ORIGINAL ARTICLE

LigaSure vs Clamp-and-Tie Technique to Achieve Hemostasis in Total Thyroidectomy for Benign Multinodular Goiter

A Prospective Randomized Study

Olivier Saint Marc, MD; Andrea Cogliandolo, MD; Arnaud Piquard, MD; Fausto Famà, MD; Rocco Roberto Pidoto, MD

Hypothesis: Occurrence of adverse effects and advantages of the LigaSure diathermy system (or LigaSure vessel sealing system) in total thyroidectomy have not been tested in prospective randomized studies comparing its use with that of the time-saving clamp-and-tie technique to ligate and divide thyroid vessels. The effectiveness of LigaSure in achieving vessel division and hemostasis remains dependent on vessel diameter, and the risk of damage to adjacent structures cannot be completely excluded. We tested the hypothesis that use of LigaSure compared with the clamp-and-tie technique can significantly and conveniently reduce operative time without increasing postoperative complications in patients undergoing total thyroidectomy for benign multinodular goiter.

Design: Prospective randomized study.

Setting: Regional hospital.

Patients: Two hundred consecutive patients with benign multinodular goiter undergoing total thyroidectomy performed by 1 of 3 surgeons.

Interventions: According to a randomized sequence, total thyroidectomy was performed in 100 patients using LigaSure and in 100 patients using the clamp-and-tie technique.

Main Outcome Measures: End points of the study included the comparative evaluation of postoperative complications, need for parathyroid gland autotransplantation, operative time, and time to hospital discharge. Preoperative, postoperative (24 hours), and 6-week follow-up serum Ca^{++} levels are also reported and compared.

Results: The postoperative complication rate was 35% overall, including all transient postoperative disturbances. The incidence of cervical hematomas was 2%, but 3 patients (1.5%), 1 in the LigaSure group and 2 in the clamp-and-tie group, required repeat operations because of respiratory tract obstruction. The incidence of permanent complications was 2.5% overall, including 3 patients (1.5%) with permanent hypocalcemia and 2 patients (1%) with permanent recurrent nerve lesions. No statistical difference in the incidence of complications was found between the 2 study groups. Similarly, no difference was found in mean hospitalization time and need for parathyroid gland autotransplantation. Preoperative, postoperative, and 6-week follow-up mean serum Ca^{++} levels were not statistically different in the 2 study groups and in the subset of patients undergoing parathyroid gland autotransplantation. Mean operative time was significantly shorter in the LigaSure group, although the mean difference between the 2 study groups was minimal (7.4 minutes). Concomitantly, there was an additional cost of 45€ (US $57.40) per operation using LigaSure.

Conclusion: The use of LigaSure is equally as safe and effective at vessel division and homeostasis as the clamp-and-tie technique, with a statistically significant (although minimal) decrease in mean operative time. Because of this minimal decrease in operative time, use of LigaSure would allow more patients to undergo total thyroidectomy each year, which would eventually help to offset its higher cost.

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Author Affiliations: Service de Chirurgie Digestive Endocrinienne et Thoracique, Centre Hospitalier Regional d'Orléans, Orleans, France (Drs Saint Marc, Piquard, and Pidoto); and Department of General Surgery, University of Messina, Messina, Italy (Drs Cogliandolo and Famà).

TOTAL THYROIDECTOMY IS INcreasingly performed for multinodular goiter because it enables definitive treatment of the disease, thus averting repeated operations and their related complications, and the removal of possible occult malignancies, which have shown significant incidence.[1,2] The most time-consuming part of the operation is the ligation and division of the thyroid vessels. Many attempts have been made to reduce the mean operative time, usually less than 90 minutes, with new methods of vessel ligation and division without in-

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creasing the risk of postoperative complications, which occur in 1% to 4.5% of patients and consist mainly of hematomas, transient or permanent injury of the recurrent nerves, and hypoparathyroidism.[3-6]

Reducing operative time with the use of new methods of vessel ligation and division has not been straightforward. For example, the use of electric monopolar coagulation is no longer recommended to decrease the occurrence of potentially life-threatening complications occasionally due to transmission of electric power and diffusion of heat to nearby tissue. Many surgeons have reverted to using the conventional clamp-and-tie technique even though use of mechanical devices such as titanium clips would shorten operative time.[7]

