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ORIGINAL ARTICLE – ENDOCRINE TUMORS

A Systematic Review and Meta-analysis Comparing the Efficacy and Surgical Outcomes of Total Thyroidectomy Between Harmonic Scalpel Versus Ligasure

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ABSTRACT

Background. Both ultrasonic coagulation (Harmonic Scalpel) (HS) and bipolar coagulation (Ligasure) (LS) are new energy devices commonly used in open thyroidectomy. This systematic review aimed at comparing the efficacy and surgical outcomes of total thyroidectomy (TT) between HS and. LS.

Methods. A systematic review of the literature was performed to identify studies comparing HS and LS. Intraoperative outcomes, surgically related complications, overall morbidity, and hospital stay were evaluated. Meta-analysis was performed using a fixed-effects model.

Results. There were 8 studies that matched the selection criteria. Of the 963 patients who underwent TT, 433 (45.0 %) used HS (HS group) while 530 (55.0 %) used LS (LS group). Compared with LS, the HS group had significantly less volume of blood loss by 2.22 ml (95 % CI = 0.26–4.23 ml) (standardized mean difference [SMD] = −0.2, 95 % CI = −0.38 to −0.02) and reduced total operating time by 3.32 minutes (95 % CI = 1.62–5.03 minutes) (SMD = −0.28, 95 % CI = −0.42 to −0.15). There was no significant difference in temporary postoperative hypocalcemia (OR = 1.29, 95 % CI = 0.88–1.90), permanent postoperative hypocalcemia (OR = 1.45, 95 % CI = 0.23–9.26), temporary recurrent laryngeal nerve (RLN) injury (OR = 1.34; 95 % CI = 0.66–2.71), permanent RLN injury (OR = 1.00; 95 % CI = 0.25–4.03), hematoma (OR = 1.00; 95 % CI = 0.3–3.31), overall morbidity (OR = 1.21, 95 % CI = 0.87–1.69), and hospital stay (SMD = −0.03; 95 % CI = −0.07 to 0.01).

Conclusions. Compared with LS, using HS in TT significantly reduced the volume of blood loss and operating time. However, the clinical significance of these findings remained questionable because the overall mean difference appeared small. There was no significant difference in the rate of complications, overall morbidity, and hospital stay between the two devices.

Thyroid surgery is a commonly performed operation, and because the thyroid gland is highly vascularized, effective hemostasis is a crucial part of the procedure.[1] With advances in technology, using new energy devices such as ultrasonic coagulation (Harmonic Scalpel, Ethicon, Cincinnati, OH) and bipolar energy (LigaSure, Valleylab, Boulder, CO [LS]) for cutting and hemostasis during thyroidectomy has become a common practice. Some institutions have adopted it as the preferred technique over the conventional technique (CT) of suture ligation and metal clips. Previous studies have demonstrated that using energy devices significantly reduces operating time and could lower total operating cost as more operations could be performed.[2–15] Some studies have also demonstrated that using energy devices reduces the rate of hypoparathyroidism after total thyroidectomy.[14,15]

However, despite the overwhelming evidence supporting the use of an energy device in thyroidectomy, it remains unclear if the 2 different energy devices, namely ultrasonic coagulation and bipolar energy, produce similar outcome. Although they are similar in that they produce rapid sealing of blood vessels, the actual mechanism is not

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the same. HS controls bleeding by sealing it with a protein coagulum at temperatures ranging from 50 to 100 °C. It denatures proteins by mechanically breaking the hydrogen bonds in protein molecules when the blade vibrates at 55.5 KHz. LS is a closed-loop instrument and occludes blood vessels and lymphatics by delivering controlled electrical energy in combination with applied physical pressure to produce a collagen seal derived from fusion of the vessel walls. To date, although numerous studies have compared the surgical outcomes of these 2 energy devices with CT, few studies have directly compared the efficacy of the two energy devices.[2–15] Furthermore, some of these studies might not have been adequately powered to demonstrate a difference in surgical outcomes. For these reasons, a systematic review and meta-analysis of clinical trials was conducted to compare the efficacy and surgical outcomes of total thyroidectomy between HS and LS.

