A meta-analysis comparing the outcomes of LigaSure Small Jaw versus clamp-and-tie technique or Harmonic Focus Scalpel in thyroidectomy
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Abstract
Background: LigaSure (LS) Small Jaw is a surgical hemostasis equipment that is newly introduced in thyroid surgery. The objective of this study is to assess the short-term efficacy and safety outcomes of LS Small Jaw compared with clamp-and-tie technique or Harmonic Focus Scalpel in thyroidectomy.

Methods: A literature search was performed in the PubMed and Embase databases (until June 12, 2016) that reported the comparisons between LS Small Jaw and other techniques in thyroidectomy. Quality assessments were performed according to The Cochrane Collaboration’s risk of bias tool and a modification of the Newcastle-Ottawa Scale in randomized controlled trials (RCTs) and non-RCTs, respectively. All statistical analyses were conducted using RevMan 5.3.

Results: Finally, 7 studies with 813 patients were included into the meta-analysis, and all included studies were comparable with moderate-to-high quality. There was significant reduced operative time in LS Small Jaw, compared with clamp-and-tie (mean difference [MD] = −17.49, 95% confidence interval [CI]: −22.20 to 12.77, \( P < 0.00001 \)) or Harmonic Focus Scalpel (MD = −2.29, 95% CI: −3.19 to 1.39, \( P < 0.00001 \)). Besides, other perioperative outcomes including intraoperative blood loss and postoperative blood loss favored LS Small Jaw compared with clamp-and-tie. In terms of complications, less-temporary hypocalcemia rate was observed in LS Small Jaw compared with clamp-and-tie (odds ratio [OR] = 0.49, 95% CI: 0.27–0.90, \( P = 0.02 \)), although no significant difference was detected compared with Harmonic Focus Scalpel (OR = 0.47, 95% CI: 0.14–1.56, \( P = 0.22 \)). Other complications such as length of hospital stay, permanent hypocalcemia, temporary or permanent recurrent laryngeal nerve palsy, and hematomas were not significant.

Conclusion: In conclusion, LS Small Jaw is more favorable than clamp-and-tie technique or Harmonic Focus Scalpel in thyroidectomy.

Abbreviations: CI = confidence interval, HR = hazard ratio, LS = LigaSure, MD = mean difference, NOS = Newcastle-Ottawa Scale, OR = odds ratio, RCT = randomized controlled trial, RLN = recurrent laryngeal nerve.

Keywords: clamp-and-tie, complications, Harmonic Focus Scalpel, LigaSure Small Jaw, meta-analysis

1. Introduction
Thyroidectomy is one of the most commonly performed procedures in head and neck surgery all over the world. Due to rich arterial and venous sources in the thyroid gland and close to the main lateral cervical vessels (carotid artery and jugular vein), recurrent laryngeal nerve (RLN), prompt and effective hemostasis in thyroid surgery is crucial.\(^1,2\) Efficacy in hemostasis may make a difference in operative time, perioperative blood loss, and degrees of injury to laryngeal nerve, parathyroid.\(^3–5\)

Ligation of blood vessels is often time consuming, and the use of sutures and their application technique requires experience and a prolonged learning curve. In recent years, several new equipments have advanced the practice of thyroid surgery, such as Harmonic Focus Scalpel and vessel sealing system.\(^6\) Harmonic Focus Scalpel is a device that is widely used in many surgical practices. Small Jaw is a new generation of the LigaSure (LS) (LigaSure, Covidien, Minneapolis, Minnesota, Minnesota, USA) for use in thyroid surgery. This device is capable of dissection, ligation, and cutting in thyroid surgery, making hemostasis more effective and operating time shorter.\(^7\) In this study, LS Small Jaw was compared with Harmonic Focus Scalpel or clamp-and-tie in terms of operative time; intraoperative blood loss; postoperative blood loss; length of hospital stay; and complications including temporary/permanent hypocalcemia, temporary/permanent RLN palsy, seromas, hematomas, and infection.
2. Methods

2.1. Study search

A systematic search was conducted in the PubMed, Embase database, and the Cochrane Central Register of Controlled Trials ClinicalTrials.gov (http://www.clinicaltrials.gov) with no limits (until June 2, 2016). Our search terms were LS Small Jaw, thyroidectomy/thyroid surgery, and surgical outcome. In addition, previously published studies on the topic of the interest were reviewed. We manually searched the references of all retrieved articles.