Recently, other easy-to-use devices such as the LigaSure (LS) diathermy system (or LigaSure vessel sealing system) (Valleylab, Boulder, Colo) have been implemented that enable simultaneous selective sealing and division of a vessel without dispersion of electric power and with less production of heat. Use of these devices are well known in abdominal surgery,[8,9] but they have also proved suitable for use in thyroid surgery.[7,10-15]

To our knowledge, adverse effects and the advantages of these new devices compared with the fastest conventional methods have not been shown in prospective randomized studies. Their effectiveness in achieving hemostasis remains dependent on vessel diameter,[16,17] and the risk of damage to adjacent structures, although significantly lower than with monopolar electric coagulation, cannot be excluded.[5,10] At the same time, the reduction in operative time that seems possible with use of the new devices[5,6,10] must be weighed against their higher cost. The purpose of our prospective randomized study was to compare postoperative outcomes in patients undergoing total thyroidectomy for multinodular goiter with the use of LS or the clamp-and-tie (CT) technique to assess whether operative time can be reduced without worsening the postoperative outcome.

METHODS

From January 1, 2004, through November 30, 2004, at the General, Endocrine, and Thoracic Surgery Department of the Regional Hospital of Orleans in France, 200 consecutive patients having benign multinodular goiter were randomized to undergo total thyroidectomy with the use of LS or CT techniques. All thyroidectomies were performed by 3 surgeons, 2 (O.S.M. and A.C.) with 10 years and 1 (A.P.) with 6 years of experience in thyroid surgery. Inclusion criteria included bilateral multinodular goiter with no suspicion of malignancy, no previous cervical surgery, no need to use the thoracic approach, and no associated parathyroid gland disease.

The surgeons were blinded to the technique to be used until one was assigned in the operating room from a randomized list engendered by statistical software (Statemate; GraphPad, Inc, San Diego, Calif). Two hundred patients were randomized into 1 of 2 groups in anticipation of 1 year's surgical activity, which was the maximum time allowed to carry out the study. The LS group included 90 women and 10 men with a mean age of 49.5±11.3 years (age range, 24-76 years); and the CT technique group comprised 74 women and 26 men with a mean age of 54.08±13.2 years (age range, 18-80 years).

End points of the study included comparative evaluation of the following outcomes: postoperative complications, need for parathyroid gland autotransplantation, operative time, and time to hospital discharge. Correlation between operative time and weight of the thyroid gland, considered relative to the size of the gland and to the difficulty of its removal, was also tested to exclude a possible interfering bias.

All specimens were fixed in 10% formalin at a pH of 7.0 and weighed by a pathologist. To test parathyroid function, serum Ca^{++} levels were determined preoperatively and at 24 hours and 6 weeks postoperatively. The operative time was calculated from skin incision to skin closure. Hospital discharge was at 24 hours after the operation if no signs of complications were present.

OPERATIVE TECHNIQUE

In the LS group, LS was the main device used except when vessels were larger than 4 mm in diameter. In 3 cases in the LS group such vessels were found in the upper pole and the surgeons ligated and divided them using conventional CT technique. In the CT group we performed the technique we had crafted and used for several years. This technique involves using the CT approach for vessels in the superior and inferior poles, and the time-saving application of titanium clips (small SurgiClip; AutoSuture, Norwalk, Conn) in the rest of the gland.

In all of the cases, total thyroidectomy was performed after identification of a recurrent laryngeal nerve and at least 1 parathyroid gland on each side. In both groups and on each side, dissection was started at the middle thyroid vein, followed by division of the superior pole. After identification of the parathyroid glands and the recurrent nerves, the inferior pole was divided and the gland was freed from its posterior vascular attachments. If the parathyroid gland appeared to be damaged or hypovascularized, we reimplanted it in the sternocleidomastoid muscle. Thyroid bed drainage was systematically avoided.

STATISTICAL ANALYSIS

Because the study was to be concluded within 1 year, 100 patients were randomized to each group based on anticipated procedures to be performed in 1 year according to the previous 2 years' experience. We verified that this number was adequate to detect an expected difference of 3.0±5.0 for continuous variables (*t* test) with a power of 0.99 at a 2-tailed significance level of $P=.05$. At the same time, for binary variables (Fisher exact test) with a power of 0.80 or higher for a difference ranging from 0.01 to 0.05 and a significance level of $P=.05$, it resulted adequately to detect a minimum difference of 0.02. Significant differences were planned to be tested appropriately with power analysis at the end of the study.

