G Chir Vol. 30 - n. 8/9 - pp. 339-344
Agosto-Settembre 2009

Thyroid tissue remnants after "total thyroidectomy"

V. D'ANDREA[1], V. CANTISANI[2], A. CATANIA[1], F.M. DI MATTEO[1], S. SORRENTI[1], R. GRECO[1], K. KYRIACOS[3], G. MENICHINI[2], E. MAROTTA[2], M. DE STEFANO[1], S. PALERMO[1], C. DI MARCO[1], E. DE ANTONI[1,3]

SUMMARY: **Thyroid tissue remnants after "total thyroidectomy".**

V. D'ANDREA, V. CANTISANI, A. CATANIA, F.M. DI MATTEO, S. SORRENTI, R. GRECO, K. KYRIACOS, G. MENICHINI, E. MAROTTA, M. DE STEFANO, S. PALERMO, C. DI MARCO, E. DE ANTONI

Total Thyroidectomy (TT) is a gold standard for benign bilateral pathologies and malignant pathologies of the thyroid. TT has numerous advantages over less radical approaches, such as the resolution of the thyroid pathology, avoidance of recurrences, and improved response to lifelong substitutive organotherapy. TT has a negligible rate of recurrence. Near Total Thyroidectomy (NTT) is associated with a low rate of recurrence. Subtotal Thyroidectomy (ST), in which a portion of the thyroid gland is deliberately left in the thyroid lodge, has a considerably higher rate of recurrence. The incidence of complications with TT is similar to that with other techniques of thyroid exeresis. However, despite the radical intent of surgeons, a real TT is not always carried out. The complete removal of all the thyroid tissue employing TT is not the norm and micro/macroscopic remnants almost always remain. The literature on these tissue remnants is often based on techniques that are not very accurate in terms of determining the diameters of the tissue remaining. In our study, conducted by colour echo-doppler of the thyroid lodge in 102 patients who had undergone TT for benign thyroid pathologies, we demonstrated significant thyroid tissue remnants after TT in 34 cases of 102 (33,3%).

Therefore, out of a total of 102 so-called "total thyroidectomies", only 68 (66,7%) were really total, whereas 12 patients (11,76%) had near total thyroidectomy, leaving tissue remnants < 1 cm, and 22 patients (21,57%) had subtotal thyroidectomy, with tissue remnants ≥ 1 cm.

RIASSUNTO: **Residuo tiroideo dopo tiroidectomia totale.**

V. D'ANDREA, V. CANTISANI, A. CATANIA, F.M. DI MATTEO, S. SORRENTI, R. GRECO, K. KYRIACOS, G. MENICHINI, E. MAROTTA, M. DE STEFANO, S. PALERMO, C. DI MARCO, E. DE ANTONI

La tiroidectomia totale (TT) è il trattamento di scelta per le patologie benigne bilaterali e patologie maligne della tiroide. TT ha numerosi vantaggi rispetto ad approcci meno radicali, quali la risoluzione della patologia tiroidea, l'assenza di recidive, e la buona risposta all'ormonoterapia sostitutiva permanente. TT ha un insignificante tasso di recidive. La tiroidectomia quasi totale (TQT) è associata ad un basso tasso di recidive. La tiroidectomia subtotale (TS), mediante la quale una porzione di parenchima tiroideo viene deliberatamente lasciata nella loggia tiroidea, è associata ad un tasso più alto di recidive. L'incidenza delle complicanze della TT è simile a quella delle altre tecniche di exeresi tiroidea. Comunque, nonostante l'intento radicale dei chirurghi, una reale TT non viene sempre portata a termine. La completa rimozione di tutto il tessuto tiroideo mediante TT non è la regola e residui micro/macroscopici sono spesso presenti. I lavori della letteratura, riguardo a questo tessuto tiroideo residuo, hanno spesso impiegato tecniche non del tutto accurate nel determinare il diametro del tessuto rimanente. Nel nostro studio, condotto mediante ecocolor doppler della loggia tiroidea in 102 pazienti che sono stati sottoposti a TT per patologie tiroidee benigne, abbiamo dimostrato la presenza di un significativo residuo di tessuto tiroideo dopo TT in 34 casi su 102 (33,3%).

