



Original research

Terminal or truncal ligation of the inferior thyroid artery during thyroidectomy? A prospective randomized trial



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ABSTRACT

Introduction: Thyroidectomy is a common procedure in general and endocrine surgery. The technique of ligation of inferior thyroid artery (ITA) has been invoked as a possible cause of appearance of postoperative hypocalcemia.

Methods: We performed a prospective randomized study involving 184 patients undergoing total thyroidectomy to evaluate the differences of truncal ligation versus distal ligation of ITA in terms of postoperative hypocalcemia, vocal fold palsy, voice and swallowing impairment. The patients were divided into group A (trunk ligation of ITA) and group B (terminal branches ligation of ITA).

Results: We evaluated postoperative PTH and calcemia (immediate, 6 and 12 months after thyroidectomy), postoperative day of discontinuation of calcium and vitamin D supplementation, voice and swallowing complaints, evaluated by mean of two specific tests available in literature, day of hospital discharge.

Conclusion: The only significant differences between the two groups were a higher immediate postoperative calcemia and a greater number of patients discharged without calcium and vitamin-D supplementation in the group B. In conclusion, no substantial differences were found between the two groups. The choice depends on the experience of the surgeon.

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1. Introduction

Thyroidectomy is one of the most common procedures in general and endocrine surgery [1]. Postoperative hypocalcemia (POHC) is the most frequent complication of this procedure [2] and it can appear temporarily, ranging from 24% to 45.5%, or become a definitive status (1.9%–33%) [3–13]. Several criteria have been invoked to explain the appearance of POHC. The surgeon's experience has been proposed as principal cause of this wide range of variability, but different conditions could be involved [10,12]. Several studies evaluate the surgical technique of ligation of inferior thyroid artery (ITA), but the choice between truncal and distal

ligation of ITA branches remains still controversial [12–16]. It has been reported that truncal ligation of the ITA not influences the function of parathyroid glands after subtotal or total thyroidectomy [12,14–16] but we have no experiences concerning the other complications and sequelae associated with thyroid surgery, such as vocal fold palsy and voice and swallowing complaints. In a previous study performed at our institution [12] we investigated some changes, mainly biochemical, of the proximal ligation of ITA compared to the distal ligation of its branches. The aim of this prospective randomized study is to confirm the previous results and to evaluate a larger range of functions and symptoms that can be associated with both modalities of approach of the ITA. The end point is to examine the real impact of truncal ITA ligation versus terminal ligation of ITA branches on postoperative clinical outcomes, such as duration of substitutive calcium treatment, length of hospital stay, vocal fold palsy incidence, voice and swallowing impairment in the postoperative period.

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2. Methods

The present study involves 184 patients underwent to total thyroidectomy at Department of General and Emergency Surgery at the University Hospital Policlinico "P. Giaccone" - Palermo, between January 2012 and May 2014. We report inclusion and exclusion criteria in Table 1. Demographic data are indicated in Table 2. The patients were scheduled for total thyroidectomy in presence of nodules >3 cm, "suspected" nodules according to the result of a fine-needle aspiration biopsy (FNAB) tracheal and/or esophageal compression due to a multinodular goiter. In the face of a solitary nodule the patients enrolled in the present study chose the total thyroidectomy according to a complete information concerning both thyroid lobectomy and total thyroidectomy. The FNABs were addressed according to the Bethesda System for reporting thyroid cytopathology [17]. Preoperative work-up included clinical examination, TSH and FT3-FT4 hormones, serum calcium preoperative levels, preoperative PTH; moreover we always performed a neck and thyroid ultrasound scan. The volume of the thyroid gland, chosen as inclusion criterium as specified in Table 1, was calculated with the following ultrasound criteria: LD x TD x TH x 0.5 (LD: longitudinal diameter of the single lobe; TD: transversal diameter; TH: lobe thickness; 0.5 is a correction factor used to transform the obtained amount from parallelepiped into an ellipsoid). The calculation of the lobe volume was made separately and the values added up later. We always investigated a thyroid autoimmunity with the evaluation of the antithyroid antibody pattern (TPO, Ab-Tg Ab), indicating the presence of Hashimoto's thyroiditis and the search of the following coexisting ultrasonographic signs: coarsened parenchymal echo texture, glandular parenchyma hypoechoic compared with a normal one, and fibrotic septations producing a pseudolobulated appearance of the parenchyma. All patients also underwent a preoperative assessment of vocal fold motility with a fiber-optic laryngoscopy. Patients with thyroid cancer, toxic goiter, associated parathyroid diseases, previous neck surgery were excluded [18–20]. Once eligibility was assessed we obtained a written informed patient's consent, the participants were randomized, using a secure web-based system, and enrolled for one of the two study arms: ITA trunk ligation (Group A) and terminal branches ITA ligation (Group B). Randomization was stratified by age and sex. The study was approved by the Ethics Committee of our institution. All procedures were performed with the same protocol of general anesthesia. All patients underwent conventional total thyroidectomy, with a collar incision 30–50 mm long, performed 2 cm above the sternal notch. In this case we no used energy-based advanced surgical instruments, such as ultrasonic or radiofrequencies dissectors nor thermal device [21–23]. All surgical procedures were total bilateral extracapsular thyroidectomies. Treatment of the upper pedicle was done by moving the

Table 1
Selection criteria.