Parametric continuous data were compared using the unpaired *t* test, with the Welch correction where appropriate, and percentages with the Fisher exact test. Correlation between outcomes and specimen weights was performed using the Pearson correlation. Statistical software used included GraphPad Prism and Statemate (GraphPad Inc, San Diego, Calif). Data are given as mean±SD. Two-tailed statistical significance was set at $P=.05$.

RESULTS

The results of our study are given in **Table 1**. The 2 study groups were statistically different for age ($P=.01$) and sex ($P=.005$). The mean weight of the thyroid glands was 45.5±31.1 g in the LS group and 48.8±45.8 g in the CT

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group (P=.56) (**Figure 1**). Thyroid disorders were distributed differently between the 2 groups, especially incidental microcarcinomas and Hashimoto thyroiditis (**Table 2**).

No mortality was observed. Morbidity was as high as 37% in the LS group and 33% in the CT group (P=.66), and in most cases included transient complications. Permanent complications were observed in 2 patients in the LS group (permanent hypocalcemia and permanent recurrent nerve lesion in 1 patient each) and in 3 patients in the CT group (permanent hypocalcemia in 2 patients and permanent recurrent nerve lesion in 1 patient) (P=NS). No patient with recurrent laryngeal nerve paralysis required intubation. Among 4 patients with postoperative cervical hematomas, 3 required reoperation (1 in the LG group and 2 in the CT group). No significant difference was found between the 2 groups insofar as need for parathyroid gland autotransplantation and mean hospitalization time (Table 1). No patient required sternotomy because of substernal extension of the goiter.

In 3 patients in the LS group, the conventional CT technique was used in an upper pole when the vessel diameter exceeded 4 mm. Mean operative time was 41.5±11.2 minutes in the LS group and 48.8±6.8 min-

Table 1. Results of the Study*

Variable	Technique Group: LigaSure† (n = 100)	Technique Group: Clamp-and-Tie (n = 100)	*P* Value
Mortality	Not observed	Not observed	
Morbidity, %	37	33	.66
Transient hypocalcemia	21	18	.72
Permanent hypocalcemia	1	2	>.99
Transient recurrent nerve lesion	12	10	.82
Permanent recurrent nerve lesion	1	1	1.00
Cervical hematoma	2	2	1.00
Parathyroid gland autotransplantation, %	42	36	.47
Operative time, mean ± SD, min	41.5 ± 11.2	48.9 ± 6.8	.001
Hospital stay, mean ± SD, d	1.08 ± 0.3	1.09 ± 0.2	.83

*Data are given as number of cases unless otherwise indicated.
†LigaSure is a diathermy system manufactured by Valleylab, Boulder, Colo.

Table 2. Pathologic Findings in the Thyroid Specimens From the Study Patients

Histopathologic Finding	Technique Group: LigaSure* (n = 100)	Technique Group: Clamp-and-Tie (n = 100)
MNG	59	61
MNG plus Hashimoto thyroiditis	23	5
MNG plus adenoma	7	15
Graves disease	7	8
Toxic MNG	3	1
Interstitial thyroiditis	1	0
Papillary microcarcinoma	13	7
Papillary carcinoma >1 cm	5	0
Follicular microcarcinoma	0	3

Abbreviation: MNG, multinodular goiter.
*LigaSure is a diathermy system manufactured by Valleylab, Boulder, Colo.