Pertanto, su di un totale di 102 cosiddette "tiroidectomie totali", solo 68 (66,7%) sono risultate realmente totali, mentre in 12 pazienti (11,76%) è stata eseguita una tiroidectomia quasi totale (TQT), essendo il tessuto tiroideo residuo < 1 cm, e in 22 (21,57%) una tiroidectomia subtotale (TS), con tessuto residuo ≥ 1 cm.

KEY WORDS: Tiroide - Tiroidectomia totale - Residuo.
Thyroid - Total thyroidectomy - Remnants.

Introduction

Considerable scientific evidence has been published in recent years (1-17) to show that in the treatment of malignant and benign thyroid nodular pathologies, total thyroidectomy (TT) is, in principle, more effective than near total thyroidectomy (NTT) or subtotal thyroidectomy (ST) in terms of:

Sapienza University of Rome
[1] Department of Surgical Sciences
(Chief: Prof. A. Redler)
[2] Department of Radiological Sciences
(Chief: Prof. R. Passariello)
[3] Specialised Degree Course "B" in Medicine and Surgery
(President: Prof. E. De Antoni)

- curing thyroid disease,
- avoiding recurrences,
- providing a better response to life-long substitutive organotherapy,
- allowing the use of thyreoglobulin (Tg) as a marker of recurrence or metastasis,
- allowing the use of radioiodine successively for diagnosis and therapy of any functioning neoplastic recurrences found.

Neoplastic thyreocytes maintain the capacity to fix radioactive iodine under thyreotropinic stimulation; this capacity, however, is considerably lower than that of normal thyroid cells (50-100 times less). Adjuvant metabolic radioiodine therapy is possible, therefore, only after the complete ablation of all the thyroid gland parenchyma. This total removal allows for the detection of any local or regional neoplastic recurrences or distal metastases and leads to a substantial improvement in disease progression through the use of radioisotope therapy (18).

TT is defined as the complete removal of visible thyroid tissue in the neck and has a negligible rate of recurrence. Similarly, NTT, which leaves <1 cm of residual parenchyma, often behind the recurrent laryngeal nerve (RLN) near Berry's ligament, is associated with a low rate of recurrence. On the contrary, ST, in which a portion of the thyroid gland is deliberately left in the thyroid lodge, has a considerably higher rate of recurrence (15).

Differentiated carcinoma of the thyroid is characterised by disease progression with a low mortality rate; however, recurrences can appear even years after surgical treatment and therefore long-term clinical monitoring protocols are required (18).

After surgery, attentive monitoring of patients with thyroid cancer is essential in order to detect local or regional recurrences and to ensure that there are no distal metastases (17).

According to recently published European and American guidelines, in the treatment of patients with differentiated thyroid cancer, ultrasound of the neck to evaluate the thyroid lodge and the lymphonode compartments of the neck is recommended at 6 to 12 months and then annually for at least 3 to 5 years, depending on the patient's risk category (1, 2, 17).

The main objectives of the follow-up are the:

- early identification of any signs of disease persistence,
- identification, in the first stage, of recurrences or metastases,
- monitoring of suppressive doses of levothyroxine.

Careful surveillance in order to identify any recurrences in apparently disease-free patients is the primary objective of long term follow-up. Postoperative evaluations include an objective examination of the neck, thyroid and laterocervical colour echo-Doppler, X-ray of the thorax to show any lung metastases, iodine-131 whole body scanning (WBS), tumor markers such as thyreoglobulin (Tg) for carcinomas of thyreocyte genesis, and calcitonin for medullary thyroid carcinoma (17).

The recurrence of papillary carcinoma in the thyroid lodge, particularly in elderly patients with extrathyroid pathology, is associated with a significant increase in the mortality rate related to cancer (17, 19, 20). Early detection of local/regional recurrences, in patients with invasive pathology is essential to achieve improved therapeutic surgical results or metabolic radiotherapy success (17).

Regarding lesions situated in the thyroid lodge of patients who had previously undergone thyroidectomy, the distinction between thyroid cancer recurrence, benign recurrence and thyroid remnants is not always straightforward based solely on ultrasound results, due to the lack of specific diagnostic criteria.

Cytopathologic examination of fine-needle aspiration samples or surgical excision of suspect nodes is sometimes necessary to determine the histological nature of such lesions (17).

We carried out colour echo-doppler examinations of the thyroid lodge in 102 TT patients to demonstrate that TT does not always correspond with the complete removal of the thyroid gland and that a significant number of TT cases should be declassified into NTT or ST.