METHODS

This systematic review and meta-analysis was conducted in accordance with the PRISMA statement.[16]

Data Sources and Searches

Studies containing data on surgical outcomes in thyroidectomy using either HS or LS were retrieved from the Scopus, Medline [PubMed] and Cochrane Library databases on July 22, 2012. We used free text search terms in "All fields"

(1) 'Thyroidectomy' OR 'Thyroid Surgery' OR 'Thyroidectomy'

(2) 'Harmonic Scalpel' OR 'Ligasure'

(3) 1 AND 2.

Study Selection

All abstracts identified by the search strategy were independently screened by 3 authors (BHL, SHN, KPW). Search results were compared, and disagreements were resolved by consensus. Full-text articles were then reviewed for closer examination if the abstracts fulfilled the inclusion criteria: (1) retrospective or prospective studies comparing surgical outcomes between LS and HS and (2) patients had to have near-total/total thyroidectomy (TT). Studies that included patients with lobectomy were included if data for the lobectomy and TT were separately reported. Also studies containing 2 or more comparative arms were included if the results for the LS and HS arms were separately reported. Studies evaluating LS or HS alone or comparing HS or LS with CT were excluded. Over the years, several newer versions/variants of the 2 technologies became available commercially. For HS, the HS-Focus became available in 2007. It has a shorter handle than the older version (Harmonic-Ace) and so is more suitable for open thyroidectomy. For LS, the LS-small-jaw (or LF1212A) became available in 2011. Unlike the older version (LS-Precise), the LS-small-jaw has an additional cutting mechanism. Both the older and newer versions were included in the meta-analysis. The reference list in each eligible article was reviewed to identify additional relevant articles missed in the initial search strategy.

Data Extraction

To assess surgical outcomes, total operating time, volume of blood loss, rates of postoperative hypocalcemia and recurrent laryngeal nerve (RLN) injury (both temporary and permanent), hematoma formation with or without re-exploration, wound complications, postoperative pain score, total cost of surgery, and length of hospital stay were retrieved. For RLN injury, we evaluated whether routine direct laryngoscopy (DL) was performed perioperatively to assess vocal cord mobility. If necessary, the corresponding author of selected publications was contacted directly for clarification of the data presented and definition of surgical outcomes. Other information extracted from each article included: study design, first authorship, country of origin, year of publication, number of patients in HS and LS groups, type and extent of procedure, patients' age, sex, body index mass (BMI), weight of excised gland, and pathology of the gland. All data were extracted onto a standardized form.

The percentage of RLN injury was calculated based on the number of nerves at risk. The overall surgical morbidity rate was calculated by dividing the total number of patients who suffered ≥1 perioperative morbidity over the total number of patients who underwent TT. If a patient suffered from ≥2 morbidities, it was counted as 1.

Data Synthesis and Meta-analysis

All the individual outcomes were integrated with the meta-analysis software Review Manager Software 5.0 (Cochrane Collaborative, Oxford, England). Standardized mean differences (SMD) were calculated for total operating time, volume of blood loss, and length of hospital stay, and odds ratios (OR) were examined for the other surgical outcomes. Results were aggregated and analyzed using a fixed-effect model. Subgroup analyses were performed to investigate whether there was a difference in surgical morbidities and operating time. Publication bias was estimated by Begg's rank correlation test and Egger's regression test.[17,18] The meta-analyses in this study were conducted using R version 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria) and the *metafor* package.[19]

RESULTS

Search Findings

Our literature review identified 518 abstracts that were potentially relevant; 501 were excluded because of duplication ($n = 72$), in a foreign language ($n = 8$), or irrelevance to the analysis ($n = 421$). Figure 1 shows the flowchart of studies retrieved and excluded. An Italian RCT was included because a fully translated English version was available during the search.[20] The full text of the 17 articles was assessed for eligibility. After closer examination, nine articles were eventually excluded. Table 1 lists these nine articles and the reason for their exclusion.

Baseline Characteristics

Table 2 shows a comparison of the baseline characteristics between these 8 eligible studies.

