

Total Thyroidectomy: the first, the best. The recurrent goiter issue

A. Cappellani, A. Zanghì, F. Cardì, A. Cavallaro, G. Piccolo, S. Palmucci*, G. Fuccio Sanzà*, M. Di Vita

Department of Surgery and Medical and Surgical Specialties, General And Breast Surgery Unit, University of Catania; *Department of Medical, Surgical and Advanced Technologies "G.F. Ingrassia", Radiology Unit, University of Catania, Italy

Abstract

Background. Redo surgery for recurrent goiter is still now, even in experienced hands, followed by higher morbidity than primary total thyroidectomy. Suppressive Levothyroxine therapy failed to improve the recurrence rate, while inducing a subclinical hyperthyroidism. Aim of this study is to verify morbidity after total thyroidectomy for benign thyroid diseases, both primary and after recurrence.

Materials and Methods. A series of 20 cases of total thyroidectomy for recurrent benign diseases (RG), performed between January 2001 and December 2013 was compared with 225 cases of primary total thyroidectomy (PT). Cancers, even incidentally diagnosed, were excluded. At least a 12 months follow up was accomplished. Due to the small size of the sample for RG, statistical analysis was performed by Fisher test only.

Results. Postoperative complications were Transient hypocalcemia: 5 (25%) in RG and 18 (8%) in PT, Permanent hypocalcemia only 2 (10%) in RG (significant for $p < 0,05$), Transient RLN deficit 5 (25%) in RG and 6 (2.6%) in PT (significant for $p < 0.05$).

Conclusions. Differences in incidence of perioperative complications cannot be advocated to justify a less than total thyroidectomy even in benign disease setting. The need for a redo surgery with its burden of morbidity is *per se* a good reason to avoid a conservative surgery. Further, suppressive therapy with Levothyroxine often fails to avoid recurrence, inducing in some cases a specific morbidity.

Our experience confirms the results of our previous experiences and of literature on this topic: the best management of recurrent goiter is its prevention by primary total thyroidectomy. *Clin Ter 2017; 168(3):e194-198. doi: 10.7417/CT.2017.2005*

Key words: complications, recurrent goiter, surgery, thyroidectomy

Introduction

The usually long time between primary surgery and recurrence of benign thyroid disease (8- 26 years in most series) has caused an underestimation of the issue. In most of cases, in fact, patients go lost at the follow up (1-5).

Nevertheless, a careful review of literature shows that this event can involve from 2 to 39% of primary less- than- total thyroidectomies (1-5). Without replacement therapy, the rate rises up to 70 % (1-5).

Such numbers have a significant value, since the need for a redo -surgery is burdened with a higher rate of permanent complications.

Since 2001, at our institution total thyroidectomy is the routinary surgery for benign thyroid disease, with the only exception of Plummer adenoma. In the same period recurrent goiters were treated with completion thyroidectomy, none of them having had primary surgery in our Unit.

We retrospectively reviewed the chart of these patients with the aim to compare morbidity of the two groups and to verify the influence of suppressive therapy on development of recurrent goiter.

Materials and Methods

All cases of total thyroidectomy performed for benign diseases from January 2001 to December 2014 at General and Breast Surgery Unit of Surgery Department of University of Catania Hospital- Policlinico were searched. Cases of Hyperthyroidism have been excluded. 245 case have been retrieved, 20 cases for recurrent goiter (RG) (none of them had been previously treated at our institution) and 225 primary total thyroidectomies (PTT).

The 20 recurrences were 12 women and 8 men, aged between 65 and 83 years old. The recurrences were diagnosed between 9 and 26 years after the initial operation (average 18,65). Four of the recurrences occurred in patients previously undergone a lobectomy and isthmusectomy. Fifteen patients had a subtotal thyroidectomy. Two of them (1 man and 1 woman) had a monolateral permanent deficit of the recurrent laryngeal nerve.

The PTT group included 147 women and 78 men, aged between 32 and 84. Demographics and characteristics of the two groups are described in Tab. 1.

Correspondence: Maria Di Vita MD, Department of Surgery and Medical and Surgical Specialties, General And Breast Surgery Unit, University of Catania, AOU Policlinico Vittorio Emanuele II, via Santa Sofia 78, 95124 Catania. E-mail: divitama@unict.it; maria.d.divita@gmail.com

Table 1. Demographics and characteristics of the two groups

	PT	RG
N	225	20
Sex ratio F/M	147/78	12/8
Age, mean (range)	51(32-84)	72 (65-83)
Previous surgery- lobectomy + isthmusectomy		4
Previous surgery- subtotal thyroidectomy		16
Previous monolateral deficit of RLN	1	2
indication for surgery		
Nodular goiter with Thy3B in 2 or more FNAC or Thy4)	179	3
Compressive symptoms	46	17

The indications for the surgical procedures were compressive symptoms (N=17), and suspected neoplasia (=3), these latter histologically not confirmed in any cases.