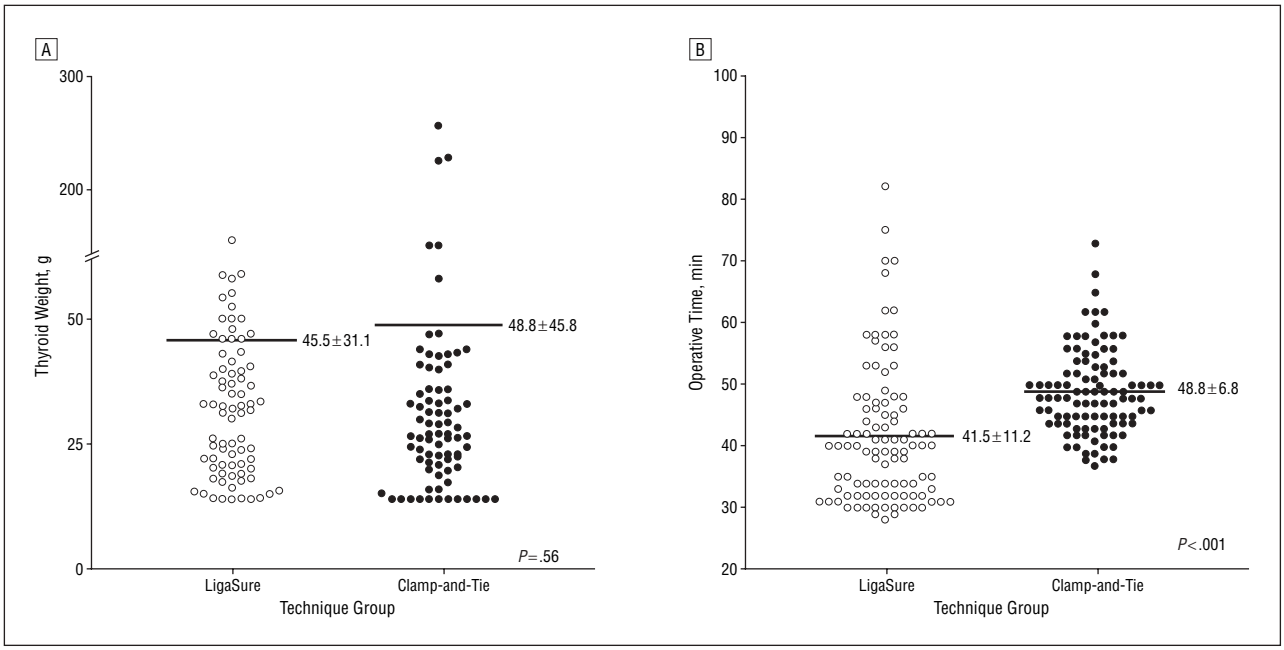

Figure 1. Scatterplots show thyroid gland weights (A) and operative times (B) in the subsets in the 2 study groups. Transverse lines and their values in the scatterplot indicate mean±SD. Thyroid gland weight was comparable in the 2 study groups. Even though statistically significant, the reduction in the mean operative time using the LigaSure diathermy system (or LigaSure vessel sealing) technique (Valleylab, Boulder, Colo) was minimal (7.4 minutes) compared with the clamp-and-tie technique.

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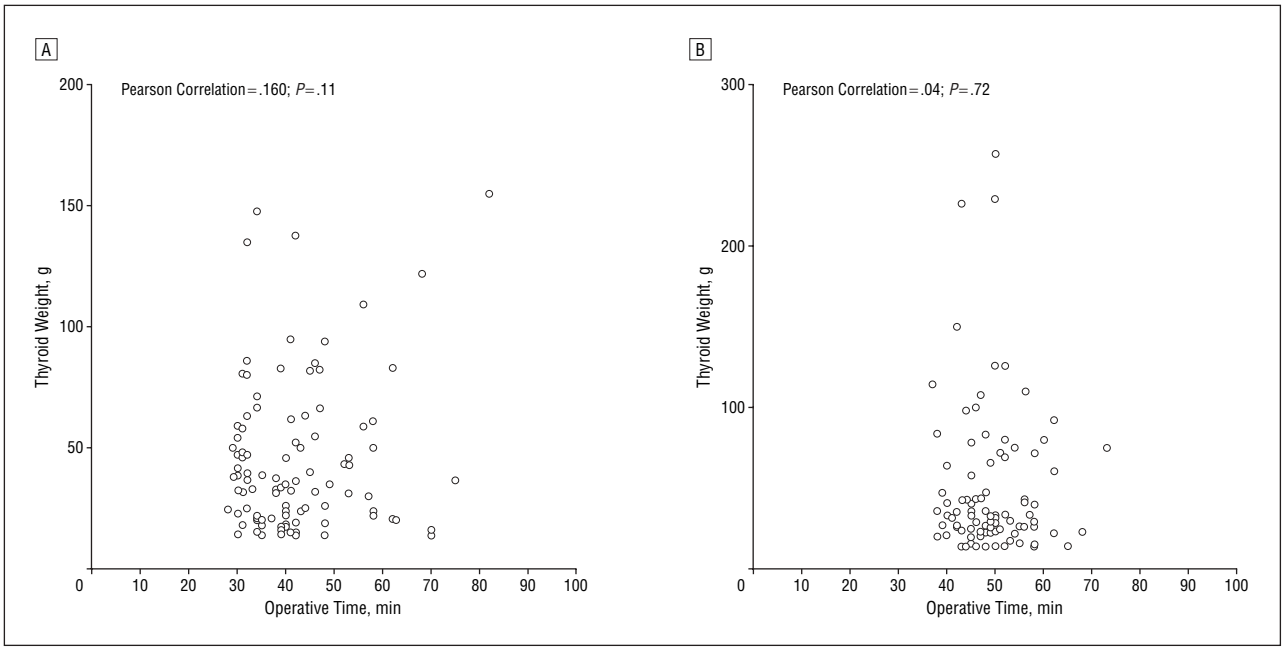

