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## The impact of thyroidectomy on parathyroid glands: A biochemical and clinical profile

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**ABSTRACT.** *Introduction:* An evaluation of PTH levels during thyroid surgery may reflect the functional status of the parathyroids and be useful in identifying patients at risk for hypocalcemia. This study aims to monitor the parathyroid function during total thyroidectomy through intra-operative serial samples for calcium and PTH. *Materials and methods:* Forty-seven patients undergoing total thyroidectomy for different diseases were selected for the study. Patients underwent serum PTH and calcium sampling at the induction of anesthesia (T0) and after the first (T1) and the second (T2) lobectomy. Serum calcium was also drafted 24 h after the operation. *Results:* Mean PTH at T0, T1, and T2 was, respectively: 32.1 pg/ml, 19.6 pg/ml, and 11.5 pg/ml. PTH was significantly higher at T0 when compared to T1 ( $p < 0.0001$ ). It was also

significantly higher at T1 than at T2 ( $p < 0.0001$ ). At T1 PTH levels were below the normal range in 20/47 cases (42.5%) and at T2 in 31/47 cases (66%). Twenty-four h after surgery, 8 patients (17%) demonstrated a biochemical hypocalcemia. A PTH value at T0 in the upper ( $>70$  pg/ml) or in the lower ( $<20$  pg/ml) limits of the normal range was statistically related to post-operative hypocalcemia ( $p = 0.017$ ). *Discussion:* The study seems to confirm that serum PTH during thyroidectomy does not represent a sensitive tool in precociously identifying hypocalcemic patients. Nevertheless, before surgery, a PTH concentration at the higher or lower normal limit may help to identify patients "at risk" of developing hypocalcemia. (J. Endocrinol. Invest. 30: 666-671, 2007)

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### INTRODUCTION

Intra-operative PTH monitoring is commonly used in patients affected with hyperparathyroidism to demonstrate the surgical removal of all the hypersecreting tissue in almost-real time, since PTH half-life is very short (1, 2). An evaluation of PTH levels during thyroid surgery may also reflect the functional status of all parathyroid tissue in the neck and may therefore be useful in the early identification of patients who will develop hypocalcemia, thus preventing the onset of hypocalcemic symptoms, as already postulated by other authors. Unfortunately there is no general agreement upon the real effectiveness of dosing PTH after thyroidectomy: in particular, the

set-point in terms of timing has a great variety according to the same authors (3-10). This study aims to monitor the parathyroid function during total thyroidectomy, indicated for different diseases, through different samples for calcium, corrected for albumin, and PTH drafted at the start of the procedure and after the first and second lobectomy. The results of the samples were then related to the post-operative calcemia.

### MATERIALS AND METHODS

Among 77 normocalcemic patients undergoing total thyroidectomy by one single surgeon (P.B.) in our department who were selected for this study, 47 were evaluated for final analyses (12 males and 35 females; mean age 45.3 yr, range 18-70 yr). Patients were excluded from the study when they demonstrated low levels of vitamin D, when they were under treatment with drugs affecting bone metabolism (bisphosphonates or vitamin D), when less than 4 parathyroid glands were identified during the operation and when one or more parathyroids were re-

*Key-words:* Thyroid surgery, thyroidectomy, intra-operative parathyroid hormone sampling, hypocalcemia.

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moved or autotransplanted. All patients were euthyroid at the time of the operation and demonstrated a pre-operative PTH in the normal range. Patients underwent serum PTH and calcium sampling from peripheral blood at the induction of anesthesia (T0), after the first (T1) and the second (T2) lobectomy. To allow a correct monitoring of parathyroid function, T1 and T2 samples were always drawn at least 5 min after the dissection of the two parathyroid glands of the ipsilateral side.

Indications for surgery were: multinodular goiter (no.=26), multinodular toxic goiter (no.=5), Graves' disease (no.=7), microfollicular nodule or Hurthle cell tumor requiring total thyroidectomy (no.=2), differentiated thyroid carcinoma (no.=7). All patients underwent total thyroidectomy. No patient affected with papillary or follicular thyroid carcinoma underwent dissection of the central neck compartment. Four patients underwent a minimally invasive video-assisted thyroidectomy (11).

