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ORIGINAL ARTICLE

THE USE OF HARMONIC SCALPEL VERSUS KNOT TYING FOR TOTAL-THYROIDECTOMY. A PROSPECTIVE RANDOMIZED STUDY

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Abstract

Aim: Thyroidectomy is a surgical procedure that requires meticulous dissection, safe anatomical exposure and effective haemostasis. The aim of the present study is to compare the use of the harmonic scalpel with conventional haemostatic techniques in patients with benign thyroid enlargement undergoing total thyroidectomy

Method: Consecutive patients treated for thyroid enlargement at our institution were evaluated for inclusion. Participants were randomly allocated to receive total thyroidectomy using harmonic scalpel (HS) or using ligature conventional thyroidectomy (CT), Study variables included operative time, length of incision, operative bleeding, postoperative drainage, hospital stay and complication.

Results: one hundred and thirty patients with benign thyroid enlargement were randomized and completed the study. The mean incision length was 5.14±1.13 cm (4 -7 cm) in HS group and 8.78±1.4 cm (6-11 cm) in CT group p=0.04. Operative time was 50.27 ± 8.03 minutes for HS and 102.38 ± 14.63 minutes for CT (p=0.001). There was a significant difference in intraoperative bleeding and postoperative drainage between the two groups. Five patients (7.7%) in CT group and two patients (3.15%) in HS group experienced transient recurrent laryngeal nerve palsy (p= 0.24) .Two patients (3.15%) in HS group suffered from manifested hypocalcaemia and six patients (9.2%) in CT groups.

Conclusion: HS is a safe, easier and effective alternative to knot tying technique for total thyroidectomy, allowing for a significant reduction of operative time, shorter incision, less intraoperative bleeding, less postoperative drainage without increasing complication rate.

Keyword: Thyroidectomy, recurrent laryngeal nerve palsy, hypocalcaemia.

INTRODUCTION

Thyroidectomy is one of the most frequently performed operations in the field of general surgery. Thyroidectomy essentially entails three steps: the identification and ligation of the feeding vessels, identification and preservation of the laryngeal nerve(s), and identification and preservation (or transplantation) of the parathyroid glands. It involves meticulous devascularization of the thyroid gland, which has one of the richest blood supplies of all organs.(1)

The gold standard for intraoperative hemostasis in thyroid surgery is suture ligation with bipolar or monopolar electrocoagulation for smaller vessels.(1)

However, the use of electrocoagulation to control bleeding carries a risk of damage to the surrounding structures because of the lateral heat dispersion.[2] Recently, several alternative methods of hemostasis, such as the harmonic scalpel, LigaSure and laser techniques, have been tested in general surgery.[3–6]

Harmonic scalpel is an alternative to traditional diathermy for achieving coagulation during surgical dissection. The harmonic scalpel was initially pioneered in laparoscopic surgery as a safe and effective method of achieving haemostasis during dissection. It has been proven to decrease operation time and complications in studies of abdominal solid organ surgery,[7] adrenalectomy,[8] and thoracic surgery.[9]

The harmonic scalpel utilizes ultrasonic energy to produce vibrations which cut and coagulate tissues. As a result, there is less spread of heat than with traditional diathermy, so that significant lateral thermal tissue damage should extend to no more than 1–2 mm, approximately half the distance of the thermal injury caused by bipolar diathermy.[10] Other advantages of this system are smokeless dissection and safety to the surgeon.[11,12]

The conventional knot tying technique requires a large number of surgical ties and therefore is time-consuming. Clips work for large vessels and were subjected to dislodgment, whereas staples are wasted and costly for multiple single vessels applications.[3] The successful introduction of the harmonic scalpel (HS), has led to a further research to compare this new technique with conventional methods for haemostasis.[7-11]

The present study was planned to compare the use of the harmonic scalpel with conventional haemostatic techniques in patients with benign thyroid swelling undergoing total thyroidectomy.

PATIENTS AND METHODS

Consecutive patients who were treated for benign thyroid enlargement by total thyroidectomy at Mansoura University Hospital, Mansoura, Egypt, during the period from February 2008 through March 2010 were eligible for the study. Exclusion criteria included patients with one lobe pathology who need hemithrodectomy, malignant thyroid, previous neck operation, or a history of neck irradiation. (We applied total thyroidectomy to patients with multinodular goiter because it is a trend in our general surgery department to prevent the recurrence of the original disease in the remained part of the gland and give the patients post-operative L. troxine in supplementary dose).

