Comparison of Completion Thyroidectomy and Primary Total Surgery for Differentiated Thyroid Cancer: A Meta-Analysis

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Summary
Background: The aim of this study was to compare the complication rates between completion thyroidectomy and primary total thyroidectomy for differentiated thyroid cancer (DTC). Methods: PubMed, the Web of Knowledge, and the China Journal Net were searched for studies concerning the treatment of DTC published in 1990–2014. A meta-analysis was performed to compare the effects of different treatments. Results: 7 studies with a total of 1,208 patients were included. There were no statistically significant differences regarding the presence of temporary recurrent laryngeal nerve (RLN) palsy, permanent RLN palsy, temporary hypocalcemia, permanent hypocalcemia, hematoma, and wound infection. Conclusions: Completion thyroidectomy can be performed with acceptable morbidity in select cases of DTC who could not be properly diagnosed perioperatively or who recurred after less than total thyroidectomy.

Introduction
Surgical treatment of thyroid diseases is still controversial, especially for differentiated thyroid cancer (DTC). The appropriate extent of thyroid surgery is mainly dependent on the age of the patient and the size and grade of the primary lesion. The American Thyroid Association (ATA) guidelines recommend that some patients with a preoperative indeterminate result who are diagnosed with malignancy after lobectomy are suitable for completion thyroidectomy (CT) [1]. But some studies indicate that CT after initial lobectomy is unnecessary after a new diagnosis of DTC [2, 3]. The issue arises from the fact that there are no randomized trials or evidence to support either surgical method.

Complications include temporary recurrent laryngeal nerve (RLN) palsy, permanent RLN palsy, temporary hypocalcemia, permanent hypocalcemia, hematoma, and wound infection. Although the complications following CT are a cause for hesitation, experience reduces the complication rates. In this study, we provide a review of the literature to determine whether there are differences in the complications of two different thyroidectomies.

Materials and Methods

Search Strategy
PubMed, the Web of Knowledge, and the China Journal Net were searched for publications from January 1990 to December 2014, without language restrictions. The search terms used were ‘completion thyroidectomy’, ‘primary total surgery’ and ‘differentiated thyroid cancer’. The reference lists of relevant studies were checked manually to locate any missing studies.

Study Selection
Identified studies were assessed for eligibility in the review by scrutinizing the titles, abstracts, and keywords of every record retrieved. Studies were restricted to those published in English and Chinese. Clinical studies concerning comparisons of any aspects between CT and primary total thyroidectomy (TT) for differentiated thyroid microcarcinoma were also included.

Data Extraction
Two coauthors (L.Y. and Z.X.) independently selected studies for inclusion and exclusion and reached a consensus when they did not agree in the initial assignment. The following variables were recorded: authors, journal and year of publication, country, sample size, study design, number of CT and TT, and complications.
publication, number of patients, patient age, histological cancer type, temporary RLN palsy, permanent RLN palsy, temporary hypocalcemia, and permanent hypocalcemia. If necessary, the corresponding authors of studies were contacted to obtain supplementary information.

Statistical Analysis

A formal meta-analysis was made for all studies, comparing the results of CT and TT for differentiated thyroid carcinoma. The outcomes used for this study were the recorded complications (temporary RLN palsy, permanent RLN palsy, temporary hypocalcemia, permanent hypocalcemia, hematoma, and wound infection). Pooled estimates of the complications were calculated using a fixed-effects model, but a random-effects model was used according to heterogeneity. The test of effect homogeneity was performed using χ² tests, with p ≤ 0.05 indicating significant heterogeneity. When the hypothesis of homogeneity was not rejected, the fixed-effects model was used to estimate the pooled effect of the outcomes; when the reverse was true, the random-effects model was also calculated. The results for each study were expressed as an odds ratio (OR) with 95% confidence intervals (CIs). The Cochrane Collaboration Review Manager (RevMan version 5.0) software was used for data analysis.

Table 1. Overview of the reviewed studies: country, patient characteristics, time to reoperation, study design

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country</th>
<th>Number of patients</th>
<th>Mean age, years</th>
<th>F/M</th>
<th>Time to reoperation</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rafferty et al. 2007 [5]</td>
<td>Canada</td>
<td>350</td>
<td>CT: 46.9</td>
<td>TT: 46.1</td>
<td>CT: 164/37 within 3 months</td>
<td>retrospective review</td>
</tr>
<tr>
<td>Gulcelik et al. 2012 [6]</td>
<td>Turkey</td>
<td>376</td>
<td>CT: 42.9</td>
<td>TT: 44.2</td>
<td>CT: 121/38</td>
<td>retrospective review</td>
</tr>
<tr>
<td>Eroğlu et al. 1998 [7]</td>
<td>Turkey</td>
<td>106</td>
<td>CT: 40.0</td>
<td>TT: 43.0</td>
<td>CT: 43/16</td>
<td>retrospective review</td>
</tr>
<tr>
<td>Rosário et al. 2007 [8]</td>
<td>Brazil</td>
<td>235</td>
<td>CT: 39.6</td>
<td>TT: 41.2</td>
<td>CT: 98/33</td>
<td>retrospective review</td>
</tr>
<tr>
<td>Merchavy et al. 2014 [9]</td>
<td>Canada</td>
<td>214</td>
<td>CT: 52.1</td>
<td>TT: 50.2</td>
<td>CT: 58/21 102 days</td>
<td>retrospective review</td>
</tr>
<tr>
<td>Mishra et al. 2002 [10]</td>
<td>India</td>
<td>143</td>
<td>CT: 39.6</td>
<td>TT: 41.4</td>
<td>CT: 34/14 most cases after 3 months</td>
<td>retrospective review</td>
</tr>
</tbody>
</table>

F = Female, M = male, CT = completion thyroidectomy, TT = Total thyroidectomy.

