



Randomised Controlled Trial

Parathyroid hormone level after total thyroidectomy using conventional versus harmonic focus technique: Prospective randomized study

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ABSTRACT

Background: Total thyroidectomy is a common procedure, we wish to examine the effects of utilizing a harmonic scalpel with traditional procedures on parathyroid hormone levels.

Patients and methods: 100 patients who underwent total thyroidectomy at the Department of General Surgery, were enrolled in this prospective randomized study, were randomly allocated into two equal groups: Group I: total thyroidectomy using a harmonic scalpel (HS) and Group II: total thyroidectomy using conventional technique.

Results: There is a significant association between the technique of surgery and the decrease in Postoperative PTH, Mean Difference, Pre and Postoperative and the change Pre PTH (p-value <0.001).

Conclusion: The postoperative serum level of parathyroid hormone declined significantly after thyroidectomy if the conventional method was used. Using HS during thyroidectomy is safe and effective with low rates of hypoparathyroidism.

1. Introduction

Total thyroidectomy is the most common endocrine surgical operation. Because the thyroid gland is one of the most vascular organs in the body, complications from intraoperative bleeding are frequent [1,2].

Hypoparathyroidism remains one of the most common complications following total thyroidectomy (TT), which may result from direct injury, devascularization, thermal trauma, oedema, or inadvertent removal of the parathyroid glands, and also depends on the extent of resection, surgical techniques, and surgeon's experience [3].

Parathyroid secretion has been shown to be decreased even in straightforward thyroidectomies without parathyroid gland accidental removal [4].

One of the most critical limiting factors in thyroid surgery morbidity and mortality is hemostasis [5].

Hemostasis during thyroidectomy can be achieved by traditional suture ligation with clamp-and-tie with or without electrocautery, whereas suture ligation is a time-consuming procedure and has a potential risk of knot slipping. In contrast, electrocautery has a potential risk of injury to surrounding tissues from dispersion of heat [6]. During

the last two decades, new energy-based devices were introduced for sutureless thyroid surgery for controlling the vascular pedicles. The Harmonic Focus (HF; Johnson and Johnson, Ethicon Endo-surgery, Cincinnati, OH, USA) is the most extensively utilized energy instrument for sutureless thyroidectomy (ST) [2,7].

By denaturing and coagulating collagen fibers, HS with ultrasonic activated shear simultaneously cuts and seals vessels are now routinely used for hemostasis in thyroid surgery [3,5].

Therefore, the aim of this study is to compare the effect of using harmonic scalpel and conventional methods during total thyroidectomy on parathyroid hormone level.

1.1. Patients and methods

The present study is a randomized clinical trial that has been conducted over 100 patients with thyroid disease who underwent total thyroidectomy operation, from April 2019 to April 2021 in the department of general surgery, were enrolled in this prospective study.

The number of cases was randomly allocated into two equal groups: Group I: total thyroidectomy using harmonic scalpel and Group II: total

; ELN, External laryngeal nerve; PTH, Parathyroid hormone; STN, Solitary thyroid nodule; RLN, Recurrent laryngeal nerve; TT, Total thyroidectomy; MNG, Multinodular goiter.

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thyroidectomy using Conventional technique. Our inclusion criteria were patients with both benign or malignant thyroid disease, and over 18 years old. The exclusion criteria were patients in toxic state, previous thyroid or neck surgery, neck irradiation, chronic renal failure, or hypoalbuminemia. The work has been reported in line with the CONSORT criteria. Patients who were eligible to these criteria were enrolled in our study after obtaining a written informed consent. This study was approved by the Faculty of Medicine for Girls Research Ethical Committee (IRB Reg. No. RHBIRB2018122001) with approval number (202107935). Registration unique identifying number (UIN): TCTR20211202001 (<https://www.thaiclinicaltrials.org/show/TCTR20211202001>).

1.1.1. Sample size calculation

Before the study, the number of patients required in each group was determined after calculating the strength according to data obtained [8]. In the S.-Q. Xu. et al. Study, parathyroid hormone "pmol/L" in the HS group was 3.25 ± 2.00 and in the CH Group was 2.80 ± 1.98 , and a large effect size ($f = 0.353$). A sample size of 47 patients in each group was determined to provide 80% power for independent samples T-test with a significance level of 5%, allocation ratio 1:1, and 95% confidence interval using G. Power 3.19.2 software.