Informed consent was obtained from all patients to be included in the study, after explanation of the nature of the disease and possible treatment. The study was approved by the local ethics committee.

All patients were subjected to careful history taking, clinical examination, and laboratory tests. Randomization was achieved through a computer-generated schedule, and the results were sealed into envelopes. The envelopes were drawn and opened by a nurse not otherwise engaged in the study in the operating room. The patients were then randomized into two groups: Group 1 underwent total thyroidectomy using harmonic scalpel for sealing of vessels and dissection (HS); group II underwent the conventional total thyroidectomy using knot tying and diathermy (CT).

Preoperative preparation was performed for patients with thyrotoxicosis by antithyroid drugs, and they were all euthyroid at the time of surgery. The routine pre-operative workup included measurement of thyroid-stimulating hormone (TSH) and thyroid hormones (T3 and T4), as well as plasma levels of total calcium. In addition, a pre-operative laryngoscopy was performed.

A prophylactic antibiotic in the form of a third-generation cephalosporin was administered 2 hours before the operation. The operation was performed with the patient in the supine position under general anesthesia with endotrachial intubation.

In our study we standardized the surgeons in the three units of general surgery department (unit 6, 7 and 8) .A Kocher incision was made at the lower neck crease two finger above suprasternal notch.

In the HS group, using the new harmonic scalpel device Focus (Ethicon Endo Surgery, Cincinnati, OH, USA) was used for cutting and coagulation. For closure of and division of superior and inferior thyroid arteries and veins we set the instrument at a power 2 i.e. more coagulation. And when smaller vessels like capsular veins we set it to the level 5 i.e. more cutting. The superior thyroid artery and vein was divided close to the gland to avoid damage to superior laryngeal nerve. And control of any bleeding from the bed using the active blade of harmonic. Finally we insert drain.

In the conventional group, mono- and bipolar coagulation, as well as ligatures, were allowed.(Monopolar diathermy was used in opening subcutaneous tissue, platysma muscles division of pretracheal fascia and strab muscles then after delivery of the lobe we use bipolar diathermy to avoid wide spread of the thermal effect of monopolar diathermy).

In both groups, the Intra-operative bleeding was estimated by weighing the gauzes before and after use. Furthermore, blood from suction (when used) was also recorded. Operation time was recorded.

Patients were discharged 24 hours after the procedure in patients without postoperative complication. Oral antibiotic coverage was recommended after discharge. Plasma levels of total calcium were measured on the first post-operative day. The need for oral substitution

with calcium and/or vitamin D analogues during hospital stay and at patient discharge was recorded together with complications.

Postoperative pain was evaluated at 12 h, 24h, and 1 w after operation using a visual analog scale (VAS)[13] with which each patients noted the severity of pain at each evaluated time using a linear between zero (no pain) and 10 (severe pain) . Postoperative analgesia in the form non-steroidal anti-inflammatory drug (NSAID) was administered intramuscularly when required. If the patients still complained of pain and required strong analgesic (1 mg/kg pethidine intramuscularly) was administered. The total dose of these medication were recorded

Follow-up was performed on postoperative day 7, and then at 1 month, 3 months, and 6 months in outpatient clinic. . Patients were also seen at our clinic if they developed symptoms between follow-up visits. At follow-up, serum thyroid hormone concentrations and serum levels of total calcium were measured, and complications recorded. Postoperative laryngoscopy was performed within 4 weeks after surgery in all patients to evaluate vocal cord function.

All assessments were conducted by investigators who were blinded to the experimental condition. The primary endpoint was operative time and secondary end points were operative bleeding, postoperative drainage, costs and complications.

The statistical analysis of the data in this study was preferred using the SPSS version 10. Analysis of data was by intension-to-treat. For continuous variables, descriptive statistics were calculated and were reported as mean + SD. Categorical variables were described using frequency distributions The Student's t- test for paired samples was used to detect differences in the means of numerical variables, Chi-square test was used for nominal variables and Fisher's exact test was used in cases with low expected frequencies. P values □ 0.05 were considered to be significant.