The preoperative evaluation always included the routine laboratory screening, FT3, FT4, TSH levels, Calcemia, PTH level, chest radiograph focusing in particular on the trachea, esophagogram in the eleven cases of recurrent goiter operated on between 2001 and 2005 and after this date a TC scan. In all cases a fiberoptic laryngoscopy has been performed.

A woman in the group of primary thyroidectomies had a monolateral permanent palsy of recurrent Laryngeal nerve discovered at preoperative laryngoscopy and possibly hesitated to a previous orotracheal intubation for abdominal surgery. She was diabetic as were 28 patients in the same group and 4 in the group of redo surgery.

The standard treatment for all recurrences was a total thyroidectomy.

In all cases the lymph nodes included in the specimen (three in one case and one in the other two) were negative for metastasis.

The recurrent laryngeal nerves (RLN) and the parathyroid glands were routinely identified. Performing this procedure has been relatively easy for the cases of previous lobectomy and isthmusectomy while in the remaining cases required longer times. In the 2 cases of permanent unilateral RLN injury from the previous operation, the nerve was not identified because of absence of thyroid tissue on that side (N=1) or because the nerve was not recognizable (N=1). In the case of previous recurrent palsy from not surgical condition, the nerves have been identified and preserved on both sides but this care did not prevent from a bilateral deficit.

During the postoperative course the serum calcium level was checked twice a day for two consecutive days in all patients. Further examinations were performed only in patients with hypocalcemia on previous evaluation or in presence of symptoms.

The laryngeal nerve function was assessed clinically. Fiberoptic laryngoscopy was only utilized in suspicious cases.

Due to the small size of the sample for RG, results were statistically analysed by Fisher test only.

Due to the nature of the study, we analysed only patients come at our observation with indications to surgery and being our institutional approach the TT we don't have information about the real incidence of recurrence after ST in our population nor there are, at our knowledge, studies of such nature published.

Results

The average surgical time for RG group cases was 124 minutes (range 88-255 minutes), as opposed to 87 minutes (range 72-170 minutes) of the primary thyroidectomy.

Three of the patients with previous lobectomy + isthmusectomy had also a significant recurrence at the site of previous surgery.

The length of hospital stay was similar in the two groups being 2 days for all patients but two. One for a bleeding in group PTT and one for symptomatic hypocalcemia in group RG .

Postoperative complications were evaluated for statistical significance by Fisher test: transient hypocalcemia (less than 7 days) was observed in 35 patients of PTT group and 5 of RG. The difference, although apparently high, was not significant (Fisher test value 0,367). Among the 35 of PTT group only two became symptomatic. One patient of PTT group and 2 from RG developed permanent hypocalcemia (more than 6 months) and are currently on oral replacement therapy. In this case the difference between groups was significant (Fisher test value 0,0214, significant for $p < 0,05$). One case of permanent RLN deficit occurred in a diabetic patient with previous monolateral palsy in PTT group and she is actually doing well with speech therapy rehabilitation; two more patients developed transient unilateral RLN deficits, which resolved within 2 months. In the RG group were observed 3 cases of transient recurrent laryngeal palsy but none of permanent paralysis. The difference between groups with regard to transient palsy was significant ($p < 0,05$), but it was not for permanent vocal cord paralysis (Fi-

Table 2. Complications in the two groups of patients (PT and RG)

Outcome	Primary Thyroidectomy (PT)	Recurrent Goiter (RG)	Statistical significance (Exact Fisher test)
Total Thyroidectomy	225	20	
Transient hypocalcemia	35 (15,55%)	5 (25%)	$p = 0.367$
Permanent hypocalcemia	1 (0,4%)	2 (10%)	$p = 0,0214$
Transient RLN deficit	3 (1,3%)	3 (15%)	$p < 0,05$
Permanent RLN deficit	1 (0,4%)	0	$p = 1$

sher test value = 1). The postoperative complications (both transient RLN palsy and permanent hypocalcemia) after redo operations were higher than those in patients who underwent primary thyroidectomy, even if the different size of the two groups limited its statistical relevance with regard to transient hypocalcemia and permanent RLN deficit. Results are described in Tab. 2.

Discussion

A recurrent goiter can be the expression either of the development of new nodules after subtotal bilateral thyroidectomy, or of the enlargement of small nodules left behind at the time of the primary operation (5); a third cause can be a compensatory hyperplasia of the residual thyroid parenchyma (6).

