Randomized Controlled Trial of Harmonic Scalpel Use During Thyroidectomy

Paolo Miccoli, FACS; Piero Berti, MD; Gian L. Dionigi, MD; Jacopo D’Agostino, MD; Cinzia Orlandini, PhD; Gianluca Donatini, MD

Objective: To compare operative factors, postoperative outcomes, and surgical complications of thyroidectomy when using the harmonic scalpel (HS) vs conventional hemostasis (CH).

Design: Single-blind, randomized controlled trial.

Setting: Department of Surgery, S. Chiara Hospital, University of Pisa, Pisa, Italy.

Patients: One hundred patients undergoing thyroidectomy.

Main Outcome Measures: Postoperative pain, drainage volume, hypocalcemia, nerve injury, and operative time.

Intervention: Patients underwent total thyroidectomy in which either the HS or CH was used.

Results: We found no significant differences between the HS and CH groups at baseline. Postoperative pain was reduced in the HS group at 24 hours (mean visual analog scale score, 3.90 vs 5.30; P < .001) and 36 hours (2.27 vs 3.95; P < .001). Drainage volume was significantly lower in the HS group (40.1 mL vs 75.4 mL; P < .001). Transient hypocalcemia was significantly lower in the HS group (5 patients [10%] vs 16 [32%; P = .01). No patients experienced nerve injury or permanent hypocalcemia. Mean operative times were shorter in the HS group (40.0 vs 46.7 minutes, P < .001).

Conclusions: Use of the HS may reduce postoperative pain, drainage volume, and transient hypocalcemia in patients undergoing thyroidectomy. Shorter operative times and improved outcomes might justify the cost of the HS compared with that of CH.

Arch Otolaryngol Head Neck Surg. 2006;132:1069-1073

The Harmonic Scalpel (HS) is an instrument that uses vibration at 55.5 kHz (ie, mechanical action) to simultaneously cut and coagulate tissue. The main advantages of ultrasonic coagulating/dissecting systems compared with a standard electrosurgical device are represented by minimal lateral thermal tissue damage (the HS causes lateral thermal injury 1-3 mm wide, approximately half that caused by bipolar systems), less smoke formation, no neuromuscular stimulation, and no electrical energy to or through the patient. Ultrasonically activated shears are safe and fast devices in laparoscopic surgery. In addition, this new technology has been widely used in several fields of surgery, including otorhinolaryngologic, gastrointestinal, vascular, and obstetric and gynecological surgery.

In the past few decades, thyroid surgery has attained a standard of excellence demonstrated by rapid patient recovery and a minimal rate of complications, such that thyroid surgery can now be performed on an outpatient basis. Hemostasis in thyroid surgery is achieved by means of the conventional clamp-and-tie technique, diathermy, hemostatic clips, and, recently, the HS. Early reports demonstrated some advantages over conventional techniques, particularly in terms of operative time and intraoperative bleeding. Later, the introduction of minimally invasive endoscopic procedures emphasized the role of the HS because its use strongly facilitated these procedures and allowed excellent hemostasis in small operative spaces, as also demonstrated by the significantly smaller incision during open surgery. Despite sporadic reports, other possible advantages have not been investigated as thoroughly, particularly the complication rate and those involving patient postoperative distress at initial deglutition and...
Table 1. Preoperative Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HS Group</th>
<th>CH Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, No. F/M</td>
<td>41/9</td>
<td>37/13</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>47</td>
<td>44</td>
</tr>
<tr>
<td>Diagnosis, No. of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multinodular goiter</td>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td>Toxic multinodular goiter</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Graves disease</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Thyroid volume</td>
<td>36.9 ± 17.2 (9-60)</td>
<td>43.0 ± 18.2 (7-60)</td>
</tr>
</tbody>
</table>

Abbreviations: CH, conventional hemostasis; HS, harmonic scalpel.

METHODS

PATIENTS

In 6 months, 100 consecutive patients underwent thyroid surgery performed by 2 of us (P.M. and P.B.). Patients were randomly assigned to either the HS group (in which the operation was performed entirely using the HS and no other hemostatic tool; 50 patients) or the CH group (in which the operation was performed using CH tools such as the resorbable ligature and bipolar diathermy; 50 patients) (Table 1). We used the Ultracision CS-14C HS (Ethicon Endo-Surgery, Inc, Cincinnati, Ohio) (Figure 1). All patients were blinded to the surgical technique used and signed an informed consent before enrollment in the trial.