Figure 2. Scatterplots show the relationship between operative time and weight of the thyroid gland in the LigaSure diathermy system (or LigaSure vessel sealing) technique (Valleylab, Boulder, Colo) (A) and clamp-and-tie (B) technique study groups. In neither group was the operative time related to the thyroid gland weight.

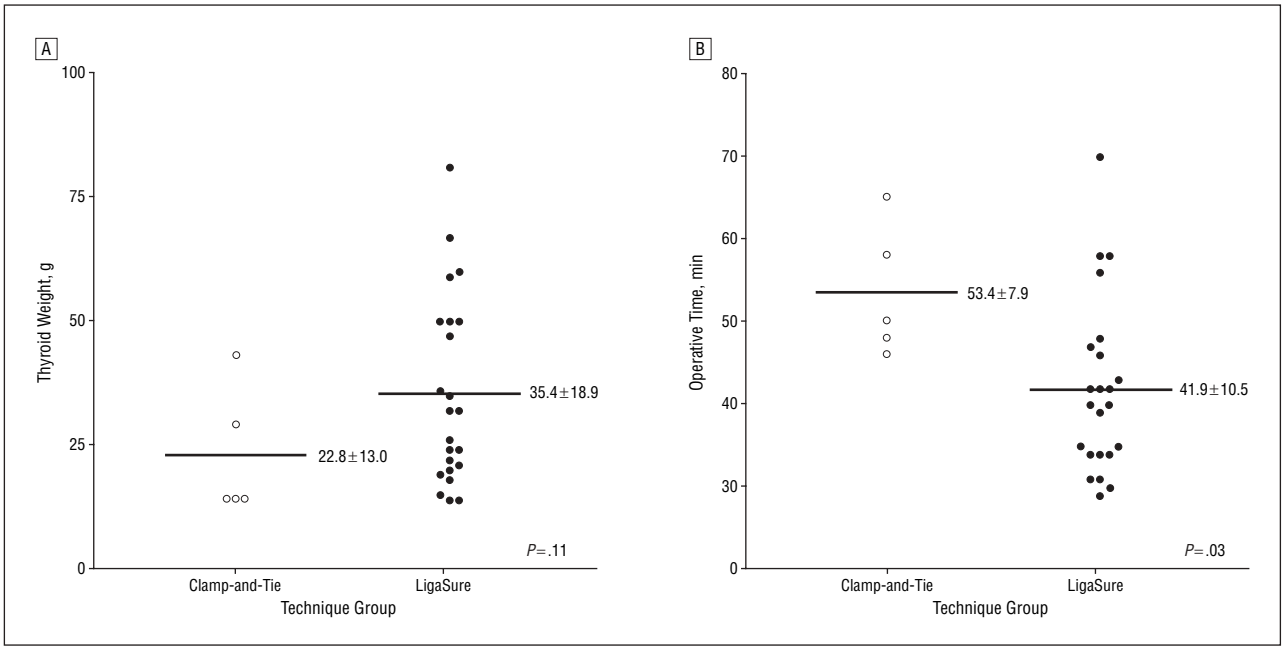

Figure 3. Scatterplots show the thyroid gland weights (A) and the operative times (B) in the subsets of patients with Hashimoto thyroiditis in both the LigaSure diathermy system (or LigaSure vessel sealing) technique (Valleylab, Boulder, Colo) (n=5) and clamp-and-tie technique (n=27) groups. The transverse lines and their values indicate mean±SD. Despite a higher mean thyroid weight, the LigaSure group shows a significant, though minimal, reduction in mean operative time.

