

## ORIGINAL ARTICLES

## THE IMPORTANCE OF THE LIGATION OF THE INFERIOR THYROID ARTERY IN PARATHYROID FUNCTION AFTER SUBTOTAL THYROIDECTOMY

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ARAÚJO-FILHO V J F de et al. - The importance of the ligation of the inferior thyroid artery in parathyroid function after subtotal thyroidectomy. *Rev. Hosp. Clín. Fac. Med. S. Paulo* 55 (4):113-120, 2000.

We prospectively studied the effects of the ligation of the inferior thyroid artery (ITA) on postoperative hypoparathyroidism in 48 patients who underwent functional subtotal thyroidectomy. Patients were randomized into two groups: A, with bilateral ligation of the ITA and B, without ligation of the ITA. Parathyroid function was checked preoperatively and after surgery by clinical examination and measurement of total calcium, intact PTH, urinary calcium, and AMPc.

**Results:** A significant incidence of postoperative hypocalcemia occurred: 17% in group A and 13% in B on the 4<sup>th</sup> postoperative day. Six months later, the incidence was 5% in Group A and 0% in Group B. These differences were not statistically significant between the two groups, and neither were any of the other clinical and laboratory observations.

**Conclusion:** The ligation of the ITA was not an important causal factor for the occurrence of postoperative hypocalcemia after subtotal thyroidectomy.

**DESCRIPTORS:** Thyroidectomy. Parathyroid glands. Hypoparathyroidism. Hypocalcemia. Surgery.

*“Thyroid vessels must be ligated somewhere. Should they be so ligated as not to cut off the blood supply of parathyroid glandules? Replying to this question is impossible without definite knowledge of the blood supply to these little bodies”*  
Halsted ; Evans - 1907<sup>1</sup>

Postoperative hypocalcemia is a relatively frequent situation after subtotal thyroidectomy for Graves' disease, with a related incidence of as high as 83%<sup>2-35</sup>. It can be transitory with regression in 6 months or, in some cases, permanent. It is a very unpleasant situation for the patient. When intensive, it can be life threatening and is therefore a very serious complication in view of the preoperative diagnosis. Some authors<sup>2, 7, 16, 35</sup> have questioned the bilateral ligation of the inferior thy-

roid artery (ITA) in subtotal thyroidectomy, which is recommended to decrease bleeding<sup>9, 36, 37, 38</sup>. It is known that almost all the blood supply to the four parathyroid glands comes from the ITA,<sup>10, 35, 39, 40</sup> so it is a logical inference that this procedure would increase postoperative hypocalcemia.

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We studied in a prospective and randomized trial the influence on the parathyroid function of bilateral ligation of the ITA in subtotal thyroidectomy for Graves' disease.

### CASUISTIC AND METHODS

Forty-eight consecutive patients underwent surgery for Graves' disease. Patients with toxic diffuse goiters were chosen because nodular goiters have

no homogeneous pattern of clinical presentation, surgical findings, nor more importantly, extent of thyroidec-tomy, which, in our opinion, would impair analysis because other factors contributing to hypocalcemia, such as direct intra-operative trauma, would be impossible to evaluate.

The patients were preoperatively randomized into two groups. In Group A, 24 patients underwent bilateral sub-total lobectomy, with the technique of capsular dissection, ligating the branches of ITA very close to the thyroid gland, and bilateral truncal ligation of the ITA<sup>1,36,41</sup>. In Group B, the surgery was the same, but without ligation of the ITA. The parathyroid glands were identified according to routine protocol, and the vascularity of the glands was evaluated at the end of the procedure. No glands required reim-planting.

All the patients had normal thyroid function with anti-thyroid medication. This control of hyperthyroidism was evaluated preoperatively by clinical examination and laboratory tests.

Parathyroid function was checked in all patients on 4 occasions: preopera-tively (-1PO), on the first and fourth day after surgery (1PO and 4PO) and at 6 months after the operation (6mPO), by clinical examination and laboratory data.

We looked for Chovstek signals pre-operatively because they occur in 5% to 15% of the normal population<sup>42, 43, 44</sup>.

Postoperatively, all patients were questioned for symptoms of hypocalcemia, such as: weakness, fatigue, ir-ritability, parastasis, cramps, anxiety, depression, and Chovstek and Trou-seau signals.