1.1.2. Randomization and allocation

The randomization of patients was done using a computerized program (SPSS), while the sealed envelopes were numbered according to the randomization tables, then packing, sealing, and envelope numbering performed carried out by neutral medical personnel (under the supervision of physicians from the Department), the number of cases included in this study was randomly allocated into two equal groups. All patients were blinded about the technique of operation, and also who assisted the outcomes.

1.1.3. Surgical procedure

All operations were done under general anesthesia with a curvilinear incision between two sternomastoid muscles and two cm above the sternal notch, and then a subplatysmal flap was done. In group I, devascularization of thyroid gland was done by harmonic scalpel (Fig. 1) whereas in group II by a conventional method with individual ligation of thyroid vessels. In both groups, identification of parathyroid glands, external laryngeal, and recurrent laryngeal nerves were done.



Fig. 1. Devascularization of thyroid gland using harmonic scalpel.

1.2. The primary outcome

postoperative parathyroid hormone level, and serum calcium level. Secondary endpoints were postoperative complication, operative time and hospital stay.

Preoperative parathyroid hormone and calcium were measured 24h before the operation. The normal range of (PTH) level is 10–69 pg/ml. The postoperative measurement was 6h at the day of operation. Cases with (PTH) level less than 10 pg/ml were considered hypoparathyroidism.

1.3. Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean \pm standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples *t*-test, Chi-square (χ^2) test and Paired sample *t*-test were used to detect any significance. Confidence interval was set to 95% and the margin of error accepted was set to 5%.

2. Results

One hundred patients who underwent total thyroidectomy were randomly divided into two equal groups; 50 patients to the harmonic scalpel group and 50 patients to the conventional group. The baseline characteristics were comparable between two groups in the term of gender, preoperative PTH, serum calcium, and preoperative diagnosis while age of patients showed a significant difference. The mean age in the harmonic group is 38.06 ± 10.79 and 33.98 ± 7.07 in the conventional group.

Both groups demonstrated a similar female to male ratio of 84% vs. 16%. The most common preoperative diagnosis was MNG with 78% in Group I (Harmonic group) while it was 70% in Group II (Conventional group) with a *p*-value of 0.165 which is not statistically significant. (Table 1).

In the harmonic group, hypocalcemia occurred in four cases (8%) and all cases were managed by calcium supplementation, and they returned to normal serum ca level within the first two weeks and the hypocalcemia was considered temporary.

Compared with the other group, six cases (12%) had hypocalcemia. Symptomatic hypocalcemia was seen in two cases, and one of those hypocalcemia cases required calcium for more than two weeks.

While comparing both groups regarding serum CA either preoperative, postoperative, Mean Diff. (pre and postoperative) and the change (pre and postoperative) there was no statistically significant difference between groups (Table 2).

In this study, there was no significant difference (*p*-value 0.787) in the preoperative serum parathyroid hormone level in both groups. After 12hr, when we measured postoperative PTH levels, Mean Diff. Pre and Postoperative and Change Pre and Postoperative, a significant statistical correlation was detected between the technique of surgery and PTH (*p*-value <0.001) (Table 3).

Postoperative PTH level declined significantly in both groups. The decline was more in conventional group than the in harmonic group. The proportion of change was higher in the conventional group -40.32 ± 16.62 V -27.47 ± 16.84 in the HS group (Fig. 2).

The operative time of the harmonic group is shorter than the conventional group Mean \pm SD 72.68 ± 8.23 and 96.22 ± 10.93 , respectively. Also, the hospital stay is longer in the harmonic group Mean \pm SD 2.28 ± 0.93 , whereas the Conventional group Mean \pm SD 1.94 ± 0.62 (Table 4).

There was no statistically significant association between the two groups in the association with other operative and postoperative complications such as RLN injury, Hematoma and Seroma (Table 4).

Table 1
Comparison between Group I: Harmonic group and Group II: Conventional group according to demographic data.