Calcium levels were corrected for albumin. PTH was measured using a 2-site chemiluminescence immunoassay (Nichols Institute diagnostic, San Juan Capistrano, CA, USA. Normal range: 15-75 pg/ml; calculated sensitivity: 1.0 pg/ml; lower limit: 0.9 pg/ml). Statistical analysis was performed using the StatView Software, version 5.0.1 and the single tests used are further specified in the results section.

## RESULTS

Mean PTH and serum calcium at T0, T1, and T2 are reported in Table 1. PTH decreased gradually from T0 to T2, while no significant modifications were observed at the same times of serum calcium levels. PTH levels at T1 were significantly lower than at T0 ( $p<0.001$ ) and at T2 were significantly lower than at T1 ( $p<0.001$ ), using the paired samples t-test. PTH levels were below the normal range in 20 out of 47 cases (42.5%) at T1 and in 31 out of 47 cases (66%) at the end of the operation (T2). Only one patient with a low (13.6 pg/ml) PTH at T1 showed a normal value (17.4 pg/ml) at T2 while the remaining 19 patients with a PTH below the

normal range at T1 confirmed an abnormal PTH level at T2. The different profiles of the PTH decay are visualized in Figure 1.

Twenty-four h after the operation, 8 patients (17%) demonstrated a biochemical hypocalcemia (mean blood calcium: 7.5 mg/dl, range: 7.0-7.8), which was symptomatic in 4. No patient developed hypocalcemia more than 24 h after surgery. All hypocalcemic patients were given calcitriol and oral calcium supplementation; at follow-up, 6 months after surgery, no patient required treatment for hypocalcemia. The biochemical and clinical features of these patients (the hypocalcemic group, HG) are summarized in Table 2.

The biochemical profiles of all patients have been further investigated with regard to the different thyroid diseases (Fig. 2). Patients affected with toxic diffuse goiter (TDG) demonstrated a greater decrease of PTH levels from T0 to T2 when compared to patients affected with other thyroid diseases ( $p=0.033$ ), result obtained with the unpaired samples t-test. Moreover, patients affected with differentiated thyroid carcinoma (DTC) when compared to other patients, demonstrated statistically significant lower levels of PTH at T2 (mean: 4.6 vs 13.0 pg/ml, SD: 6.28 vs 10.3;  $p=0.025$ ). No other differences have been demonstrated between patients affected with different thyroid diseases (data not reported but available upon request to the authors).

When comparing patients belonging to the HG with all other patients, no significant difference has been obtained as for: age at operation, gender, thyroid disease, pre-operative levels of serum calcium (data not reported but available upon request to the authors). Even the difference between the starting and final PTH levels (T0-T2) is not significant between the two groups (Fig. 3).

Using the ROC curve we obtained the best sensitivity (83%) and specificity (62.5%) (odds ratio=8.06) for PTH values between 20 and 70 pg/ml. When evaluating the post-operative outcome it was demonstrated that a starting value in the upper ( $\geq 70$  pg/ml) or in the lower ( $\leq 20$  pg/ml) limits of the normal range is

Table 1 - Mean and median results obtained at the different times of the operation.

	T0 (mean/median)	T1 (mean/median)	T2 (mean/median)	P
PTH	32.1±14.6 (Range: 15.1-70.6)	19.6±12.8 (<0.9-60.0)	11.5±10.0 (<0.9-40.6)	T0-T1: <0.001 T1-T2: <0.001
Ca	9.2/9.3 (8.2 - 10.0)	9.1/9.2 (8.2 - 10.0)	9.1/9.2 (8.2 - 10.0)	ns

T0: at induction of anesthesia; T1: first lobectomy; T2: second lobectomy.

