

# SURGICAL PRACTICE AND RISK FACTORS IN THE TREATMENT OF PATIENTS WITH BENIGN THYROID DISEASES

LORANT KISS<sup>1</sup>, MIHAI FAUR<sup>2</sup>, ROLAND KISS<sup>3</sup>

<sup>1,2,3</sup>“Lucian Blaga” University of Sibiu, County Clinical Emergency Hospital of Sibiu

**Keywords:** thyroid carcinoma, hyperthyroidism, thyroidectomy

**Abstract:** The extent of surgery for unilateral or bilateral disease is controversial. Bilateral resection should be associated with low recurrence rates, but with a higher technical morbidity. The aim of this study is to present our experience with benign thyroid diseases treated by either subtotal, total or near total thyroidectomy, and the existence of cold nodules and the frequency of thyroid carcinoma in hyperthyroid patients. **Methods:** There were reviewed the medical records of 815 patients who underwent operations for toxic multinodular goiter-struma (TMS) (n=298), Graves' diseases (SD) n=341, and toxic adenoma (TA) n=176 between January 1990 and April 2013. During this period of time, the patients underwent subtotal unilateral or total thyroidectomy for benign disease. **Results:** The incidence of thyroid carcinoma was of 6.4% (352/815); cold nodules were found in 292 (36%) of the patients and no cold nodules were found in 523 (63%) of the patients. In SD, 3.7% of the patients had carcinoma, its incidence in the patients with TMS being of 6.3%. The recurrence rate in the lobectomy group was of 11%, versus 3% after total thyroidectomy. However, patients in the lobectomy group had a much lower complication noted (2%) versus 9% after thyroidectomy (p=0.007). **Conclusions:** In patients with MMS, 89% of those with unilateral resection did not require further surgery. The morbidity after unilateral thyroidectomy was lower than for bilateral resection. The present data support the recommendation for the unilateral lobectomy in the selected cases with symptomatic unilateral MMS.

## INTRODUCTION

Thyroidectomies are one of the most common elective surgical procedures in the western world and USA. About 50 000 thyroidectomies are performed in USA every year.(1)

Sokal et al. showed that patients with hyperthyroidism had a higher incidence of thyroid carcinoma than the patients with euthyroidism (2), and other studies have also found that thyroid carcinoma is highly frequently associated with Graves's disease (SD) and hyperthyroidism.(3-9)

Multinodular goiter (MMS) is the most common form of benign thyroid disease, affecting 5 % to 7 % of the world's population.(10,11)

Indications for surgical therapy in MMS include syndromes of compression, suspected malignancy, hyperthyroidism and cosmetics. Surgery may involve either unilateral or bilateral thyroidectomy depending on the extent of the disease and on the surgeon's decision.(12,13)

The extent of surgery, however, for symptomatic MMS is controversial. The recurrence rate for unilateral thyroidectomy has been reported from 10% to – 26% (14,15), and unilateral or subtotal resection was accepted, but with a higher recurrence rate associated with it because potential goitrogenic tissue remains in situ.(16,17)

Total thyroidectomy offers a lower recurrence rate, but it can be associated with a higher complication rate.(18,19,20)

The most common complications after thyroidectomies are hematoma, permanent hyperparathyroidism, lesion of the recurrent nerve and transient post-operative hypocalcemia.(21,22,23)

## PURPOSE

The aim of this study was to present the risk factors for malignancy in surgical patients with SD, TMS and TA with the determination of the impact of age, presence of cold nodules and the incidence of thyroid carcinoma and hyperthyroidism.

## METHODS

The medical records of 815 patients who underwent operations for toxic multinodular goiter (TMS) (n=298), Sroves' disease (SD) (n=341) and toxic adenoma (TA) n=176 were reviewed between January 1990 and April 2013. The diagnosis of hyperthyroidism was primarily based on the presence of signs of hyperthyroidism, elevated T4 and thyroid-stimulating hormone (TSH) levels.

Patients who had hyperthyroidism with multiple nodules but who did not have the clinical and biochemical signs of SD were defined to have TMS.

Hyperthyroid patients without signs of SD with remaining suppressed gland, on scintigraphy they were defined to have TA. In 443 (54%) of patients, ultrasonography was performed. In 81 patients (10%), thyroid fine-needle puncture was performed together with cytological examinations. Thyroid resection specimens were fixed in formalin for 24 hours and then histopathologically examined. In presence of any tumours the tumour diameter was the maximum diameter assessed from the histopathological point of view. For the statistical analysis, chi-square tests were used and p<0,5 was accepted as indicating a significant difference.

All patients had preoperative chest X-rays. If the MMS was obviously bilateral on physical examination, CT (computer tomography and/or cervical ultrasound was not always obtained before bilateral resection). If a unilateral MMS

<sup>1</sup>Corresponding author: Kiss Lorant, B-dul Corneliu Coposu, Nr. 2-4, Sibiu, România, E-mail: drkisslorant@yahoo.com, Tel: +40269 215050  
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## CLINICAL ASPECTS

was suspected on physical examination, these patients underwent preoperative imaging to confirm the unilateral character of the lesions, unilateral lobectomy being planned.

