

Type of Operation for Toxic Adenoma, Toxic Multinodular Goitre and Graves' Disease

S. Lanitis, K. Karkoulias, G. Sourtse, V. Ganis

Abstract

Many countries and medical associations have developed guidelines for the management of benign thyroid conditions, including the surgical management of toxic thyroid goitres and the toxic solitary thyroid adenoma. Our aim is to provide evidence to support or reject different kind of operations used for the management of toxic thyroid conditions i.e. toxic goitre and toxic solitary nodule. Hyperthyroidism affects 1.2% of the general population. The main cause is Graves' Disease (50-80%) followed by the toxic multinodular goitre (TMNG), toxic adenoma (TA) and, finally, thyroiditis (10%). Management includes antithyroid medications, iodine ablation (I^{131}) and surgical resection of the gland. According to the American thyroid association, if surgical management is selected, it is highly recommended to proceed with a total or near-total thyroidectomy in order to minimize the recurrences. This kind of operation is associated with an almost 0% recurrence rate as opposed to subtotal thyroidectomy which is associated with an 8% recurrence rate at 5-year follow-up. The incidence of malignancy in patients with Graves' disease is less than 2%. In about one-third of patients, there will be regression of the disease. For the patients who are under medical or surgical management, the recurrence rate is almost 50% if only antithyroid medications are used, 21% after I^{131} ablation, and 5% after surgery. The evidence from the literature shows that TT is associated with a lower recurrence rate and the same incidence of permanent serious complications. ST is associated with a lower rate of temporary hypoparathyroidism. In terms of the development of ophthalmopathy, both the comparison of RCT and non-RCT showed no significant difference between the two approaches. For the management of the toxic thyroid lesions, most guidelines recommend the following:

Solitary toxic thyroid nodule - the recommended operation is unilateral total thyroid lobectomy.

This operation is associated with less than 1% treatment failure and only 2.3% hypothyroidism.

Toxic multinodular goitre - it is recommended to proceed with total or near-total thyroidectomy.

The incidence of malignancy is 3%-9%, hence, this operation is adequate for such lesions; the recurrence rate is less than 1% and the patient becomes euthyroid soon after surgery.

- For the benign toxic solitary nodule, a total lobectomy can be performed.
- For the benign toxic multinodular goitre, total thyroidectomy is the procedure of choice since it may decrease the recurrence rate, can decrease the reoperation rate, can reduce the overall morbidity associated with a reoperation, and can successfully manage "occult" thyroid cancers
- The operation should be performed by an experienced surgeon so as to ensure that the risk of permanent complications (i.e. RLN palsy and hypoparathyroidism) is less than 1-2%.

Key words: Toxic adenoma; toxic multinodular goitre; Graves' Disease

Introduction

Many countries and medical associations have developed guidelines for the management of benign thyroid conditions that include the surgical management of toxic thyroid goitres and toxic solitary thyroid adenoma. This paper was based on the following guidelines and sources:

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European society for medical Oncology (ESMO) 2012, American Association of clinical endocrinologists (AACE) 2010, National Comprehensive Cancer Network (NCCN) 2013, German Association of Endocrine Surgeons (GAES) 2011, 2013, American Thyroid Association (ATA) 2009, British Thyroid Association and Royal college of physicians (BTA) 2007, AACE/AME/ETA 2010, European Thyroid Association (ETA). Moreover, in an attempt to provide the best possible evidence, data from randomized control trials (RCTs) and meta-analyses were also used.

As is clearly stated in most guidelines, the objective of the surgical procedure is the safe and definite management

of thyroid pathology [1]. Our aim is to provide evidence to support or reject different kinds of operations performed for the management of toxic thyroid conditions i.e. toxic goitre and toxic solitary nodule.

Discussion

It is well known that thyroid nodules are common in the general population. Despite the fact that only 4-8% is clinically detectable, a higher percentage can be found with the US with a range between 13-67%. Moreover, in post-mortem specimens thyroid nodules can be found in about 50 % of the population [2]. Many studies have shown that malignancy can manifest in 5% of these nodules irrespective of their size [3].

With regard to the evaluation and management of thyroid nodules, the algorithm proposed in the NCCN guidelines Version 2.2013 recommends that the assessment for suspicious lymph nodes begins with a thyroid stimulating hormone (TSH) and a neck US evaluation apart from the thyroid, the central and lateral cervical compartments. If the TSH is low, radioiodine imaging is indicated to clarify whether there is an autonomously functioning nodule ("hot"); a "hot" nodule needs to be treated medically, accordingly. A scan that shows a "cold" or "warm" nodule indicates that the workup should proceed as for non-toxic lesions, i.e. based on the clinical and sonographic features, a fine needle aspiration of the suspicious nodes is recommended to exclude malignancy. Nodules suspicious for malignancy demand a different algorithm which is not within the scope of this paper. For nodules that do not meet the criteria for FNA or for those considered benign by FNA, surveillance with US is recommended every 6-12 months. If no malignancy is found at the preoperative workup, patients can be managed either medically or surgically. Is not within the interest of this paper to set the indications for surgery. The aim of this paper is to present the facts, the pros and cons of each operation and provide evidence concerning the ideal operation which combines safety with the most definite results.