2.2. Study selection

The inclusion criteria were as follows: the studies that estimated the impact of surgical instruments on thyroidectomy, surgical procedure comparing LS Small Jaw and clamp-and-tie or Harmonic Focus Scalpel, the studies providing short or surgical outcomes, and available data for each surgical regimen. The exclusion criteria were as follows: the patients in studies underwent other treatment such as hematectomy, just 1 surgical regimen (LS Small Jaw) was reported, other surgical technique such as LS precise was compared, and studies lacking available data.

Search results were imported into bibliographic citation management software (EndNote X7, Endnote, Thomson Scientific, Philadelphia, Pennsylvania, USA). The authors screened imported titles and abstracts to identify potential studies, and then, full texts were carefully read to match the inclusion and exclusion criteria. Disagreements were resolved through discussion or asking for advice from the corresponding author.

2.3. Data extraction and quality assessment

The first 2 authors independently extracted data from potential included studies. Baseline information included first author, published year, number of patients, intervention, study design, and country. The following outcome data were extracted: operative time; intraoperative blood loss; postoperative blood loss; length of hospital stay; and complications including temporary/permanent hypocalcemia, temporary/permanent RLN palsy, hematomas, and infection.

As for study qualitative assessment, we used The Cochrane Collaboration’s risk of bias tool[9] to evaluate the quality of randomized controlled trials (RCTs). Six domains including random sequence generation, allocation concealment, blinding of participants and researchers, blinding of outcome assessment, incomplete outcome data, and selective reporting were independently taken into evaluating risk of bias. For non-RCTs, a modification of the Newcastle-Ottawa Scale (NOS)[9] with 3 domains of selection, comparability, and outcome was induced. Five main factors were investigated: operation indication, operation type (total thyroidectomy or hemithyroidectomy), age, sex, and body mass index. Out of a total of 6 stars, studies that valued more than 4 stars were recognized as being moderate-to-high quality.

2.4. Statistical analysis and outcome definition

We analyzed the data using (Review manager, Cochrane, London, United Kingdom) (Version 5.3). Odds ratios (ORs) or hazard ratios (HRs) along with 95% confidence intervals (CI) were used for analyzing dichotomous data and mean differences (MDs) along with 95% CI for continuous data. Heterogeneity test, in order to measure the variation among included studies, was expressed with the I² index and P value. In addition, substantial significance was set when P<0.10, thus a random effect model was used, and sensitivity analysis was performed by sequentially omitting each study to test the influence of individual study. When, P≥0.10, a fixed-effect model was induced. For outcomes, the value of P<0.05 was considered to indicate statistical significance.

Intraoperative and postoperative blood losses were estimated. Postoperative complications were recorded till discharge from hospital. Permanent hypocalcemia or RLN palsy was followed till 6 to 12 months after surgery.

3. Results

3.1. Characteristics of studies

The flow diagram of the detailed selection process is summarized in Fig. 1. Briefly, a total of 16 abstracts were identified after removing out duplications in the primary electronic and manual searches. After screening the potential full texts of hit abstracts, 7 studies including a total of 813 patients who underwent thyroidectomy compared the surgical outcomes between LS Small Jaw and clamp-and-tie/Harmonic Focus Scalpel.[10–16] Among them, 5 studies (386 patients) compared LS Small Jaw and clamp-and-tie,[10,11,13,15,16] and the residual 2 studies (427 patients) compared LS Small Jaw and Harmonic Focus Scalpel for thyroidectomy.[12,14] The baseline characteristics of all studies are listed in Table 1.

3.2. Quality judgments of studies

LS Small Jaw is an emerging instrument used in thyroidectomy. It is not hard to randomly allocate thyroidectomy into LS Small Jaw or other instruments. So the included 4 of total 7 researches were prospective randomized studies[10,11,13,14] and another 3 studies were 2 retrospective controlled studies[15,16] and 1 prospective...
nonrandomized study.\cite{12} As for qualitative assessment, Table 2 showed the evaluation of each study followed by The Cochrane Collaboration's risk of bias tool and modified NOS. All included studies were comparable with moderate-to-high quality.

