| Tumor recurrences         | 6             | 398            | 1,170  | 0.54       | 0.22    | 1.32         | 0.18         | 0           |

Abbreviations: ET, endoscopic thyroidectomy; LN, lymph node; OT, open thyroidectomy; RLN, recurrent laryngeal nerve; sTg, stimulated thyroglobulin; WMD, weighted mean difference.
to 3.34, \(P=0.54\), no heterogeneity existed across studies \((I^2=0\%)\), and no significant differences between the ET and OT groups were observed (Table 3 and Figure 4A–F).

**Meta-analysis of oncological results**

The sTg levels were available in two studies.\(^{26,32}\) The ET group had lower proportions of having sTg <1.0 ng/mL (OR 0.33, 95% CI 0.13 to 0.81, \(P=0.02\)). No heterogeneity among studies existed \((I^2=0\%)\).

Six studies recorded tumor recurrences,\(^{26,29–32,36}\) and three studies reported no tumor recurrences during the follow-up period. Analysis of the pooled data showed that the two groups did not differ significantly (OR 0.54, 95% CI 0.22 to 1.32, \(P=0.18\)). No heterogeneity among studies was observed \((I^2=0\%)\) (Table 3 and Figure 5).

**Subgroup analysis**

We conducted a subgroup analysis according to the extent of thyroidectomy. The results of the subgroup analysis were roughly consistent with the previous outcomes. However, the volume of drainage (WMD 100.31, 95% CI –33.67 to 234.29, \(P=0.14\)) and transient RLN palsy (OR 1.58, 95% CI 0.66 to 3.79, \(P=0.31\)) were comparable between the ET and OT groups in TT. In addition, the hospitalization period

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**Table 3**

| Study or subgroup | ET | Mean (95% CI) | SD | Total | Mean (95% CI) | SD | Total | Weight (%) | Mean difference IV, random, 95% CI | Year | Mean difference IV, random, 95% CI |
|------------------|----|---------------|---|-------|---------------|---|-------|------------|-----------------------------------|------|-----------------------------------|
| Chung 2007       | 165.1 | 0 | 103 | 111.4 | 0 | 198 | 12.8 | 50.12 (40.92, 59.32) | 2007 | - |
| Hong 2011        | 121.65 | 20.78 | 57 | 71.53 | 29.43 | 60 | 12.8 | 55.00 (46.22, 61.78) | 2011 | - |
| Kim 2011         | 136 | 31 | 95 | 81 | 16 | 138 | 13.4 | 55.00 (46.22, 61.78) | 2011 | - |
| Tae 2011         | 192.4 | 56.3 | 31 | 101.6 | 33.3 | 36 | 8.2 | 90.80 (68.10, 113.50) | 2011 | - |
| Lee 2012         | 138.4 | 36.9 | 37 | 112.3 | 14 | 41 | 11.6 | 26.10 (13.46, 38.74) | 2012 | - |
| Park 2016        | 123.9 | 39.3 | 50 | 70.7 | 22.3 | 102 | 12.0 | 53.20 (41.48, 64.92) | 2016 | - |
| Kim 2016         | 139.56 | 0 | 173 | 119.67 | 0 | 830 | - | - | 2016 | - |
| Tan 2015         | 95 | 15 | 34 | 33 | 5 | 30 | 13.8 | 62.00 (56.65, 67.35) | 2015 | - |
| Huang 2016       | 142.5 | 36.9 | 75 | 111.5 | 21.2 | 123 | 12.8 | 31.00 (21.85, 40.15) | 2016 | - |
| Xiang 2016       | 187 | 51 | 49 | 135 | 53 | 47 | 8.8 | 52.00 (31.18, 72.82) | 2016 | - |
| Ren 2017         | 169 | 56.489 | 20 | 127.74 | 42.051 | 35 | 6.6 | 41.26 (12.85, 69.67) | 2017 | - |

**Figure 2**

Forest plot and meta-analysis of (A) operative time; (B) number of retrieved lymph nodes; (C) blood loss. Abbreviations: ET, endoscopic thyroidectomy; OT, open thyroidectomy.
was comparable between the two groups in LTT (OR 0.81, 95% CI –0.19 to 1.82, \( P = 0.11 \)). The concrete results of the subgroup analysis are summarized in Table 4.

**Pooled surgical outcomes**
Table 5 shows the pooled surgical outcomes of patients between ET and OT groups from all eligible studies.