Laboratory tests were obtained on the 4 occasions by measurement of total calcium, phosphate, albumin, hema-tocrit, pH, and intact PTH, determined from fasting blood samples collected at 8 a.m. Urine tests of calcium, phos-phate, creatinine, and AMPc were also made at the same time, in the 24-hour urine samples.

Total calcium was corrected for al-bumin and pH, as is usually recom-mended<sup>9, 10, 19, 34, 45, 46, 47, 48, 49</sup>.

Hypocalcemia was defined for cor-rected calcium levels lower than 4mEq/l<sup>9, 16, 44, 50, 51</sup>.

Urinary calcium was corrected for urinary creatinine, for better evalua-tion<sup>52</sup>.

The statistical study, done by the Mathematics Institute of the University of São Paulo, was designed to compare the mean values of each laboratory pa-rameter at the 4 times in the same group, and between the groups. The significance level was 0.05.

## RESULTS

The mean age in Group A was 33.3 years, with an s.d. of 12.1. In Group B it was 31.8 years, with a s.d. of 10.1. In both groups 96% were female.

The mean preoperative value of al-bumin for the 48 patients was 4.6 g/dl and a pH 7.34.

As seen in Tables 1, 2 and in Fig-ure 1, the mean total and corrected cal-cium was lower for the immediate postoperative days in both groups, but there were no differences between groups.

The percentage of patients with postoperative hypocalcemia was very high in both groups, (Fig. 2), but again, no difference between groups was ob-served.

Only one patient of Group A and none in Group B had permanent hy-pocalcemia.

Intact PTH was measured at the 4PO and 6mPO only. The observed values showed an increase that was similar in both groups.

All the other laboratory parameters showed some expected variations but without significant difference between the groups.

Clinical evaluation showed that the signs and symptoms of hypocalcemia increased with time (Fig. 3) with a

**Table 1** - Laboratory data in Group A (with truncal ligation of the ITA). Mean (s.d.).

Group A	-1 PO	1 PO	4 PO	6m PO	Normal
Calcium	4.67(0.31)	4.40(0.42)*	4.36(0.52)*	4.63(0.40)	>4.0 mEq/l
Calcium (corrected)	4.61(0.32)	4.46(0.44)	4.36(0.59)	4.49(0.38)	>4.0 mEq/l
PO4	3.78(0.59)	3.52(0.61)	3.80(0.85)	4.01(0.74)	2.3-4.5mg/dl
PTH			21.2(11.4)	24.9(12.6)**	12-72pg/ml
Calcium/C (ur.)	0.11(0.07)	0.09(0.08)	0.17(0.13)	0.10(0.09)	<0.2
PO4 (ur.)	0.55(0.37)	0.66(0.42)	0.45(0.29)	0.52(0.31)	0.4-1.3g/24h
AMPc (ur.)	2577(2551)	2222(1798)	3275(3473)	2794(2494)	3340-5880nMol/24h
Hematocrit	41.75(3.67)	38.99(4.2)	37.82(3.7)*	39.30(4.1)	37-47%

\*= Significant difference comparing with -1 PO.

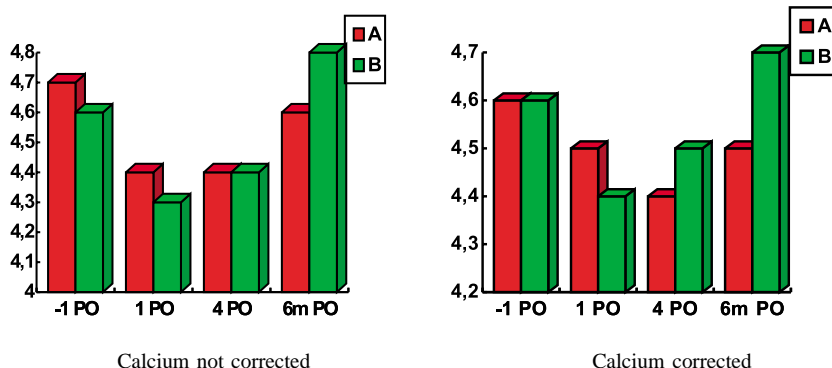
\*\*= Significant difference comparing with 4 PO.

