



**ORIGINAL ARTICLE**

# Surgical treatment of Graves disease

Vergilius José Furtado de Araújo Filho<sup>1</sup>, Erivelto Martinho Volpi<sup>1</sup>, Flávio Carneiro Hojaij<sup>2</sup>, Wellington Alves Filho<sup>1</sup>, Arthur Vicentini da Costa Luiz<sup>1\*</sup>, Claudio Roberto Cernea<sup>1</sup>, Lenine Garcia Brandão<sup>1</sup>

## Abstract

**Introduction:** There is no proved superiority between surgical and non-surgical treatment for Graves' disease up to now. **Objective:** To evaluate our surgical experience in the treatment of Graves' disease. **Materials and Methods:** A total of 96 patients with Graves' disease underwent thyroidectomy from 2002 to 2012. All patients were operated on under euthyroid condition, achieved by the use of antithyroid drugs associated to beta-blockers. Follow-up period ranged from 1 to 10 years. **Results:** All patients developed hypothyroidism. There was no recurrence. The main complications observed were transient hypoparathyroidism in 23 cases (24%), transient hoarseness in 7 patients (7%), hematoma in the immediate post-operative period in 2 cases (2%) and permanent hypoparathyroidism in 1 patient (1%). No death was observed in this series. The time of hospitalization varied from 1 to 5 days and 78% of the patients were discharged in the first postoperative day. **Conclusion:** Thyroidectomy is effective and safe, with low complication rates.

**Keywords:** graves disease; thyroid diseases; thyroidectomy.

## Introduction

Graves' disease is the most frequent cause of hyperthyroidism, accounting for 60-80% of the cases, with a prevalence of 0.05% in women and 0.005% in men. It was simultaneously first described at two different locations by Basedow (Germany) and Graves (Ireland), in the 1840s decade. Its etiopathogenesis was described in the 20<sup>th</sup> Century, with the discovery of thyrotropin receptors and anti-receptors antibodies, establishing its autoimmune background. The production of immune complexes may lead to several inflammatory processes, such as periorbital soft tissue swelling and tibia myxedema.<sup>1-3</sup> Hyperthyroidism is also an affection with multisystemic consequences, such as cardiovascular impairment and alterations in neurovegetative and bone metabolism. Seldom is Graves' disease asymptomatic, what makes the treatment of this condition the best approach for most cases.<sup>1,2,4</sup> Thyrotropin receptors are stimulated by autoimmune antibodies, therefore increasing thyroid hormone production and also developing gland hypertrophy.

There is no superiority between surgical and non-surgical treatment of toxic diffuse goiter. The approaches differ among services and countries. In Japan, for example, surgery is widely used, and radioactive iodine is usually avoided.

<sup>1</sup>Universidade de São Paulo (USP), Faculdade de Medicina, Disciplina de Cirurgia de Cabeça e Pescoço, São Paulo, SP, Brasil

<sup>2</sup>Universidade de São Paulo (USP), Laboratório de Anatomia e Cirurgia Vascular (LIM02), São Paulo, SP, Brasil

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The later, however, is the preferred modality by North Americans. In Europe, goiter treatment diverges among different countries.<sup>1,3,5</sup>

Treatment options to toxic diffuse goiter are surgery (thyroidectomy), radioactive iodine ablation and medical treatment with antithyroid drugs. Radioactive iodine ablation was first described in 1946 and has been widely used since then. Its major advantages are the relative low cost and safety among high-risk surgical patients. The main disadvantages of radioactive iodine treatment include long period until euthyroidism is established (at least four months), 3% per year rate of hypothyroidism development and frequent necessity of more than one dose. Medical treatment with antithyroid drugs consists in the use of thionamides, such as methimazole and propylthiouracil, which act inhibiting iodide incorporation into tyrosine residues and iodotyrosil coupling to form iodothyronine, thus affecting thyroid hormones synthesis. These drugs have a latency period that varies between 2 to 6 weeks until symptom relief. The recurrence rate is up to 60% after 6 months of the beginning of the treatment. Also, patients with large goiters and/or severe hyperthyroidism rarely maintain disease remission for long periods.