### RESULTS

Data from the patients with MMS, SD and TA are shown in table no. 1.

**Table no. 1. Characteristics of the patients with MMS, SD and AT**

Total: n=815	SD n=341	TMS n=298	AT n=176
Age (mean +/- SD)	38 +/- 10.2	49 +/- 12.5	48 +/- 11.0
Age of the patients with/without carcinoma	42.8 +/- 11.0 38.1 +/- 12.0	51 +/- 13.2 49 +/- 12.6	57.2 +/- 9.0 47.2 +/- 11.0
Patients with cold nodules n (%)	9(3.0)	205(68.8)	77(43.8)
Patients with palpable cold nodules n (%)	9(3.0)	101(34.0)	4(2.3)
Patients with non palpable cold nodules n(%)	0	103(34.7)	73(41.5)
Gender (F/M)	266/74	260/38	147/29
Patients with no cold nodules n (%)	331(97)	92(31)	99(56)
Patients thyroid carcinoma	12(3.8)	18(6.4)	21(12.0)
Patients with papillary microcarcinoma, with thyroid carcinoma n (%)	10/12(85.0)	10/18(58%)	15/21(71)

In 75% of lobectomies, the presence of compression syndrome represented the indication for resection and in 30%, the serious optalmopathy was the second most frequent indication in the patients with SDL, as shown in table no. 2.

**Table no. 2. Patients with SD, MMS, AT and the indication for thyroidectomy**

Indication	SD (%)	TMS n (%)	TA n (%)
Large goiter with compression	183(53)	266(89)	172(97,6)
Ophthalmopathy	102(30)	0	0
Substernal goiter	0	21(7,4)	0
Suspicious or malignant Fine Needle Aspiration Biopsy (FNAB) results	5(1.8)	9(3.3)	4(2.3)

Of the 815 patients, 292 (36%) had cold nodules, and 523 (64%) did not have cold nodules. In 526 patients (6.5%), the presence of thyroid carcinoma was found.

The incidence of carcinoma was of 3.8% in SD, 6.4% in TMS and 12% in TA, with a mean incidence of 4.9% in men and 6.8% in women. Older patients ( $\geq 50$  years) had a significantly higher incidence of carcinoma than the younger people, 10.2% vs. 4.3% ( $p=0.002$ ). In presence of cold nodules and hyperthyroid function, the frequency of carcinoma is presented in table no. 3.

In 45% of the patients with thyroid carcinoma, palpable cold nodules were present in 15% of cases and 85% of tumours, they were incidental.

In SD, bilateral thyroidectomy was performed in 164 (48%) patients and 176 (52%) underwent near total or total thyroidectomy. Frozen section analysis was performed in 33 of cases. The frequency of carcinoma was significantly higher in SD patients with palpable cold nodule 20% ( $p=0.007$ ).

The histopathological features of thyroid carcinoma larger than 1 cm found in the patients with hyperthyroidism are presented in table no. 4.

**Table no. 3. Thyroid carcinoma in patients with hyperthyroidism and cold nodules**

	SD= 341	TMS (n=298)	TA n=176	Total: 815
Carcinoma with cold nodules n%	1/9 (20.0)	17/205 (8.6)	18/7 (23.0)	36/291 (13%)
Carcinoma with no cold nodules n%	10/331 (3.3)	0/92	3/99 (30)	14/523 (29%)
Carcinoma with palpable cold nodules n%	1/9 (20%)	11/101 (11)	3/4 (75.0)	15/113 (14.6)
Carcinoma with no palpable cold nodules n%	10/331 (3.3)	6/196 (3.6)	18/172 (10)	33/694 (50)
p	0.007	0.006	0.001	0.001

**Table no. 4. Histopatological features of thyroid carcinoma larger than 1 cm in hyperthyroidism**

Histopatology	SD	TMS	TA	Total
Size (mm)	14	10-26	18-41	10-41
No microcarcinoma local invasion (n%)	0	1(12.0)	3(50)	4(25.0)
Invasion of thyroid capsule n%	2(100)	0	0	2(12.5)
Extrathyroid extension n%	0	4(50.0)	3(50.0)	7(43.8)
Multicentricity n%	0	3(37.5)	0	3(18.7)
Total	2	8	6	16

In toxic multinodular goiter, 68.8% of the patients had cold nodules, 34% of them were palpable and 34.7% of the cold nodules were nonpalpable. In 47% of the cases ultrasonography was performed.

Bilateral subtotal thyroidectomy, near total and total thyroidectomy were performed in 69%, 23% and 8% of the patients with TMS.

In the present study, the patients with and without thyroid carcinoma did not differ significantly in terms of their mean age ( $p=4$ ). In 17(6.4%) of all cases, we found papillary carcinoma the majority (58%) of which were PMC.