**Publication bias**
Figure 6 shows a funnel plot of the studies reporting on transient RLN palsy. Begg’s test (\( P = 0.276 \)) and Egger’s test (\( P = 0.753 \)) showed no statistical publication bias in the studies reporting on transient RLN palsy.

**Discussion**
PTC is a subtype of differentiated thyroid cancer and surgery remains the primary therapeutic method for thyroid cancer. However, an obvious scar on the neck left after conventional OT causes psychological concerns in patients. With the popularity of endoscopic instruments, ET has been an attractive alternative to open surgery for the treatment of PTC. Owing to the limited number of studies comparing the outcomes between ET and OT, the general application of ET for PTC remains controversial. Unlike the previous meta-analysis, which included patients with PTMC only, our study also recruited patients with tumor sizes larger than PTMC. Furthermore, many new studies with a greater number of patients have been published in recent years. Therefore, we aimed to perform a comprehensive systematic review and meta-analysis to identify the clinical value of ET in adult patients with PTC.

The results of our meta-analysis showed that the operative time in the ET group was longer than that in the OT group. This may be attributed to three reasons. First, more time is...
needed to create the skin flap.\textsuperscript{31,32} Second, the meticulous bleeding control and careful lymph-node dissection require longer operation times.\textsuperscript{7,30} Third, surgeon experience and skills affect the operation times.\textsuperscript{19,29,37} The volume of fluid drainage and the time taken to remove the drainage tube in the ET group were much greater than in the OT group. It has been suggested that more dissection is needed to achieve the necessary working space.\textsuperscript{28} Furthermore, the longer postoperative hospitalization period in ET suggests a longer recovery period than for OT, especially when performing TT.

In terms of the number of lymph nodes dissected, our meta-analysis demonstrated that there was no significant

\begin{table}[h]
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\begin{tabular}{llllllll}
\hline
Study or subgroup & ET Events & Total & OT Events & Total & Weight (\%) & Odds ratio M–H, random, 95\% CI & Year & Odds ratio M–H, random, 95\% CI \\
\hline
Chung 2007 & 26 & 103 & 5 & 198 & 14.8 & 13.03 (4.83, 35.18) & 2017 & \\
Kim 2011 & 2 & 95 & 1 & 138 & 5.6 & 2.95 (0.26, 32.96) & 2011 & \\
Hong 2011 & 2 & 57 & 2 & 60 & 7.3 & 1.05 (0.14, 7.75) & 2011 & \\
Tae 2011 & 2 & 31 & 1 & 36 & 5.5 & 2.41 (0.21, 27.98) & 2011 & \\
Lee 2016 & 9 & 75 & 4 & 233 & 12.7 & 7.81 (2.33, 26.16) & 2016 & \\
Park 2016 & 4 & 50 & 7 & 102 & 12.1 & 1.18 (0.33, 4.24) & 2016 & \\
Kim 2016 & 12 & 173 & 33 & 830 & 17.9 & 1.80 (0.91, 3.56) & 2016 & \\
Tan 2015 & 1 & 34 & 0 & 30 & 3.5 & 2.73 (0.11, 69.60) & 2015 & \\
Huang 2016 & 2 & 75 & 3 & 123 & 8.3 & 1.10 (0.18, 6.71) & 2016 & \\
Xiang 2016 & 2 & 49 & 0 & 47 & 3.8 & 5.00 (0.23, 106.95) & 2016 & \\
Ren 2017 & 2 & 20 & 4 & 35 & 8.4 & 0.96 (0.14, 5.18) & 2017 & \\
\hline
Total (95\% CI) & 762 & 1,832 & 100 & 2.64 (1.36, 5.11) & & & & \\
\end{tabular}
\caption{Table A}
\end{table}

