Surgical treatment of Graves' disease: subtotal thyroidectomy might still be the preferred option

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Key words: *hyperthyroidism; Graves' disease; total thyroidectomy; subtotal thyroidectomy; amount of the thyroid remnant.*

Summary. *Objective. The aim of this prospective study was to report our results after thyroidectomy for Graves' disease. In addition, the relationship between the thyroid remnant and postoperative thyroid function was studied.*

Material and methods. Forty-nine consecutive patients were operated on for Graves' disease. The indications for surgery were persistent or recurrent hyperthyroidism after medical treatment in 34 patients (69.4%), mechanical symptoms due to a large goiter in 7 (14.3%), increased ophthalmopathy in 7 (14.3%), and allergy to antithyroid medications in 1 patient (2.0%). Total thyroidectomy (TT) was performed in 28 and subtotal thyroidectomy (STT) in 21 patients. Follow-up lasted 24 to 70 months.

Results. There was no statistically significant difference in the rate of postoperative complications comparing TT and STT. The patients who underwent TT had no recurrence during a mean follow-up of 47 months. After STT, with the mean weight of the thyroid remnant 3.0±1.0 g, there was no relapse of Graves' disease during a mean follow-up of 52 months. After STT, postoperative hypothyroidism developed in 14 patients (66.7%); 7 patients (33.3%) remained euthyroid during follow-up. Comparison of the euthyroid patients and the hypothyroid patients revealed no difference in the weight of the remnant (3.3 g vs. 2.8 g), but a statistically significant difference occurred in the weight of the resected gland (61.0 g vs. 94.4 g, P=0.026) and in the proportion of the remnant (5.6% vs. 3.3%, P=0.030).

Conclusions. Both TT and STT are safe procedures regarding postoperative complication rate. STT with the thyroid remnant of about 3 g allows to permanently cure hyperthyroidism ensuring the euthyroid state in a significant proportion of patients. Postoperative thyroid function after STT is best predicted by the proportion of the remnant.

Introduction

Graves' disease (GD) is the most common cause of hyperthyroidism. There are currently three different treatment options for GD: surgery, antithyroid drugs, and radioiodine ablation. Surgery is usually not the first-line treatment, and it is indicated mainly in patients with large goiters and symptoms of mechanical compression and with severe ophthalmopathy, as well as in patients who have failed antithyroid drug or radioiodine treatment. The issue of the extent of thyroidectomy for GD remains controversial. Recent reports advocate conflicting approaches ranging from subtotal (STT) (1–3) to total thyroidectomy (TT) (4–6).

The purpose of this study was to report our results obtained with thyroidectomy for GD. In addition, the relationship between the thyroid remnant and postoperative thyroid function was studied.

Material and methods

This prospective study comprised 49 patients operated on for GD consecutively between January 2000 and November 2003. All patients were operated on by one of the three surgeons experienced in thyroid surgery.

The diagnosis of GD was verified either by determination of thyroid-stimulating hormone receptor antibodies (TSH-R-Ab) (detectable in 43 patients; 87.7%) or clinical signs of endocrine ophthalmopathy (present in 28 cases; 57.1%) combined with hyperthyroidism.

Altogether 41 women (83.7%) and 8 men (16.3%), with a mean age of 42.4±15.2 years (range 14–75), were included in the study. Of these 49 patients, 45 (91.8%) had been treated with antithyroid drugs alone or in combination with β-adrenergic blocking drugs

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(n=12; 24.5%), with thyroid hormone substitution (n=5; 10.2%), or with a combination of the two. Four patients (8.1%) had received only β-blockers. All patients were routinely treated with the Lugol solution for 10 days before the operation.

The indications for surgery were persistent or recurrent hyperthyroidism after medical treatment in 34 patients (69.4%), mechanical symptoms due to a large goiter in 7 (14.3%), increased endocrine ophthalmopathy in 7 (14.3%), and allergy to antithyroid medications in 1 patient (2.0%).

The decision about the extent of thyroidectomy was based solely on the fact whether the patient had ophthalmopathy or not.