These studies were published between January 2008 and April 2012; 5 studies were prospective randomized trials (RCT), and the remaining 3 were retrospective studies (RS).[20–27] There were 963 patients included; 433 (45.0 %) used HS (HS group), and 530 (55.0 %) used LS (LS group). In terms of type of device used, 2 studies published in 2008 used an older version of the HS (Harmonic-Ace), while the latter 6 studies after 2009 used a newer version of HS (Harmonic Focus).[20–27] In terms of the type of LS, only the latest study used the latest version of LS (Ligasure small-JAW) with the rest using the LS-Precise.[27] Also, five studies included a mix of benign and malignant thyroid diseases while the remaining 3 studies included benign diseases only.[20–27] Age at operation was comparable in 6 of

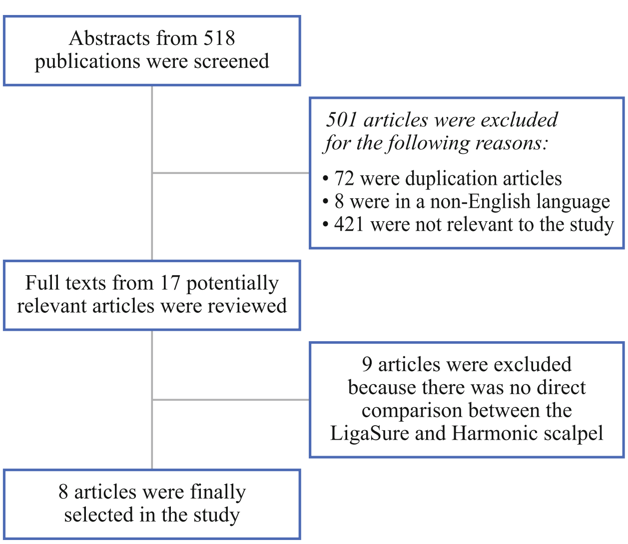


FIG. 1 Flow diagram for study selection

8 studies, and the sex ratio was comparable in seven of eight studies.[20–27] BMI was only available in two studies and was comparable between the HS and LS group.[25,27] Weight of excised thyroid gland and type of pathology (benign vs malignant) were comparable in 6 studies.[20,21,23,25–27] The mean weight of excised gland thyroid in the HS group ranged from 33.2 to 96.5 grams, while the mean in the LS group ranged from 35.3 to 90.9 g.

Surgical Outcomes

Table 3 lists the surgical outcomes in the 8 eligible studies. Figure 2a shows the forest plot for blood loss. The estimated blood loss was specifically reported in 4 of 8 studies.[21–24] The mean estimated blood loss in HS group was 21.87 ml compared with 24.02 ml in the LS group. Quantitative meta-analysis revealed a significantly less blood loss in the HS group when compared with the LS group (SMD = −0.2, 95 % CI =−0.38 to −0.02). The overall mean difference in blood loss was 2.22 ml (95 % CI = 0.26–4.23 ml). The potential publication bias was not significant, as confirmed by Begg analysis (Kendall's tau = 0.6667, $p = .333$) and the Egger regression test ($z = 0.4040$, $p = .6862$).

Figure 2b shows the forest plot for operating time. The total operating time was reported in all 8 studies, but only 2 studies explicitly defined operating time as the duration from skin incision to skin closure [21,23] In the HS group, the mean operating time was 88.40 minutes compared with 94.83 minutes in the LS group. Quantitative meta-analysis of these 8 studies confirmed that the HS group had an overall mean reduction in operating time of 3.32 minutes (95 % CI = 1.62–5.03 minutes), and this difference was statistically significant (SMD = −0.28, 95 % CI = −0.42 to −0.15). There were 3 studies that had significant time reduction of 35, 27, and 15 minutes, respectively[22,23,26] When only the 5 RCTs were analyzed[20,22,24, 26,27] the operating time remained significantly shorter in the HS group when compared with the LS group (SMD = −1.29, 95 % CI = −1.55 to −1.07). However, the potential publication bias appeared significant, as confirmed by the Egger regression test ($z = -5.0726$, $p < .001$). There was a tendency for the smaller studies favoring shorter operating time in the HS group.