A recurrence can arise from a parenchyma never before treated, after lobectomies or lobectomies + isthmusectomies (false recurrence) or from residual parenchyma after subtotal or near total thyroidectomies. In three of four cases of recurrence after lobectomy we found the glandular enlargement involving not only the residual lobe but also the remnant at the side of previous surgery.

But even after a total thyroidectomy a recurrence can be observed, arising in ectopic thyroid tissue or from structures embryologically related to the development and migration of thyroid buds (i.e. thyreoglossal duct, pyramidal lobe, thyreothymic remnant, tubercle of Zuckerkandl) (7).

The large meta-analysis by Cirocchi, Trastulli et al. has reported only 1 recurrence in 425 cases of PTT (0.2%) compared to 8.4% (53/632) in patients treated with subtotal thyroidectomy (8) confirming that PTT is the only way to prevent recurrence and the exceptionality of such event after PTT.

In these cases the treatment will be more complex and require a very rigorous surgical indication. In our experience we never met such occurrence.

Some authors limit the definition of recurrent goiter to cases in which an echographic volume greater than 20 cc and/or new nodules of volume greater than 0.5 cc are found (9).

In our series the mean volume was 41 cc (range 28- 60 cc) for recurrent goiter and 45 (32- 65cc) for primary ones.

The recurrence rates of goiter, either symptomatic or asymptomatic nodules, after conservative treatment have been reported between 2.5% up to 73% (average 10%) (1-5), and it is usually associated with euthyroid multinodular goiters and, mostly, with a larger glandular remnant (10).

The recurrences after the apparent removal of the entire affected glandular tissue could be due to the polyclonal origin of the thyroid nodules (11), or to the polyclonal growth potential of morphologically and functionally independent cell aggregates present in the entire gland (12).

Multinodular goiter should be so considered as a disease of the entire gland, even if apparently limited to a lobe, and, as such, it should be treated with a total thyroidectomy (4).

After a total thyroidectomy, we would face a recurrence only in case of a non-recognized or ectopic thyroid remnant (7). Nevertheless, the debate on this approach for a benign disease is still open.

In favour of conservative approach is reported the avoidance of lifelong replacement therapy and of complications as injuries to the RLN or permanent hypoparathyroidism. (13).

Further, the observation that not all the recurrence need surgery lead some author to still advocate a more individualized selection of the extent of resection for endemic goiter (13,14). In addition, some Authors suggest that the risk of missing an occult cancer is very small and that Levo-Thyroxin could not be everywhere or at every time available (13-15).

This last issue is becoming actual in many countries in these last years (16) but we think that it can't be utilized as a rule on a worldwide basis.

On the other hand, it is very difficult, among the largely variable descriptions of techniques, understanding what is the ideal thyroid residual tissue that would prevent the risk of hypothyroidism and it is almost impossible to leave enough functioning thyroid tissue without exposing the patient to an unacceptable risk of recurrence (2,3,17).

Indeed, most patients will need replacement therapy because of a persistent subclinical hypothyroidism with difficulty to achieve a good hormonal compensation (15,17).

Marchesi et al. in 1998 in their experience of 108 subtotal thyroidectomies and 451 total thyroidectomies for multinodular euthyroid goiter concluded that there is no "hormonal" benefit in conservative surgeries, while total thyroidectomy, instead, reduces the recurrences by 26%. The same Author reported significant transient complications in about 50% of patients undergone surgery for recurrent goiter (18).

Even the entity of the hormonal treatment, suppressive or replacement therapy, after conservative surgery, has been largely questioned, with controversial results.

Most studies agree about the need for some form of treatment, being the recurrence rate excessively higher in patient not treated with levothyroxine than in those treated (42 -57% vs 5% - 28% (2).

However, a report with 30-year follow-up showed that the recurrence rates were similar (41% and 45%) in treated and untreated patients (19).

In a recent study comparing two groups of patients with recurrent goiter, undergone either suppressive or replacement therapy, the former had a significantly shorter interval between first intervention and redo surgery but this could be related to a more rigorous follow up in this group of patients (1). This report supports and confirms the opinion that the administration of levo-thyroxine cannot prevent all recurrences.

Because LT4 suppressive therapy results, by definition, in subclinical hyperthyroidism, treated patients may be at increased risk for atrial fibrillation, other cardiac abnormalities, or reduced bone density. These possibilities, combined with the uncertainty regarding efficacy, has led to recommendations that vary depending upon the age, sex, and menopausal status of the patient

In addition, if we consider that the recurrences usually become evident after 8-10 years from the initial treatment, it is likely that we will encounter higher recurrence rates as the follow-up period extends (19). In the groups studied by Miccoli in the cited article the mean intervals from first operation to recurrence were 24 and 27 years (1).