TT (n=28) was chosen for patients with ophthalmopathy. In the rest of the cases (n=21), STT (unilateral total and contralateral subtotal lobectomy) was performed. The total weight of the remnant was intended to be between 2 g and 4 g. Actually, a 1.5–5 g remnant of the thyroid tissue was left behind. The weight of the thyroid remnant was determined by a technique described previously (7). A tissue segment was cut from the resected part of the thyroid, trimmed to the size of the thyroid remnant, and weighed. The weight of the resected thyroid tissue was also determined.

Postoperatively, signs or symptoms of low serum calcium levels and voice complaints were recorded. In the case of voice complaints, the patients were evaluated for recurrent nerve palsy by an ear, nose, and throat physician.

Follow-up lasted 24 months to 70 months (mean 49 months). All patients were followed up for 3–4 weeks, 6 months, and then yearly after the operation. Follow-up examination included clinical evaluation and measurement of the serum concentration of free thyroxine (fT4) and thyrotropin (TSH). Patients with subnormal fT4 (reference range 10.3–24.5 ρmol/L) and/or elevated TSH (reference range 0.4–4.0 mIU/L) levels at the follow-up blood test were regarded as having postoperative hypothyroidism, and for them thyroxine replacement was prescribed. Postoperative or recurrent hyperthyroidism was defined as persistently elevated fT4 and/or suppressed TSH levels.

Statistical analysis was performed using the statistical software Stats Direct version 2.4.4. The mean values were presented as the mean ± standard deviation (SD) and compared with the use of Student's t test. Comparison of the percentages was carried out by using Fisher's exact test. All p values were two-sided. The level of significance was set at $P<0.05$.

Results

Postoperative complications were minimal (Table 1). There was no mortality. We did not observe statistically significant difference in the rate of postoperative complications comparing two procedures, TT and STT.

The patients who underwent total thyroidectomy developed no recurrence during a mean follow-up of 47 months. During a mean follow-up of 52 months, no relapse of GD after STT was observed in patients with a mean weight of thyroid remnant being 3.0±1.0 g. All patients who underwent TT received thyroxine replacement at discharge and remained dependent on thyroxine to maintain the euthyroid status during follow-up.

After STT, 14 patients (66.7%) developed postoperative hypothyroidism and required thyroxine replacement, while 7 patients (33.3%) remained euthyroid during follow-up. The patients treated by STT were further divided into two groups according to the postoperative functional status of the thyroid (Table 2). The patients in both groups were comparable with reference to the weight of the thyroid remnant but differed significantly regarding the weight of the resected thyroid, which was larger in the hypothyroid group than in the euthyroid group (94.4±34.3 g *vs.* 61.0±16.5 g, P=0.025). We found that all patients with Graves'

Table 1. **Postoperative complications after surgery for Graves' disease**

Complication	TT (n=28) n (%)	STT (n=21) n (%)
Transient hypocalcaemia	3 (10.7)	2 (9.5)
Permanent hypocalcaemia	0	0
Transient recurrent nerve palsy	0	1 (4.8)
Permanent recurrent nerve palsy	0	0
Postoperative bleeding	0	0

TT – total thyroidectomy; STT – subtotal thyroidectomy.

Table 2. **Peri- and postoperative findings in the patients treated by subtotal thyroidectomy**

Finding	Euthyroidism (n=7)	Hypothyroidism (n=14)	P
Mean weight of the resected thyroid, g	61.0±16.5	94.4±34.3	0.026
Mean weight of the thyroid remnant, g	3.3±1.2	2.8±0.9	0.309
Mean proportion of weight of the thyroid remnant in total weight of the thyroid, %	5.6±2.3	3.4±2.0	0.030