Although all studies reported postoperative hypocalcemia in the HS and LS groups, the definition varied between studies. Table 4 shows the definitions of temporary and permanent hypocalcemia. There were some subtle differences between the 8 studies. Although definition of hypocalcemia was verified with the corresponding author in 4 studies, standardization was not possible because of the variability.[20,24,25,27] Nevertheless, assuming all studies used similar definition of temporary and permanent

TABLE 1 The nine articles that were excluded after reviewing the full-length text

First author	Journal	Year, country	Title	Main reason for exclusion
Shemen[9]	*Otolaryngol Head Neck Surg*	2002, United States	Thyroidectomy using the harmonic scalpel: analysis of 105 consecutive cases	Study compared HS with conventional technique.
Ortega[4]	*J Laparaendosc Adv Surg Tech A*	2004, Spain	Efficacy and cost-effectiveness of the UltraCision harmonic scalpel in thyroid surgery: an analysis of 200 cases in a randomized trial.	Study compared HS with conventional clamp and tie technique.
Kirdak[10]	*World J Surg*	2005, Turkey	Use of ligasure in thyroidectomy procedures: results of a prospective comparative study	Study compared LS with conventional clamp and ligation technique.
Parmeggiani[11]	*G Chir*	2005, Italy	Major complications in thyroid surgery: utility of bipolar vessel sealing (LigaSure Precise)	Study compared LS with traditional coagulation.
Cordon[6]	*Surgery*	2005, Mexico	A randomized, prospective, parallel group study comparing the Harmonic Scalpel to electrocautery in thyroidectomy	Study compared HS with standard electrocautery techniques.
Franko[7]	*Am Surg*	2006, United States	Safely increasing the efficiency of thyroidectomy using a new bipolar electro sealing device (LigaSure) versus conventional clamp-and-tie technique	Study only compared LS with conventional silk tie techniques.
Miccoli[8]	*Arch Otorhinolaryngol Head Neck Surg*	2006, Italy	Randomized controlled trial of harmonic scalpel use during thyroidectomy	Study compared HS and conventional hemostasis.
Foreman[12]	*Ann R Coll Surg Engl*	2009, United Kingdom	The use of the harmonic scalpel in thyroidectomy: "beyond the learning curve"	Study compared HS with conventional technique.
Markogiannakis[28]	*Surgery*	2011, Greece	Thyroid surgery with the new harmonic scalpel: a prospective randomized study	Study compared HS (Focus) with Harmonic Ace.

HS Harmonic scalpel, *LS* LigaSure

TABLE 2 The eight eligible published studies comparing baseline characteristics between Harmonic scalpel (HS) and Ligasure (LS)

First author/ year	Study design	No. of patients		Mean (SD/range) age (years)		Sex ratio		Mean (SD/range) weight of excised gland (g)	Final pathology		Matching between HS and LS
		HS	LS	HS	LS	HS (M:F)	LS (M:F)		Benign	Malignant	
Manouras[21] 2008	RS	144	148	51.6 (13.2)	52.8 (13.4)	30:114	33:115	HS = 63.5 (29.8) LS = 64.1 (34.2)	HS = 107 LS = 112	HS = 37 LS = 36	1, 2, 4, 5
Sartori[22] 2008	RCT	50	50	–	–	–	–	–	HS = 47 LS = 42	HS = 3 LS = 8	1, 2, 4, 5
McNally[23] 2009	RS	15	59	49.1 (15.6)	50.4 (13.9)	2:13	13:46	HS = 41.3 (26.6) LS = 67.4 (66.4)	HS = 2 LS = 8	HS = 1 LS = 51	1, 2, 4, 5
Pons[24] 2009	RCT	20	20	–	–	–	–	–	HS = 20LS = 20	HS = 0 LS = 0	–
Di Renzo[20] 2010	RCT	31	31	50.5 (12.1)	51.1 (12.1)	8:23	9:22	HS = 96.5 (46.5) LS = 90.9 (26.7)	HS = 31 LS = 31	HS = 0 LS = 0	1, 2, 4, 5
Rahbari[25] 2011	RCT	45	45	46.1	48.7	9:36	9:36	HS = 33.2 (32.6) LS = 35.3 (35)	HS = 20 LS = 22	HS = 25 LS = 23	1, 2, 3, 4, 5
Zarebczan[26] 2011	RS	36	87	42 (14)	49 (15)	4:32	12:75	HS = 35.5 (36.5) LS = 44.7 (43.1)	HS = 23 LS = 60	HS = 13 LS = 27	2, 4, 5
Dionigi[27] 2012	RCT	92	90	40.8 (20–79)	41 (20–83)	17:75	20:70	HS = 49 (26–86)[a] LS = 51 (28–140)[a]	HS = 92 LS = 90	HS = 0 LS = 0	1, 2, 3, 4, 5