Patients and methods

A retrospective analysis of patient database of the Department of Radiological Sciences was conducted to identify all the patients who had undergone total thyroidectomy for benign thyroid pathologies.

During the follow-up, at intervals of 6-12 months, all the patients were first prescribed: - thyroid hormones, in their free fraction (FT3, FT4); TSH (thyroid-stimulating hormone); thyreoglobulin and/or antithyreoglobulin antibodies during suppressive and/or substitutive hormonal therapy; colour echo-Doppler of the neck and, in the case of doubtful ultrasound results, scintigraphy.

Ultrasound of the neck is recommended to evaluate the thyroid lodge and the lymphonode compartments at 6 and 12 months, and then yearly for a period of time that depends on the risk category of the patient. All the patients in this study underwent an ultrasound of the neck within a year of surgery. A Technos MPX, Esaote, Genova, Toshiba Aplio VX, Osaka, Japan, equipped with a high frequency linear probe (7.5-13 MHZ) was used. The examination was conducted by an expert operator to detect the presence of any residual thyroid tissue and/or other neck pathologies. When residual thyroid tissue was found, at least two diameters were measured and ultrastructural and vascularization evaluations were carried out.

A total of 102 patients were selected who had undergone ultrasound examination of the neck during follow-up after total thyroidectomies carried out at different Hospitals for benign thyroid pathologies from January 2004 to December 2007, 12 males and 90 females (ratio M/F = 1/7,5), mean age 57 years (range 18–81 years).

Results

Thyroid gland remnants were found in 33.3% of the total cases examined (34/102); of these, 32 patients were female and 2 were male M/F = 1/16); the mean age was 56.9 years (range 34–79 years). Therefore, there were no significant differences in terms of age or sex. The mean maximum diameter of the gland remnants observed in the thyroid lodge was 10.58 mm (range 4–30 mm).

Of these 34 cases, 22 (64,7%) showed a maximum diameter of tissue remnants of ≥ 1cm, while in 12 cases (35.3%), the maximum diameter of gland parenchyma was < 1cm.

Therefore, out of a total of 102 TTs, only 68 (66,7%) were effectively total, whereas 34 (33.3%) were shown to be less than total; specifically 12 patients of 102 (11.76%), who instead of having undergone a TT, had had an NTT, leaving parenchyma remnants <1cm; while 22 (21.57%) patients really underwent an ST, with tissue remnants ≥1cm.

In 10 of the 34 cases (29.4%) the thyroid parenchyma remnants were found to be bilateral in the thyroid lodge, while in 24 cases (70.6%) it was unilateral. Of the latter, 9 cases (37.5%) were on the right and 15 cases (62.5%) on the left.

Discussion

TT has numerous advantages over less radical approaches, such as the resolution of the thyroid pathology, avoidance of recurrences, and improved response to life-long substitutive organotherapy. TT allows the use of thyreoglobulin (Tg) as a marker of recurrences and metastases, and also the subsequent use radioiodine for diagnosis and treatment of functioning metastases. Despite the fact that TT as the initial treatment remains controversial, it is nonetheless recommended for the treatment of the majority of patients with benign or malignant thyroid pathologies (1, 2, 16).

Although papillary carcinoma has a disease progression that is not highly aggressive and the mortality rate is not high, recurrences can occur even many years after surgical treatment (18-21). Recurrence of papillary carcinoma in the thyroid lodge, particularly in elderly patients with extrathyroid pathologies, carries a significantly increased risk of mortality (17, 22, 23). Early diagnosis of local/regional recurrences in patients with invasive diseases is, therefore, important to achieving greater surgical therapeutic success and/or more effective radio-metabolic treatment. Thus, long-term monitoring protocols are essential with such patients (18).

The extension of TT to benign thyroid pathologies is still a matter of discussion. The object of surgical treatment is to ensure the best therapeutic treatment with the lowest possible risk of complications and to avoid the need to reoperate the neck. TT is the treatment of choice when the thyroid pathology involves both lobes and if there is a high risk of recurrence, as in multinodal benign goitre, Flaiani-Graves-Basedow disease and cancer (6, 24, 25). Some surgeons maintain that the morbidity of non-total operations is lower than TT (24, 26, 27); therefore, they generally prefer ST for benign pathologies. In agreement with certain authors, TT may be preferable in order to achieve the complete eradication of the disease and to prevent recurrences, to facilitate radioiodine treatment and to eliminate the risk that the irradiated thyroid can degenerate into a malignant state (24, 28). Arguments against this strategy are based on a higher rate of complications, in particular, lesion of the recurrent nerve and hypoparathyroidism and the need for life-long substitutive organotherapy (24, 29-31).