RESULTS

The study flow chart is shown in Figure 1. Of 157 consecutive patients seen during the recruiting period, 130 patients (27 men and 103 women) were eligible and entered the study. The mean age was 38.53 ± 12.13 (range, 12–79) years. These patients were randomly divided into two groups (65 patients in HS group and another 65 patients in conventional group) the two groups were matched for age, sex, pathological diagnosis. All patient demographics characters are shown in Table 1.

The mean incision length was 5.14 ±1.13 cm (4-7 cm) in HS group and 8.78±1.4 cm (6-11 cm) in CT group p=0.04. The operative time was significantly shorter in HS group compared to conventional group (50.27±8.03 minutes; range, 35-65 min vs 102.38±14.63 min; range, 70-120 min; p=0.001). There was a significant difference in intraoperative bleeding between the two group (6.18±3 ml in HS group vs 99.07±52.5 ml in CT p=0.001). Table 2.

The total postoperative drainage fluid volume was significantly less in HS group than in CT group (5.6±3.48 ml vs. 68.07±23.26 ml p=0.001). The hospital stay significantly longer in CT group than in HS group Table 2.

Five patients (7.7%) in CT group and two patients (3.15%) in HS group experienced transient recurrent nerve palsy (p= 0.24). However, only one patient in CT group developed permanent recurrent paresis. Two patients (3.15%) in HS group suffered from manifested hypocalcaemia and need calcium substitution and six patients (9.2%) in CT groups developed manifest hypocalcaemia and need calcium 6 month after surgery. One postoperative bleeding required reoperation was observed in CT group. Table 2.

The incidence of postoperative pain (po-pain) needs analgesics is significantly more in traditional group at 12 h postoperatively (52(80%) vs 34 (52.3%) P = 0.001), and at 24 h postoperative (40 (61.5%) vs 28 (43.1%) P=0.03) but the incidence of postoperative pain at 1 week differs but not reach a significance between both groups Table 2. VAS in HS group was lower than in traditional group, the difference is significant at 12 h postoperative (3.62+1.21 vs 6.23+1.76 P= 0.003), but the difference was insignificant at 24 h and 1 week postoperative Table 2.

The costs were significantly higher in HS group than in CT group (380.76 ± 33.74 euros vs. 301 ±32.23 euros).

Tables 1. Demographic data in harmonic scalpel thyroidectomy group (HS) and conventional thyroidectomy group (CT).

	HS	CT	95% CI of the differences		
			lower	upper	
Age (years/0)	41.81±13.4 (16-79)	36.24±12.62 (12-72)	1.0499	10.0886	0.6
Sex					0.21
male	11 (16.9%)	16 (24.6%)			
female	54 (83.1%)	49 (75.4%)			
Pathology					
Multinodular goiter	47 (72.3%)	46 (70.8%)			0.35
Thyrotoxicosis	18(27.7%)	19 (29.2%)			

Tables 2. Comparison of the operative and postoperative data of patients of HS group and CT group.

	HS	CT		95% CI of the differences	
				lower	upper
Incision length (cm)	5.14+1.13 (4-7)	8.78 +1.4 (6-11)	0.04	-3.0866	-2.1904
Number of ligature	0	21.92+7.7 (14 -35)	0.001	-23.8346	-20.0115
Operative bleeding (ml)	6.18+3 (0-10)	99.07+52.5 (20-200)	0.001	-121.7990	-95.9856
Operative time (min)	50.27+8.03 (35-65)	102.38+14.63 (70-120)	0.001	-56.2046	-48.0108
Weight (gm)	169.30+48.65 (70-250)	172.38+42 (85-258)	0.3	-18.8470	12.6932
Drain (ml)	5.6+3.48 (0-20)	68.07+23.26 (0-100)	0.001	-68.2499	-56.7039
Hospital stay (hours)	15.95+5.88 (11-35)	47.63+23.22 (12-120)	0.001	-37.5578	-25.7960
Presence of Po-pain*					
12 h	34 (52.3%)	52(80%)	0.001		
24 h	28 (43.1%)	40 (61.5%)	0.03		
1 w	2 (3.1%)	5 (7.7 %)	0.24		
VAS of Po-Pain					
12 h	3.62+1.21	6.23+1.76	0.003	-3.1386	-2.0921
24 h	2.57+1.32	3.92+1.18	0.53	-1.7861	-.9216
1w	.75+1.16	1.69+1.06	0.94	-.5530	-1.3240
Complication					
Transient RLN palsy	2 (3.15)	5 (7.7%)	0.24		
Permanent RLN	0	1 (1.5)	0.31		
Hypocalcaemia	2 (3.15%)	6 (9.2%)	0.14		
Coasts (euros)	380.76 ± 33.74	301 ±32.23	0.001	67.6237	90.5302