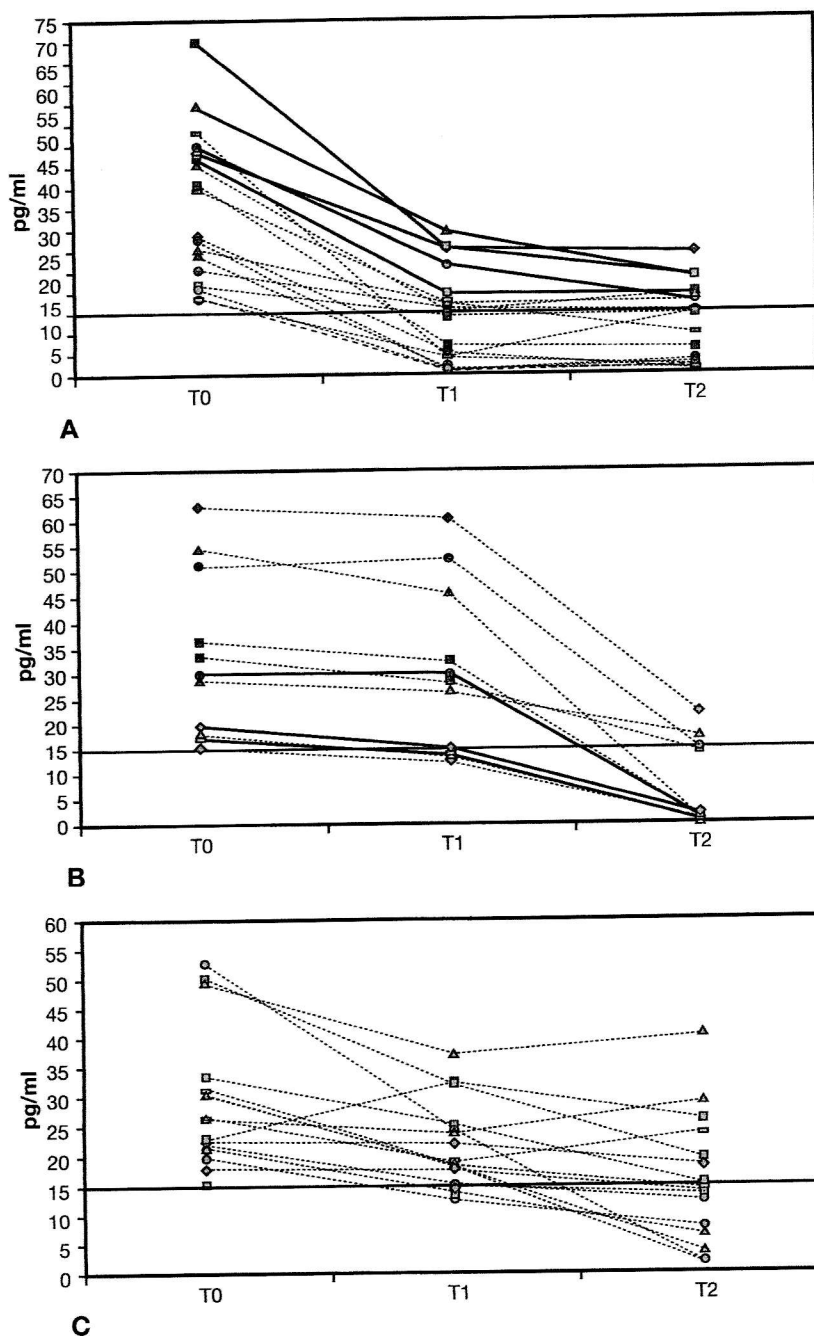


Fig. 1 - The different profiles of PTH decay in our series of patients: the first group (A), composed of 19 patients demonstrates the sharper decrease of PTH after the first lobectomy; the second group (B), composed of 12 patients, after the second lobectomy. The third group (C, 16 patients) is composed of the remaining patients. Thicker lines evidence patients with a hypocalcemic outcome. It is worth noting that patients who will develop hypocalcemia do not demonstrate a "typical" decay profile. The bold line indicates the lower limit of the normal range of PTH. T0: at induction of anesthesia; T1: first lobectomy; T2: second lobectomy.

statistically related to post-operative hypocalcemia (Fisher's exact  $p$ -value = 0.017).

#### DISCUSSION

The study confirms that serum calcium level does not represent a sensitive tool in precociously

identifying hypocalcemic patients since the concentration at the beginning and at the end of the surgical procedure is almost identical in all patients.

On the other hand, PTH levels demonstrate a significant drop in concentration from the start to the end of the procedure, thus confirming the reliable

Table 2 - Demographic, clinical and biochemical profile of the 8 patients with post-operative hypocalcemia.

