

# Hyperthyroidism and concurrent thyroid carcinoma

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**Abstract.** – In the last twenty years, medical studies have reported a significant increase in thyroid neoplasms among patients with hyperthyroidism.

Aim of the present work is to reconsider the real incidence of this not uncommon association and to establish a model for surgical treatment of hyperthyroidism for a possible concurrence with thyroid carcinoma.

At the Department of Surgical Sciences and Applied Medical Technologies "La Sapienza" Rome's University, during the period 1994 to 1999, an homogeneous group of 82 patients was surgically treated for hyperthyroidism.

Of our patients, fifty-four (66%) had a "multinodular toxic goiter" (MTG), twenty (24%) a "functional autonomous nodule" (FAN) while the remaining patients were affected by Graves' disease.

The surgical procedures adopted were:

- 1) total extracapsular ipsilateral lobectomies and isthmectomies in sixteen patients with FAN;
- 2) total extracapsular thyroidectomy in all patients with MTG and with Graves' disease and in the remaining four patients with FAN after a long time treatment with thyrostatic drugs.

On six (7%) of our patients we found out a thyroid carcinoma: five with MTG and one with Graves' disease. However, no association with thyroid carcinoma was observed in anyone with FAN.

The correct treatment of thyroid surgical diseases is a single definitive operative approach. The procedure must be a total thyroidectomy in MTG and Graves' disease. However, in patients with FAN it's possible, after careful evaluation, to carry out a total extracapsular ipsilateral lobectomy with isthmectomy, justified by the normal morphology of the remaining thyroid tissue.

It is always possible, in these cases, a subsequent complete exeresis if a carcinoma is present in the removed lobe.

**Key Words:**

Hyperthyroidism, Thyroid neoplasms, Thyroid carcinoma.

## Introduction

In the last twenty years, medical studies have reported a significant increase in thyroid neoplasms among patients with hyperthyroidism<sup>1-3</sup>.

Hyperfunctioning diseases of thyroid have always been thought as " unsuspected lesions" because past theories have suggested that hyperthyroidism protects from thyroid cancer owing to a lack of stimulation to thyroid tissue itself by TSH<sup>4</sup>.

Aim of the present work is to reconsider the real incidence of this not uncommon association and to establish a model for surgical treatment of hyperthyroidism for a possible concurrence with thyroid carcinoma.

## Methods

At the Department of Surgical Sciences and Applied Medical Technologies "La Sapienza" Rome's University, during the period 1994 to 1999, an homogeneous group of 82 patients was surgically treated for hyperthyroidism.

Of our patients, fifty-four (66%) had a "multinodular toxic goiter" (MTG), twenty (24%) a "functional autonomous nodule" (FAN), while the remaining patients were affected by Graves' disease (Table I).

Most of our patients were women (73%) and the average age was 52. The preoperative diagnostic protocol used included, for all patients, complete hormonal dosages as follows: T3, T4, FT3, FT4 and TG; as well as antithyroglobulin and antiperoxides antibodies and the TSH dosage using the IRMA method. In

Table I.

Patients with hyperthyroidism surgically treated		
MTG	54	66%
FAN	20	24%
Graves'	8	10%
Total	82	100%

addition, instrumental investigatory means were employed, including ultrasounds and thyroid scanning with Tc 99 or with I 131 and, where necessary, T3 suppression test or TSH Releasing Hormone test (TRH).

Cytologic preoperative sampling was often carried out on MTG dominant nodules and on cold areas in Graves' disease; in none of these patients, however, a preoperative diagnosis of thyroid carcinoma was performed.

Compressive symptoms, ineffectiveness, or failure to follow the medical treatment and recurrence of disease, made surgery advisable.

The surgical procedures adopted were:

- 1) total extracapsular ipsilateral lobectomies with isthmectomies in sixteen patients with FAN;
- 2) total extracapsular thyroidectomy in all patients with MTG and with Graves' disease and in the remaining four patients with FAN after a long time treatment with thyrostatic drugs (Table II).

An intraoperative histological examination was carried out almost exclusively on total ipsilateral lobectomies and isthmectomies, often not diagnostic in follicular lesions. This procedure wasn't performed in patients who had undergone to a total thyroidectomy.

Table II.

Surgical procedures in hyperthyroidism	
Total ipsilateral lobectomies + isthmectomies	16 FAN
Total thyroidectomies	54 MTG 8 Graves' 4 FAN
Total	82

## Results

On six (about 7.0%) of our patients we found out a thyroid carcinoma: five of the fifty-four MTG and one of the eighth with Graves' disease. However, no association with thyroid carcinoma was observed in any patient with FAN (Table III).

The six patients with cancer were all female. Total thyroidectomy was performed at first in all cases.

We had four papillary, one follicular and one medullary carcinomas. In the majority of cases (3/4), the lesion was at the first stage (less than a centimetre); in just one case, with medullary carcinoma, the lesion measured 1.2 centimetres.

In all patients, the diagnosis was made only after definitive histological studies.

About forty days after surgery, all patients underwent a "radioiodine whole body scanning" (WBS). Radioactive <sup>131</sup>Iodine for remnant thyroid ablation has been used in all patients except for medullary carcinoma. None of our patients at follow-up had, up till now, a recurrence (Table IV).