Po-Pain……..Postoperative pain.
VAS……..visual analogue scale.

DISCUSSION

The thyroid is a highly vascularised organ, and therefore it is important to achieve good haemostasis during thyroid surgery. Total thyroidectomy is the treatment of choice for many thyroid diseases.[1-3] Thyroidectomy is a surgical procedure which requires meticulous dissection, safe anatomical exposure, and effective hemostasis. Using ligatures are probably the most common way to accomplish a good haemostasis but it is time-consuming; therefore, many devices have been introduced over the years, in clinical practice, to save time and to decrease postoperative complications.[1-4]

The conventional knot tying technique in a resectional surgical procedure as thyroidectomy requires a large number of surgical ties and therefore is time-consuming. Reduction of the time spent with the conventional ligature can significantly reduce the operative time in this procedure.[14,15]

Still, bleeding can sometimes be troublesome, and therefore, new techniques for haemostasis have been sought. Conventional haemostatic techniques in thyroidectomy include knot tying and electro-coagulation. The successful introduction of the harmonic scalpel (HS), a device that cuts and coagulates simultaneously using high frequency mechanical energy], has led to a further research to compare this new technique with conventional methods for haemostasis.[12]

The development of ultrasonically activated coagulating shears in the early 1990s has provided an alternative to other methods of controlling blood vessels. The device divides tissue by using high-frequency ultrasonic energy transmitted between the instrument blades. The active blade of the instrument vibrates longitudinally against an inactive blade.[16] This mechanical action disrupts protein hydrogen bonds within the tissue. This takes place at a relatively low temperature (80°C) causing a lesser tissue injury (< 1.5 mm) compared with both electrocautery (6mm) and laser (3 mm).[17,18] Because the water in the tissue does not boil due to this mild increase in temperature, the proteoglycans and collagen fibers in the tissue become denatured and mix with intracellular and interstitial fluids to form a gluelike substance
(a coagulum).[19]

The harmonic scalpel is ideally suited to dissection around the thyroid gland. The thyroid has a rich blood supply, with vessels entering the gland superiorly, laterally and inferiorly. Each vessel must be securely occluded and divided to perform a safe and expeditious operation. In addition, lying in close proximity to the thyroid and its rich vasculature lie important structures including the parathyroid glands and the recurrent laryngeal nerves which can be damaged not only directly, but indirectly by lateral spread of thermal energy.

The harmonic scalpel should not be used to seal vessels larger than 3 mm. The harmonic scalpel was shown to cause less peripheral tissue damage than electrocautery.[16-19] In the present study, the superior and inferior thyroid arteries were sealed with no complications or difficulties with the harmonic scalpel using power level 2.

Although total thyrodectomy for the thyroid gland have a high rate of success in terms of local control of the disease, the disadvantages of these procedures are obvious; and the importance of maintaining function of the RLNs and parathyroids has surfaced as an equally important issue.[20,21]

In our study HS could allow to perform total thyroidectomy by a smaller skin incision than in conventional thyroidectomy this results was reported in many studies. [14,22,23]

In our study the operative time was significantly shorter in HS group compared to conventional group (50.27±8.03 minutes; range, 35-65 min vs 102.38±14.63 min; range, 70-120 min ; p=0.001).These findings are consistent with several other studies, which have also shown thyroid surgery performed with the harmonic scalpel to be more efficient than that performed using conventional methods. Voutilainen et al reported that average operating room time savings with the Harmonic scalpel was 35.8 minutes, with no difference in complications between harmonic scalpel and traditional groups.[3-5] Kilicl etal.,[24] and Zarebczan etal.,[25] reported similar results to our study with use of the harmonic scalpel reducing operative time for thyroid surgery by an average of 18%.