Patients	Age	Diagnosis	Ca T0	PTH T0	PTH T1	PTH T2	Ca D1
PI	29	DTG	9.5	29.5	29.4	1.1	7.0
PII	25	DTG	9.1	70.6	27.4	21.1	7.5
PIII	56	MNG	9.3	48.6	23.7	16.1	7.8
PIV	59	MNG	9.1	57.0	30.6	20.9	7.6
PV	55	MNG	9.4	47.1	27.0	26.2	7.8
PVI	34	PTC	8.2	16.6	13.5	<0.1	7.6
PVII	52	PTC	9.1	19.3	14.4	1.5	7.5
PVIII	66	RMNG	8.2	15.1	14.2	14.2	7.7

DTG: diffuse toxic goiter, MNG: multinodular goiter, PTC: papillary thyroid carcinoma, RMNG: recurrent multinodular goiter. Ca T0: pre-operative blood calcium, Ca D1: blood calcium 24 h after the operation. PTH T0: PTH at induction of the anesthesia, PTH T1: PTH 2 to 5 minutes after the first lobectomy, PTH T2: PTH 2 to 5 minutes after total thyroidectomy.

role of PTH in monitoring parathyroid function also during thyroidectomy. The significant decrease of PTH demonstrated during the operation in almost every patient of our series reveals that in patients undergoing thyroidectomy, parathyroid function is impaired by the surgical manipulation of the glands, reaching levels under the normal range in as much as 66% of patients. When taking into exam the measurements after the first lobectomy (T1), we can consider that in 42% of cases the PTH levels have already reached a concentration below the lower limit. This allows us to speculate that even the manipulation of only 2 parathyroids may

have an impact on the PTH secretion, especially considering that all patients had 4 parathyroids visualized.

Besides, the sharper drop obtained in patients affected with TDG can be explained by the higher, though not significantly evident, pre-operative levels of PTH (mean PTH at T0 in TDG patients: 40.5 pg/ml vs 31.2 pg/ml in patients affected with other diseases). Furthermore, even if our data show that the parathyroid function might seem more impaired in patients undergoing surgery for differentiated thyroid carcinoma, maybe suggesting a more aggressive operation, this speculation cannot be confirmed

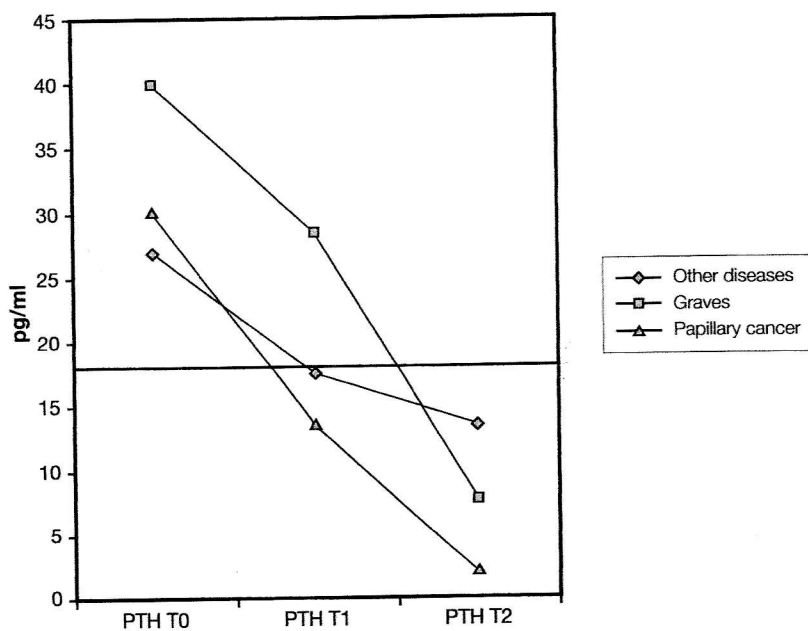


Fig. 2 - The different profiles of PTH mean decay according to three classes of thyroid diseases: Graves' disease, thyroid cancer and other diseases. T0: at induction of anesthesia; T1: first lobectomy; T2: second lobectomy.