Exclusion criteria included previous neck operation, a history of neck irradiation, or the need for central or lateral compartment lymphadenectomy.

The patients were stratified in terms of age, preoperative diagnosis, and thyroid size to generate homogeneous groups. A total thyroidectomy for benign or malignant thyroid disease was performed with the patient under general anesthesia and with endotracheal intubation in all cases. A complete preoperative assessment (serum thyrotropin levels, ultrasonography to evaluate nodule size and gland volume, and fine-needle aspiration cytology) was obtained in all patients.

Outcomes of the study included operative time, fluid content in the suction balloon (drainage volume) during the first 24 hours after surgery, postoperative pain, and incidence of complications (rate of hypocalcemia and laryngeal nerve injury). Suction drainage was used to evaluate the overall amount of blood loss after the procedure and to assess the actual difference between the groups. Drainage collection is not routinely used in open thyroidectomy and is never used for minimally invasive video-assisted thyroidectomy. The drains were removed 24 hours after surgery.

Both preoperative and postoperative recurrent laryngeal nerve status were determined by indirect laryngoscopy, performed by an otolaryngologist from the Department of Otolaryngology at S. Chiara Hospital. In all patients, serum calcium levels were obtained the first postoperative day and then weekly for 3 weeks. Patients with low calcium levels on the first postoperative day were asked to return the next day to have the level rechecked.

Patients were given acetaminophen, 1000 mg every 8 hours, for the first 24 hours after surgery. Pain assessment was analyzed according to patient responses to a visual analog scale (VAS) and a verbal response scale (VRS). Pain assessment was completely unaware of the surgical instrumentation used during the procedure collected all data relative to postoperative pain.

The VAS consisted of a printed 10-cm horizontal line anchored by the descriptors “no pain” (minimum, on the left end of the scale) and “worst pain imaginable” (maximum, on the right end). All subjects were in good general health, had no known neurological disorders, and were taking no medications. Patients used the VAS to assess their level of pain when they started deglutition and early feeding (generally 24 and 36 hours after the operation). They were also asked to describe the anatomical location of the pain, in particular to differentiate postoperative surgical incision pain from back or neck pain not due to the surgical procedure. To avoid any setting bias, the clinician always moved the scale’s indicator to the horizontal midpoint before the instrument was handed to the patient for a response.

The VRS offered 5 options: 0 for no; 1, light; 2, endurable; 3, strong; and 4, unendurable pain. The patients graded their pain at 24 and 36 hours after surgery.

Patients were also asked to contact the Department of Surgery at the University of Pisa after discharge for any postoperative complication such as neck hematoma or seroma and wound infection.

The ethical committee of the Department of Surgery approved the study protocol. All patients gave informed written consent. The results were analyzed using the 2-sample t test and χ² test. P < .05 was considered statistically significant.

RESULTS

Table 1 gives the preoperative characteristics of the patients. All patients underwent total thyroidectomy and no lymph node dissection was performed. We included patients with benign thyroid disease and low-risk (pT1N0M0) papillary carcinoma, limiting the trial.
to patients who would not need lymph node dissection. Patients presenting with large goiters, extensive Graves disease, and invasive cancers were excluded from the study. The groups were well matched for all preoperative characteristics.

All operative factors, postoperative outcomes, and surgical complications for the groups are presented in Table 2. Differences in operative time and 24-hour drainage volume were statistically significant between the groups (P<.001). Additional knotting or electrocautery was not necessary in the HS group. Postoperative transient biochemical hypoparathyroidism occurred more frequently in the CH group than in the HS group. Biochemical hypoparathyroidism was defined as a serum calcium level below 8.0 mg/dL (2.00 mmol/L) (reference range, 8.0-10.5 mg/dL [2.00-2.62 mmol/L]). In the CH and HS groups, 16 patients (32%) and 5 patients (10%), respectively, required oral calcium carbonate supplementation postoperatively, although these patients showed no clinical symptoms of hypocalcemia. This difference was statistically significant (P=.01) (Table 2). The lowest serum calcium level was 7.7 mg/dL (1.92 mmol/L) in the CH group vs 7.8 mg/dL (1.88 mmol/L) in the HS group. All patients recovered completely, and no definitive hypoparathyroidism was registered.