Injury to the recurrent laryngeal nerve during thyroidectomy is a serious and disabling complication. It may be temporary or permanent, with temporary injury often taking several months to recover.[26] In the literature, the rate of a temporary injury of the recurrent laryngeal nerve after thyroidectomy is reported to be is around 5 to 7% and 0.9 to 2.4% for permanent damage.[27-29]

In the present study, seven patients experience a transient paresis of the recurrent laryngeal nerve, two patients in the HS group and five patients in the conventional group. At follow-up with indirect laryngoscopy, 4 to 6 weeks after the operation, all these seven patients had normal vocal cord function. In our harmonic scalpel group there were no cases of permanent recurrent laryngeal injury. Most studies have demonstrated low rates with no difference in recurrent laryngeal nerve injury compared to conventional techniques.[6,15,23]

Hallgrimsson P et al[30] in his study reported that an increased risk for transient paresis associated with the use of harmonic scalpel compared to conventional techniques ($p \leq 0.005$, 9.7% vs. 1.4%) However, there was no difference in permanent injury and the rates decreased with increasing experience. although the safety margin was 5 mm by Hallgrimsson P et al, the harmonic device has in some instances been too close to the recurrent laryngeal nerve, e.g. at the ligament of Berry. This would then explain the somewhat high rate of transient recurrent nerve palsy. There is a debate between different studies using the harmonic scalpel in how haemostasis is accomplished close to the recurrent laryngeal nerve. Some surgeons do not use any ligatures or clips at all in thyroidectomies, whereas others use ligatures when in close association with the nerve or parathyroid glands.[5]

Incidence of temporary and of permanent suppression of the parathyroid varies from study to study, Reported incidence of permanent suppression ranges from 0% to 69%,[30,31] but with larger trials of longer duration estimating an incidence typically of between 1 and 6% of patients overall.[32-34] Temporary suppression is similarly variable, but with typically larger numbers of patients affected. In the present study, two patients (3.15%) in HS group suffered from manifested hypocalcaemia and need calcium substitution and six patients (9.2%) in CT groups developed manifest hypocalcaemia and need calcium 6 month after surgery. and no patients in our study suffered from permanent hypoparathyroidism.
(Postoperative hypocalcaemia & hypoparathyroidism were related to the type of operation not the pathology of operation as we did total thyroidectomy in simple multinodular goiter and hyperthyroidism).

Haemostasis is achieved well with the use of the harmonic scalpel. Only one patient in conventional thyroidectomy required a return to theatre for post-operative bleeding. There was a significant difference in intraoperative bleeding between the two group (6.18±3 ml in HS group vs. 99.07±52.5 ml in CT p=0.001). Other studies have also demonstrated no difference in bleeding between techniques.[8,15] One study did demonstrate a decrease in blood loss with the use of the harmonic scalpel.[35]

Emam et al.[36] evaluated aspects of the safety of ultrasonic dissection using the harmonic scalpel by assessing thermal mapping of dissected tissues on various power settings. At the maximal power setting of five, much greater temperature rises were recorded in the surrounding tissues compared to a power setting of three. Thus, when using the harmonic scalpel near important structures such as the recurrent laryngeal nerve and parathyroids the surgeon should use power level 3 to ensure ultrasonic dissection with the harmonic scalpel is entirely safe.

Perko[37] showed that the width of lateral thermal damage was also proportional to the duration of application of the scalpel to the tissues even with standard output power 3; a 5-s application resulting in a mean thermal injury width of 0.0522 mm and a 10-s application producing a mean injury width of 0.1544 mm.

In our study the incidence of postoperative pain that needs analgesics is significantly more in traditional group at 12 h and 24 hours postoperatively. VAS in HS group was lower than in traditional group, the difference is significant at 12 h postoperative. This results may attributed to longer time of operation in traditional group , more traction on the neck muscle, thermal injury, and more length of incision

Celestino Pio Lombardi et al[15] concluded that HS is a safe and cost-effective alternative to knot tying technique for CT, allowing for a significant reduction of operative time (about 30%) without increasing complications rate and overall costs of the procedure. The significant shorter operative time could ultimately determine the possibility to perform more procedure in the same operative session with a potential better utilization of health resources and reduction of the waiting list, with overall costs saving.

