Post thyroidectomy thyroid tissue remnant: Comparison between tie ligation and LigaSure by post-operation ultrasonography and technetium uptake

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ABSTRACT

Introduction: Thyroidectomy can be done using different methods. In this study, post thyroidectomy thyroid remnant was compared between tie ligation and LigaSure.

Methods: Thirty-two patients undergoing thyroidectomy were equally grouped into tie ligation (A) and LigaSure (B). The duration of operation, estimated surgical blood loss, drain discharge, pre and post-operation calcium and parathormone levels, and pre and post-operation subjective assessment of the vocal cord function were collected. Thyroid bed technetium uptake (TTU) and ultra-sonographies were done, respectively, within 3 and 7-14 days after surgery, and thyroid tissue remnant was evaluated.

Results: Duration of the operation was longer in group A. Surgery-related blood loss and drain discharge, changes of calcium, parathormone and quality of voice before and after surgery were similar between the two groups. Three patients had sonographically remarkable post-surgical thyroid remnant; all operated by tie ligation, the difference with group B was insignificant. TTU was similar between groups A and B.

Conclusion: Although LigaSure reduces the operation time with similar operation outcomes, the indicators of thyroid tissue surgical remnants are similar between the two sterategies.

Keywords: Thyroidectomy; LigaSure; Tie ligation; Technetium uptake; Thyroid tissue remnant.

INTRODUCTION

Thyroid cancer is the most common endocrine cancer. Surgical removal of the tumor is the main stem of the treatment. Many cases undergo radioactive iodine therapy after surgery. The loco-regional recurrence and distant metastases are the unfavorable aspects of the disease with bone, lung, and brain metastases as life-threatening consequences. The recurrence and metastases are directly correlated with insufficient tumor resection [1]. Also, failure of the radioiodine therapy is more encountered in patients with tumoral remnants after incomplete surgeries. Many questions are raised about the optimal way to document the surgical remnant of the tumor/thyroid and the way to minimize it. The neck ultrasonography (NUS) is the optimal diagnostic modality for detection, evaluation, and follow-up of the thyroid nodules [2]. Unfortunately, the NUS is not either sensitive or specific for evaluation of tumoral remnant at the thyroid bed after thyroid surgery. The whole body iodine scan after therapy is optimal for detection of thyroid bed and tumoral remnant as well as locoregional recurrence [3]; however, the use of diagnostic radioiodine imaging before radioiodine therapy is limited due to the induced radio-resistance [4, 5]. An alternative way for evaluation of thyroidal tissue remnant after surgery can be technetium-99m pertechnetate (Tc-99m) imaging [6, 7]. The procedure has been previously described as neck technetium uptake [8] which could be implied for assessment of thyroid bed technetium uptake (TTU). The procedure could be used for post-surgery conditions to evaluate the need for radioiodine therapy (RIT) or radioiodine dose determination as well as in the broader context of thyroid cancer treatment including evaluation of response after RIT.

The remnant after the total thyroidectomy procedures is a challenging issue, complicated further by the limited accuracy of imaging as mentioned above, which includes information to select the forthcoming therapy. The thyroid or thyroid tumor remnant is reasonably related to the method and technique of the surgery and the experience of the surgeon. Different thyroidectomy methods are ranging from radical to less invasive surgeries. The extent of the surgery is tailored for the extension of the tumor and the final goal would be negative margins and no post-operation tumoral remnant [9]. Also, the tool for the surgery varies from the established and rather conventional tie ligation to more recent equipment-dependent methods using heat and ultrasound waves for resection and hemostasis. Presumably, the tools used in the thyroidectomy may correlate with the consequence of surgery and the extent of the tumor remnant. In the current study, a newly available technology, LigaSure, is compared with the conventional tie ligation method. The operations were total thyroidectomy without neck dissection to harmonize the effect of the extent of the surgery. Certain surgery related indices including surgery time and bleeding as well as remnant imaging including NTU and TTU were employed for determination of post-surgery thyroid remnant.

