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Analysis of the role of thyroidectomy and thymectomy in the surgical treatment of secondary hyperparathyroidism☆

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ABSTRACT

Purpose: Parathyroidectomy can be subtotal or total with an autograft for the treatment of renal hyperparathyroidism. In both cases, it may be extended with bilateral thymectomy and total or partial thyroidectomy. Thymectomy may be recommended in combination with parathyroidectomy in order to prevent mediastinal recurrence. Also, the occurrence of thyroid disease observed in patients with hyperparathyroidism is poorly understood and the incidence of cancer is controversial. The aim of the present study was to report the experience of a single center in the surgical treatment of renal hyperparathyroidism and to analyse the role of thyroid and thymus surgery in association with parathyroidectomy.

Materials and methods: We analysed parathyroid surgery data, considering patient demographics, such as age and gender, and surgical procedure data, such as type of hyperparathyroidism, associated thyroid or thymus surgery, surgical duration and mediastinal recurrence. Histopathological results of thyroid and thymus samples were also analysed.

Results: Medical records of 109 patients who underwent parathyroidectomy for secondary hyperparathyroidism were reviewed. On average, thymectomy did not have impact on time of parathyroidectomy ($p = 0.62$) even when thyroidectomy was included ($p = 0.91$). Intrathymic parathyroids were detected in 7.5% of the thymuses removed and papillary carcinoma was detected in 20,8% of thyroid tissue samples. Two patients showed recurrence of supernumerary intrathymic parathyroids and a single case of mediastinitis was observed.

Conclusions: Parathyroidectomy with thymectomy and/or thyroidectomy has an important role in the treatment of renal hyperparathyroidism since thyroid cancer can frequently occur and require surgery. Thymectomy should be considered to avoid recurrence and a risky re-operation.

1. Introduction

Hyperparathyroidism in chronic renal disease (CRD) occurs as a result of low levels of calcitriol, which promotes hypocalcaemia and is also intensified by hyperphosphatemia. In this condition, there is an increased release of parathyroid hormone (PTH) due to a constant effect on calcitriol and calcium receptors, which renders the glands refractory to increases of calcium levels [1–4]. Patients for whom drug therapy fails to reduce PTH levels, the remaining therapy is parathyroidectomy (PTX) [5].

Parathyroidectomy can be subtotal or total with an autograft. In both cases, parathyroid surgery may be associated with bilateral cervical thymectomy [2] and/or thyroidectomy [6,7]. The thymus is the most common site of occurrence of supernumerary parathyroid tissue or ectopic glands [8]. Thus, thymectomy may be recommended in association with PTX to prevent mediastinal recurrence [8–14]. The concomitant thyroid disease observed in patients with hyperparathyroidism is poorly understood and the incidence of thyroid cancer in these patients is controversial. It has been suggested that this association is not random as was previously thought [4–7]. If this association is confirmed, thyroidectomy would be considered for treatment and prevention of cancer.

The aim of the present study was to report the experience of a single center with the surgical treatment of hyperparathyroidism in CRD, considering the roles of thyroid and thymus in a concomitant approach.

☆ There are no potential or real conflicts of interest.

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2. Methods

The medical records of patients submitted to subtotal or total parathyroidectomy with autograft for hyperparathyroidism between 2008 and 2013 were analysed. Patient data such as age and gender, preoperative diagnoses such as secondary or tertiary hyperparathyroidism, thyroid nodule investigation according to American Thyroid Association criteria were reviewed. Fine needle aspirations guided by ultrasound were done by radiology team. All patients had parathyroid scynthygraphy Sestamibi as a preoperative exam localization. Surgical data such as associated thyroid or thymus surgery, time of surgery and mediastinal recurrence were reviewed. Histopathologic results of thyroid and thymus samples were also analysed. PTH levels were measured before and 6 months after surgery to assess the success of the procedure. The study was approved by the Research Ethics Committee of the Institution.

Four groups were compared to determine the influence of thymectomy and thyroidectomy on surgery duration: standard parathyroidectomy (group A) and parathyroidectomy/thymectomy (group B). Since many patients underwent two thyroidectomy procedures, we also compared a group of parathyroidectomy/thyroidectomy (group C) and parathyroidectomy/thyroidectomy/thymectomy (group D). Time of surgery was measured in minutes, and the mean of each group of patients was compared. Statistical analysis was performed by the *t*-test to compare the duration of surgery in the different groups using GraphPad Prism software.