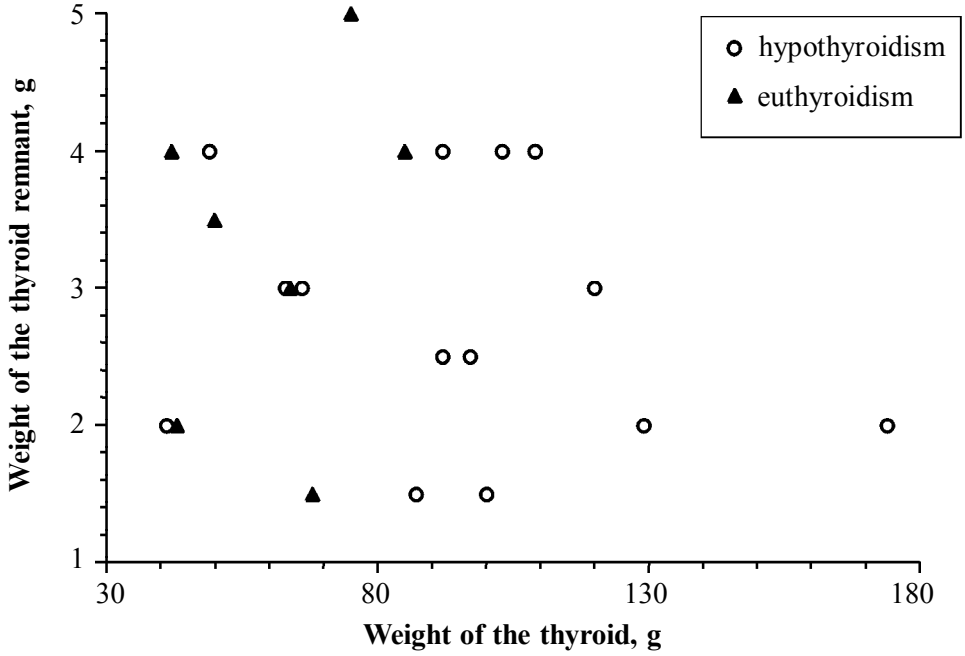

Fig. **Distribution of the patients treated by subtotal thyroidectomy on the basis of postoperative functional status of the thyroid, the weight of the thyroid, and the weight of the thyroid remnant**

gland larger than 87 g became hypothyroid after STT (Fig.). The proportion of the weight of the thyroid remnant in the total weight of the thyroid was significantly higher in the euthyroid group (5.6±2.3%) compared with the hypothyroid group (3.4±2.0%, P=0.030).

Discussion

Like many other authors (5, 6, 8), we did not observe any statistical difference in this prospective trial comparing the complication rates of the two procedures, TT and STT. Our preference for TT in this trial was based on the belief that TT is superior in patients with ophthalmopathy. However, recent prospective randomized studies have revealed no difference in postoperative changes in Graves' ophthalmopathy regarding total *versus* subtotal thyroidectomy (1, 9). Although TT prevents relapse of the disease, it will leave the patient hypothyroid postoperatively. Many surgeons do not regard this as a complication (10, 11); yet, postoperative hypothyroidism cannot be the goal of surgery, either. Therefore, if the euthyroid patient is the goal, some functioning thyroid tissue should be preserved. The size of the thyroid remnant is still the most powerful factor related to postoperative thyroid function (3, 4, 8, 12). The problem is how much of the thyroid remnant should be left behind to best ensure the euthyroid state and at the same time to permanently cure hyperthyroidism.

According to literature data, the weight of thyroid remnant should be less than 4.0 g to avoid postoperative hyperthyroidism (1, 12). Our data were consistent with this recommendation. We did not observe relapses of GD after STT in patients with a mean weight of the thyroid remnant being 3.0 g during the mean follow-up of 52 months. However, the euthyroid state was achieved only in one-third of the patients. Therefore, we hypothesized that in certain circumstances

larger remnant size could even ensure the euthyroid state for a higher number of patients postoperatively, without triggering recurrent hyperthyroidism. As the patients with a large Graves' gland were more likely to become hypothyroid after resection in our study, we presumed that probably the size of the thyroid remnant was too small in the case of large Graves' gland to ensure the euthyroid state. This opinion was supported by the finding that the proportion of the remnant was significantly higher in the euthyroid patients compared with the hypothyroid patients (5.6% *vs.* 3.4%). At the same time, we did not find a difference in the weight of the remnant (3.3 g *vs.* 2.8 g) when comparing the euthyroid *vs.* hypothyroid patients. It seems that the proportion of the weight of the thyroid remnant in the total weight of the thyroid is a more powerful factor for determining postoperative thyroid function than the weight of thyroid remnant itself. It means that when deciding on the amount of the remnant one should evidently take into account thyroid size.