Damage of the recurrent laryngeal nerve did not occur. One patient in the HS group experienced a wound infection. That patient was treated conservatively with daily medications, local drainage, and antibiotic therapy. The mean postoperative hospital stay was similar in both groups (mean, 2 days). According to the VAS and VRS scores, patients in the HS group experienced significantly less pain compared with patients in the CH group. The differences in VAS scores between the HS and CH groups were statistically significant at 24 and 36 hours (P<.001) (Table 2 and Figure 2). The difference in the VRS score between the groups was not statistically significant at 24 hours after surgery; however, the 36-hour score demonstrated a clear, statistically significant difference between the groups (P<.001) (Table 2).

Table 2. Operative and Postoperative Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>HS Group</th>
<th>CH Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time, mean ± SD (range), min</td>
<td>40.0 ± 6.8 (25-60)*</td>
<td>46.7 ± 10.8 (30-60)</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Postoperative drainage at 24 h, mean ± SD (range), mL</td>
<td>40.1 ± 25.4 (5-120)*</td>
<td>75.4 ± 43.4 (0-230)</td>
</tr>
<tr>
<td>Transient postoperative complications, No. of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>5†</td>
<td>16</td>
</tr>
<tr>
<td>Recurrent laryngeal nerve palsy</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pain score, mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS at 24 h</td>
<td>3.90 ± 1.74*</td>
<td>5.30 ± 1.44</td>
</tr>
<tr>
<td>VAS at 36 h</td>
<td>2.27 ± 1.47*</td>
<td>3.95 ± 1.45</td>
</tr>
<tr>
<td>VRS at 24 h</td>
<td>1.83 ± 0.96</td>
<td>2.04 ± 0.65</td>
</tr>
<tr>
<td>VRS at 36 h</td>
<td>1.02 ± 0.80*</td>
<td>1.63 ± 0.63</td>
</tr>
</tbody>
</table>

Abbreviations: CH, conventional hemostasis; HS, harmonic scalpel; VAS, visual analog scale; VRS, verbal response scale.

*P<.001.
†P = .01.

COMMENT

Prospective, randomized studies on the use of the HS in thyroid surgery have shown that this instrument has several advantages in open traditional10-12,14,15 and minimally invasive13 operations compared with CH. In the present study, we prospectively evaluated these possible advantages, checking all of the end points already examined individually in previous studies.10-16

Ultrasonically activated shears allow a 10% to 35% savings in operative time vs CH.8,11,15 Our experience (a mean time reduction of 14.3%) confirms these data (P<.001) and is shared by other recently published studies.15,16 The time savings, although statistically significant, does not seem to have great clinical relevance.

The reduction of postoperative pain in patients in the HS group was an important outcome of our study. This factor has been rarely examined11 and the results are controversial, probably because of the difficulty in evaluating such an outcome objectively and particularly when trying to analyze only the pain arising from the operative field, which might be affected by the use of a supposedly less traumatic hemostatic tool. For this reason, we used pain during initial deglutition and early feeding as our end point, excluding the cervical distress linked with neck hyperextension during the operation. The data show that patients in the HS group had a less painful postoperative course, as demonstrated by the mean VAS scores at 24 and 36 hours and the mean VRS score at 36 hours after surgery (P<.001 for all comparisons). A possible explanation is that the HS causes reduced tissue injury, with no neuromuscular stimulation (as would be induced by electrocautery). Thus, even though the mean ± SD VRS score at 24 hours postoperatively was only slightly decreased in the HS group (1.83±0.96 vs 2.04±0.65 for the CH group), the 36-hour values showed significantly reduced pain (P<.001), demonstrating faster recovery for patients in the HS group.

Furthermore, the use of the HS would allow reduced traction and reduced manipulation of the thyroid, particularly when dividing the upper pedicle and transect-
ing the superior pole, as claimed by Shemen. In his report, Shemen demonstrated that a smaller incision was possible for patients undergoing thyroidectomy with the HS because of increased control of the upper thyroid vessels when using this device. The reduced tissue injury and the better hemostasis are confirmed by the statistically significant reduction of drainage volume during the first 24 hours for patients in the HS group (P < .001). That reduction draws attention to the great sealing capacity of this device. After using the HS, some investigators reached similar conclusions regarding postoperative drainage, whereas others did not. We attribute these results to our careful selection of patients, avoiding the use of HS for large goiters, extensive Graves disease, and invasive cancers. Use of the HS for lymph node dissection has not yet been evaluated, and such studies would be helpful.