3. Results

Data of 109 patients submitted to renal PTX were analysed. Patients (51 men and 58 women) were 32–57 years old [mean (x) ± SD = 46 ± 7.8 years]. Patients diagnosed with secondary hyperparathyroidism had mean calcium levels of 1.17 ± 0.25 mg/dl and mean PTH levels of 1930.3 ± 595.68 pg/ml. Of these patients, nine underwent total thyroidectomy, due suspect nodules; 16 underwent partial thyroidectomy, 4 for unilateral thyroid nodule, 8 with intent to warrant margins of resection and 5, because one or more parathyroid was not found (Table 1). In patients diagnosed with tertiary hyperparathyroidism, the mean calcium level was 1.49 ± 0.26 mg/dl and the mean PTH level was 969 ± 899 pg/ml. Of these, only one patient underwent total thyroidectomy and 3 underwent partial thyroidectomy. No patients were taking calcimimetcs drugs before surgery, since it was not available in Brazilian public health system at the moment of the study. On patients also submitted to thyroidectomy, five patients had temporary unilateral recurrent laryngeal nerve palsy.

The mean duration of surgery was compared between the group of patients exclusively submitted to standard PTX and a group of patients who were submitted to PTX plus thymectomy. Standard PTX lasted 135.7 ± 58.3 min, and PTX associated with thymectomy lasted 129.2 ± 46.2 min. Specific analyses were carried out in patients submitted to associated thyroidectomy. Analysis of the group with a thyroid approach showed that PTX alone lasted 185.5 ± 93.4 min and PTX associated with thymectomy lasted 182.1 ± 55.1 min (Table 2). In both groups, thymectomy did not affect the duration of surgery ($p = 0.62$ for PTX alone and $p = 0.91$ for PTX associated with thymectomy).

Table 2
Comparison of the duration of surgery among the groups submitted to parathyroidectomy (PTX) (A), to PTX plus thymectomy (TMX) (B), to thyroidectomy (TRX) (C) or to both procedures (D).

Duration of surgery (minutes)	Without TRX	With TRX
PTX	A = 59 (135.7 ± 58.3)	C = 10 (185.5 ± 93.4)
PTX/TMX	B = 26 (129.2 ± 46.2)	D = 14 (182.1 ± 55.1)

Table 3
Histological results of the excised thyroid and thymus.

Histopathologic results			
Thyroid		Thymus	
Thyroid without abnormalities	6	Thymus without abnormalities	37
Goitre	6	Intrathymic parathyroids	3
Thyroiditis	4		
Papillary carcinoma	5		

Biopsy results revealed the presence of three intrathymic parathyroids among the 40 patients who underwent prophilactic thymectomy. Patients with a preoperative diagnosis of mediastinal parathyroid were not considered. Among the 24 patients who underwent thyroidectomy, we found six goitres, four cases of thyroiditis and five papillary carcinomas (Table 3). Size nodules of Papillary thyroid carcinomas ranged from 0.8 cm a 2.2 cm in greater diameter, being 4 T1N0MO and 1 T2N0 M0. One patient had a carcinoma of 1,1 cm at the superior right lobe and a 0,2 cm microcarcinoma in the left lobe. The second patient had a 2,2 cm carcinoma in the right lobe and a 0,2 cm microcarcinoma in the left lobe. The third patient had 2 carcinoma nodules of 0,6 cm and 0,1 cm in the left lobe and also a 0,1 cm microcarcinoma in the right lobe. In this patient was detected a metastasis inside the thymectomy. The fourth patient had a 0,9 cm carcinoma in the posterior face of left lobe and a 0,8 cm carcinoma in the right lobe. The fifth patient had T1 carcinoma in the right lobe. Three patients who were not submitted to prior thymectomy had mediastinal recurrence and required reoperation.

4. Discussion

The approach to the thyroid gland in the surgical treatment of secondary hyperparathyroidism is a frequent occurrence and should be considered during the preoperative evaluation. The identification of thyroid nodules during sonographic evaluation of the parathyroid glands provides a preliminary assessment and permits an adequate surgical program. Most authors agree that thyroid micronodules should not be analysed for cytology. However, it is necessary to decide whether micronodules should be punctured in patients who will undergo PTX, considering the possibility of reoperation with an increased risk of a bilateral approach and the risk of malignancy.

Papillary carcinomas were identified in 20.8% of the thyroids removed from the present patients. It is noteworthy that the diagnosis of malignancy was not made in the presurgical evaluation of any patients. Thus, the incidence of papillary carcinoma was higher than expected even when compared to thyroid analysis in the autopsies of individuals

Table 1
Preoperative calcium ion and parathyroid hormone (PTH) levels in patients with secondary and tertiary hyperparathyroidism and the type of thyroidectomy performed. Normal Values: *1.12–1.32 mmol/l; **8–70 pg/ml. PTX – parathyroidectomy.