Demographic data	Group I: Harmonic group (n=50)	Group II: Conventional group (n=50)	Total (n=100)	Test	p-value
Age (years)					
Mean ± SD	38.06 ± 10.79	33.98 ± 7.07	36.02 ± 9.31	t=2.236	0.028*
Range	20–69	23–52	20–69		
Gender					
Female	42 (84.0%)	42 (84.0%)	84 (84.0%)	$\chi^2=0.000$	1.000
Male	8 (16.0%)	8 (16.0%)	16 (16.0%)		
Preoperative diagnosis					
LT STN	3 (6.0%)	5 (10.0%)	8 (8.0%)	$\chi^2=6.494$	0.165
MNG	39 (78.0%)	35 (70.0%)	74 (74.0%)		
RT STN	4 (8.0%)	5 (10.0%)	9 (9.0%)		
Secondary toxic goitre	4 (8.0%)	5 (10.0%)	9 (9.0%)		
Type of lesion					
Colloid Goitre	12 (24.0%)	14 (28.0%)	26 (26.0%)	$\chi^2=6.022$	0.537
Follicular adenoma	15 (30.0%)	9 (18.0%)	24 (24.0%)		
Follicular Carcinma	2 (4.0%)	4 (8.0%)	6 (6.0%)		
Follicular hyperplasia	14 (28.0%)	15 (30.0%)	29 (29.0%)		
Hashimoto thyroiditis	4 (8.0%)	2 (4.0%)	6 (6.0%)		
Hurthle cell adenoma	0 (0.0%)	2 (4.0%)	2 (2.0%)		
Medullary carcinoma	0 (0.0%)	1 (2.0%)	1 (1.0%)		
Papillary Carcinoma	3 (6.0%)	3 (6.0%)	6 (6.0%)		

Using: t-Independent Sample t-test; χ^2 : Chi-square test. p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS

Table 2
Comparison between Group I: Harmonic group and Group II: Conventional group according to serum CA.

Serum CA	Group I: Harmonic group (n=50)	Group II: Conventional group (n=50)	Total (n=100)	t-test	p-value
Preoperative					
Mean ± SD	9.28 ± 0.37	9.21 ± 0.63	9.25 ± 0.51	0.679	0.499
Range	8.7–10.2	8.6–12.6	8.6–12.6		
Postoperative					
Mean ± SD	8.81 ± 0.56	8.73 ± 0.50	8.77 ± 0.53	0.750	0.455
Range	7–10	7.1–9.8	7–10		
Mean Diff. Pre and Post					
Mean ± SD	-0.47 ± 0.52	-0.48 ± 0.77	-0.48 ± 0.65	0.076	0.939
Range	-2.3–0	-5.2–0	-5.2–0		
Change Pre and Post					
Mean ± SD	-5.04 ± 5.51	-4.93 ± 6.49	-4.99 ± 5.99	-0.087	0.931
Range	-24.73–0	-41.27–0	-41.27–0		

Using: t-Independent Sample t-test; p-value>0.05 NS.

3. Discussion

Total Thyroidectomy is associated with significant complications, and surgical techniques are one of the important factors which may affect the rate of post thyroidectomy complications [4].

Hypoparathyroidism is one of the most common and important post

thyroidectomy complications. Due to variations in the parameters used to diagnose hypoparathyroidism, the incidence of hypoparathyroidism after thyroidectomy is variable, it was 5% in a study by Ref. [8], 1.6–83% [9], and 1.2–40% [10].

Different cutoff values have been reported to define Hypocalcemia less than 7 mg/dL [11], less than 8.0 mg/dL [12], less than 8.5 mg/dL [13–15].

Postoperative hypocalcemia may be due to either transient or permanent hypoparathyroidism. Permanent hypoparathyroidism occurs in less than 3% of patients, whereas transient postoperative hypocalcemia is much more common [10].

Hypoparathyroidism may be due to accidental parathyroid gland removal or vascular injury [9] Laboratory assessment of parathyroid function includes PTH and serum ca level [9].

Now, energy-based devices can be used in thyroid surgery for achieving hemostasis and dissection. Nonetheless, some assumptions should be avoided with the use of the energy-based device in critical regions close to the parathyroid glands, and the conventional suture ligation technique should be used [10].

A harmonic scalpel was used for dissection and hemostasis, as good Hemostasis allows identification and protection of parathyroids, superior and recurrent laryngeal nerves. Also, it permits the ligation of vessels with a diameter of less than 3 mm. Some studies have suggested that using a harmonic scalpel on larger vessels, such as the superior thyroid vessels, may be beneficial [16].

We investigated the effect of HS versus traditional thyroidectomy on serum levels of PTH and serum calcium. We found that there was a greater decrease in serum calcium and PTH in the traditional thyroidectomy group than HS group, but it was statistically significant for PTH hormone but not for serum calcium.

Several randomized trials on the use of ultrasonic dissection devices in thyroid surgery have consistently observed that not only the surgery time was significantly reduced in comparison to conventional dissection techniques but also the rates of postoperative hypocalcemia decreased [17].