Inclusion	Exclusion
Thyroid nodule > 3 cm (if consenting)	Thyroid carcinoma
Nodule Bethesda I–II – III–IV	Diabetes
Multinodular euthyroid goiter	Obesity
Thyroid volume ≤ 80 ml	Coagulopathy
	Liver disease
	Hypoalbuminemia
	Hashimoto's thyroiditis
	Toxic goiter
	Previous neck surgery
	Preoperative vocal fold palsy
	Coexistent hyperparathyroidism
	Intraoperative parathyroid removal

Table 2
Demographic data.

	Group A	Group B	p-value
Age (mean)	46.2 ± 13.66	44.8 ± 13.74	N.S.
Gender:			
- Female	61	58	
- Male	58	24	N.S.
Thyroid volume (mean)	50.52 ± 16.7	52.12 ± 17.95	N.S.
Preoperative PTH (mean)	51.16 ± 8.44	50.26 ± 8.88	N.S.
Preoperative calcemia (mean)	9.22 ± 0.71	9.15 ± 0.71	N.S.

upper thyroid pole laterally, exploring the intercricothyroidal space to avoid any injury to a low-situated nerve, and separately ligating the branches of the superior thyroid artery as low as possible. The truncal ITA ligation was performed in the group A looking for the artery medially to the carotids, and laterally to the recurrent laryngeal nerves and sectioning the artery between two ties. In the group B the terminal branches of the ITA were ligated separately (if the artery was previously divided in two or more branches) close to the thyroid capsule and medially to the inferior laryngeal nerve. The laryngeal nerves (superior and inferior) as well as the inferior and superior parathyroid glands were carefully visualized looking for the usual landmarks (Zuckermandl's tuberculum for both sides and tracheo-esophageal groove on the left side). All procedures were performed by the same surgical team experienced in thyroid surgery. The operative time was evaluated from skin incision to the last skin suture. We considered the serum calcium and plasmatic PTH levels in preoperative period and 24 h after the thyroidectomy. The normal range for calcemia was 8.6–10.2 mg/dL; the normal PTH value was 15–65 pg/ml. Transient hypocalcemia was defined when serum calcium level dropped back down the normal range. In these circumstances, patients were also clinically assessed for the presence of Chvostek's and Trousseau's signs and other symptoms of hypocalcemia, such as peripheral or oral paresthesia, seizure, and laryngospasm. A fiber optic laryngoscopy was done once again 24 h after surgery. At discharge, calcium and calcitriol were suggested in case of need: an empirical daily dosage of 0.75 mg of calcitriol + 1000–1500 mg of calcium was suggested if calcemia after 24 h was 8 ± 0.1 mg/dL; we administered 1–1.25 mg of calcitriol + 2000–3000 mg of calcium for progressively inferior values of calcemia. These dosages were progressively reduced after periodic controls. We recommended a new serum calcium dosage 24 h after the patients were discharged and on the fourth and the seventh postoperative days for any further therapeutic adjustment. We administered the minimal dose of calcium and vitamin D needed to maintain calcemia of ≥ 8.0 mg/dL. We considered also the length of hospital stay and the duration of administration of calcium and vitamin D (postoperative days). Our experience with functional esophageal surgery and histological findings of nerve degeneration in other diseases [24–26] led us to study also this specific postoperative outcome. So, the vocal and swallowing function were investigated with two questionnaires available in the literature [1]. These questionnaires were administered to the patients in the preoperative period and 30 days after the surgical operation. The results obtained in the postoperative time were compared with the preoperative ones and the results were led to two categorical variables: worsening – no worsening. Finally, we took into consideration the records of the clinical and laboratory tests at 6 and 12 months after surgical operation. Statistical analysis: Intercooled Stata, version 9.0 (Stata Corp, College Station, TX), was used for the analysis. The association between the surgical technique and quantitative variables was assessed with the Student's t test. The association between categorical variables and surgical technique was assessed using the χ^2 test or Fisher's exact

test as appropriate. A P value ≤ 0.05 was considered statistically significant.