**Table 2** - Laboratory data in Group B (without truncal ligation of the ITA). Mean (s.d).

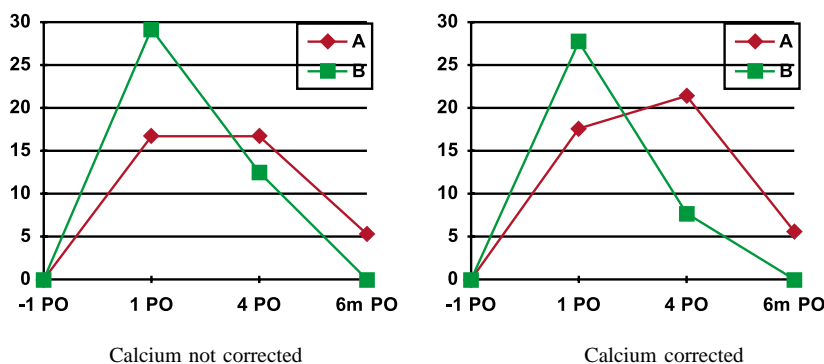
Group B	-1 PO	1 PO	4 PO	6m PO	Normal
Calcium	4.61 (0.30)	4.25 (0.58)*	4.44 (0.52)*	4.63(0.40)	>4.0 mEq/l
Calcium (corrected)	4.65(0.34)	4.42(0.48)*	4.54 (0.42)	4.65 (0.23)	>4.0 mEq/l
PO4	3.81 (0.60)	3.80 (0.71)	3.96 (0.58)	3.51 (0.62)	2.3-4.5mg/dl
PTH			17.0 (12.3)	24.2(13.8)**	12-72pg/ml
Calcium/C (ur.)	0.12(0.06)	0.10(0.06)	0.09(0.07)	0.09(0.03)	<0.2
PO4 (ur.)	0.42(0.23)	0.47(0.24)	0.66(0.48)	0.78(0.49)	0.4-1.3g/24h
AMPc (ur.)	2616(2780)	1916(1505)	3114(2395)	2962(2883)	3340-5880nMol/24h
Hematocrit	41.76(5.53)	38.33(5.0)	36.28(4.7)*	38.85(5.7)	37-47%

\*= Significant difference comparing with -1 PO.

\*\*= Significant difference comparing with 4 PO.



**Figure 1** - Mean values of total calcium and corrected calcium in both groups at the 4 times. No significant difference between the groups was observed.



**Figure 2** - Percentage of patients with postoperative hypocalcemia in both groups at the 4 times. No significant difference between the groups was observed.

higher incidence in the late period. Again, there were no differences between the groups.

When we matched the levels of calcemia with clinical signs and symp-

toms in the early postoperative period, there was a good relationship between symptomatic patients and calcium levels. However, most patients with hypocalcemia were asymptomatic

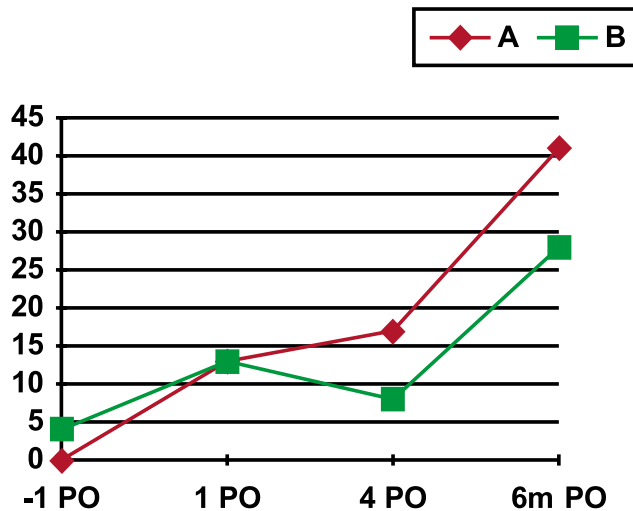
(81.8%). In the late period, only one patient was hypocalcemic, and she was asymptomatic. Ten other patients complained of symptoms indicating hypocalcemia; all of them had normal corrected calcium.