METHODS

From March 2017 to December 2017, 32 patients undergoing total thyroidectomy were recruited. The patients had suspicious thyroid nodules for malignancy (n=8), multinodular goiter (n=20), or grave's disease (n=4). The study protocol was confirmed by the university research ethics committee. Informed consent was collected. The participants were randomly classified into two groups (11 females in each). Patients in group A were operated using conventional tie ligation (n=16), and in group B were operated employing LigaSure (n=16). Two authors contributed in the surgeries including an attending/supervising surgeon (i.e. AA) and NM who was the chief resident of surgery at the time of study aided the attending surgeon. Two different operation rooms were employed for either surgery with tie ligation or LigaSure. Patients were blindly allocated to the

operating rooms and correspondingly tie ligation (group A) or LigaSure (group B) methods. Surgery approaches were essentially identical. The randomization was done with simple alternative allocation of the participants to either operation rooms based on the admission order. Serum calcium and PTH levels were measured before surgery. Duration of operation and the number of wet gauzes along with the visual assessment of their percentage saturation were collected. For bleeding estimation, the number of complete wet gauzes (i.e. almost 100% saturation) multiplied by 10cc was calculated [10]. Also, serum calcium and PTH levels were measured in the surgery night serum samples. A questionnaire was filled before and after surgery to quantify the quality of the voice. The questionnaire consisted of 5 questions with 0-2 scores for each. Four questions were directed to subjective patient's assessment of his/her voice strength, recent voice change, spontaneous aspiration experience, and suffocation feeling, the 5^{th} question directed the accompanying family person and questioned his/her assessment of patient's voice strength. The sum of scores was registered before surgery and on the day of discharge, 2-3 days post-operation. Occurrence of clinical hematoma and seroma, as well as drainage volume, were collected. The patients were followed to verify the pathology of the thyroid.

Within 3 days post-operation, the surgical site thyroid remnant was imaged using IV injections of 185 MBq freshly eluted technetium. The exact injection dose was measured by subtraction of pre and post-injection syringe dose measured using a dose calibrator (Model 4001M Mini Bin, Jackson, USA). The syringe was counted before injection for 40 seconds at a distance of 25 cm from the camera surface (Sopha medical, Leuhr 140, France). The injected count was calculated as:

$$\text{Injected count} = \frac{\text{Preinjection count} * \text{Injected dose}}{\text{Preinjection dose}}$$

The patient's neck was imaged two times: at 25 cm from the camera for 40 seconds for calculations and to collect 200K counts at the shortest camera-neck position for visual assessment. Two rectangular equal region of interests (ROI) of about 2000-3000 pixels were drawn over the neck, and shoulder as background. TTU was calculated based on the following formula:

$$\text{TTU} = \frac{\text{Neck ROI count} - \text{Background ROI count}}{\text{Injected count}}$$

The 200 k-count images were visually evaluated for the presence of thyroid/thyroid tumor remnant by the consensus of two nuclear physicians.

NUSs were done by a single experienced radiologist 7-14 days after surgery by ultrasound (Philips Affiniti 50 Ultrasound, Bothell, Washington). The clinical, laboratory, nuclear medicine, and sonographic indices were compared between patients who underwent tie ligation and LigaSure operations. Data were explored then Chi-square, T-test, and Mann Whitney U test was employed when appropriate. For the assessment of the effect of surgical technique on the changes of calcium and parathormone, analysis of covariance (general linear model) was applied. SPSS version 22 and a p significance level of 0.05 were used.

RESULTS

Patients (22 females and 10 males) aged 42.3 ± 14.2 with no remarkable difference between groups (42.9 ± 15.4 vs 41.8 ± 13.3 for A and B, respectively). Eleven patients in each group were females and 5 were males. Eight patients had pathologically proven papillary thyroid cancer 4 in each group. Pre-surgical suspicion for malignancy was high in 2 and 3 patients in groups A and B,