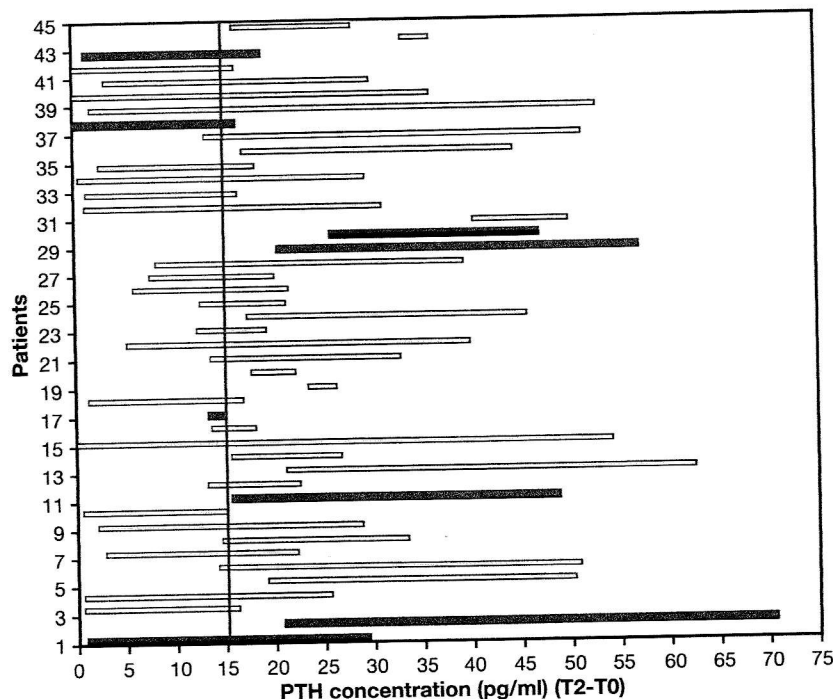


Fig. 3 - The difference in PTH concentration from T0 (at induction of anesthesia) to T2 (second lobectomy). The bold line indicates the lower limit of the normal range of PTH. Hypocalcemic patients are evidenced in black. Patients who will develop hypocalcemia do not demonstrate a significant difference between T2 and T0 when compared to normocalcemic patients.

since hypocalcemic events in these patients are no longer frequent.

In our series, 8 patients (17%) demonstrated biochemical hypocalcemia 24 h after thyroidectomy; this result is in line with those described in the literature, in which the rate of transient hypocalcemia after thyroidectomy ranges from 1.7% to more than 30% (12-18). Among the 8 hypocalcemic patients, only 4 demonstrated a PTH under normal levels at the end of the procedure, confirming that intra-operative PTH assay immediately after the thyroidectomy cannot be considered useful in assigning the patient to a "high-risk" group of developing hypocalcemia. We can also add that, immediately after the operation, a PTH level in the normal range cannot be considered a safe parameter in terms of developing post-operative hypocalcemia, as described by other authors (19).

The only feature that we found significantly related to post-operative hypocalcemia is the pre-operative PTH level: a hormonal concentration in the higher or lower normal limit might help to identify patients "at risk" of developing hypocalcemia after surgery. In conclusion, from the results of this study we can affirm that the parathyroid function is impaired in almost every patient submitted to thyroidectomy, as demonstrated by the significant drop of PTH from the start to the end of the operation. Moreover, since a significant drop in PTH is already demonstrated af-

ter the first lobectomy in almost half of the cases, we can postulate that one or two parathyroids can influence the secretion of PTH as a whole. Nevertheless, the parathyroid function is normally impaired for a very short time, since out of the 60% of patients who demonstrate a PTH level under the normal range immediately after the thyroidectomy, only a minority (17%) developed a transient hypocalcemia. Finally, in our series, only a pre-operative factor such as the PTH concentration can identify patients "at risk" of developing post-operative hypocalcemia, since neither intra-operative nor post-operative PTH levels are significantly related to hypocalcemia. A pre-operative evaluation of PTH may then be suggested to associate patients to a "high-risk" category of developing post-operative hypocalcemia. Further studies, performed on wider series of patients, have yet to be made to confirm the reliability of this latter result.

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