The study of Pelizzo et al., 2014 [18] found that after total thyroidectomy using Focus Harmonic Scalpel, hypoparathyroidism was 45.2 (48%), compared to 51.7 (54.26%) with conventional hemostasis. As a result, they came to the conclusion that the Focus Harmonic Scalpel could protect the parathyroid gland and likewise lowering the risk of hypoparathyroidism.

These results are consistent with the reports of Y. F. Duan et al., 2013 [16] and (S.-Q. Xu et al., 2019 [8]). This indicates that Focus Harmonic Scalpel has certain advantages for conventional hemostasis in protecting parathyroid glands.

FOCUS Harmonic Scalpel is supposed to be a more reliable and safe instrument that can take place of the clamp-and-tie technique in total thyroidectomy [16].

Even when comparing another energy device as LigaSure with conventional surgery regarding Transient hypoparathyroidism and permanent hypoparathyroidism following thyroidectomy. It was significantly associated more with the conventional technique [3]. This finding supports the idea of better hemostasis is associated with good preservation of parathyroid function.

In contrast, impaired postoperative parathyroid function with lower PTH level was noticed in total harmonic scalpel thyroidectomy than in the classic clamp-and-tie group [4].

Also, in a study conducted by Jiang et al., 2020 [3] compared two groups, the first group uses harmonic scalpel only and the other group used harmonic scalpel in addition to clamp and tie HS-CAT when the dissection is close to the parathyroid.

Their findings showed that hypoparathyroidism within the first 24h is significantly associated with HS-CAT more than the HS group. This significant association was not found 2 months after surgery. This conclusion is linked to the CAT approach, which preserves tiny vessels better than HS, lowering the risk of temporary hypoparathyroidism.

Table 3

Comparison between Group I: Harmonic group and Group II: Conventional group according to PTH.

PTH	Group I: Harmonic group (n=50)	Group II: Conventional group (n=50)	Total (n=100)	t-test	p-value
Preoperative					
Mean ± SD	38.65 ± 5.99	39.13 ± 11.05	38.89 ± 8.84	-0.271	0.787
Range	25-60	23.1-79	23.1-79		
Postoperative					
Mean ± SD	28.06 ± 7.46	22.74 ± 7.22	25.40 ± 7.78	3.623	<0.001**
Range	7.9-42	9.1-39.2	7.9-42		
Mean Diff. Pre and Post					
Mean ± SD	-10.59 ± 6.34	-16.40 ± 10.36	-13.49 ± 9.03	3.379	<0.001**
Range	-32--2	-60.4--2	-60.4--2		
Change Pre and Post					
Mean ± SD	-27.47 ± 16.84	-40.32 ± 16.62	-33.90 ± 17.85	3.840	<0.001**
Range	-78.05--6.06	-76.46--6.45	-78.05--6.06		

Using: t-Independent Sample t-test.

p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS

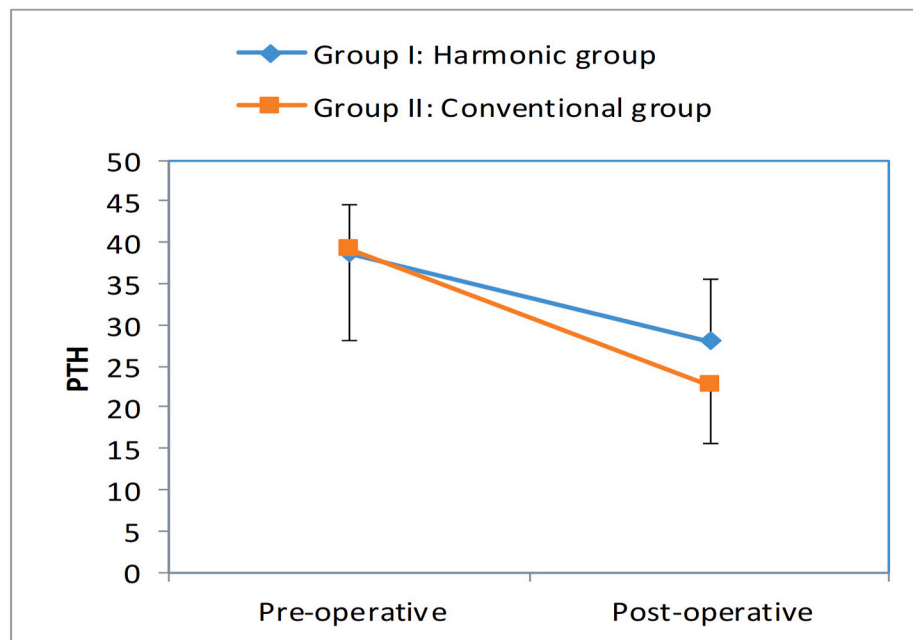


Fig. 2. Comparison between Pre-operative and Post-operative according to PTH in each group.