respectively. Other operation indications were non-oncologic considerations. The pathologic findings are presented in Table 1. The sonographic estimation of thyroid volume before surgery was 662.9 ± 823.4, similar in both groups (675.9 ± 762.7 vs. 649.9 ± 905.1 m^3; p=0.9). Time of surgery was significantly longer for tie ligation surgeries (93.9 ± 26.0, 111.3 ± 15.8, 75.3 ± 21.5 min in total group A and group B, respectively; p=0.000), but no remarkable difference was detected for the estimated blood loss and post-operation drain discharge between two groups (Table 2). No hematoma was reported. Seroma formation at first clinical follow-up was noticed in 4 (25%) and 2 (12.5%) patients of groups A and B (p=0.36), respectively. TTU measured 1.8% ± 1.6 (Figure 1) without any significant differences between groups A and B (1.6± 0.4 vs. 1.9± 0.4; p=0.7). TTU more than 2% was more prevalent in the ligaSure group, but the difference was not significant (all patients: 35.5%, ligaSure: 43.8%, and tie ligation: 26.7%; p=0.32). Out of all sonographies, 3 patients (9.4%) were reported to have remarkable post-surgical thyroid remnant; all of them were operated by tie ligation method (18.8%; p= 0.069). Pre and post-operation serum calcium levels as well as baseline vitamin D levels were statistically similar between groups. Parathormone levels were remarkably lower in tie ligation group either pre-operatively (Table 2) but the decrement in calcium and parathormone values showed no significant interaction effect for the technique of surgery (for calcium, partial eta was 0.000 and P=0.969; for Parathormone, partial eta was 0.008 and p= 0.498; Figure 2). Rank analysis of the scores derived from the questionnaires about the quality of vocal cord function before or after surgery showed no remarkable difference between groups (mean rank were 17.3 vs.15.7 before surgery and 14.8 vs. 18.3 after surgery for groups A and B, respectively).
Other main outcomes of the surgeries are presented in Table 2 compring the results in groups A and B.

DISCUSSION

There are remarkable debates concerning the privilege of different surgical methods for thyroidectomy. We compared a new instrument-assisted technique, ligaSure, with the conventional tie ligation method. We showed the use of ligation has a remarkable shorter duration of surgery with equal outcomes. Voice quality scores were the same between the methods. Thyroid tissue remnant estimates by sonography and technetium uptake were statistically similar. For proper decision-making to choose between two methods, the ease of the surgery by ligaSure and the savings of operation bedtime should be balanced against the higher cost. There are conflicting available reports about the privileges of newly-developed surgical instrumentations namely harmonic and ligaSure in terms of shorter surgery time, less nerve injury, lower prevalent hematoma/seroma, better complete tissue resection, and less frequent parathyroid ischemia [11-15].
The percentage of sonographically reported post-surgical thyroid remnant was higher for tie ligation surgery, albeit insignificantly. We believe the sonography might detect the granulation tissue around the stitches as thyroid remnant tissue. It is confirmed that early post-operation neck sonography is not reliable [16], hence prohibited by many guidelines [17, 18]. The echogenicity of the granulation and thyroid tissue are similar, but visualization of hyper-echogenic tie knots within the granulation tissue may provide a lead for proper differentiation. Although the sonography operator of the current study was an experienced attending radiologist, the differentiation of the inflammation/granulation change versus infiltrative tissue or thyroid remnant was not possible in these cases.

We adopted the method for calculation of TTU from one of our previous publications in patients with Graves' disease for post-thyroidectomy patients. TTU was insignificantly higher in patients operated using ligaSure and the percentage of high TTUs (>2%) was 17% higher in these patients, however, the difference was insignificant probably due to the small sample size. Inflammation of the surgery site may have contributed to this finding. Resulting in more Technetium accumulation at the thyroid surgical site due to inflammatory hyperemic reaction. Consequently, the higher TTU, even it was statistically significant, could have been unimportant [19].

The cost analysis between the two groups may provide further insight into the privilege or drawbacks of traditional tie ligation and equipment-dependent LigaSure methods, which is lacking in the current paper. According to the results of the current study, the surgeons may be reassured that the use of the traditional tie ligation method may not remarkably change the surgical outcome. Nevertheless, long interval follow-ups are needed to evaluate the outcome for tumor recurrence or complete remission.