\begin{table}[h]
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\begin{tabular}{llllllll}
\hline
Study or subgroup & ET Events & Total & OT Events & Total & Weight (\%) & Odds ratio M–H, fixed, 95\% CI & Year & Odds ratio M–H, fixed, 95\% CI \\
\hline
Chung 2007 & 0 & 103 & 1 & 198 & 18.0 & 0.64 (0.03, 15.75) & 2007 & \\
Tae 2011 & 0 & 31 & 0 & 36 & Not estimable & & & \\
Kim 2011 & 2 & 95 & 0 & 138 & 7.0 & 7.41 (0.35, 156.03) & 2011 & \\
Hong 2011 & 1 & 57 & 0 & 60 & 8.3 & 3.21 (0.13, 80.49) & 2011 & \\
Park 2016 & 2 & 50 & 4 & 102 & 44.4 & 1.02 (0.18, 5.77) & 2016 & \\
Lee 2016 & 1 & 75 & 0 & 233 & 4.2 & 9.40 (0.38, 233.27) & 2016 & \\
Kim 2016 & 1 & 173 & 3 & 830 & 18.1 & 1.60 (0.17, 15.50) & 2016 & \\
Xiang 2016 & 0 & 49 & 0 & 47 & Not estimable & & & \\
Ren 2017 & 0 & 20 & 0 & 35 & Not estimable & & & \\
\hline
Total (95\% CI) & 653 & 1,679 & 100 & 2.04 (0.80, 5.23) & & & & \\
\end{tabular}
\caption{Table B}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{llllllll}
\hline
Study or subgroup & ET Events & Total & OT Events & Total & Weight (\%) & Odds ratio M–H, random, 95\% CI & Year & Odds ratio M–H, random, 95\% CI \\
\hline
Chung 2007 & 26 & 103 & 35 & 198 & 18.0 & 1.57 (0.88, 2.80) & 2007 & \\
Tae 2011 & 0 & 31 & 0 & 36 & Not estimable & & & \\
Kim 2011 & 24 & 95 & 38 & 138 & 17.8 & 0.89 (0.49, 1.61) & 2011 & \\
Tan 2015 & 0 & 34 & 1 & 30 & 3.8 & 0.29 (0.01, 7.26) & 2015 & \\
Park 2016 & 13 & 50 & 23 & 102 & 16.3 & 1.21 (0.55, 2.64) & 2016 & \\
Kim 2016 & 22 & 173 & 246 & 830 & 18.7 & 0.35 (0.22, 0.55) & 2016 & \\
Xiang 2016 & 29 & 49 & 14 & 47 & 15.8 & 3.42 (1.47, 7.96) & 2016 & \\
Ren 2017 & 2 & 20 & 9 & 35 & 9.6 & 0.32 (0.06, 1.66) & 2017 & \\
\hline
Total (95\% CI) & 555 & 1,416 & 100 & 0.93 (0.46, 1.87) & & & & \\
\end{tabular}
\caption{Table C}
\end{table}
Figure 4 Forest plot and meta-analysis of (A) transient RLN palsy; (B) permanent RLN palsy; (C) transient hypocalcemia; (D) permanent hypocalcemia; (E) hematoma or bleeding; (F) seroma.

Abbreviations: ET, endoscopic thyroidectomy; M–h, Mantel–Haenszel; OT, open thyroidectomy; RLN, recurrent laryngeal nerve.

difference between the ET and OT groups. This finding may indicate that the clearance of lymph nodes is comparable between the two groups. The previous meta-analysis showed that the number of lymph nodes dissected is less in the ET group, but no significant difference existed in the subgroup analysis, which is in concordance with our result.

RLN palsy and hypocalcemia are the major complications of thyroid surgery. Our meta-analysis showed that ET was associated with a significantly greater risk of transient RLN palsy than OT, which was not consistent with the previous meta-analysis. In the sensitivity analysis, the significant difference still existed. It is worth noting that endoscopic magnification with high-definition monitors is better for detecting the RLN. However, the similar or even worse risk of transient RLN palsy in ET relative to OT remains disappointing. Chung et al reported that 25.2% (26/103) of patients experienced transient RLN palsy and proposed that thermal damage caused by the ultrasonic scalpel may injure the RLN. Tan et al adopted the same viewpoint. Another reason may be that ET represents a different anatomic surgery approach, which is not familiar to traditional thyroid surgeons. Sun and Dionigi proposed that surgeons must have an excellent understanding of the RLN in terms of identification and suggested that intraoperative neural
monitoring may be a good choice to avoid RLN palsy.\textsuperscript{41} It was an interesting finding that in the subgroup analysis, transient RLN palsy was comparable between the two groups in TT, but not in LTT. We consider that the risk of transient RLN palsy can be greatly reduced as long as the surgeon is experienced in ET, and good exposure and protection of the RLN are achieved during surgery. In addition, there were no significant differences between the two groups in terms of

![Figure 5](image_url) Forest plot and meta-analysis of (A) number of sTg < 1 ng/mL; (B) number of tumor recurrences.