utes in the CT group (Δ=−7.3; Δ95% confidence interval, −9.97 to −4.80; $P<.001$; power=1.00) (Figure 1). No relationship between operative time and thyroid weight was found between the 2 study groups (**Figure 2**). In the patients with Hashimoto thyroiditis, the mean weight of the thyroid glands was 35.8±18.9 g in the LS group and 22.8±13.0 g in the CT group, and the mean operative time was 41.9±10.5 and 53.4±7.9 minutes, respectively (**Figure 3**). Preoperative, postoperative (24 hours), and 6-week serum Ca^{++} levels in all patients in both study groups and the subset of patients undergoing parathyroid gland autotransplantation are shown in **Figure 4**.

All patients with postoperative hypocalcemia were discharged on a therapeutic regimen of oral calcium and cholecalciferol, which was continued until normalization of the calcium level. In 21 patients in the LS group and 18 patients in the CT group with postoperative hypocalcemia, the serum Ca^{++} levels were normalized within 4 weeks.

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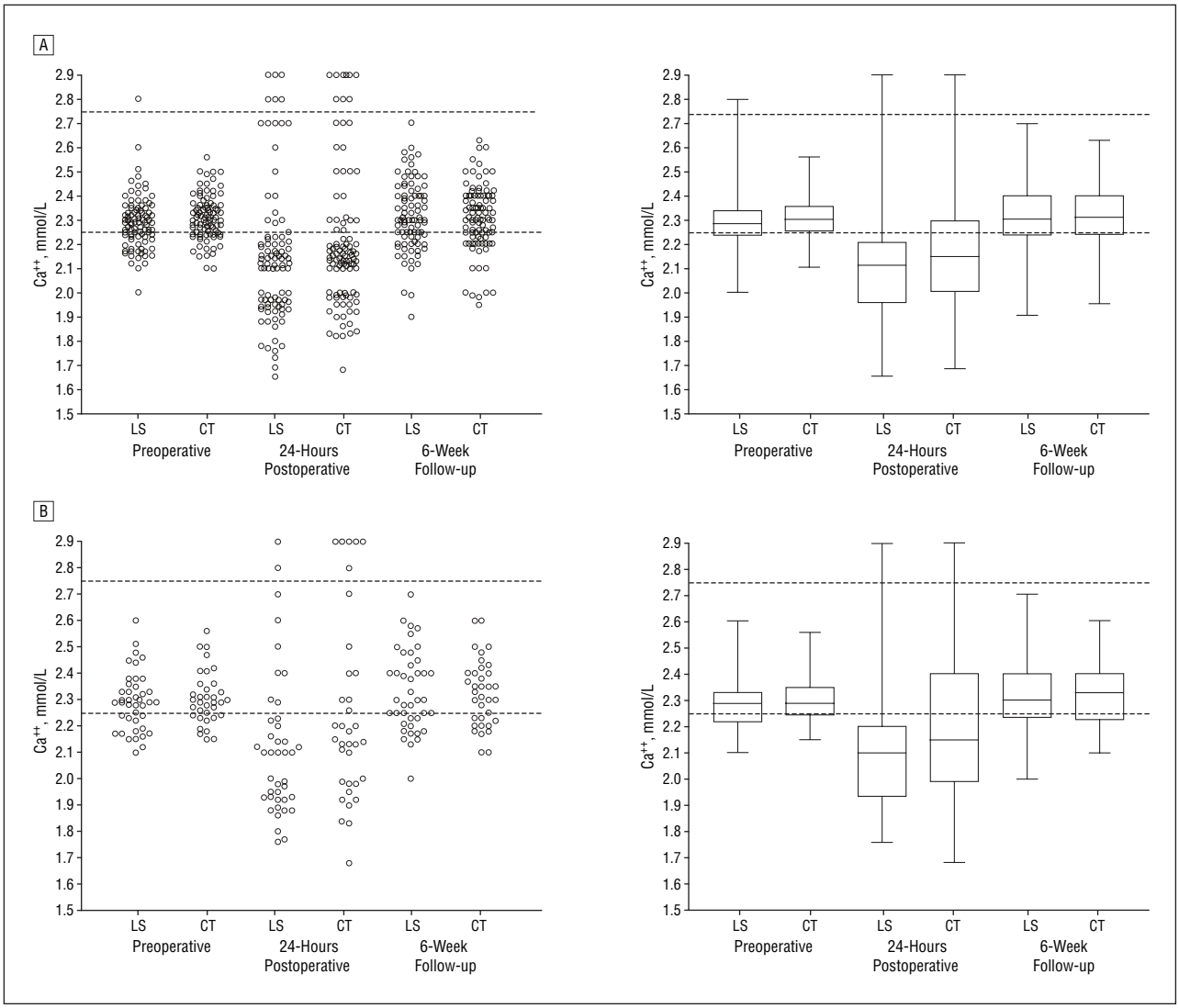