The study is limited by two major factors: first, the sample size is small; and second, the study may not be extrapolated because it was a single center study. Furthermore, the nonspecific uptake of technetium in the surgical bed three days after surgery as a result of inflammation and hyperemic reaction could be high hence timing of our measurement could have been inappropriate. The timing was set because the levothyroxine replacement after thyroidectomy should be started as soon as possible which inhibits the Tc-99m uptake at the thyroid bed or tumoral remnants. Nevertheless, this remarkable flaw should be considered when interpreting the results.

CONCLUSION

The outcome of thyroidectomy by tie ligation and LigaSure is similar except for a longer operation time for tie ligation. Direct higher cost for LigaSure and indirect cost burden for the longer occupation of operation room should be balanced to choose between the methods.

REFERENCES

1. Pisanu A, Saba A, Podda M, Reccia I, Uccheddu A. Nodal metastasis and recurrence in papillary thyroid microcarcinoma. Endocr. 2015;48(2):575-81.
2. Russ G, Bigorgne C, Royer B, Rouxel A, Bienvenu-Perrard M. The thyroid imaging reporting and data system (TIRADS) for ultrasound of the thyroid. J Radiol. 2011;92(7-8):701-13.
3. Cailleux AF, Baudin E, Travagli JP, Ricard M, Schlumberger M. Is diagnostic iodine-131 scanning useful after total thyroid ablation for differentiated thyroid cancer? J Clin Endocrinol Metab. 2000;85(1):175-8.
4. Tuttle RM, Tala H, Shah J, Leboeuf R, Ghossein R, Gonen M, Brokhin M, Omry G, Fagin JA, Shaha A. Estimating risk of recurrence in differentiated thyroid cancer after total thyroidectomy and radioactive iodine remnant ablation: using response to therapy variables to modify the initial risk estimates predicted by the new American thyroid association staging system. Thyroid. 2010;20(12):1341-9.
5. Schneider DF, Ojomo KA, Chen H, Sippel RS. Remnant uptake as a postoperative oncologic quality indicator. Thyroid. 2013;23(10):1269-76.
6. Giovanella L, Suriano S, Ricci R, Ceriani L, Anton Verburg F. Postsurgical thyroid remnant estimation by 99mTc-pertechnetate scintigraphy predicts radioiodine ablation effectiveness in patients with differentiated thyroid carcinoma. Head Neck. 2011;33(4):552-6.

7. Kueh SS, Roach PJ, Schembri GP. Role of Tc-99m pertechnetate for remnant scintigraphy post-thyroidectomy. Clin Nucl Med. 2010;35(9):671-4.
8. Zhao H, Liu CH, Cao Y, Zhang LY, Zhao Y, Zhang X, Lin YS, Xia Y, Liu YW, Liu HF, Li XY. An immediate postoperative response to therapy assessment can help avoid unnecessary RAI therapy. Front Oncol. 2022;12:947710.
9. Tarasova VD, Tuttle RM. A risk-adapted approach to follow-up in differentiated thyroid cancer. Rambam Maimonides Med J. 2016;7(1):e0004.
10. Ali Algadiem E, Aleisa AA, Alsubaie HI, Buhlaiqah NR, Algadeeb JB, Alsneini HA. Blood loss estimation using gauze visual analogue. Trauma mon. 2016;21(2):e34131.
11. AlJuraibi W, Ahmed MR, Saber A. Use of ligasure sealing versus conventional suture-ligation in total thyroidectomy. J Surg. 2016;4(3-1):34-8.
12. Markogiannakis H, Kekis PB, Memos N, Alevizos L, Tsamis D, Michalopoulos NV, Lagoudianakis EE, Toutouzas KG, Manouras A. Thyroid surgery with the new harmonic scalpel: a prospective randomized study. Surg. 2011;149(3):411-5.
13. Pons Y, Gauthier J, Ukkola-Pons E, Clément P, Roguet E, Poncet J-L, Conessa C. Comparison of LigaSure vessel sealing system, harmonic scalpel, and conventional hemostasis in total thyroidectomy. Otolaryngol Head Neck Surg. 2009;141(4):496-501.
14. Cannizzaro MA, Bianco SL, Borzì L, Cavallaro A, Buffone A. The use of FOCUS Harmonic scalpel compared to conventional haemostasis (knot and tie ligation) for thyroid surgery: a prospective randomized study. Springerplus. 2014;3(1):639.
15. Kuboki A, Nakayama T, Konno W, Goto K, Nakajima I, Kanaya H, Hirabayashi H, Haruna SI. New technique using an energy-based device versus conventional technique in open thyroidectomy. Auris Nasus Larynx. 2013;40(6):558-62.
16. Liu R, Zhang B. Role of ultrasound in the management of thyroid nodules and thyroid cancer. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2017;39(3):445-50.
17. Leenhardt L, Erdogan M, Hegedus L, Mandel S, Paschke R, Rago T, Russ G. 2013 European thyroid association guidelines for cervical ultrasound scan and ultrasound-guided techniques in the postoperative management of patients with thyroid cancer. Eur Thyroid J. 2013;2(3):147-59.
18. Haugen BR. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: what is new and what has changed? Cancer. 2017;123(3):372-81.
19. Shapiro B, Rufini V, Jarwan A, Geatti O, Kearfott KJ, Fig LM, Kirkwood ID, Gross MD. Artifacts, anatomical and physiological variants, and unrelated diseases that might cause false-positive whole-body 131-I scans in patients with thyroid cancer. Semin Nucl Med. 2000;30(2):115-32.