Even though, the surgical procedure shows off as a resolute option,<sup>6-8</sup> the surgical treatment of enlarged thyroid glands is truly a challenge. Enlarged glands (at least twice a normal volume) present exuberant vascularity with fragile vessels and a friable parenchyma. Subtotal thyroidectomy was the standard procedure for Graves' disease. The purpose of this operation was to solve hyperthyroidism, leaving some thyroid tissue behind. The major limitation of this technique relies in the difficulty to establish how much thyroid tissue should be preserved in order to maintain euthyroidism without the recurrence of the disease. Many studies have shown high efficacy on its treatment with the complete removal of the thyroid gland, especially when performed by experienced surgeons. Previous aspects such as morbidity and mortality rates are no longer justified when analyzing the vast literature, which shows total thyroidectomy as the preferred treatment for Graves' disease.

This study aims to show the surgical outcome of a group of patients treated of toxic diffuse goiter.

## Methods

The present study is a part of a scientific project approved by the Ethics Committee of the Institution Review Board of (IRB) of our institution, entitled "Study of the Complications of Thyroidectomies Performed in a Teaching Institution, 2011".

Patients' data were obtained by review of medical records.

A total of 96 patients diagnosed with Graves' disease were treated with surgery (thyroidectomy) in the period between 2002 and 2012. They were referred to the Head and Neck Surgery Department with an already established diagnosis of Graves' disease due to clinical features and confirmed high levels of thyroid antibodies - thyroid stimulating hormone receptor antibodies (TRAb), thyroid peroxidase antibodies (TPOAb), and thyroglobulin antibodies (TgAb).

Patients were consecutively included in this study, with no inclusion/exclusion criteria other than the diagnostic of Graves' disease. All patients were operated on by one of the first 3 authors. The chosen technique (total or subtotal thyroidectomy) was determined by the surgeon's preference, the presence of suspicious nodules and technical difficulty during the procedure.

Twelve patients had nodules diagnosed in the preoperative ultrasound, none of them underwent fine needle aspiration before the surgery.

We collected the following data: age, gender, volume of thyroid gland, clinical treatment, or not, with antithyroid drugs and/or beta-blockers, date and extension of surgery. The mean age was 34 years old, varying from 7 to 71; and 83 patients (86%) were female (Table 1).

All patients were operated on in a clinically and laboratorial euthyroidism condition, achieved by the use of antithyroid drugs, sometimes associated to beta-blockers (32 patients, 33%) in the preoperative period. Seven patients could not be treated with antithyroid drugs due to prior allergic conditions, so they received beta-blockers alone before surgery. In this series, no preoperative potassium iodine therapy was done.

We considered as subtotal thyroidectomy the excision of all thyroidal tissue but a fragment of 1.0 x 1.0 cm (1.0 mL).

The postoperative follow-up period ranged from 1 year up to 10 years.

## Results

Of the 96 patients included in this study, 89 (93%) were treated with total excision of thyroid gland, while seven (7%) underwent subtotal thyroidectomy.

**Table 1.** Graves' disease patients' demographic information.

	n	%
Gender		
Male	13	13.5
Female	83	86.5
Age		
0-9	1	1.0
10-19	4	4.2
20-29	24	25.0
30-39	38	39.6
40-49	15	15.6
50-59	9	9.4
60-69	3	3.1
70 or +	1	1.0
Extension		
Total	89	92.7
Subtotal	7	7.3
Malignancy		
Yes	9	9.4
No	87	90.6

n = number of patients.

The age of patients varied between 7 and 71 years old, and the mean age was 36 years old. The mean thyroid gland volume at neck ultrasonography was 37mL, and surgical specimens varied between 9mL and 150mL [mean 24mL ( $\pm 25.8$  mL)]. Pathological results showed 9 cases of thyroid cancers (9.4%) and 87 cases of adenomatous goiter (90.6%), associated or not to chronic thyroiditis – Table 1.

All patients, including those submitted to subtotal thyroidectomy, developed hypothyroidism. There were no cases of hyperthyroidism recurrence during the follow-up period of the study. Transient hypoparathyroidism occurred in 23 cases (24%) and one patient (1%) presented permanent hypoparathyroidism. Transient hoarseness was observed in 7 patients (7%), whereas there was no case of permanent voice impairment. Two patients developed hematoma in the immediate post-operative period, which were solved surgically, with good evolution afterwards. There was no death observed in the study's period.

Time of hospitalization varied between one to five days, whereas 78% of the cases had hospital discharge on the first post-operative day.