The efficacy of suppressive treatment with L-tiroxina is still controversial (24, 32-36); substitutive organotherapy in TT patients can be considered as a dependence, but more than half of the patients who undergo Dunhill Procedure (DP) or ST need to take L-tiroxina (24). DP is a technique of thyroid removal first carried out at the beginning of the last century by Sir Thomas P. Dunhill (1876-1957), who used the procedure for toxic goitre. This procedure consists in the removal of a lobe, the isthmus and from half to two thirds of the contralateral lobe (24, 37). The term DP was used with reference to treating Graves' disease by certain authors (24, 38, 39).

It has been suggested that TT is a gold standard for diffuse bilateral pathologies and malign pathologies of the thyroid. Another factor in favour of TT is the risk of cancer onset or recurrence in residual thyroid tissue after NTT (40). The incidence of complications with TT is similar to that with other techniques of thyroid exeresis, thus, TT could be adopted for surgical treatment also in cases of benign thyroid pathology. In addition, reoperation of the neck carries a higher risk of morbidity; therefore, the authors consider TT to be the treatment of choice, despite the need for life-long substitutive organotherapy (24).

TT has a low risk of local/regional recurrence and facilitates detection of metastases both through serum Tg assessment and through ^{131}I WBS (13, 14, 16). Furthermore, TT can improve survival in high-risk patients without increasing surgical morbidity, if carried out expertly (41).

Some authors carry out TT from one side and ST from the other for benign thyroid pathologies such as Graves' disease and nodular goitre (24, 26, 27). It has been observed that TT is indicated for Graves' disease

and that it is as safe as ST (24, 26, 39); Koyuncu et al. (24) performed TT also for other benign thyroid diseases (24).

Pappalardo et al. (42) compared TT and DP during a long-term follow-up period, and they saw recurrences in 10 (14%) of 72 patients operated on with ST (24). Koyuncu et al. (24) compared three different techniques of thyroid removal: TT, ST and DP. The rate of paralysis of the RLN with TT compared with ST was 0-1% e 1-3%, respectively (24, 43-45). The rate of permanent hypoparathyroidism with TT compared with ST was 0-3,8% and 0-0,2% respectively (24, 43, 44). The most important factor in the prevention of complications with thyroidectomy is the use of an appropriate surgical technique; the identification and conservation of the parathyroid and recurrent laryngeal nerve during surgery is considered the most valid method of avoiding more serious complications. Routine identification and conservation of these organs and their vascularization leads to a reduction of complications to the minimum (24). The study of Koyuncu et al. (24) did not show any permanent paralysis of the RLN in any of the 3 groups.

It is a common opinion that, despite the radical intent of surgeons, a real TT is rarely carried out. Remnants of thyroid tissue are often found and usually treatment with radioiodine (RAI, ^{131}I) is necessary for the complete ablation of the remaining material (16, 46).

The literature on these tissue remnants is not very recent and is often based on techniques that are not very accurate in terms of determining the diameters of the tissue remaining (16, 47-49).

The first study in this area was in 1942 when Reinhardt employed autoradiography with ^{131}I and observed thyroid tissue remnants in 7 of 12 rats that had undergone TT (16, 50). After this initial research, numerous clinical studies almost always demonstrated the presence of functioning thyroid tissue after TT, so much so that in certain centres, after ablative surgical treatment, therapy with radioiodine was carried out without a preliminary WBS (16, 50-52). The study of Salvatori et al. (16) showed that in 93.1% of TT, some residual thyroid tissue remains. In fact, these authors showed that only 6.9% of patients were clear of thyroid tissue after TT; 381 patients had residual thyroid tissue inside and 236 outside of the tumoural bed. The criteria defining the success of a thyroid ablation specify the complete removal of every visible functioning area in the thyroid lodge, a 24-h ^{131}I quantitative neck uptake (RAIU test) lower than 1% and a serum Tg off LT4 (serum Tg levels measured after L-T4 withdrawal; TSH > 30 µUI/ml) less than 2 ng/ml in the absence of Tg Ab. That study showed that many patients had thyroid remnants contralaterally of the affected lobe, demonstrating that attention is focused primarily of the diseased lobe in the case of unilateral pathology (16).