Table 2. Overview of the reviewed studies: study duration, patient source, histological type

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Study duration</th>
<th>Patient source</th>
<th>Histological type</th>
</tr>
</thead>
</table>

CT = Completion thyroidectomy, TT = total thyroidectomy.

Results

Study Selection

We identified 143 potentially relevant articles (fig. 1). After exclusion of duplicate references, non-relevant literature, and those manuscripts that did not satisfy the inclusion criteria, 34 candidate articles were considered for the meta-analysis. After careful review of the full texts of these articles, 7 studies were included. The study characteristics are summarized in tables 1 and 2.

The patient demographics for the 7 studies are presented in table 1. CT was performed 10 days after the initial operation in all cases. All papers were retrospective chart reviews. The publication dates ranged from 1990 to 2014. The study sizes ranged from 106 to 376 patients.

Although one included study [8] failed to cover the examination of complications, the other included studies indicated that postop-
erative laryngoscopy was performed and serum calcium concentrations were assessed routinely. Temporary RLN palsy occurred in 10.1% (75/741) and 8.1% (57/702) of the patients in the CT and TT groups, respectively. The permanent RLN palsy rates were 1.8% and 1.1% in the CT (12/682) and TT (7/655) groups, respectively. There were no significant differences in the occurrence of temporary RLN palsy (OR = 1.19, 95% CI 0.81–1.75, P = 0.63; fig. 2) or permanent RLN palsy (OR = 1.54, 95% CI 0.62–3.79, P = 0.35; fig. 2). The prevalence of temporary hypocalcemia was 14.9% in the CT group versus 15.4% in the TT group, without significant differences (OR = 0.75, 95% CI 0.38–1.51, P = 0.42; fig. 3) in the random-effects model. The prevalence of permanent hypocalcemia was 2.8% in the CT group versus 3.3% in the TT group, without significant differences (OR = 0.86, 95% CI 0.47–1.57, P = 0.63; fig. 2) in the fixed-effects model. 3 studies reported hematoma and wound infection, and there were no significant differences in the occurrences (OR = 1.00, 95% CI 0.31–3.26, P = 1.00 and OR = 1.58, 95% CI 0.46–5.43, P = 0.47; fig. 2).

**Discussion**

CT plays an important role in the treatment of patients with DTC. Recently, not all patients have undergone TT, which is the preferred operation for cancer treatment. One of the reasons is the difficulty of perioperative diagnosis of cancer which can lead to inappropriate procedures. When the results of fine-needle aspiration (FNA) cytology or inefficient intraoperative frozen-section examinations are reported as indeterminate, a lobectomy or near-total thyroidectomy is performed. Once the final pathology is reported as DTC, reoperative thyroidectomy will be indicated in these patients [11]. CT is still believed to cause increased complication rates [12], and complications like RLN injury and hypoparathyroidism are reasons for hesitation, especially for inexperienced surgeons. However, other authors in the literature report that high-volume surgeons perform with lower rates of complications [13].

Our study was a systematic review of the available literature, examining complications in patients with DTC undergoing CT and TT. The reported complication rate of pooled temporary RLN palsy was 10.1% in the CT group and that of pooled permanent RLN palsy was 1.8%. The incidence of pooled temporary hypopar-
athyroidism was 14.9% and that of pooled permanent hypoparathyroidism was 2.8%, in the CT group. Our meta-analysis showed that CT led to similar complications as TT (figs. 2 and 3).

The rate of pooled temporary hypocalcemia seems to be very low in our study. So we reviewed a large number of publications and found that the incidence of temporary hypocalcemia varies from as low as 1% to as high as 50% of patients who underwent TT [14–18]. Most series report an incidence of around 20–40%.

Some studies that were designed to decrease the complication risk have focused on the timing of completion surgery and conclude that CT should be performed either within 10 days of the primary operation or beyond a minimum of 3 months in order to avoid strong postoperative adhesions [14, 19, 20]. In our series, the risk of complications seemed similar regardless of the time interval after the initial surgery. The result may be attributed to careful identification of the recurrent nerves and parathyroid glands.

Cervical lymph node dissection may increase the rate of transient and permanent hypocalcemia, which is usually explained by the higher opportunity of unplanned removal or devascularization of the parathyroid glands during dissection. In our meta-analysis, only 2 of the included studies [5, 9] mentioned central lymph node dissection as part of the surgical procedure. One of these 2 studies [9] did not consider the presence of lymph nodes in the surgical specimens, and the other one [5] found a similar incidence of hypocalcemia. Although our study cohort was short of these data, some authors indicated that central lymph node dissection was not a risk factor for postoperative hypocalcemia [21, 22].

Radioiodine ablation of the remnant lobe is an alternative choice to achieve a CT. However, it is feared that multiple doses of 131I to ablate large thyroid remnants may produce radiation thyroiditis, odynophagia, cervical edema, etc. Thus, the adverse reactions limited this approach [23].

There are some limitations to our study. First, most of the included studies were single-center retrospective chart reviews with inherent limitations such as selection bias and inaccurate or missing data reports. Second, most of the trials did not report central lymph node dissection or radioiodine ablation. Hence, our findings must be interpreted with caution. To date, no randomized controlled trial has been completed to compare CT with TT for DTC.

Conclusions

CT can be performed with acceptable morbidity in select cases of DTC who could not be properly diagnosed perioperatively or who recurred after less than TT.

Disclosure Statement

No conflict of interest exits regarding the submission of this manuscript.

References

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