## Discussion

Graves' disease treatment options include medical treatment, radioactive iodine therapy and surgery. Medical treatment can be efficient in case of clinical remission, otherwise a definitive treatment should be considered. Definitive treatment can be done by surgical resection or radioactive iodine ablation.<sup>1,2,5,6</sup>

When choosing definitive a treatment it is necessary to analyze each patient's characteristics in order to select the more appropriate option. It may be useful to establish some criteria when choosing surgical approach. We selected some characteristics that can be used as criteria to determine surgery: Thyroid nodule with malignancy or suspicious for malignancy; local compressive symptoms; pregnancy expectations; and severe ophthalmopathy.

However, is surgical treatment efficient and safe? Our results demonstrated that it is. We achieved successful hyperthyroidism control without recurrences, with low hospital permanence, minimum complication rates or permanent sequels. Our results are also comparable with those found in the vast literature. Our complication rates are identical when compared to other casuistic throughout different experienced services. Genovese et al.<sup>8</sup>, in 2013, showed after extended revision that surgical treatment is, at least, more efficient than radioactive iodine ablation. And they went beyond, success rates were remarkably higher with total thyroidectomy. They also showed a low rate of permanent sequels (1%), again coincident with our data.

In other series we have found coincident data when analyzing the complication rates. It is safe to say that, despite the impression that hypocalcemia and hematomas are more frequent after toxic goiter surgery than normal thyroid operations, this effectively does not occur. Scerrion et al.<sup>9</sup> demonstrated not only success in the resolution of hyperthyroidism, but also a real improvement in quality of life.

The occasional finding of well-differentiated thyroid carcinomas associated to toxic diffuse goiters corroborates the indication of surgical treatment. In the present study the incidence was 9.4% (similar to the literature<sup>10</sup>), and some of these tumors had local invasion and lymph node metastasis. Other than that, bulky reduction of thyroid mass contributes to lowering antibodies levels and consequently immune complex formation, thus reducing exophthalmos and myxedema.<sup>3,7,9-11</sup>

Analyzing other studies<sup>7-9</sup> and based in our series, we could point two fundamental causes of the good results obtained: adequate preoperative evaluation and the fact that the operation was always performed by skilled experienced surgeons, habituated to this procedure. Preoperative evaluation of patients is fundamental, aiming to obtain normal levels of free thyroxin levels (fT4). When there is any contraindication for the use of antithyroid drugs, beta-blocker should be used.

Regarding the surgical experience, American Thyroid Association (ATA) Guidelines<sup>1</sup> had already pointed out the influence of the surgeon's experience with operative complication rates. It is recommended that the physician perform at least 20 thyroidectomies per year. Parenchyma changes, glandular enlargement, high vascularity and impaired clinical conditions associated to the disease are among some of the factors that imposes the necessity of a highly qualified surgical team in order to obtain the best results for each case.

## Conclusion

Surgical treatment for toxic diffuse goiter is a definitive treatment modality, with low recurrence and complication rates when performed at optimized settings, including good preoperative evaluation and surgical team composed by experienced surgeons. Thus, it is a powerful therapeutic option, with results sometimes much better than other options of treatment.

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**\*Correspondence**

Arthur Vicentini da Costa Luiz  
 Universidade de São Paulo (USP),  
 Faculdade de Medicina, Disciplina de  
 Cirurgia de Cabeça e Pescoço  
 CEP 05403-900, São Paulo (SP), Brasil  
 Tel.: + 55 (11) 2661-6425  
 E-mail: dr.avicentini@gmail.com

**Authors information**

VJFAF - Professor at the School of  
 Medicine, Universidade de São Paulo  
 (FMUSP). EMV - PhD in Sciences at the  
 School of Medicine, Universidade de  
 São Paulo (FMUSP). FCH - Professor at  
 the Anatomy Laboratory and Vascular  
 Surgery (Medical Investigation  
 Laboratory 02) at School of Medicine,  
 Universidade de São Paulo (FMUSP).  
 WAF - PhD in Sciences at the School  
 of Medicine, Universidade de São  
 Paulo (FMUSP). AVCL - Head and Neck  
 Surgeon at the School of Medicine,  
 Universidade de São Paulo (FMUSP).  
 CRC - Professor at the School of  
 Medicine, Universidade de São Paulo  
 (FMUSP). LGB - Professor at the  
 School of Medicine, Universidade de  
 São Paulo (FMUSP)

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