In the present study, we found significant levels of thyroid tissue remnants after TT in 34 cases of 102 (33.3%). Ultrasound evaluation of the neck showed 12 cases (11.7%), which should be re-classified as NTT (remnants < 1 cm), and 22 (21.6%) as ST (remnants ≥ 1 cm); thyroid remnants as large as 3 cm of parenchyma were observed (range 0.4-30 mm).

The 6.9 % of effective TT found by Salvatori et al. (16) is not excessively low considering that the authors evaluated the presence or absence of thyroid remnants using the most accurate qualitative and quantitative diagnostic available and they established a strict cut-off value and highly specific criteria to define thyroid remnants. In particular, they scanned the neck using therapeutic doses of radioiodine; a very accurate diagnostic method to detect thyroid remnants due to the high photon stream and the consequent elevated thyroid remnant to the background radioactivity ratio (16, 53). This 6.9% of patients without thyroid remnants, which was considered high by the authors, could be explained by the fact that they decided to evaluate only patients operated on by surgeons expert in endocrinology (16).

Sosa et al. (54) demonstrated that the individual experience of the surgeon was significantly associated with the rate of post-thyroidectomy complications and the duration of postoperative hospitalization. He found a relationship between the experience of the surgeon and postoperative clinical progression in thyroid surgery. It is not surprising that the expertise of the surgeon can influence the percentage and the diameters of thyroid tissue remnants after TT (16).

In patients with thyroid tissue remnants, analysis of the distribution of ^{131}I has shown that a significant number of functioning tissue foci situated at the extreme superior pole and in the pyramidal lobe, and these results could be explained by anatomical and pathophysiological reasons (16). Fratkin et al. (55) demonstrated that an area of difficulty for surgeons is Berry's ligament, a small, dense portion of the mid-posterior area of the thyroid capsule, which in any case is rather variable. This ligament links the thyroid tightly to the antero-lateral face of the trachea; the RLN runs inside this ligament for a few millimetres. Thus, in an attempt to avoid damaging this nerve, incomplete resection of the thyroid gland in this area may result in foci of ^{131}I uptake in postoperative scans.

In conclusion, TT is the surgical intervention of choice in malignant thyreopathologies and also in diffuse benign diseases affecting both lobes. It leads to a percentage of complications similar to NTT and ST, therefore, in our opinion, it represents the gold standard not only for malignant thyroid pathologies, but also for the majority of benign thyroid diseases. When carried out in specialized centres for thyroid surgery, the rate of complications is low. However, the complete removal of all

the thyroid tissue employing TT is not the norm and micro/macroscopic remnants almost always remain (47, 48).

All patients undergoing TT, and not only those operated on for cancer of the thyroid, should be re-examined 6 months after the operation with a colour echodoppler of the thyroid lodge and reclassified on the basis of tissue remnants as follows:

A) Total Thyroidectomy (TT) = absence of macroscopic thyroid tissue remnants;
B) Near Total Thyroidectomy (NTT) = presence of thyroid tissue remnants < 1 cm;
C) Subtotal Thyroidectomy (ST) = presence of thyroid tissue remnants ≥ 1 cm.