## Discussion

About the incidence of thyroid neoplasms, recent reports have shown the greater frequency of association of thyroid carcinomas with euthyroidism ( $\approx 14.3\%$ )<sup>3,5,6</sup>. The concurrence with hyperthyroidism is present in about 5% of cases on increase in the last few years<sup>7-12</sup>.

This is due to remarkable developments in preoperative cytological sampling, to increase of surgical thyroid exeresis and to improvement of pathological report through multiple specimens.

Table III. Patients with hyperthyroidism and thyroid carcinoma.

	Hyperthyroidism	Thyroid ca
MTG	54	5
FAN	20	0
Graves'	8	1
Total	82	6

Table IV. Hyperthyroidism and thyroid carcinoma.

Pat	Sex	Age	Disease	Surg procedures	Pathol	TNM	FU/m
1) BA	F	67	MTG	Total thyroidectomy	Follic ca	I (0.4 cm)	54 ned*
2) ZE	F	74	MTG	Total thyroidectomy	Papill ca	I (0.7 cm)	26 ned*
3) RS	F	72	MTG	Total thyroidectomy	Med ca	II (1.2 cm)	9 ned*
4) LT	F	66	MTG	Total thyroidectomy	Papill ca	I (0.4 cm)	48 ned*
5) ND	F	51	MTG	Total thyroidectomy	Papill ca	I (0.5 cm)	32 ned*
6) VL	F	38	Graves'	Total thyroidectomy	Papill ca	I (0.5 cm)	18 ned*

\*No evidence disease.

In most cases, carcinomas are occult, smaller than 1 cm in size and located adjacently to or near hyperfunctioning thyroid areas, but almost never within them<sup>13</sup>.

In MTG the incidence of papillary microcarcinomas, varies with an average frequency of 6,2%<sup>1,2</sup>.

In FAN, the incidence is at its lowest among the various hyperthyroidisms (2.4%). The carcinoma, usually papillary and almost never functioning, is always occult in hyperfunctioning tissue and this condition doesn't allow easy identification<sup>12,14</sup>.

In patients with Graves' disease it is easy to establish, through thyroid scanning and before surgical procedure, a "cold" area in a tissue with diffuse distribution of activity, which will be positive in about 50% of cases as thyroid carcinoma<sup>3,15-16</sup>.

Although the incidence of such association is not very high, at 3.9%, it should be stressed that the thyroid-stimulating immunoglobulins of this disease may interfere with neoplastic growth allowing a rapid increase of tumour with premature diffusion.

The results of our series confirm greater incidence of carcinoma in MTG, compared with Graves' disease and especially with FAN.

Patients with MTG were undergone to surgery for mechanical symptoms of obstruction or for oncological risk.

Surgical exeresis is the first treatment for FAN; in some cases, however, the radioiodine therapy is possible.

In Graves' disease surgery is recommended only in those patients unsuccessfully treated with medical or radioiodine therapy. Preoperative cytological sampling ultrasound guided, is advisable in MTG or Graves' disease.

An intraoperative pathological specimen is usually superfluous, because total thyroidectomy avoids postoperative report of carcinoma.

This procedure, however, is essential in FAN where only a total ipsilateral lobectomies and isthmectomies is indicated. Indeed, a postoperative examination of tissue removed during surgery will supply the most complete diagnostic information.

Surgical options are essentially as follows: an extracapsular total ipsilateral lobectomy and isthmectomy, a "near-total" thyroidectomy and a extracapsular total thyroidectomy. In our opinion, confirmed by all current studies, the "near-total" thyroidectomy should be abandoned owing to the risk of a recurrence especially in Graves' disease. The prevention of complications, such as recurrent palsy and hypocalcemia, doesn't depend on the type of surgery used but on the surgical technique adopted<sup>17</sup>.

The correct treatment of thyroid surgical diseases is a single, definitive operative approach. The procedure must be a total thyroidectomy in MTG and Graves' disease. However, in patients with FAN it's possible, after careful evaluation, to carry out a total ipsilateral lobectomy and isthmectomy, justified by the normal morphology of remaining thyroid tissue.

It is always possible, in these cases, a subsequent complete exeresis if a carcinoma is present in the removed lobe. In patients with FAN, in long-term thyrostatic treatment it is preferable to do at first a total thyroidectomy, owing to the high oncological risk.

In fact, there's a significant increase in recurrent laryngeal injury, from 1.5 to 11%, in re-operated patients<sup>18</sup>.

In conclusions hyperthyroidism with thyroid carcinoma is an event more frequent than in the past, due to improvements in pre-operative and postoperative diagnosis. In this experience, we found a thyroid carcinoma in six of 82 patients with hyperthyroidism (about 7%).

On MTG and Graves' disease, clinical suspect should be aroused in nodules with mutated clinical features such as the "cold" areas with rapid growth in hyperfunctioning tissue and after long periods of treatment with thyrostatic drugs.

Biological and clinical behaviour of these microscopic tumours is very similar to classic neoplasms except in Graves' disease where the etiology of disease can give origin to early neoplastic diffusion.

For an ideal surgical approach it's preferable to carry out, if possible, a preoperative histological identification.

On MTG and Graves' disease total thyroidectomy appears to be the best surgical procedure, while total ipsilateral lobectomy and isthmectomy followed, if necessary, by total exeresis, is more recommended in FAN.

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