Matching: *1* age, *2* sex, *3* body mass index (BMI), *4* weight of excised thyroid gland, *5* final pathology

M male, *F* female, *RCT* randomized controlled trial, *RS* retrospective study

[a] Only thyroid volume (ml) was given

hypocalcemia, the overall temporary hypocalcemia rate in the HS group was comparable to that of the LS group (84 of 433 [19.4 %] and 82 of 530 [15.5 %], respectively; OR = 1.29, 95 % CI = 0.88–1.90), while the overall permanent hypocalcaemia was also similar between the HS and LS groups (1 of 312 [0.3 %] and 0 of 314 [0.0 %], respectively; OR = 1.45, 95 % CI = 0.23–9.26).

Similar to hypocalcemia, the definition of temporary and permanent RLN injury varied between studies (see Table 4). Routine preoperative DL was performed in seven studies, and routine postoperative DL for documenting bilateral vocal cord movement was performed in 5 studies.[20–27] The cumulative temporary RLN palsy (risk per nerve) was comparable between the HS and LS groups (16 of 776 [2.1 %] and 17 of 970 [1.8 %], respectively) (OR = 1.34, 95 % CI = 0.66–2.71). The cumulative permanent RLN palsy (risk per nerve) was also comparable between the HS and LS groups (0 of 826 [0.0 %] and 2 of 1,020 [0.2 %], respectively) (OR = 1.00, 95 % CI = 0.25–4.03).

The rate of hematoma was reported in all 8 studies. The cumulative hematoma rate was comparable between the HS and LS groups (2 of 433 (0.5 %) and 5 of 530 (0.9 %), respectively) (OR = 1.00, 95 % CI = 0.3–3.31). The overall morbidity rate ranged between 3.3 and 64 % in the HS group and between 6.1 % and 46 % in LS group. The overall morbidity after thyroid surgery with HS was not statistically different from the LS group (110 of 433 (25.4 %) versus 117 of 530 (22.1 %), OR = 1.21, 95 % CI = 0.87–1.69).

Although the length of hospital stay was reported in 5 studies, 1 study did not provide the SD for HS and LS groups and so only 4 studies were included in the meta-analysis.[20,21,24,26,27] There were two studies that defined it as the duration from the day of admission to the date of discharge, while 1 study defined it as the duration of postoperative stay.[20,21,27] One study did not provide a definition.[26] The mean in the HS group was 1.28, while the mean in the LS group was 1.06 days. There was no significant difference between the 2 groups (SMD = −0.03, 95 % CI = −0.07 to 0.01).

There were 2 studies that reported similar postoperative pain score/analgesic requirement.[24,27] Total operating cost were compared in 2 studies; 1 study found the total operating cost in the HS group was significantly lower than the LS group ($p < 0.001$), while another study found similar cost between HS and LS groups.[24,25]

DISCUSSION

The technology in surgery is constantly evolving, and so it is difficult to compare to the efficacy and surgical outcomes of 2 different energy devices because each energy device is often replaced by a newer version every

TABLE 3 Comparison of surgical outcomes between Harmonic scalpel (HS) and Ligasure (LS) groups in the eight studies