References

1. Pacini F, Schlumberger M, Dralle H, et al. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. Eur J Endocrinol 2006; 154:787-803.
2. Cooper DS, Doherty GM, Haugen BR, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2006; 16:109-42.
3. Zambudio AR, Rodriguez J, Riquelme J, et al. Prospective study of postoperative complications after total thyroidectomy for multinodular goiters by surgeons with experience in endocrine surgery. Ann Surg 2004; 240:18-25.
4. Müller PE, Kabus S, Robens E, Spelsberg F. Indications, risks, and acceptance of total thyroidectomy for multinodular benign goiter. Surg Today 2001; 31:958-62.
5. Mishra A, Agarwal A, Agarwal G, Mishra SK. Total thyroidectomy for benign thyroid disorders in an endemic region. World J Surg 2001; 25:307-10.
6. Gough IR, Wilkinson D. Total thyroidectomy for management of thyroid disease. World J Surg 2000; 24:962-5.
7. Friguglietti CU, Lin CS, Kulcsar MA. Total thyroidectomy for benign thyroid disease. Laryngoscope 2003; 113:1820-6.
8. Colak T, Akca T, Kanik A, et al. Total versus subtotal thyroidectomy for the management of benign multinodular goiter in an endemic region. ANZ J Surg 2004; 74:974-8.
9. Bron LP, O'Brien CJ. Total thyroidectomy for clinically benign disease of the thyroid gland. Br J Surg 2004; 91:569-74.
10. Hisham AN, Azlina AF, Aina EN, Sarojah A. Total thyroidectomy: the procedure of choice for multinodular goitre. Eur J Surg 2001; 167:403-5.
11. Gibelin H, Sierra M, Mothes D, et al. Risk factors for recurrent nodular goiter after thyroidectomy for benign disease: case-control study of 244 patients. World J Surg 2004; 28:1079-82.
12. Ayache S, Tramier B, Chatelain D, et al. Evolution of the thyroid surgical treatment to the total thyroidectomy. Study of about 735 patients. Ann Otolaryngol Chir Cervicofac 2005; 122:127-33.
13. Esnaola NF, Cantor SB, Sherman SI, et al. Optimal treatment strategy in patients with papillary thyroid cancer: a decision analysis. Surgery 2001; 130:921-30.
14. Mazzaferri EL. An overview of the management of papillary and follicular thyroid carcinoma. Thyroid 1999; 9:421-7.
15. Snook KL, Stalberg PL, Sidhu SB, et al. Recurrence after total thyroidectomy for benign multinodular goiter. World J Surg 2007; 31:593-8.
16. Salvatori M, Raffaelli M, Castaldi P, et al. Evaluation of the surgical completeness after total thyroidectomy for differentiated thyroid carcinoma. Eur J Surg Oncol 2007; 33:648-54.
17. Shin JH, Han BK, Ko EY, Kang SS. Sonographic findings in the surgical bed after thyroidectomy: comparison of recurrent tumors and nonrecurrent lesions. J Ultrasound Med 2007; 26:1359-66.
18. De Antoni E. Il carcinoma differenziato della tiroide. Collana Monografica della Società Italiana di Chirurgia. Torino: UTET; 2006.
19. Caballero-Calabuig E, Cano-Terol C, Sopena-Monforte R, et al. Influence of the thyroid remnant in the elevation of the serum thyroglobulin after thyroidectomy in differentiated thyroid carcinoma. Importance of the diagnostic iodine total-body scanning. Eur J Nucl Med Mol Imaging 2008; 35:1449-56.
20. Mazzaferri EL, Kloos RT. Clinical review 128: Current approaches to primary therapy for papillary and follicular thyroid cancer. J Clin Endocrinol Metab 2001; 86:1447-63.
21. National Comprehensive Cancer Network (NCCN). Thyroid carcinoma. Clinical practice guidelines in oncology, version 1. Fort Washington: NCCN; 2005.
22. McConahey WM, Hay ID, Woolner LB, et al. Papillary thyroid cancer treated at the Mayo Clinic, 1946 through 1970: initial manifestations, pathologic findings, therapy, and outcome. Mayo Clin Proc 1986; 61:978-96.
23. Grant CS, Hay ID, Gough IR, et al. Local recurrence in papillary thyroid carcinoma: is extent of surgical resection important? Surgery 1988; 104:954-62.
24. Koyuncu A, Dökmetas HS, Turan M, et al. Comparison of different thyroidectomy techniques for benign thyroid disease. Endocr J 2003; 50:723-7.
25. Siragusa G, Lanzara P, Di Pace G. Subtotal thyroidectomy or total thyroidectomy in the treatment of benign thyroid disease. Our experience. Minerva Chir 1998; 53:233-8.
26. Andåker L, Johansson K, Smeds S, Lennquist S. Surgery for hyperthyroidism: hemithyroidectomy plus contralateral resection or bilateral resection? A prospective randomized study of postoperative complications and long-term results. World J Surg 1992; 16:765-9.
27. Tschantz P, Sohrabi N, Dojcinovic S, Chèvre F. Surgical indications and techniques in Basedow's disease, multinodular goiter and thyroid cancers. Rev Med Suisse Romande 2001; 121:337-9.
28. Liu Q, Djuricin G, Prinz RA. Total thyroidectomy for benign thyroid disease. Surgery 1998; 123:2-7.
29. Cady B, Sedgwick CE, Meissner WA, et al. Risk factor analysis in differentiated thyroid cancer. Cancer 1979; 43:810-20.
30. Sugino K, Ito K, Nagahama M, et al. Surgical management of Graves' disease -10-year prospective trial at a single institution. Endocr J 2008; 55:161-7.
31. Lepner U, Seire I, Palmiste V, Kirsimägi U. Surgical treatment of Graves' disease: subtotal thyroidectomy might still be the pre-