Hyperparathyroidism type	PTX	Calcium (mg/dl)*	PTH (pg/ml)**	Total thyroidectomy	Partial thyroidectomy
Secondary	91	1.17 ± 0.25	1930.3 ± 595,68	9	16
Tertiary	18	1.49 ± 0.26	969 ± 899	1	3

whose cause of death is not connected to the thyroid gland. Some authors reported thyroid carcinomas in 2% to 17% of patients with secondary hyperparathyroidism [15–17]. On this basis, the present data corroborate previous studies that identified an increased risk of papillary carcinoma in individuals with CRD [6]. Although we have not analysed all patients included but only those underwent thyroidectomy.

Although most thyroidectomy patients had thyroid nodules, some operated patients had a normal thyroid. It is likely that the position of the parathyroid gland influenced the surgeon in the decision to remove the gland. Parathyroid glands usually have an intrinsic relationship with thyroid tissue, often making it impossible to remove the diseased gland safely regarding the margins of resection. Closely attached glands without a dissection plane favour the decision to remove the thyroid lobe. Moreover, the lack of identification of one or more parathyroid glands may justify thyroid gland removal so that intrathyroidal parathyroid glands will be removed, preventing the persistence of hyperparathyroidism.

In the present study, three of the 40 patients who underwent thymectomy had an intrathymic parathyroid. Those parathyroid glands were not identified in prior investigation by scynthygraphy. Although it is considered the main exam to ectopic parathyroid investigation, authors have been found low accuracy in identify all hyperplasic glands. This finding is lower compared with data published by other authors who reported a detection rate of up to 15% of intrathymic glands [8,9]. This discrepancy can occurs maybe because this is a retrospective study based on partial thymectomy, differently of other studies based on total thymectomy or studies based on corpse dissection, where all thymus can be valued. However, among patients who did not undergo thymectomy, three subjects had relapsed or persistent hyperparathyroidism. One patient had persistent hyperparathyroidism duo to an intrathymic mediastinal parathyroid and underwent re-operation twice. Another patient presented mediastinitis as a postoperative complication and required drainage and antibiotic administration. A third patient underwent two operations to remove mediastinal parathyroid tissue, but without reduction of PTH levels, suggesting a likely mediastinum parathyromastosis. This demonstrates that mediastinal transcervical reoperations may yield unsatisfactory results with a high risk of complications and failure.

The thymus approach during PTX has been controversial. Some authors recommend thymectomy to reduce the risk of persistence and recurrence of hyperparathyroidism from an intrathymic supernumerary gland. Other authors perform the procedure in cases of multiple endocrine neoplasias at risk of thymoma development, counterindicating the procedure in chronic renal patients. Some surgeons do not perform the procedure in order to reduce the surgical time. Our study suggests that the duration of surgery does not seem to be affected by the association of thymectomy. Bilateral cervical thymectomy is a relatively quick procedure when performed by experienced surgeons. It is likely that the differences in the patients studied were influenced by the location of the parathyroid glands. Topical parathyroid glands in the usual position tend to be identified and removed quickly, whereas ectopic glands require further neck exploration and consequently a longer surgical time. The thyroid gland approach requires a longer surgical time since it requires identification and careful dissection of the recurrent laryngeal nerve [2].

This is retrospective analysis of thyroid and thymus surgery recommendation in patients with secondary and tertiary hyperparathyroidism. Since this is a controversial issue, there was not a uniform criteria between different surgeons. The decision to make a resection of thyroid was made before or during surgery. Ultrasound findings of thyroid nodules or suspect cytology of malignancy made possible a preoperative recommendation of associated thyroid surgery. However patients with normal thyroid and intraoperatively findings of closely attached parathyroids without a dissection plane favour the decision to remove the thyroid lobe. Thymectomy, in our center, were recommended when four parathyroid were not found in the neck. More recently, thymectomy has been recommended in all parathyroidectomy.

The choice of clinical measures for previous assessment of all thyroid nodules and a better standardized histopathological analysis of the thymus removed could provide more reliable data. In addition, a prospective study assessing the aspects covered in the present investigation should be conducted to confirm the present findings.

5. Conclusion

Performing thymectomy does not seem to increase the average surgical time needed to perform PTX. Thymectomy may be important to avoid reoperations that expose the patients to the risk of serious complications. Thyroidectomy is a procedure frequently associated with PTX and, therefore, is important for the evaluation of thyroid nodules, especially for the higher risk of papillary carcinoma among patients with chronic renal disease.

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