Hyperthyroidism affects 1.2% of the general population. The main cause is Graves' disease (50-80%) followed by toxic multinodular goitre (TMNG), toxic adenoma (TA) and finally thyroiditis (10%). Management includes antithyroid medications, Iodine ablation (I^{131}) and surgical resection of the gland (level of evidence A) [4].

According to the American thyroid association, if the surgical approach is selected it is highly recommended to proceed with a total or near total thyroidectomy in order to minimize recurrences. This kind of operation is associated with almost 0% recurrence rate as opposed to subtotal thyroidectomy which is associated with a 8% recurrence rate at 5-year follow-up (level of evidence A) [4]. The same

guidelines indicate that the procedures should be carried out by an experienced surgeon to ensure that permanent hypoparathyroidism is less than 2%, permanent recurrent laryngeal nerve palsy is less than 1%, the reoperation/haemorrhage rate is under 0.3%-0.7% and that overall mortality is less than 1/10.000 operations [4].

Graves' Disease

The incidence of malignancy in patients with Graves' disease is less than 2%. About one-third of patients will manifest regression of the disease. For those under medical or surgical management, the recurrence rate is almost 50% where only antithyroid medications are used, 21% after I^{131} ablation and 5% after surgery. Moreover, surgery is the preferred treatment for patients with ophthalmopathy, in pregnancy, in patients with pressure symptoms and in those with suspicious nodules [5]. The only question that has to be answered is that of which operation fulfills the criteria to the procedure of choice - total thyroidectomy (TT) or subtotal thyroidectomy (ST).

Two major questions need to be answered to decide on the most appropriate operation: (a) what is the recurrence rate for each procedure? and (b) what is the effect on the evolution of ophthalmopathy?

We must also bear in mind that we are dealing with a benign condition; therefore, when choosing the appropriate operation, we must also consider the associated problems following each procedure, especially morbidity. When we talk of morbidity in thyroid surgery, we mainly refer to temporary or permanent recurrent laryngeal palsy and hypoparathyroidism. This leads us to yet another question that needs to be answered: how safe is each procedure?

Nowadays, there is a trend to perform total or near total thyroidectomy for most thyroid pathologies. In order to support this practice and decide which is the most appropriate operation, we must answer two important questions: (a) is total Thyroidectomy necessary for the management of a benign condition such as Graves' disease? and (b) is TT a safe operation when performed by experts?

A recent meta-analysis of the available four RCTs showed the following [5]:

Figure 1 [5]. Results of the meta-analysis on the recurrence rate and ophthalmopathy progression after TT or ST.

In 674 cases of Graves' disease managed either with TT (N=342) or with ST (N=332), the cumulative recurrence rate for ST was 7.83% as opposed to 0.87% for TT, which was statistically very significant ($p=0.0003$).

In 299 cases of Graves' disease managed either with TT (N=151) or ST (N=148), the cumulative progression rate of ophthalmopathy for ST was 11.48% while for TT it was 10.59% which was not statistically significant ($p=0.80$).

Complications

The cumulative temporary hypoparathyroidism rate for ST was 12.21% while for TT it was 32.5% which was statistically very significant ($p < 0.0001$); hence, ST leads to a lesser temporary hypoparathyroidism.

The cumulative permanent hypoparathyroidism rate for ST was 0.9% as opposed to 2.62% for TT, but this was not statistically significant ($p = 0.13$).

The cumulative temporary RLNP rate for ST was 3.21% while for TT it was 3.43%, which was not statistically significant ($p = 0.85$).

The cumulative permanent RLNP rate for ST was 0.9% and for TT it was 1.46%, but this was not statistically significant ($p = 0.52$).

This study concluded that TT is associated with a lower recurrence rate and the same incidence of permanent serious complications. ST was associated with a lower rate of temporary hypoparathyroidism.

The same year (2013), a systematic review on the same subject included 4 RCTs and 19 Non-RCTs with a total of 1665 patients submitted to TT and 1577 patients who underwent ST [6]. Notably, malignancy was found in 4.7% of the patients.