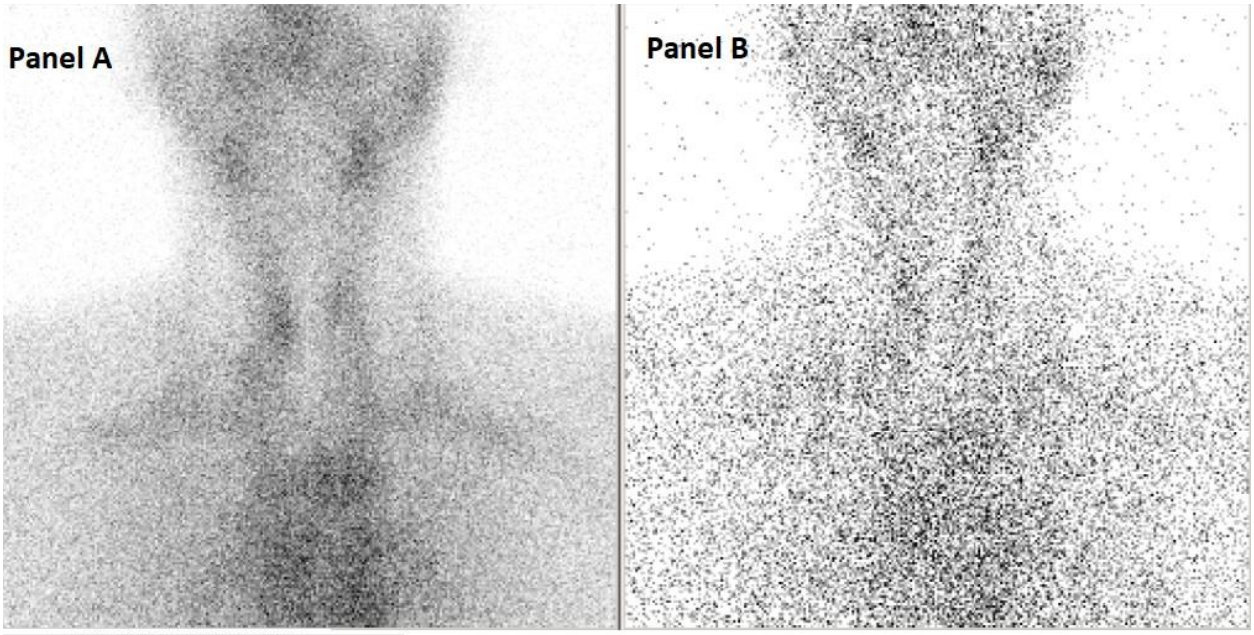
Table 1. The pathologic findings are presented

LigaSure	MNG 7 (21.8); PTC 4 (12.5); nodular hyperplasia 2 (6.2); follicular adenoma 2 (6.2); and grave's disease 1 (3.1).
Tie ligation	Diffuse hyperplasia 5 (15.6); PTC 4 (12.5); nodular hyperplasia 3 (9.3); MNG 3 (9.3); and follicular hyperplasia 1 (3.1).