In toxic adenoma (TA), the lobe contralateral to the lobe with TA was significantly suppressed and invisible onjscintigraphy. In TA bilateral, subtotal thyroidectomy was performed in 52% of the cases, near total or total thyroidectomy was performed in 31% patients and lobectomy and istmus resection were performed in 17%, unilateral lymph node dissection was performed in one patient with PMC and lymph node metastases.

The histopathological examination reveals coexisting thyroid nodules in the contralateral lobe of toxic adenoma in 77 (44%) patients.

In patients with bilateral MMS, all surgeons performed total thyroidectomy. In patients with MMS unilateral, we preferred total resection, in order to prevent recurrence and a possible thyroid microcarcinoma in the remaining tissue.

The recurrence rate after uni and bilateral resection is shown in table no. 5

**Table no. 5. Recurrence and complication rates**

Groups	Recurrence rate (%)	Complication rate (%)	Hypocalcemia (%)
Unilateral resection	11	2	0
Bilateral resection	3	9	6
p-value	029	007	049

Patients in the unilateral group had a recurrence rate of 11%. In the bilateral resection group, the recurrence rate was

## CLINICAL ASPECTS

3%. The total complication rate, however, was significantly higher in the bilateral group, especially with regard to postoperative hypocalcemia. The overall complication rate was 9% in the patients in the bilateral groups compared to 2% in the unilateral group ( $p=0.007$ ).

The rate of transient postoperative hypocalcemia in the bilateral group was of 6% versus 0% in the unilateral group ( $p=0.049$ ).

### DISCUSSIONS

In the present study, we investigated the results of the surgical treatment in benign thyroid diseases and the incidence of thyroid carcinoma in the patients with hyperthyroidism. Thyroid carcinoma was found in 6.5% of the patients with hyperthyroidism.

The surgical procedure of choice for symptomatic MMS remains controversial.

In the past, most surgeons have performed unilateral or subtotal thyroidectomy because of its lower complication rate, but this attitude can lead to the need for reintervention if the symptoms reoccur.

More recently, total thyroidectomy has been preferred by some surgeons because of its lower recurrence rate.(10,11)

The prevalence of palpable thyroid nodules in SD was 15%, but studies of US survey have found as high as 34%.(24-27)

Thyroid nodules have been associated with an increased risk of malignancy in SD in 5% (5.28), but in SD patients with palpable cold nodules, this incidence is of 46%.(3,5,8,20,28,24,27)

Kroimpsetal (28) found that 17% of non palpable nodules in SD patients, contained thyroid carcinoma.

In our study, the most common indications for surgery in SD were a large goiter with compressive effects and serious ophtalmopathy rather than the presence of a suspicious nodule.

The most common complications of thyroid surgery are hematoma, recurrent laryngeal nerve injury permanent hyperparathyroidism, and transient postoperative hypocalcemia hematoma usually occurs within 24 hours of surgery. The incidence of hematoma is <1% to 2% of all thyroidectomise.(30)

Permanent damage to the recurrent laryngeal nerve occurs in 0% to 4% of cases.(30,31)

We found that the incidence of thyroid carcinoma in TMS was of 6.4%, which is consistent with the rates (5-8.2%) found in previous studies.(29,32-34)

The common indications for surgery in TMS are massive enlargement with compressive symptoms, substernal extension and suspicious of malignancy.(32,35) In present study, 90% of the patients with TMS had surgery for compressive symptoms.

In the present study, the incidence of thyroid carcinoma in patients with TA was of 12.0%, in other studies, the incidence of carcinoma ranged from 2.5-4.4%.(6,29,36,33)

The complication rates in patients undergoing unilateral thyroidectomy have been reported in several studies, with hematoma in 0% and laryngeal nerve injury occurred in 0% to 3% of patients, and rarely temporary hypocalcemia.

In comparison, the complication rates in total thyroidectomy are higher, hematoma occurs in 0.4% of cases, permanent hypoparathyroidism occurred in 1% to 5% and temporary hypoparathyroidism in 5% to 30% of patients.

The rate of recurrent laryngeal nerve injury was the same as in unilateral thyroidectomy (0% to

3%).(11,12,18,30,37)

The recurrence rate for MMS in patients undergoing unilateral thyroidectomy is of 1.2% to 26%, the recurrence rate for patients undergoing total thyroidectomy is of 3%.

### CONCLUSIONS

The complications for the patients undergoing unilateral thyroidectomy for unilateral MMS disease are significantly lower than that for the patients with total thyroidectomy with the recurrence rate of unilateral thyroidectomy higher than total thyroidectomy. Cold nodules are frequent in hyperthyroid patients, cold nodules in older patients ( $\geq 50$  years) are significant risk factors for thyroid carcinoma in hyperthyroid patients.

Thyroidectomy may be adequate for hyperthyroid patients with cold nodules or for nodules with suspicious sonographic features, but malignancy cannot be excluded.

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