In a previous study by our group, the HS proved to be safe, with good control of the blood vessels and no bleeding after surgery. Other authors have reported better vessel control, which allowed use of a smaller incision. Routine use of the HS in minimally invasive video-assisted thyroidectomy has confirmed for us that the shears facilitates performance of the operation in a restricted field.

Finally, our data demonstrate that the complication rate in the HS group might be significantly reduced, but this could be evaluated for transient hypocalcemia only (5 patients [10%] vs 16 [32%]; P = .01). Incidences of definitive hypoparathyroidism and recurrent nerve palsy were too low to reach statistical significance in this type of prospective study. Similar results for transient hypocalcemia were reported by Meurisse et al, although their results were not statistically significant. Our results seem to support the hypothesis stated by Cordon et al that the reduced tissue injury resulting from less heat generated by the HS might lead to a reduced risk of impaired vascularity in the parathyroid glands.

On the other hand, a major criticism of the HS is its cost: the HS is disposable and expensive and must be considered an additional cost in the diagnosis related group’s Medicare hospital payment system. However, when the reduced operative time is considered, the device actually might be cost-effective, although others do not agree. Furthermore, if additional studies can confirm the trends noted by us and others of a reduced complication rate and avoidance of drainage, the overall cost problems linked with the use of HS could disappear. Finally, our experience suggests that manual tying can be completely avoided, and the absence of a need for ligatures is an additional, although marginal, cost savings.

Despite the safety demonstrated by the HS in several studies, specific training and experience in the use of the device are necessary because the active blade in inexperienced hands can easily injure surrounding vital structures. As with any other innovative technique, a learning curve is strongly advisable; according to Voutilainen.
and Haglund,12 approximately 10 hours of experience is required. We recommend supervision by a senior endocrine surgeon with surgical teaching responsibility during the first procedures, until a standardization of the technique is achieved.13,19 We stress, however, that such supervision and the learning curve might be considered additional costs in the early stage of HS use.

In conclusion, we have demonstrated that the HS is a useful device in thyroid surgery and may reduce postoperative pain, blood loss, and the rate of complications (eg, transient hypocalcemia). Shorter operative time and improved patient outcomes suggest a wider use of the HS in thyroid surgery and justify its cost over that of CH. Further research might study the efficacy of the HS in revision neck surgery and lymphadenectomy.

Submitted for Publication: March 3, 2006; final revision received April 23, 2006; accepted June 2, 2006.
Correspondence: Paolo Miccoli, FACS, or Gianluca Donatini, MD, Department of Surgery, S. Chiara Hospital, Via Roma 67, 56100 Pisa, Italy (p.miccoli@dc.med.unipi.it or giacko76@hotmail.com).
Author Contributions: Dr Miccoli had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Miccoli, Berti, and Donatini. Acquisition of data: D’Agostino and Donatini. Analysis and interpretation of data: Orlandini and Donatini. Drafting of the manuscript: Dionigi, D’Agostino, Orlandini, and Donatini. Critical revision of the manuscript for important intellectual content: Miccoli, Berti, and Donatini. Statistical analysis: Orlandini. Obtained funding: Miccoli. Administrative, technical, and material support: Miccoli. Study supervision: Miccoli and Donatini.
Financial Disclosure: None reported.
Funding/Support: Ethicon Endo-Surgery, Inc, provided the technology (harmonic scalpel) used in the trial.
Role of the Sponsor: Ethicon Endo-Surgery, Inc, did not participate in the data collection, study analysis, or interpretation of the results.

REFERENCES


**Correction**

**Error in Byline.** In the Original Article titled “Randomized Controlled Trial of Harmonic Scalpel Use During Thyroidectomy,” published in the October issue of the ARCHIVES (2006;132:1069-1073), an error occurred in the presentation of the third author’s name in the byline on page 1069. The byline should have appeared as follows: “Paolo Miccoli, FACS; Piero Berti, MD; Gianlorenzo Dionigi, MD; Jacopo D’Agostino, MD; Cinzia Orlandini, PhD; Gianluca Donatini, MD.”