**Abbreviations:** ET, endoscopic thyroidectomy; M–h, Mantel–Haenszel; OT, open thyroidectomy; sTg, stimulated thyroglobulin.

### Table 4: Meta-analysis of the subgroups according to the extent of thyroidectomy

| Outcomes                  | No of studies | No of patients | OR/ WMD | 95% CI          | P-value | I^2 (%) |
|---------------------------|---------------|----------------|---------|-----------------|---------|---------|
| **TT**                    |               |                |         |                 |         |         |
| Operative time            | 4             | 269            | 410     | 47.40           | 34.18, 60.61 | <0.00001 | 84      |
| No of retrieved LNs       | 4             | 269            | 410     | −0.10           | −0.50, 0.30 | 0.63    | 0       |
| Blood loss                | 2             | 125            | 225     | 2.35            | −7.27, 11.97 | 0.63    | 79      |
| Volume of drainage        | 2             | 145            | 240     | 100.31          | −33.67, 234.29 | 0.14    | 94      |
| Hospitalization period    | 2             | 145            | 240     | 0.33            | 0.10, 0.56 | 0.005   | 0       |
| Transient RLN palsy       | 4             | 269            | 410     | 1.58            | 0.66, 3.79 | 0.31    | 0       |
| Permanent RLN palsy       | 3             | 194            | 287     | 1.89            | 0.49, 7.33 | 0.36    | 20      |
| Transient hypocalcemia    | 3             | 194            | 287     | 1.48            | 0.68, 3.20 | 0.32    | 70      |
| Permanent hypocalcemia    | 3             | 194            | 287     | 1.35            | 0.46, 3.99 | 0.58    | 0       |
| Hematoma or bleeding      | 3             | 219            | 308     | 2.93            | 0.61, 14.02 | 0.18    | 0       |
| Seroma                    | 2             | 170            | 261     | 0.67            | 0.10, 4.55 | 0.68    | 0       |
| **LTT**                   |               |                |         |                 |         |         |
| Operative time            | 4             | 148            | 166     | 45.96           | 29.33, 62.59 | <0.00001 | 90      |
| No of retrieved LNs       | 4             | 203            | 364     | −0.89           | −2.48, 0.70 | 0.27    | 90      |
| Blood loss                | 2             | 54             | 65      | 6.52            | −0.72, 13.76 | 0.08    | 46      |
| Duration of drainage      | 2             | 54             | 65      | 2.20            | 1.82, 2.59 | <0.00001 | 0       |
| Volume of drainage        | 2             | 54             | 65      | 114.99          | 99.74, 130.24 | <0.00001 | 0       |
| Hospitalization period    | 3             | 114            | 136     | 0.81            | −0.19, 1.82 | 0.11    | 95      |
| Transient RLN palsy       | 4             | 186            | 358     | 2.83            | 1.26, 6.36 | 0.01    | 44      |
| Permanent RLN palsy       | 3             | 152            | 328     | 5.29            | 0.54, 52.22 | 0.15    | 0       |
| Transient hypocalcemia    | 2             | 54             | 65      | 0.31            | 0.07, 1.36 | 0.12    | 0       |
| Hematoma or bleeding      | 4             | 148            | 166     | 2.20            | 0.62, 7.84 | 0.22    | 0       |

**Abbreviations:** ET, endoscopic thyroidectomy; LN, lymph node; LTT, less than total thyroidectomy; OT, open thyroidectomy; RLN, recurrent laryngeal nerve; TT, total thyroidectomy; WMD, weighted mean difference.
Table 5  Pooled surgical outcomes between ET and OT groups from all eligible studies