First author (year)	Mean (SD) operating time (minutes)	Mean (SD) blood loss (ml)	Hypocalcemia (%)		RLN injury (%)		Hematoma[a] (%)	Overall morbidity[b] (%)	Mean (SD) hospital days
			Temporary	Permanent	Temporary	Permanent			
Manouras[21]/ 2008	HS = 73.8 (13.8)	HS = 24 (10)	HS = 5 (3.5 %)	HS = 0 (0 %)	HS = 2 (0.7 %)	HS = 0 (0 %)	HS = 1 (0.7 %)	HS = 10 (6.9 %)	HS = 1.5 (0.5)
	LS = 74.3 (14.2)	LS = 26 (13)	LS = 4 (2.7 %)	LS = 0 (0 %)	LS = 2 (0.7 %)	LS = 0 (0 %)	LS = 1 (0.7 %)	LS = 9 (6.1 %)	LS = 1.5 (0.5)
Sartori[22] 2008	H S = 94 (24)	HS = 97 (19)	HS = 30 (60 %)	NR	HS = 1 (1 %)	HS = 0 (0 %)	HS = 1 (2 %)	HS = 31 (62 %)	NR
	LS = 129 (32)	LS = 111 (34)	LS = 22 (44 %)		LS = 1 (1 %)	LS = 0 (0 %)	LS = 0 (0 %)	LS = 23 (46 %)	
McNally[23]/	HS = 88.0 (14.0)	HS = 47 (70.4)	HS = 0 (0.0 %)	NR	HS = 1 (3.3 %)	HS = 0 (0 %)	HS = 0 (0 %)	HS = 1 (6.7 %)	NR
2009	LS = 115 (38.3)	LS = 49.4 (44.7)	LS = 7 (11.9 %)		LS = 2 (1.7 %)	LS = 1 (0.8 %)	LS = 2 (3.3 %)	LS = 12 (20.3 %)	
Pons[24]/ 2009	HS = 114 (9)	HS = 23 (19)	HS = 0 (0.0 %)	NR	HS = 1 (2.5 %)	NR	HS = 0 (0 %)	HS = 2 (10 %)	HS = 2.6
	LS = 122 (10)	LS = 21 (17)	LS = 1 (5 %)		LS = 1 (2.5 %)		LS = 0 (0 %)	LS = 3 (15 %)	LS = 2.6
Di Renzo[20]/ 2010	HS = 62.7 (14.1)	NR	HS = 10 (32.3 %)	HS = 0 (0 %)	HS = 1 (1.6 %)	HS = 0 (0 %)	HS = 0 (0 %)	HS = 11 (35.5 %)	HS = 2.2 (0.3)
	LS = 68.9 (7.4)		LS = 10 (32.3 %)	LS = 0 (0 %)	LS = 0 (0 %)	LS = 0 (0 %)	LS = 0 (0 %)	LS = 10 (32.3 %)	LS = 2.3 (0.4)
Rahbari[25]/ 2011	HS = 184.2 (66.2)	NR	HS = 10 (22.2 %)	HS = 0 (0 %)	NR	HS = 0 (0 %)	HS = 0 (0 %)	HS = 14 (31.1 %)	NR
	LS = 187.6 (52.6)		LS = 11 (24.4 %)	LS = 0 (0 %)		LS = 0 (0 %)	LS = 0 (0 %)	LS = 17 (37.8 %)	
Zarebczan[26]/ 2011	HS = 59 (11)	NR	HS = 3 (8.3 %)	NR	HS = 4 (5.6 %)	HS = 0 (0 %)	HS = 0 (0 %)	HS = 7 (19.4 %)	HS = 0.9 (0.2)
	LS = 74 (17)		LS = 12 (13.8 %)		LS = 5 (2.9 %)	LS = 1 (0.6 %)	LS = 2 (2 %)	LS = 20 (23.0 %)	LS = 1.1 (0.4)
Dionigi[27] 2012	HS = 76 (10)	NR	HS = 26 (28.3 %)	HS = 1 (1.1 %)	HS = 6 (3.2 %)	HS = 0 (0 %)	HS = 0 (0 %)	HS = 35 (38.0 %)	HS = 2 (0.2)
	LS = 73 (9)		LS = 15 (16.7 %)	LS = 0 (0 %)	LS = 6 (3.3 %)	LS = 0 (0 %)	LS = 0 (0 %)	LS = 23 (25.6 %)	LS = 2 (0.1)

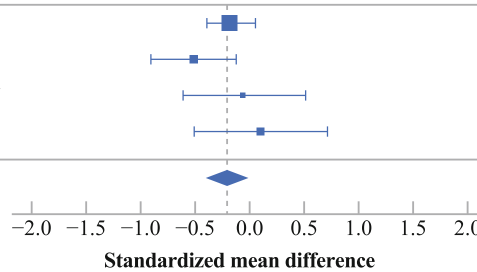
RCT randomized controlled trials, *RS* retrospective study, *NR* not reported, *RLN* recurrent laryngeal nerve, *RLN* injury, superior laryngeal nerve injury, and wound complications (such as hematoma, seroma, infection, burn)