There are several advantages conferred by the harmonic device to the technique of thyroidectomy. Because the scalpel tip and shaft are of narrow caliber, the device can access tight spaces. The scalpel reliably seals the feeding vessels, enabling the surgeon to use smaller incisions. It transmits little heat to the surrounding structures and thus has a limited tissue interface. One of the advantages of the use of HS and consequent avoidance of manual tying could be the possible reduction of human resources in the operating room. In other words, surgeons could theoretically accomplish thyroidectomy without any assistant by using HS.[15,23]

Conclusion: HS is a safe, efficacious and cost-effective alternative to conventional total thyroidectomy (knot tying technique), allowing for a significant reduction of operative time, shorter length of the incision, less intraoperative bleeding, less postoperative drainage without increasing complications rate.

REFERENCES

1. Gluckman JL. Total thyroidectomy. In: Bailey BJ, Calhoun KH, editors. Atlas of head and neck surgery: otolaryngology, 2nd ed.Philadelphia: Lippincott Williams & Wilkins. 2001:228–9.

2. Miccoli P, Materazzi G, Miccoli M, Frustaci G, Fosso A, Berti P. Evaluation of a new ultrasonic device in thyroid surgery: comparative randomized study. Am J Surg. 2010;199:736-40.

3. Siperstein AE, Berber E, Morkoyun E. The use of the harmonic scalpel vs conventional knot tying for vessel ligation in thyroid surgery. Arch Surg. 2002;137:137–42.

4. Yildirim O, Umit T, Ebru M, Bulent U, Belma K, Belma K, et al. Ultrasonic harmonic scalpel in total thyroidectomies. Adv Ther. 2008;25:260-5.

5. Voutilainen PE, Haglund CH. Ultrasonically activated shears in thyroidectomies: a randomized trial. Ann Surg. 2000;231:322–8.

6. Rahbari R, Mathur A, Kitano M, Guerrero M, Shen WT, Duh QY, et al. Prospectrive Randomized Trial of Ligasure Versus Harmonic Hemostasis Technique in Thyroidectomy: Ann Surg Oncol. 2010.

7. Takao S, Shinchi H, Maemura K, Aikou T. Ultrasonically activated scalpel is an effective tool for cutting the pancreas in biliary-pancreatic surgery: experimental and clinical studies. J Hepatobiliary Pancreat Surg. 2000;7:58-62.

8. Siperstein AE, Berber E, Engle KL, Duh QY, Clark OH. Laparoscopic posterior adrenalectomy: technical considerations. Arch Surg. 2000;135:967-971.

9. Aoki T, Kaseda S. Thoracoscopic resection of the lung with the ultrasonic scalpel. Ann Thorac Surg. 1999;67:1181-1183.

10. Ecker T, Carvalho AL, Choe JH, Walosek G, Preuss KJ. Hemostasis in thyroid surgery: harmonic scalpel versus other techniques- a meta-analysis: Ototolaryngol Head Neck Surg. 2010;143:17-25.

11. Emam TA, Cuschieri A. How safe is high-power ultrasonic dissection? Ann. Surg. 2003;237:186–91.

12. Amaral JF. The experimental development of an ultrasonically activated scalpel for laparoscopic use. Surg. Laparosc. Endosc. 1994;4:92–9.

13. Huskisson EC. Measurement of pain. Lancet. 1974:1127-31.

14. Viapiano J, Wards DS. Operating room utilization: the need for data. Int Anesthesiol Clin. 2000;38:127–40.

15. Celestino Pio Lombardi, Marco Raffaelli, Americo Cicchetti, Marco Marchetti, Carmela De Crea, Rossella Di Bidino, et al. The use of "harmonic scalpel" versus "knot tying" for conventional "open" thyroidectomy: results of a prospective randomized study. Langenbecks Arch Surg. 2008;393:627–31.

16. McCarus SD. Physiologic mechanism of the ultrasonically activated scalpel. J Am Assoc Gynecol Laparosc. 1996;3:601-8.

17. Hambley R, Hebda PA, Abell E, Cohen BA, Jegasothy BV. Wound healing of skin incisions produced by ultrasonically vibrating knife, scalpel, electrosurgery, and carbon dioxide laser. J Dermatol Surg Oncol. 1988;14:1213-17.