**DISCUSSION**

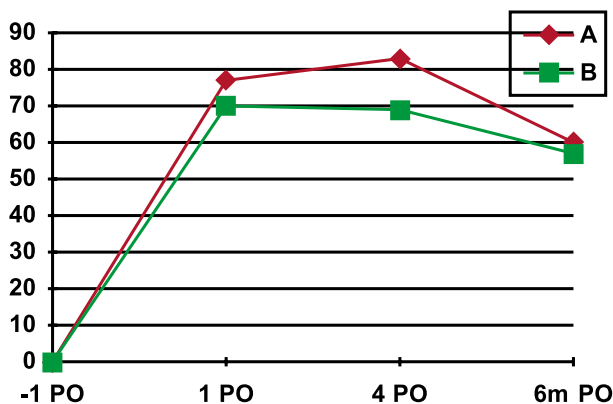
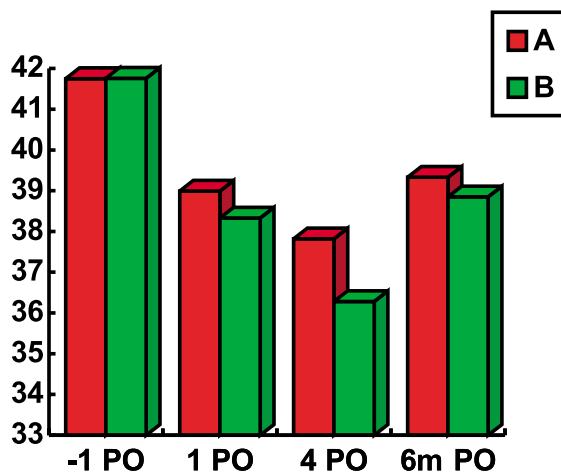
Subtotal thyroidectomy is a very good therapeutic option for patients with toxic diffuse goiter. It is a safe and fast method with very low mortality and excellent results<sup>11, 34, 53, 54,55, 56, 57</sup>. The main complications of this operation are related to the recurrent<sup>58</sup> and superior<sup>59</sup> laryngeal nerves and the parathyroid glands. When subtotal thyroidectomy is performed by an experienced surgeon, the incidence of these complications is very low.

Transient hypoparathyroidism after a subtotal thyroidectomy has an incidence as high as 83%<sup>2-35</sup>. Most authors believe that the hypofunction of these glands occurs because of ischemia, secondary to ligation of the ITA. This is a logical inference, since we know that the blood supply to the parathyroid glands comes mainly from this vessel.

Many papers<sup>2, 10, 13, 16, 17, 19, 35, 43, 63, 64</sup> recommend not ligating the ITA. The ligation should be made as distal as possible, near the capsule of the thy-



**Figure 3** - Percentage of patients with symptoms and/or signals of hypocalcaemia in both groups at the 4 times. No significant difference between the groups was observed.



**Figure 4** - Hematocrit values and percentage of patients with low Ht in both groups at the 4 times. No significant difference between the groups was observed.

roid gland. On the other hand, some authors<sup>9, 11, 12, 37, 38</sup> recommend ligating the ITA, arguing that the risks of more intra-operative bleeding and damage to the recurrent laryngeal nerve are higher, and the benefits are theoretical and not proven.

We chose to limit our study to toxic diffuse goiter, because in this kind of thyroid surgery, the risk of direct damage of the parathyroid gland or its thin vascularization is about the same in all patients. This is not true in other bilateral procedures made for nodular goiters or malignant tumors.

The high incidence (30%) of post-operative hypocalcemia (Fig. 1) is similar to that reported by others<sup>9, 51</sup>. It is statistically different from the uncorrected calcemia in both groups when compared to preoperative levels. With the corrected calcemia, the differences were lower and not statistically significant (Fig.1). Ligation of the ITA was apparently not the cause of the hypocalcemia, since there was no difference between the two groups. This was the same conclusion of Drezner et al.<sup>65</sup>, Cakmakli et al.<sup>48</sup>, Kalliomaki et al.<sup>60</sup>, and Nies et al.<sup>66</sup>. Only one patient became definitively hypocalcemic in Group A, but this occurrence was not statistically significant.