### 3.3. Outcomes

In terms of operative time, all 7 studies were pooled in the analysis. Among them, 5 of total 7 researches compare LS Small Jaw with clamp-and-tie, and there is significant reduced operative time in LS Small Jaw group (MD = −17.49, 95% CI: −22.20 to 12.77, \( P < 0.00001 \)).\cite{10,11,13,15,16} The other 2 studies reported the similar significant reduced operative time when LS Small Jaw is compared with Harmonic Focus Scalpel (MD = −2.29, 95% CI: −3.19 to 1.39, \( P < 0.00001 \)) (Fig. 2).\cite{12,14} Moreover, funnel plot of operative time in all studies showed no obvious evidence of publication bias (Fig. 3). In addition, other perioperative outcomes including intraoperative blood loss and postoperative

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**Table 1**

| Reference                  | No. of patients | Intervention                                      | Study design                        | Country      |
|----------------------------|-----------------|---------------------------------------------------|-------------------------------------|--------------|
| Bircan et al\cite{10}      | 32              | LigaSure Small Jaw vs clamp-and-tie                | Prospective randomized controlled   | Turkey       |
| Coiro et al\cite{11}       | 95              | LigaSure Small Jaw vs clamp-and-tie                | Prospective randomized controlled   | Italy        |
| Hammad et al\cite{12}      | 161             | LigaSure Small Jaw vs Harmonic Focus Scalpel       | Prospective controlled              | USA          |
| Hirunwiwatkul and Tungkavichagul\cite{13,14} | 20              | LigaSure Small Jaw vs clamp-and-tie                | Prospective randomized controlled   | Thailand     |
| Hwang et al\cite{14}       | 64              | LigaSure Small Jaw vs Harmonic Focus Scalpel       | Prospective randomized controlled   | Korea        |
| Kuboki et al\cite{15}      | 39              | LigaSure Small Jaw vs clamp-and-tie                | Retrospective controlled            | Japan        |
| Molnar et al\cite{16}      | 10              | LigaSure Small Jaw vs clamp-and-tie                | Retrospective controlled            | Romania      |

**Table 2**

| Selection                  | Comparability | Outcome assessment | Random sequence generation | Allocation concealment | Blinding of participants and researchers | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Quality judgment |
|----------------------------|---------------|--------------------|-----------------------------|------------------------|------------------------------------------|---------------------------------|------------------------|-------------------|-------------------|
| Bircan et al\cite{10,12}   | +             | ?                  | +                           | +                      | +                                       | +                               | +                      | ++++              | +     |
| Coiro et al\cite{11,12}    | +             | ?                  | +                           | +                      | +                                       | +                               | +                      | +++               | +     |
| Hammad et al\cite{12,13,14} | ★★ ★ ★ ★ ★ ★ | ★★ ★ ★ ★ ★ ★       | ★★ ★ ★ ★ ★ ★ ★ ★           | ★★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ | ★★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ | ★★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ | ★★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ | ★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★★
blood loss, favoring LS Small Jaw, compared with clamp-and-tie are shown in Table 3.

With respect to complications, temporary/permanent hypocalcemia, temporary/permanent RLN palsy, hematomas, and infection were recorded into analysis. Temporary hypocalcemia was assessed in 2 of total 7 studies, showing no significant difference between LS Small Jaw and Harmonic Focus Scalpel for thyroidectomy (OR = 0.47, 95% CI: 0.14–1.56, P = 0.22) (Fig. 4).\(^\text{12,14}\) However, less-temporary hypocalcemia rate in LS Small Jaw was highly significant than clamp-and-tie in 4 studies (OR = 0.49, 95% CI: 0.27–0.90, P = 0.02) (Fig. 4).\(^\text{10,11,15,16}\) In the quantitative analysis of temporary RLN palsy, 6 studies reported available data,\(^\text{10–12,14–16}\) and LS Small Jaw did not bring any significant benefits compared with whether clamp-and-tie (HR = 0.97, 95% CI: 0.41–2.28, P = 0.94) or Harmonic Focus Scalpel (HR = 0.73, 95% CI: 0.33–1.64, P = 0.45) (Fig. 5). Other complications such as length of hospital stay, permanent hypocalcemia, permanent RLN palsy, and hematomas are briefly detailed in Table 3. Specially, 1 secondary complication, infection was not demonstrated in 3 studies with no significance within groups.\(^\text{11,14,15}\)

