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ORIGINAL ARTICLE

# Terminal ligature of inferior thyroid artery branches during total thyroidectomy for multinodular goiter is associated with higher postoperative calcium and PTH levels

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## KEYWORDS

Thyroid;  
Inferior thyroid  
artery;  
Total thyroidectomy;  
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PTH

## Summary

**Purpose:** To evaluate the impact of truncal versus terminal branch ligature of the inferior thyroid artery (ITA) on postoperative calcium and PTH plasma levels in patients undergoing total thyroidectomy for multinodular goiter.

**Methods:** A prospective randomized study was performed comparing a group of patients that underwent either truncal ligature of the ITA (group 1) or terminal ligature of ITA branches (group 2).

**Results:** A series of 126 consecutive patients with non-toxic euthyroid multinodular goiter underwent total thyroidectomy. Truncal ligature of the ITA was performed in 63 patients (group 1) and terminal branch ITA ligature in 63 patients (group 2). Postoperative ionized serum calcium (mmol/L) at 24 hours was significantly lower in group 1 than in group 2 patients ( $1.22 \pm 0.06$  vs.  $1.25 \pm 0.05$ ,  $P < 0.05$ ) and at 48 hours ( $1.20 \pm 0.05$  vs.  $1.23 \pm 0.05$ ,  $P < 0.05$ ). Mean postoperative PTH levels (pg/mL) at 4 hours after thyroidectomy were significantly lower in group 1 than in group 2 patients ( $22.32 \pm 11.64$  vs.  $25.82 \pm 12.87$ ,  $P = 0.044$ ). Mean hospital stay (hours) was higher in group 1 than in group 2 patients ( $87.47 \pm 41.04$  vs.  $70.34 \pm 24.82$ ,  $P < 0.05$ ).

**Conclusion:** This study shows that terminal ligature of ITA branches during total thyroidectomy for multinodular goiter is associated with higher mean postoperative calcium and PTH levels, and shorter hospital stay. However, no significant difference in terms of permanent hypoparathyroidism was observed between the two groups.

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## Introduction

Postoperative transient hypocalcemia is observed in 0.4 to 26.8% of patients after subtotal thyroidectomy [1,2]. After total thyroidectomy, an even higher incidence of transient hypocalcemia has been reported in some series ranging from 24 to 45.5% [2–5]. The incidence of permanent postoperative hypoparathyroidism has been estimated at 1.9–2.5% of patients after subtotal thyroidectomy [2,6] and at 0.3–3.5% after total thyroidectomy [2,3,7,8]. Surgeon's experience as well as other criteria have been proposed to explain observed variations in the incidence of postoperative transient permanent hypoparathyroidism. The role of proximal inferior thyroid artery (ITA) ligation or distal ligation of ITA branches has also been proposed but remains controversial. Several previous series reported that truncal ligation of the ITA may not be associated with functional alteration of the parathyroid glands after subtotal thyroidectomy [9–12]. The aim of this study was to prospectively compare the impact of truncal ITA ligation versus terminal ligation of ITA branches on postoperative calcium and parathyroid-hormone (PTH) levels in patients undergoing total thyroidectomy.

## Materials and methods

A prospective randomized study of consecutive patients with euthyroid bilateral multinodular goiter was performed in the department of general surgery and organ transplantation at the university of Palermo between January 2006 and January 2009. Preoperative work-up included clinical examination, neck and thyroid ultrasound scan, as well as assay of TSH and thyroid hormone. A preoperative assessment of vocal cord mobility (indirect laryngoscopy) was made in all patients. Indications for total thyroidectomy were tracheal and/or oesophageal compression as well as large sized nodules (> 3 cm). Patients with thyroid cancer (either suspected preoperatively or confirmed by histology), associated parathyroid diseases, age less than 18 years, skeletal diseases, and previous blood transfusions were excluded. We also excluded patients in which the histological examination of the thyroid showed the presence of parathyroid tissue within the thyroid specimen.

Once eligibility was assessed and patient's consent was obtained, participants were randomized, using a secure web-based system that was maintained by the coordinating center, and enrolled in one of the two study arms: ITA trunk ligation (group 1) and terminal branch ITA ligation (group 2). Randomization was stratified by age and sex.