Another important parameter of parathyroid function is the level of intact PTH<sup>44,61,62, 67, 68, 69,70,71,72</sup>. We have not seen the often-reported undetectable levels,<sup>70,72,73</sup>. All of our hypocalcemic patients had low levels of PTH. On the other hand, 10.7% of the levels were low in normal calcemic patients. This is also reported by Endres et al.<sup>72</sup> and shows that intact PTH is a sensitive method but is too nonspecific for the diagnosis of hypoparathyroidism. Comparing the PTH levels at the 4PO and 6mPO (Tables 1 and 2), we can see a statistically significant increase in both groups, but again, there was no difference between groups; therefore, ligation of the ITA did not

seem related to the alterations of the PTH.

All other laboratory data showed expected variations, but they were too nonspecific. We did not see a statistically significant difference between the groups at any time.

A very interesting observation was the decrease of hematocrit levels in the immediate postoperative periods in both groups, showing a statistical significance at the 4PO when compared to preoperative levels. The number of patients with low hematocrit levels was high at 4PO (83% and 69% respectively in Groups A and B). In the later period, about 60% of patients in both groups had not reached preoperative levels (Fig 4). This shows that even with all the usual operative care of an experienced surgical team, intra-operative bleeding in subtotal thyroidectomy for Graves' disease is frequent and intense. In contrast with reports from some authors<sup>9, 36, 37, 38</sup>, the bilateral

truncal ligation of the ITA did not reduce the blood loss.

Another very significant observation is the low reliability of clinical observations when evaluating postoperative hypocalcemia in thyroidectomies. It has been reported that most hypocalcemic patients are asymptomatic<sup>11, 16, 44, 74, 75, 76, 77</sup>. This was also true in our study, since 77.8% of our hypocalcemic patients had no symptoms. On the other hand, when symptomatology occurred in the early postoperative period, we observed low or very close to low normal calcium levels. We have to agree with other authors<sup>11, 16, 20, 43, 63, 77</sup> who recommend routine determination of corrected total or ionized calcium in the early postoperative period after thyroidectomies because of the frequent absence of clinical manifestations in the presence of hypocalcemia.

In the late postoperative period, we saw a significant increase of symptoms even in 32.3% of patients with normal

calcemia. This curious finding can be easily explained by the nonspecific nature of these symptoms and the possibility that they were suggested to the patients by insistent interrogation, as has also been postulated by other authors<sup>75, 76, 77, 78</sup>. The only definitively hypocalcemic patient was asymptomatic, as they usually are<sup>16, 74</sup>. At this time, we think that it is very important to confirm the clinical suggestion of hypocalcemia with determination of calcium levels to avoid unnecessary treatment and, more importantly, to prevent the cataracts that occur at a high incidence (up to 50%) in hypocalcemic patients<sup>79, 80, 81, 82</sup>.

We do not perform, or recommend, bilateral truncal ligation of the ITA in subtotal thyroidectomy for Graves' disease, since we think it is not necessary, but our results, as well as those of others, indicate that the ligation of the ITA does not appear to alter the function of the parathyroid glands in these operations.

## RESUMO

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ARAUJO-FILHO V J F de e col. – A importância da ligadura da artéria tireoidiana inferior na função paratireoidiana após tireoidectomia subtotal. *Rev. Hosp. Clín. Fac. Med. S. Paulo* 55(4):113-120, 2000.

Com o objetivo de observar os efeitos da ligadura da artéria tireoidiana inferior (ITA) no hipoparatiroidismo, 48 pacientes submetidos à tireoidectomia subtotal funcional foram estudados de forma prospectiva. Dois grupos

foram randomizados, A: com a ligadura troncular bilateral da ITA e B: sem a ligadura troncular da ITA.

A função paratireoidiana foi verificada no período pré-operatório e após a cirurgia através de exame clínico e dosagens de cálcio total, PTH, cálcio urinário e cAMP.

Os resultados demonstraram incidência importante e significativa de hipocalcemia pós-operatória, de 17% no grupo A e 13% no grupo B no 4º PO. Seis meses após, a incidência foi

de 5% no grupo A e 0% no grupo B. Estas diferenças não foram estatisticamente significativas entre os dois grupos, nem nenhum dos outros dados clínicos ou laboratoriais estudados.

Concluimos que a ligadura da ITA não é um fator causal importante de hipocalcemia pós-operatória após tireoidectomia subtotal.

**DESCRITORES: Tireoidectomia. Glândulas paratireóides. Hipoparatiroidismo. Hipocalcemia. Cirurgia.**

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