18. Armstrong DN, Ambroze WL, Schertzer ME, Orangio GR. Harmonic scalpel vs electrocautery hemorrhoidectomy: a prospective evaluation. Dis Colon Rectum. 2001;44:558-64.

19. Kanehira E, Omura K, Kinoshita T, Kawakami K, Watanabe Y. How secure are the arteries occluded by a newly developed ultrasonically activated device? Surg Endosc. 1999;13:340-2.

20. Parker DJ, Krupa K, Esler R, Vujovic P, Bennett IC: Use of the harmonic scalpel in thyroidectomy: ANZ J Surg. 2009;79:476-80.

21. Turkay Kirdak, Nusret Korun, Halil Ozguc. Use of Ligasure in Thyroidectomy Procedures: Results of a Prospective Comparative sudy World J. Surg. 2005;29:771–4.

22. Larry Shemen. Thyroidectomy using the harmonic scalpel: Analysis of 105 consecutive cases. Otolaryngol Head Neck Surg. 2002;127:284-8.

23. Miccoli P, Berti P, Dionigi Gian L, D'Agostino J, Orlandini C, Donatini G. Randomized controlled trial of harmonic scalpel use during thyroidectomy. Arch Otolaryngol Head Neck Surg. 2006;132:1069–73.

24. Kilic M, Keskek M, Ertan T, Yoldas O, Bilgin A, Koc M. A prospective randomized trial comparing the harmonic scalpel with conventional knot tying in thyroidectomy. Adv. Ther. 2007;24:632–8.

25. Zarebczan B, Mohanty D, Chen H. A Comparison of the Ligasure and Harmonic Scalpel in Thyroid Surgery: A Single Institution Review: Ann Surg Oncol. 2011;18:214-8.

26. Chiang FY, Wang LF, Huang YF, Lee KW, Kuo WR. Recurrent laryngeal nerve palsy after thyroidectomy with routine identification of the recurrent laryngeal nerve. Surgery. 2005;137:342–7.

27. Jiang H, Shen H, Jiang D, Zheng X, Zhang W, Lu L, Jiang Z, Qiu M: Evaluation the safety of the Harmonic Scalpel around the recurrent laryngeal nerve:ANZ J Surg. 2010;80:822-6.

28. Horne SK, Gal TJ, Brennan JA. Prevalence and patterns of intraoperative nerve monitoring for thyroidectomy. Otolaryngol Head Neck Surg. 2007;136:952–6.

29. Hermann M, Alk G, Roka R, Glaser K, Freissmuth M. Laryngeal recurrent nerve injury in surgery for benign thyroid diseases Ann Surg. 2002;235:261–8.

30. Hallgrimsson P, L. Lovén, J Westerdahl, Anders BergenfelzUse of the harmonic scalpel versus conventional haemostatictechniques in patients with Grave disease undergoing total thyroidectomy: a prospective randomised controlled trialLangenbecks Arch Surg. 2008;393:675–80.

31. Ohman U, Granberg PO, Lindell B. Function of the parathyroid glands after total thyroidectomy. Surg. Gynecol. Obstet. 1978;146:773–8.

32. Clark OH. Total thyroidectomy: the treatment of choice for patients with differentiated thyroid cancer. Ann. Surg. 1982;196:361–70.

33. Jacobs JK, Aland JWJ, Ballinger JF. Total thyroidectomy: a review of 213 patients. Ann. Surg. 1983;197:542–9.

34. Salander H, Tisell LE. Incidence of hypoparathyroidism after radical surgery for thyroid carcinoma and autotransplantation of parathyroid glands. Am. J. Surg. 1977;134:358–62.

35. Marchesi M, Biffoni M, Cresti R. Ultrasonic scalpel in thyroid surgery. Chir. Ital. 2003;55:299–308.

36. Emam TA, Cuschieri A. How safe is high-power ultrasonic dissection? Ann. Surg. 2003; 237: 186–91.

37. Perko Z, Pogorelic Z, Bilan K. Lateral thermal damage to rat abdominal wall after harmonic scalpel application. Surg. Endosc. 2006;20:322–4.