| Outcomes                           | ET       | OT       | References |
|-----------------------------------|----------|----------|------------|
| **Intraoperative outcomes**       |          |          |            |
| Operative time (minutes)          | 142.0±45.9 | 92.3±36.6 | 7, 27–31, 34–36 |
| No of retrieved LNs               | 4.3±4.1  | 4.7±4.0  | 7, 27–31, 33–35 |
| Blood loss (mL)                   | 19.6±24.5 | 14.5±9.8 | 7, 31, 34, 36 |
| **Postoperative outcomes**        |          |          |            |
| Duration of drainage (days)       | 5.9±1.9  | 4.6±2.0  | 31, 34, 36  |
| Volume of drainage (mL)           | 202.3±142.0 | 112.7±56.9 | 28, 29, 31, 34, 36 |
| Hospitalization period (days)     | 5.3±2.5  | 4.8±2.9  | 27–30, 34, 36 |
| Transient RLN palsy, n (%)        | 64 (8.3) | 60 (3.3) | 7, 26–29, 31–36 |
| Permanent RLN palsy, n (%)        | 7 (1.1)  | 8 (0.5)  | 26–29, 32–36 |
| Transient hypocalcemia, n (%)     | 116 (20.9)| 366 (25.8)| 26, 28, 29, 31, 32, 34–36 |
| Permanent hypocalcemia, n (%)     | 10 (1.9) | 31 (2.2) | 26, 28, 29, 32, 34–36 |
| Hematoma or bleeding, n (%)       | 13 (1.9) | 17 (1.1) | 7, 26–32, 35, 36 |
| Seroma, n (%)                     | 10 (3.9) | 9 (2.5)  | 7, 27–29    |
| **Oncological outcomes**          |          |          |            |
| sTg, 1.0 ng/ml, n (%)             | 9 (31.0) | 176 (51.3)| 26, 32      |
| Tumor recurrences, n (%)          | 6 (1.5)  | 31 (2.6) | 26, 29–32, 36 |

Abbreviations: ET, endoscopic thyroidectomy; LN, lymph node; OT, open thyroidectomy; RLN, recurrent laryngeal nerve; sTg, stimulated thyroglobulin.

permanent RLN palsy, transient hypocalcemia, permanent hypocalcemia, hematoma or seroma.

Oncological outcomes, such as tumor recurrences and completeness of thyroid resection, are highly valued by surgeons. According to the American Thyroid Association guidelines, sTg may be helpful in predicting disease status. Only two studies recorded the number of patients with sTg <1 ng/mL and our results demonstrated that the OT group may be associated with cleaner resection. Similarly, Kim et al found that the ET group showed higher postoperative thyroglobulin levels (2.4±6.3 ng/mL) than the OT group (0.8±2.0 ng/mL). This indicates that OT is superior to ET in sTg levels presenting completeness of thyroid resection. In contrast, Jeong et al enrolled 275 PTMC patients who underwent ET and reported that all thyroidectomized patients had <1 ng/mL of postoperative serum thyroglobulin. With regard to tumor recurrences, the results showed no significant differences between the two groups, and three studies reported no tumor recurrences during the follow-up period. However, the results should be interpreted with caution. This is because, first, there were still insufficient available data on sTg levels. Second, data on postoperative follow-up were lacking and follow-up times were too short, because most PTCs have a slow progression and a good prognosis, with a 10-year survival rate of more than 90%. Third, tumor characteristics such as tumor size were not well matched between the two groups. Thus, unlike surgical-related outcomes, oncological outcomes are difficult to compare. Randomized controlled trials with long-term follow-up assessment are needed to further evaluate oncological outcomes.

There are several limitations in our meta-analysis. First, all studies included were non-randomized controlled trials, which could lead to a higher risk of potential selection and reporting bias than randomized controlled trials. Second, some heterogeneity was observed for certain results. This may be related to differences among patient and tumor characteristics, the surgeons’ experience and the surgical approaches. Third, transoral endoscopic thyroidectomy (TOET) has received attention in recent years, but no reports have compared OT with TOET in total thyroid cancer. Most patients who undergo TOET have benign lesions, and many reports are on initial experiences or robot-assisted surgery. In addition, cosmetic results and quality of life are difficult to assess because of the few well-accepted tools available to study such outcomes.
Conclusion
Compared with OT, ET is disappointing in terms of operation and drainage time, amount of drainage fluid, hospital stay and transient RLN palsy, whereas other complications appear comparable. In addition, despite the similar tumor recurrence rates, the level of surgical completeness in ET may not be as good as that in OT. Therefore, the application of ET for patients with PTC should be conducted carefully, and further prospective studies with longer follow-up are needed to evaluate the oncological effectiveness of ET.

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Author contributions
J Zhou and L Wang designed the study; J Zhou and C Chen wrote the manuscript; C Chen, S Huang, A Huang, Y Jia and J Wang analyzed the data and interpreted the results. All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure
The authors report no conflicts of interest in this work.

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