3.4. Heterogeneity

High heterogeneity was only detected concerning intraoperative blood loss (I\(^2\) = 76%, P = 0.02), and then, sensitivity analysis was conducted by omitting each single study. Study from Hammad et al\(^\text{12}\) contributed high weight in the outcome, and there was significant reduced intraoperative blood loss in LS Small Jaw group after omitting it (P = 0.04).

| Number of studies | Patients | Test of heterogeneity | MD/OR (95% CI) | P for effect size | Analysis model |
|-------------------|----------|-----------------------|----------------|------------------|----------------|
| **Intraoperative blood loss** | 2 | 115 | 115 | 76 | 0.04 | Random |
| **Postoperative blood loss** | 2 | 115 | 115 | 8 | 0.30 | Fixed |
| **Length of hospital stay** | 3 | 81 | 75 | 35 | 0.21 | Fixed |
| **Permanent hypocalcemia** | 4 | 176 | 170 | 0 | 0.57 | Fixed |
| **Permanent RLN palsy** | 4 | 176 | 170 | 0 | 0.73 | Fixed |
| **Hematomas** | 4 | 176 | 170 | 0 | 0.53 | Fixed |

\(\text{CI} = \text{confidence interval, MD} = \text{mean difference, OR} = \text{odds ratio, RLN} = \text{recurrent laryngeal nerve.}\)
4. Discussion
This meta-analysis is specifically designed to compare the short- and long-term outcomes between LS Small Jaw and other hemostasis techniques (clamp-and-tie and Harmonic Focus Scalpel) in thyroidectomy. Finally, after pooling enough eligible data from patients who underwent thyroidectomy, LS Small Jaw is proven favorable with regard to operative time and temporary hypocalcemia, as well as equal perioperative bleeding and RLN injury.

As a novel instrument for surgical hemostasis, LS Small Jaw was initially used during thyroidectomy in 2011, which mainly sealed vessels up to 7 mm in diameter.\[10,17\] Previous studies have shown controversial results in terms of operative time, perioperative bleeding, temporary hypocalcemia, and RLN injury. Therefore, our meta-analysis mainly focuses on the safety of this innovation instrument.

Our meta-analysis demonstrates favorable perioperative outcomes including shorter operative time and less perioperative blood loss in LS Small Jaw. Those benefits are in accordance to previous preliminary outcomes,\[11,13\] likely supporting the popularization of LS Small Jaw in thyroidectomy. Moreover, LS Small Jaw connects with better control of hemostasis, which may bring about reduced operative bleeding, as well as reduced operative duration and shorter hospitalization.

As for complication, the data on permanent hypocalcemia and RLN palsy are not significant. However, temporary hypocalcemia, a crucial endpoint for assessing the safety of LS Small Jaw instrument, is significantly less compared with clamp-and-tie, although no significant difference is observed compared with Harmonic Focus Scalpel. Theoretically, since LS Small Jaw and Harmonic Focus Scalpel are both energy-based devices, they are predicted to have similar outcomes in terms of postoperative hypocalcemia. However, lack of sufficient data (only 2 studies) leads these results to be interpreted carefully.\[12,14\] Concerning the safety of LS Small Jaw in thyroidectomy, the usage of LS Small Jaw in thyroidectomy not only reduces the incidence of short-term hypocalcemia, but also acquires comparable long-term hypocalcemia and RLN palsy.

In terms of sensitivity analysis, the primary pooled estimation of the outcomes is consistent with that of the sensitivity analysis when 1 study was extracted out, which may indicate that our pooled results had good quality.

Finally, there are some limitations in our research: first, although most included studies are prospective, RCTs and non-RCTs are pooled for some outcomes because of the lack of available data and studies. Second, relatively high heterogeneity among studies was estimated for intraoperative blood loss. Lastly, the fact that not all included studies were RCTs may decrease the power of our outcome. So, caution should be taken to explain the pooled results because of the limitations of our study.

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