Table 2. Comparison of the outcomes of the surgery between 2 groups of patients operated with tie ligation and LigaSure

	Tie ligation	LigaSure	Total	Sig
Pre-operation calcium (mg/dl)	9.3 (0.5)	9.1 (0.7)	9.2 (0.6)	0.359
Post-operation calcium (mg/dl)	8.4 (0.5)	8.2 (0.8)	8.3 (0.7)	0.454
Pre-operation PTH (ng/ml)	50 (28.3)	81.1 (41.2)	65.6 (38.2)	0.019
Post-operation PTH (ng/ml)	20.4 (17.8)	41.3 (27.6)	30.9 (25.2)	0.016
25-OH-Vitamin D (pg/ml)	25.5 (12.5)	30 (18)	27.7 (15.4)	0.419
Pre-operation voice evaluation index†	1 (0-2)	0 (0-1.8)	0.5 (0-2)	0.724
Post-operation voice evaluation index†	0 (0-1)	0.5 (0-1.8)	0 (0-1)	0.722
Duration of surgery (min)	111.3 (15.8)	75.3 (21.5)	93.3 (26.0)	0.000
Estimated blood loss (Gauze number)	7.8 (3.1)	6.1 (3.6)	6.9 (3.4)	0.182
Volume of post-operation drain discharge	66.9 (41.3)	45.9 (17.7)	56.4 (33.1)	0.072

Data are mean and standard deviation in parentheses generally but median (quartiles) when indicated by †.
Independent sample T tests were done except where nonparametric test was used when indicated by †.



ROI color	Count per pixel	Total Count	Area	Max Count	Min Count
	1	2631	2500	7	
	1	3218	2500	8	

Fig 1. The standard and 40 min images purposed for calculation as well as region of interests and counts of a typical patient

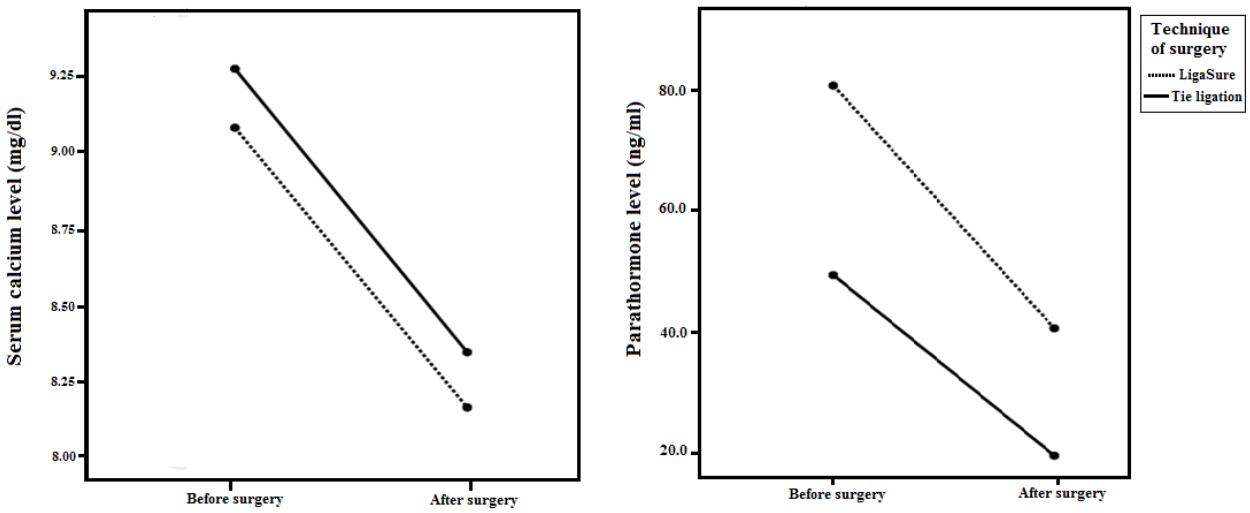


Fig 2. The comparison of decrements calcium and parathormone levels before and after surgery in two groups of patients operated by tie ligation and ligaSure methods