Conclusions

Summarizing our data, it can be concluded that both TT and STT are safe procedures regarding postoperative complication rate. STT with the thyroid remnant accounting for about 3 g allows to permanently cure hyperthyroidism and to ensure the euthyroid state in a significant proportion of patients. Postoperative thyroid function after STT is better predicted by the proportion than by the weight of the thyroid remnant.

Greivso ligos chirurginis gydymas: dalinė tiroidektomija vis dar naudojamas gydymo metodas

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Raktažodžiai: hipertiroidizmas, Greivso liga, radikali tiroidektomija, dalinė tiroidektomija, liekamasis skydliaukės kiekis.

Santrauka. *Tikslas*. Pateikti Greivso ligos chirurginio gydymo, t. y. tiroidektomijos, rezultatus. Taip pat tirtas ryšys tarp liekamojo skydliaukės kiekio ir skydliaukės funkcijos po operacijos.

Tirtųjų kontingentas ir tyrimo metodai. Buvo operuoti 49 ligoniai, sergantys Greivso liga. Indikacijos operacijai buvo nuolatinis ar pasikartojantis hipertiroidizmas po medikamentinio gydymo (37 (69,4 proc.) ligoniai), mechaniniai simptomai dėl padidėjusios skydliaukės (7 (14,3 proc.) ligoniai), padidėjusi oftalmopatija (7 (14,3 proc.) ligoniai) ir alergija antitiroidiniams vaistams (1 (2,0 proc.) ligonis). Radikali tiroidektomija atlikta 28 ligoniams, dalinė – 21. Stebėsenos trukmė – nuo 24 iki 70 mėn.

Rezultatai. Palyginus radikalią ir dalinę tiroidektomijas, reikšmingo komplikacijų po operacijos dažnio nenustatyta. Ligoniams, kuriems padaryta radikali tiroidektomija, vidutiniškai 47 mėn. stebėsenos laikotarpiu ligos atkryčio neužregistruota. Atlikus dalinę tiroidektomiją, ligoniams, kuriems palikta vidutiniškai 3,0±1,0 g svorio skydliaukė, Greivso ligos atkryčio vidutiniškai 52 mėn. stebėsenos laikotarpiu neužregistruota. Atlikus dalinę tiroidektomiją, hipotiroidizmas po operacijos pasireiškė 14 ligonių (66,7 proc.), 7 ligoniams (33,3 proc.) stebėsenos laikotarpiu skydliaukės funkcija išliko normali. Palyginus ligonius, sergančius hipotiroidizmu ir kurių skydliaukės funkcija atsikūrė, statistiškai reikšmingo liekamojo skydliaukės svorio skirtumo nerasta (3,3 g *vs.* 2,8 g), tačiau pastebėtas statistiškai reikšmingas pašalintos liaukos svorio (61,0 g *vs.* 94,4 g, p=0,026) ir skydliaukės likučio svorio dalies nuo bendrojo skydliaukės svorio (procentais) skirtumas (5,6 proc. *vs.* 3,3 proc., p=0,030).

Išvados. Įvertinus komplikacijų dažnį po operacijos, nustatyta, kad radikali ir dalinė tiroidektomija yra saugios procedūros. Dalinė tiroidektomija, kurios metu paliekama apie 3 g skydliaukės liekana, sudaro sąlygas hipertiroidizmui išgydyti užtikrinant normalią skydliaukės funkciją daugeliui ligonių. Skydliaukės funkcija, atlikus dalinę tiroidektomiją, geriausiai numatoma įvertinus skydliaukės likučio svorio dalį nuo bendrojo skydliaukės svorio (procentais).

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