Figure 4. Scatterplots and box-whiskers graphs of preoperative, postoperative (24 hours), and 6-week serum Ca^{++} levels in the patients in the study groups (A) and the subset of patients undergoing parathyroid gland autotransplantation (B). Box-whisker graphs show the 25th to 75th percentile range (box), with 95% confidence intervals (whiskers) and median values (transverse lines inside the boxes). No statistical difference was found between the 2 study groups at the respective times. CT indicates the clamp-and-tie technique group; LS, LigaSure diathermy system (or LigaSure vessel sealing) technique (Valleylab, Boulder, Colo) group.

In the LS group, 94 patients were discharged on postoperative day 1, and 5 on postoperative day 2, and 1 patient underwent repeat operation because of a cervical hematoma on postoperative day 4. In the CT group, 91 patients were discharged on postoperative day 1, and 9 on postoperative day 2. All patients without malignancy were prescribed lifelong hormone therapy, and patients with malignancy were treated postoperatively with iodine 131.

COMMENT

The LS technique enables surgeons to apply high current (4 A) and low voltage (<200 V) to achieve simultaneous vessel sealing and division. The device acts through denaturation of the collagen and elastin in the vessel wall. The pressure applied by the scissors opposes the walls to allow the proteins to form a seal. Microscopically, it is possible to verify that internal elastic lamina is preserved and collagen bundles form across the previous lumen.[16] The device has received acceptance worldwide in several surgical fields. It is claimed to be safe and effective because it allows vessel sealing and division without dispersion of electric power and with little or no production of heat. In thyroid surgery, there is an additional reason to use it. Partial or total thyroidectomy requires microsurgical techniques because a number of minute vessels must be divided. Use of the LS technique is likely not only to shorten operative time but also to enable surgeons to feel comfortable with it.

Postoperative outcome with LS has been controversial. Petrakis et al,[10] in a retrospective case-control study, reported fewer complications and shorter operative and hospitalization times in the LS group. Other retrospective and prospective but not randomized studies did not

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find any differences between complication rates and hospitalization times.[5,7,11] Operative time was substantially reduced in studies by Shen et al[5] and Kirdak et al[7] but not by Kiriakopoulos et al.[11]

In our study, the use of the LS technique was as safe as the conventional CT technique. No difference was found in the incidence of postoperative complications and postoperative discharge in the 2 study groups (Table 1). Our postoperative complication rate was 35% overall when transient postoperative disturbances were included, and 2.5% when only permanent damage to the parathyroid glands and laryngeal nerves was included. It is probable that we found no difference in postoperative outcomes between the 2 study groups because the same surgical procedure was used in both groups, with the same risks.

The incidence of cervical hematomas in our series of patients was 2%. Three patients (1.5%), 1 in the LS group and 2 in the CT group, required reoperation because of respiratory tract obstruction, but active bleeding was found in only 1 patient, in the CT group. It is well known that reoperation because of respiratory tract obstruction after total thyroidectomy is not unequivocally related to the occurrence of a postoperative cervical hematoma. Postoperative bleeding into the deep cervical space usually occurs within the first 4 hours after the procedure.[18,19] However, respiratory tract obstruction may also arise from laryngeal edema, usually occurring within 12 hours after surgery. Laryngeal edema may occur from a discrete hematoma in the thyroid bed or from trauma after endotracheal intubation.[20] Such problems are rare, with only 1% to 2% of patients requiring reoperation to control hemorrhage and approximately 0.1% to 0.3% of patients requiring tracheostomy.[21] In addition, the presence of intraoperative hypotension could result in the surgeon overlooking some small vessel that should be sealed, thus leading to postoperative cervical hematoma.