3. Results

The two groups were homogeneous in terms of demographic data: age, gender, thyroid volume, preoperative calcemia and PTH (Table 2). No significant differences were found between the two groups, in terms of postoperative PTH. The difference in serum calcium levels was significant in the early postoperative evaluation ($p < 0.03$). As the average of the calcemia evaluated in the first postoperative day was less than 8 mg/dL in the group A, some differences were found in the discontinuation of the substitutive calcium and vitamin D treatment: in fact, twice the patients of the group B were discharged without indication for substitutive calcium and vitamin D treatment ($p < 0.04$), but these differences disappeared ever since the first outpatient control, that is to say in the fourth postoperative day. No differences concerning the postoperative complications and symptoms potentially associated to thyroidectomy, such as inferior laryngeal nerve palsy, voice and swallowing impairment score, were found in our series. Interestingly, the day of discharge was slightly, although not significantly influenced from the technique adopted, in fact the number of patients discharged in the second postoperative day was moderately greater in the group A, probably as a consequence of the greater drop of serum calcium levels, in this group, early in the postoperative period (Table 3).

4. Discussion

The hypoparathyroidism is the most frequent, and one of the most feared complications of total or subtotal thyroidectomy. The main cause seems to be the impairment of parathyroid blood supply subsequent to surgical manipulation. The possible causes are the excision of one or more parathyroid gland or an insufficiency of parathyroid blood supply subsequent to surgical manipulation [12,27]. The accidental parathyroid removal is a rare event, mainly due to an intrathyroidal or subcapsular parathyroid gland [28–30]. The occurrence of this event more frequently depends on the type and extent of thyroidectomy, specific thyroid diseases and surgical team experience. The present study involves a

homogeneous group of patients with euthyroid goiter in the absence of neoplasm. All procedures were performed by a team of experienced surgeons who used the same surgical technique in all patients. Moreover, the variables taken into consideration were not only the blood calcium or parathyroid hormone levels, that had been evaluated in previous studies [11–16], but the impairment of functions involving the upper esophagus and the larynx admitting that some pathophysiological changes could be influenced by a worsening in blood supply. This hypothesis could be supported by the evidence of the anastomoses between parathyroid circulation and peritracheal and periesophageal arteries [31–34]. The present study confirms the results of a previously published meta-analysis [35–38], that evaluated the moderate influence of different surgical techniques in post-thyroidectomy calcemia, and the previous results found at our institution that showed the association of the distal ligation of ITA branches during total thyroidectomy with higher mean postoperative calcium and PTH levels. In any case, no conclusive results in favor of proximal or distal ligation have been reported in the literature: on the one hand the distal ligation of ITA is a simple surgical manoeuvre, that allows to isolate carefully inferior parathyroid gland preserving the inferior laryngeal nerve. On the other hand, if the surgeon, in a specific situation, needs to ligate the ITA along the main trunk, for obtaining a better bleeding control, we can affirm that it is not a dangerous surgical choice.

5. Conclusion

Actually the advantages of the distal ligation of ITA branches seems to be limited to the immediate postoperative period. The trend in the subsequent postoperative days is in fact a substantial likeness in terms of results of both techniques. Furthermore in our experience we no find differences in terms of complications and/or postoperative complaints, such as voice or swallowing impairment. In conclusion, we can affirm that the choice between the two techniques depends on the experience of the surgeon and the need in specific events that could happen during the development of this specific procedure.

Ethical approval

None.

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Author contribution

Romano Giorgio: study design and writing.
Scerrino Gregorio: study design and writing.
Profita Giuseppe: data collections and data analysis.
Amato Giuseppe: data collections and data analysis.
Salamone Giuseppe: data collections and data analysis.
Di Buono Giuseppe: data collections, data analysis and writing.
Lo Piccolo Clotilde: data collections and data analysis.
Sorce Vincenzo: data collections and data analysis.
Agrusa Antonino: study design and writing.
Gulotta Gaspare: study design.

Conflicts of interest

Romano Giorgio and other co-authors have no conflict of interest.

Table 3

Results. p.o. = postoperative; VIS = voice impairment score; SIS = swallowing impairment score.

	Group A	Group B	p-value
p.o. PTH	40.48 \pm 13.73	41.87 \pm 13.89	N.S.
PTH after 6 months	47.17 \pm 10.72	45.64 \pm 10.71	N.S.
PTH after 12 months	47.87 \pm 10.79	46.45 \pm 10.82	N.S.
p.o. calcemia	7.9 \pm 0.64	8.1 \pm 0.60	<0.03
Calcemia after 6 months	8.7 \pm 0.41	8.8 \pm 0.52	N.S.
Calcemia after 12 months	8.9 \pm 0.45	8.8 \pm 0.49	N.S.
Treatment discontinuation:			
- None at discharge	10	21	<0.04
- Within 4 days	31	32	N.S.
- Within 7 days	33	30	N.S.
- Beyond 7 days	17	7	N.S.
- Long term	1	2	N.S.
VIS 30 days after surgery			
- Normal	62	65	
- Impaired	30	27	N.S.
SIS 30 days after surgery			
- Normal	73	69	
- Impaired	19	23	N.S.
p.o. day discharge			
- I	54	67	
- II	38	25	<0.06

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