Table 4

Comparison between Group I: Harmonic group and Group II: Conventional group according to operative time and postoperative complications.

		Group I: Harmonic group (n=50)	Group II: Conventional group (n=50)	Total (n=100)	Test	p-value
Operative Time (min)	Mean ± SD	72.68 ± 8.23	96.22 ± 10.93	84.45 ± 15.25	t=12.171	<0.001**
	Range	55-90	70-120	55-120		
Hospital stay (days)	Mean ± SD	2.28 ± 0.93	1.94 ± 0.62	2.11 ± 0.80	t=2.157	0.033*
	Range	1-6	1-4	1-6		
Parathyroid Number Identified and Preserved						
2		5 (10.0%)	5 (10.0%)	10 (10.0%)	χ ² =0.800	0.670
3		13 (26.0%)	17 (34.0%)	30 (30.0%)		
4		32 (64.0%)	28 (56.0%)	60 (60.0%)		
Postoperative complications						
ELN injury		4 (8.0%)	2 (4.0%)	6 (6.0%)	χ ² =12.254	0.140
Heamatoma		1 (2.0%)	0 (0.0%)	1 (1.0%)		
Hypocalcemia		3 (6.0%)	4 (8.0%)	7 (7.0%)		
RLN Injury		1 (2.0%)	0 (0.0%)	1 (1.0%)		
RLN Injury&Hypocalcemia		1 (2.0%)	2 (4.0%)	3 (3.0%)		
Seroma		1 (2.0%)	0 (0.0%)	1 (1.0%)		
No		39 (78.0%)	42 (84.0%)	81 (81.0%)		

Thermal injury of HS which can be in the form of as spasm or irreversible protein denaturation, can be mitigated by vasodilation, parathyroid cell regeneration, and reperfusion from the collateral blood supply [3].

Because of the good hemostasis established by devices such as the HS and LS, the operative time was reduced. The reduction in surgical time could be attributable to a reduction in the time necessary for the

hemostasis of the thyroid gland's blood vessels. Other factors that may shorten the operative time as skills and experience of surgeons using these devices could be the reason for the reduction in surgical time [5, 16,19,20].

In our study, the operative time for the harmonic group is shorter than conventional group. Another advantage of HS is the absence of smoke and the lack of electric energy passing through the body of the patient [5].

Other complications as RLN injury, Hematoma, and Seroma showed no statistically significant association when comparing both groups with p value 0.140. (Table 4). These results are similar to findings obtained by Refs. [9,21].

Dehal and colleagues investigated 147,344 thyroid and parathyroid procedures and reported a hematoma in the neck was found in 1.5 percent [22]. Ramouz et al. found that 70 of 6,830 hematomas required exploration in a large case-controlled study, accounting for 1.02 percent of all hematomas and found no significant difference in postoperative hematoma formation between the Ligasure small jaw and Harmonic scalpel groups [23].

A meta-analysis included 47 RCTs with a total of 6219 patients: 2671 were operated with harmonic scalpel, 813 with LigaSure, and 2735 with traditional hemostasis. There was no difference in the frequencies of transient recurrent laryngeal nerve palsy or hematoma between the three procedures [24].

Long-term follow-up and the small number of cases in this study are the study's limitations.

4. Conclusion

The postoperative serum level of parathyroid hormone was significantly declined after thyroidectomy when the conventional method is used. Using HS during thyroidectomy is safe and effective with lower rates of hypoparathyroidism.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

IRB approval (Reg. No. RHBIRB2018122001) with approval number (202107935), This study was approved by the Faculty of Medicine for Girls Al Azhar university Research Ethical Committee.

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Author contribution

All authors has contributed in study design, data collection, data analysis, writing the paper.

Consent to participate

Informed consent was obtained from all individual participants who took part in the study.

Registration of research studies

1. Name of the registry:Thai Clinical Trials Registry (TCTR)
2. Unique Identifying number or registration ID:Registration unique identifying number (UIN): TCTR20211202001

3. Hyperlink to your specific registration (must be publicly accessible and will be checked):(https://www.thaiclinicaltrials.org/show/TCTR20211202001).

Guarantor

Hany Abdelfatah Elhady.

Declaration of competing interest

The authors declare there is no conflict of interest to be declared.

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