Even if most patients are placed, after conservative surgery, under therapy with L-Thyroxin, some authors still recommend to avoid total thyroidectomy because of an alleged higher rate of complications (14) such as iatrogenic unilateral or bilateral RLN injury or permanent hypothyroidism.

Nevertheless, in many series the incidence of such complications after total thyroidectomies for benign diseases is not significantly higher than after conservative interventions or even lower (12).

Performing a conservative surgery (i.e. sub-total thyroidectomy) doesn't eliminate the need of visualizing the RLN and the parathyroids. Seiler et al reported a decrease of RLN injuries from 2.7% in partial resections (from 1972 to 1990), to 0.7% in more radical approaches (total hemi-thyroidectomy with contralateral subtotal thyroidectomy, at a minimum) in the years 1991 to 1996 (12). Our paradoxical result with permanent laryngeal palsy occurred in a diabetic patient who already had a permanent vocal cord paralysis, related to a previous abdominal surgery with orotracheal tube. This event suggests that the contralateral deficit could be related to factors different from thyroidectomy.

The incidence of hypoparathyroidism has decreased, as well (from 3.6% to 1%) (14,20). They related this apparently paradoxical result to the routine intraoperative visualization of the laryngeal recurrent nerve and of parathyroids in total or near total thyroidectomy.

Nevertheless, the permanent hypoparathyroidism is directly related to the surgical technique. Thomusch found that the independent risk factors for hypoparathyroidism were a total thyroidectomy, the bilateral central ligation of the inferior thyroid arteries; the identification and preservation of only one or, worse, no parathyroids (21). Even the use of devices as Focus® seems not to be useful to decrease the risk for this complications (22).

A further incentive to choose total thyroidectomy instead than subtotal thyroidectomy could be found in the possibility to prevent leaving occult cancers in situ. The already cited work by Cirocchi et al supports this view showing that the incidence of cancer discovered after TT is higher than after ST (34/465, 7.3% for TT and 41/669, 6.1%, for ST, $p=0.27$) (8).

Since total thyroidectomy is gaining worldwide acceptance, surgery for recurrent goiter should become more rare but, due to the long time interval between primary surgery and recurrence, this occurrence still happens (1-4, 23). As a consequence we still face with the specific issues related to recurrence: the indications to the treatment and the treatment technique itself.

Obviously, the surgical indications are the same as for primary goiter:

- suspect neoplasia;
- hyperthyroidism;
- tracheal deviation or compression;
- mediastinal syndrome;
- cosmesis

But, being the risk of complications significantly higher in completion thyroidectomy, the indications have to be selected very carefully and alternatives to surgery should be taken in consideration. In fact, the incidence of RLN lesions, both unilateral and bilateral, have been reported up to 5 times higher in redo operation compared to primary

operation, even if performed by a same surgical team (20). Although in some series the permanent palsy of RLN is as rare after redo surgery as after primary surgery (1), the permanent hypoparathyroidism seems to occur much more frequently after redo-operation (0.5-9.5%) compared to primary surgery (0.4%) (18, 19).

In case of hyperthyroidism or compressive symptoms, some authors advocate the use of radio Iodine, at least for poor surgical candidates (24,25). The radioiodine therapy is well tolerated and often a single dose is able to achieve the result that will become evident after a latency of 2-3 months. This time could be too long if the indication to surgery is given by compressive symptoms. In addition, if the goiter is larger than 60 g, especially in Graves' disease, it can be more difficult to achieve the control of the disease (2). Thus, some drugs like amiodarone, or previous administration (within six months) of an iodine contrast, can reduce the uptake of the isotope and consequently, the efficacy of the treatment. A further contraindication to the sole use of isotope is the suspect of neoplastic nodules. In these cases the isotope can be utilized only as a bridge to surgery (24).

In evaluating the fitness of the patient for surgery, advanced age (over 75) should not be considered per se a contraindication to thyroid surgery (25). In our series, 4 of the 20 RG and 24 of the 225 PT were older than 75 and none of them developed any complication, doing as well as younger patients.

Conclusions

In conclusion, even in specialized referral centers, the intervention for recurrent goiters is burdened by significantly higher risks for complications than the primary total thyroidectomy, especially for permanent hypocalcemia and transient laryngeal palsy.

Total thyroidectomy has been, in our experience, the only intervention capable of preventing relapses also allowing an easier control of hypothyroidism and the removal of microscopic foci of cancer. The risk for permanent RLN palsy or hypoparathyroidism has not been higher than with less than total thyroidectomies, not justifying, in our opinion, a conservative approach in principle.

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