[a] Including hypocalcemia

[b] With or without re-exploration

(a)

1st author & year	Harmonic Scalpel n	Harmonic Scalpel blood loss	Harmonic Scalpel sd	LigaSure n	LigaSure blood loss	LigaSure sd	SMD [95% CI]
Manouras et al., 2008	144	24	10	148	26	13	−0.17 [−0.40, 0.06]
Sartori et al., 2008	50	97	19	50	111	34	−0.50 [−0.90, −0.11]
McNally et al., 2009	15	47	70.4	59	49.4	44.7	−0.05 [−0.61, 0.52]
Pons et al., 2009	20	23	19	20	21	17	0.11 [−0.51, 0.73]
Fixed-effect overall estimate							−0.20 [−0.38, −0.02]



(b)

1st author & year	Harmonic Scalpel n	Harmonic Scalpel mean time	Harmonic Scalpel sd	LigaSure n	LigaSure mean time	LigaSure sd	SMD [95% CI]
Manouras et al., 2008	144	73.8	13.8	148	74.3	14.2	−0.04 [−0.27, 0.19]
Sartori et al., 2008	50	94	24	50	129	32	−1.23 [−1.66, −0.80]
McNally et al., 2009	15	88	14	59	115	38.3	−0.76 [−1.35, −0.18]
Pons et al., 2009	20	114	9	20	122	10	−0.82 [−1.47, −0.18]
Direnzo et al., 2010	31	62.7	14.1	31	68.9	7.4	−0.54 [−1.05, −0.04]
Rahbari et al., 2011	45	184.2	66.2	45	187.6	52.6	−0.06 [−0.47, 0.36]
Zarebzan et al., 2011	36	59	11	87	74	17	−0.96 [−1.37, −0.55]
Dionigi et al., 2012	92	76	10	90	73	9	0.31 [0.02, 0.61]
Fixed-effect overall estimate							−0.28 [−0.42, −0.15]

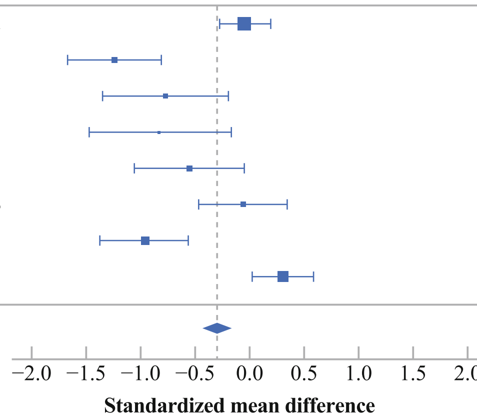


FIG. 2 Forest plots. **a** For blood loss. **b** For operating time

4–5 years. Furthermore, the choice often depends on many factors and not just on efficacy or surgical outcomes alone. Some of these factors include how ergonomic the device is (perhaps, affected by personal preferences) and how experienced or comfortable the surgeon is with the device. Nevertheless, a direct comparison between the two different energy devices is important because thyroidectomy remains a commonly performed operation, and the cost of these devices accounts for a substantial proportion of the total procedure cost (15–20 %).[24,25]

Our meta-analysis showed that using HS in TT resulted in significantly reduced blood loss and shortened total operating time when compared with LS. In some ways, these outcomes are interrelated because less operating time would lead to reduced volume of blood loss. However, since the overall mean [SE] difference in blood loss and operating time between HS and LS appeared small (2.22 [1.28]) ml and 3.32 [0.87] minutes, respectively), it does raise the issue of whether these findings are actually clinically relevant and significant. Nevertheless, it is worth noting that 3 studies did have significant time reduction of 35, 27, and 15 minutes, respectively, and they were significantly greater than the pooled result of 3.32 minutes.[22,23,26] In the Egger regression analysis of the operating time, it appeared that there might have been some publication bias with the smaller-sized studies favoring the HS group. Although it was equally important to show that both energy devices had similar complication rates (in terms of temporary and permanent hypocalcemia, temporary and permanent RLN injury, hematoma formation or postoperative bleeding as well as overall morbidity, this part of analysis was somewhat weakened by the non-standardization in definitions (Table 4). Nevertheless, the implication is that if a surgeon prefers one particular device, there is no need to switch from one device to another.