When all patients were included, the recurrence rate after TT was 0.42% while for ST it was 8.11%, confirming once again that significantly more recurrences occurred after ST ($p < 0.0001$). This was also true for comparisons that included either only RCTs or Non-RCTs.

As concerns the evolution of ophthalmopathy, both the

comparison of RCTs and Non-RCTs showed no significant difference between the two approaches ($p = 0.76$).

In terms of complications, it was found that temporary hypoparathyroidism was higher in the TT group (27.9% vs. 9.48%) which was very significant ($p < 0.0001$) during both the overall and the independent comparisons (RCT and non-RCT).

In respect to permanent hypoparathyroidism, in contrast to the findings of the RCT comparison that found no statistically significant difference between TT and ST, the comparison of Non-RCTs showed that more patients who underwent TT (3.76% vs. 0.86%) developed this complication ($p = 0.001$). This was also the case in the overall analysis.

In relation to permanent RLN palsy, no significant difference was found between the two operations in either of the comparisons.

Guidelines

Most guidelines recommend the following for the management of toxic thyroid lesions.

- The recommended procedure for a solitary toxic thyroid nodule is unilateral total thyroid lobectomy [1]. This operation is associated with less than 1% treatment failure and only 2.3% hypothyroidism.
- Total or near total thyroidectomy is recommended for toxic multinodular goitre [1]. The incidence of malignancy is 3%-9% rendering this procedure adequate for such lesions. The recurrence rate is less than 1% and the patient becomes euthyroid soon after the operation.

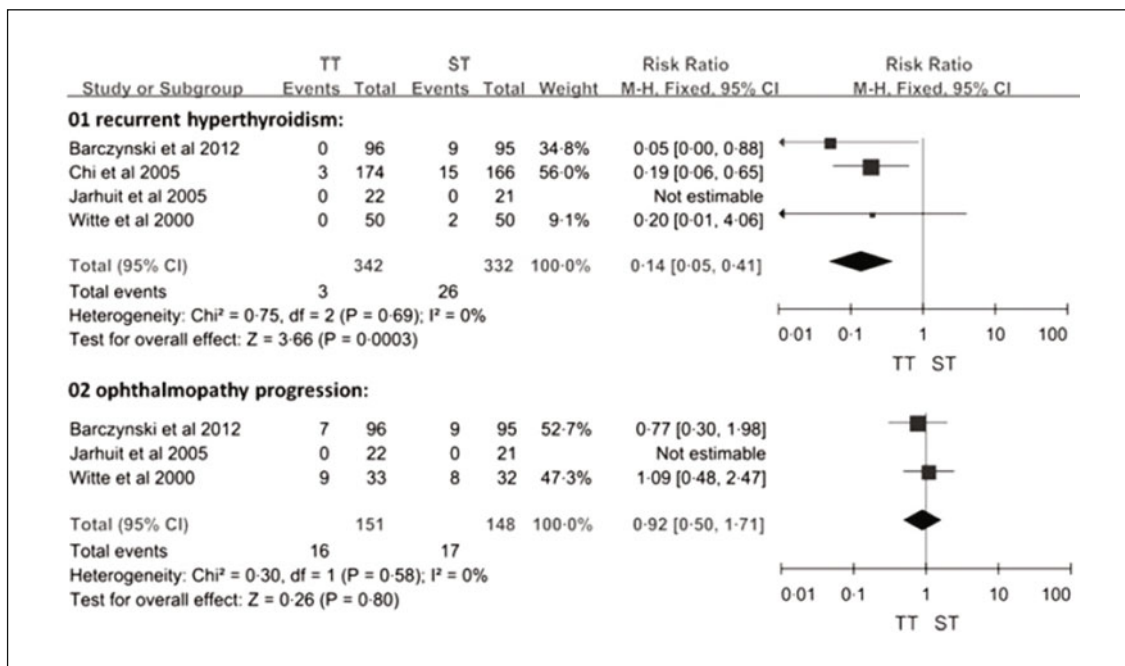


Figure 1.

- Total or near total thyroidectomy is also indicated for Graves' disease [1,5-9]. The incidence of malignancy is less than 2% in these patients [1]. Nevertheless, more recent publications suggest that even in Graves' disease, the incidence of malignancy can reach almost 5% [6].

Conclusions

- For a benign toxic solitary nodule, a total lobectomy can be performed.
- The procedure of choice for benign toxic multinodular goitre is total thyroidectomy since it may decrease the recurrence rate, can decrease the reoperation rate, can decrease the overall morbidity associated with a re-operation, and can successfully manage "occult" thyroid cancers.
- The operation should be performed by an experienced surgeon so as to reduce the risk of permanent complications (i.e. RLN palsy and hypoparathyroidism) to less than 1-2%.

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