In our study, as many as 33% of patients in the LS group and 38% of patients in the CT group had transient complications involving the parathyroid glands or laryngeal nerves. This was not unexpected. Some studies[22,23] have reported that transient hypoparathyroidism may be noted in as many as 15% of patients when only clinical symptoms are considered but in as many as 80% of patients when laboratory criteria are used. In the studies of Delbridge et al,[24] as many as 32% of patients who underwent total thyroidectomy required calcium supplementation 3 to 6 weeks after surgery. Transient recurrent nerve paralysis has been observed in 8.7% to 39.0% of patients[25,26] and is not completely avoidable even with systematic laryngeal nerve identification.[24,27]

Permanent complications after total thyroidectomy in our series included permanent hypocalcemia in 3 patients (1.5%) and permanent recurrent nerve lesions in 2 patients (1%), with no statistical difference between the 2 study groups. These adverse events could not be related to recognizable technical errors or to the 2 methods of dissection and vessel sealing used. After total thyroidectomy, the complication rate for permanent damage to the parathyroid glands or laryngeal nerves usually ranges from 1% to 4.5%, depending on surgeon experience, thyroid gland weight, and underlying thyroid disease.[2,24,27-30] After subtotal thyroidectomy to treat benign thyroid disease, permanent damage to the parathyroid glands and recurrent nerves is likely in about 1% of patients.[28,31,32]

We prevented inadvertent damage to recurrent nerves by systematic, careful identification, and minimized long-term effects of inadvertent damage to the parathyroid glands by performing gland autotransplantation at the sternocleidomastoid muscle because of suspected insufficient blood supply.[33-35] Transient or permanent nerve lesions and the need for parathyroid gland autotransplantation did not differ between the 2 groups of patients (Table 1). In addition, parathyroid gland autotransplantation yielded good results, with no differences between the 2 study groups (Figure 4).

The only significant advantage of using the LS technique in our study was reduction in the mean operative time by 7.4 minutes, which can be considered irrelevant. In consideration of its cost, this minimal reduction in mean operative time would not seem to justify the use of LS rather than the CT technique for thyroidectomy. However, some considerations lead to different conclusions. First, reduction in operative time with LS seems to be an unbiased result because we found no correlation between thyroid gland weight and operative time (Figure 2). This was verified in the subset of patients with Hashimoto thyroiditis in whom there was a significant reduction in mean operative time in the LS group despite a higher mean weight of the glands (Figure 3). Second, and more important, based on our cost analysis, the observed 7.4-minute reduction in mean operative time with the use of LS could allow about 30 additional operations to be performed each year. Compared with the CT technique, which requires 2 clip devices per thyroidectomy, LS costs 45€ (US $57.40) more per thyroidectomy, after an initial cost of 20 000€ (US $25 510). Performance of additional operations each year might well justify the additional costs of LS, especially in centers dedicated to endocrine surgery.

In conclusion, our study shows that the use of the LS technique can reduce operative time without significantly modifying postoperative results because it allows faster but equally safe and effective vessel sealing and division compared with the conventional CT technique. Although the reduction in mean operative time was only 7.4 minutes in our study, this could be important in a center specializing in endocrine surgery, where the higher cost of using the LS device might be compensated for within a year as a result of being able to perform more thyroidectomies.

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Correspondence: Olivier Saint Marc, MD, Service de Chirurgie Digestive Endocrinienne et Thoracique, Centre Hospitalier Regional d'Orléans, 14 Avenue de l'Hôpital, 45 067 Orléans Cedex 2, France (olivier.saintmarc@chr-orleans.fr).
Author Contributions: *Study concept and design:* Saint Marc, Cogliandolo, and Pidoto. *Acquisition of data:* Saint Marc, Cogliandolo, Piquard, and Famà. *Analysis and interpretation of data:* Cogliandolo and Pidoto. *Drafting of the manuscript:* Pidoto. *Critical revision of the manuscript for important intellectual content*: Saint Marc and Cogliandolo. *Statistical analysis:* Pidoto. *Administrative, tech-*

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nical, and material support: Famà. *Study supervision:* Saint Marc.

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