One important reason why the LS group might have had a longer operating time was because the older version of LS (LS-precise) did not have a cutting device, and so the surgeon had to perform two separate surgical steps instead of 1 step as in the HS group. In fact, a recent RCT comparing the operating time between HS-Focus and the newer version of LS (LS-small-jaw) had similar mean operating time (76 vs. 73 minutes, p = ns). However, the sample calculation in this RCT was to detect a PTH difference of 5 pg/mL and not on operating time or other surgical outcomes.[27]

Despite being the largest comparison of efficacy and outcomes between HS and LS, because of the low incidence of complications in general, some of the nonsignificant findings might have been related to the underpower of the

TABLE 4 Definitions of postoperative hypocalcemia and recurrent laryngeal nerve injury in the eight studies

First author (year)	Temporary hypocalcemia	Permanent hypocalcemia	Preoperative DL	Temporary RLN injury	Permanent RLN injury	Postoperative DL
Manouras[21]/ 2008	Symptoms with calcium <8.5 mg/dL	Patients who required permanent calcium supplement	Routine	Voice abnormalities and/or vocal cord palsy for ≤1 month by DL	Voice abnormalities and/or vocal cord palsy for >1 month by DL	Selective, based on postoperative voice quality
Sartori[22] 2008	Symptoms with ionized calcium <1.14 mmol/L for <6 months	Persistent symptoms with ionized calcium <1.14 mmol/L for >6 months	Routine	Vocal cord palsy confirmed by DL, no duration mentioned	Persistent vocal cord palsy by DL	Selective, based on postoperative voice quality
McNally[23]/ 2009	Defined as mild hypocalcemia for symptomatic patients who are easily controlled with calcium and calcitriol supplement	Patients who required permanent oral or intravenous calcium supplement (no specific given)	Routine	Vocal cord palsy confirmed by DL	Persistent vocal cord palsy confirmed by DL	Routine, 2 weeks after operation
Pons[24]/ 2009[a]	When the ionized calcium was <1.80 mmol/L for ≤1 month after the surgery	When the ionized calcium was <1.80 mmol/L for >1 month after the surgery	Routine, day before operation	Vocal cord palsy for ≤1 month after the surgery	Vocal cord palsy for >1 month after the surgery	Routine, 1 month after operation
Di Renzo[20]/ 2010[a]	Total calcium <8 mg/dL for ≤1 year	Persistent total calcium <8 mg/dL for >1 year	Routine	Hoarseness of voice and vocal cord palsy for ≤ 1 year	Hoarseness of voice and vocal cord palsy > 1 year	Routine, 1 month after surgery
Rahbari[25]/ 2011	Transient post-operative calcium <8 mg/dL	Permanent post-operative calcium <8 mg/dL	Not reported	Transient hoarseness	Permanent hoarseness	Not reported
Zarebczan[26]/ 2011[a]	Symptomatic or serum calcium <8 mg/dL for ≤6 months	Symptomatic or calcium <8 mg/dL for >6 months	Routine	Vocal cord palsy by DL for ≤6 months	Vocal cord palsy by DL for >6 months	Routine, 3–6 months after operation
Dionigi[27]/ 2012[a]	Symptomatic or serum calcium <2.2 mmol/L for ≤12 months	Symptomatic or serum calcium <2.2 mmol/L for >12 months	Routine, 24–48 hours before by an independent laryngologist	Any reduced vocal cord movement for ≤12 months	Any reduced vocal cord movement for >12 months	Routine, 1–2 days after and periodically at 1, 2, 4, 6, and 12 months after surgery until full cord recovery

RLN recurrent laryngeal nerve, *DL* direct laryngoscopy, *PTH* parathyroid hormone

[a] Studies that had been verified with the corresponding author

meta-analysis. To confirm our findings, a multicenter prospective randomized trial is required.

In conclusion, compared with LS, using HS in TT significantly reduced blood loss and operating time. However, the clinical relevance of these findings remained questionable because the overall mean difference appeared small, and with the availability of the newer version of LS this difference may become even smaller. There was no significant difference in the rate of complications, overall morbidity, and hospital stay between the two devices.

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