All procedures were performed with the same protocol of general anesthesia. In group 1 patients, ITA truncal ligation was performed lateral to the recurrent laryngeal nerve on both sides. In group 2 patients, terminal branches of the ITA were ligated close to the thyroid capsule and medial to the recurrent laryngeal nerve. The recurrent nerves as well as the inferior and superior parathyroid were carefully exposed and preserved for secure visualization. All procedures were performed by a single surgeon. Operating time was evaluated from skin incision to the last skin suture. In all patients, determination of ionized calcium, serum phosphorus and alkaline phosphatase levels was performed preoperatively, at 24, 48, 72 hours and on the 30th day after surgery. Ionized calcium levels were measured by indirect potentiometry with a ion-selective electrode at correction to pH 7.4 using a Nova 7 analyzer (Nova biomedical, Darmstadt, Germany;

coefficient of variation 3.5% per  $x = 1.19$  mmol/L). We also evaluated PTH plasma levels at 4 hours after surgery.

Normal range for blood ionized calcium, serum phosphorus and alkaline phosphatase were considered respectively as 1.16–1.32 mmol/l, 2.7–4.5 mg/dl and 64–270 U/L. PTH levels were defined as normal when the PTH was greater or equal to 10 pg/ml. Transient hypocalcemia was defined when the ionized calcium was less than 1.16 mmol/l and when signs and symptoms of neuromuscular irritability required treatment for less than six months, while permanent hypoparathyroidism was diagnosed when the treatment period exceeded six months. Postoperative calcium therapy was started only when the serum calcium levels were less than 1.16 mmol/l and when symptoms of hypocalcemia were present. The mean duration of hospital stay (hours) was also evaluated for each patient. Patients were clinically assessed postoperatively at 24, 48, 72 hours and on day 30 for the presence of Chvostek's and Trousseau's signs and other symptoms of hypocalcemia, such as peripheral or oral paresthesia, seizure, and laryngospasm. All patients underwent clinical and laboratory (ionized serum calcium assay) follow-up at 5 and 8 months postoperatively for potential permanent hypoparathyroidism.

Statistical analysis – mean patient age, operating time, hospital stay, serum ionised calcium, phosphatemia (preoperatively and postoperatively at 24, 48, 72 hours and 30 days) were evaluated and compared between the two groups using Student's *t*-test. Transient hypocalcemia was analyzed by means of the  $\chi^2$  test. Fischer's exact test was used for non-parametric data.

## Results

A prospective randomized study of 126 consecutive patients who underwent total thyroidectomy for euthyroid bilateral multinodular goiter was performed. In group 1, 63 patients underwent truncal ITA ligation: 16 men and 47 women, mean age  $37.2 \pm 9.1$ ). In group 2, 63 patients underwent ligation of the terminal ITA branches proximal to the thyroid capsule: 16 men and 47 women, mean age  $38.1 \pm 10.1$ ). In both groups, the preoperative mean values of ionised calcium and phosphoremia were similar (Table 1). Mean operating time (minutes) was shorter in group 1 than in group 2 ( $83.6 \pm 15.7$  [range 68–138] versus  $106.3 \pm 24.24$  [range 84–205]) ( $P < 0.05$ ). No postoperative recurrent laryngeal nerves injuries was observed.

Mean ionized calcium levels were significantly lower in the ITA truncal ligation group (group 1) than in group 2 patients at 24 hours ( $1.22 \pm 0.06$  vs.  $1.25 \pm 0.05$ ,  $P < 0.05$ ) and 48 hours after thyroidectomy ( $1.20 \pm 0.05$  vs.  $1.23 \pm 0.05$ ,  $P < 0.05$ ). However, no statistical difference in ionized calcium levels remained significant between the two groups at 72 hours and 30 days after surgery (Table 1). In addition, serum phosphate levels was significantly higher in group 1 at 24 hours ( $3.88 \pm 0.59$  vs.  $3.59 \pm 0.61$ ,  $P < 0.05$ ) and 48 hours after thyroidectomy ( $3.98 \pm 0.55$  vs.  $3.70 \pm 0.60$ ,  $P < 0.05$ ). Serum alkaline phosphatase levels were within the normal range and similar in both groups preoperatively, at 24, 48, 72 hours after thyroidectomy and on postoperative day 30.

Postoperative hypocalcemia was observed in 31 patients (24.6%) at 24 hours after thyroidectomy in all patients from both groups. Postoperative hypocalcemia occurred significantly more frequently in group 1 than in group 2 (33.3% vs. 15.8%,  $P < 0.05$ ) (Table 2). Mean postoperative

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