ferred option. Medicina (Kaunas) 2008; 44:22-6.
32. Ambrosi A, Pezzolla A, Barone G, et al. Clinical study of residual function and recurrences in patients after partial thyroidectomy for non-toxic nodular goiter. Ann Ital Chir 1994; 65:543-6.
33. Berglund J, Bondesson L, Christensen SB, et al. Indications for thyroxine therapy after surgery for nontoxic benign goitre. Acta Chir Scand 1990; 156:433-8.
34. Hedman I, Jansson S, Lindberg S. Need for thyroxine in patients lobectomised for benign thyroid disease as assessed by follow-up on average fifteen years after surgery. Acta Chir Scand 1986; 152:481-6.
35. Westermark K, Persson CP, Johansson H, Karlsson FA. Nodular goiter: effects of surgery and thyroxine medication. World J Surg 1986; 10:481-7.
36. Geerdsen JP, Hee P. Nontoxic goiter. II. A study of the pituitary-thyroid axis in 14 recurrent cases. Acta Chir Scand 1982; 148:225-7.
37. Vellar ID. Thomas Peel Dunhill: pioneer thyroid surgeon. Aust N Z J Surg 1999; 69:375-87.
38. Alsanea O, Clark OH. Treatment of Graves' disease: the advantages of surgery. Endocrinol Metab Clin North Am 2000; 29:321-37.
39. Müller PE, Bein B, Robens E, et al. Thyroid surgery according to Enderlen-Hotz or Dunhill: a comparison of two surgical methods for the treatment of Graves' disease. Int Surg 2001; 86:112-6.
40. Perri S, Mariani G, Trunfio A, et al. Total thyroidectomy in the surgical treatment of thyroid disease a retrospective clinical study. Minerva Endocrinol 2001; 26:41-51.
41. Schlumberger M, Pacini F. Thyroid Tumors. Paris: Edition Nucleon; 2003.
42. Pappalardo G, Guadalaxara A, Frattaroli FM, et al. Total compared with subtotal thyroidectomy in benign nodular disease: personal series and review of published reports. Eur J Surg 1998; 164:501-6.
43. Campana FP. Total thyroidectomy of goiter. G Chir 1997; 18:467-9.
44. Foster RS Jr. Morbidity and mortality after thyroidectomy. Surg Gynecol Obstet 1978; 146:423-9.
45. Perzik S. The place of total thyroidectomy in the management of 909 patients with thyroid disease. Am J Surg 1976; 132:480-3.
46. Wartofsky L, Sherman SI, Gopal J, et al. The use of radioactive iodine in patients with papillary and follicular thyroid cancer. J Clin Endocrinol Metab 1998; 83:4195-203.
47. Huić D, Medvedec M, Dodig D, et al. Radioiodine uptake in thyroid cancer patients after diagnostic application of low-dose 131I. Nucl Med Commun 1996; 17:839-42.
48. Leger FA, Izembart M, Dagousset F, et al. Decreased uptake of therapeutic doses of iodine-131 after 185-MBq iodine-131 diagnostic imaging for thyroid remnants in differentiated thyroid carcinoma. Eur J Nucl Med 1998; 25:242-6.
49. Bajén MT, Mañé S, Muñoz A, García JR. Effect of a diagnostic dose of 185 MBq 131I on postsurgical thyroid remnants. J Nucl Med 2000; 41:2038-42.
50. Reinhardt WO. Method for determing completeness of thyroidectomy using radioactive iodine. Proc Soc Exp Biol Med 1942; 50:81-4.
51. de Klerk JM, de Keizer B, Zelissen PM, et al. Fixed dosage of 131I for remnant ablation in patients with differentiated thyroid carcinoma without pre-ablative diagnostic 131I scintigraphy. Nucl Med Commun 2000; 21:529-32.
52. Salvatori M, Perotti G, Rufini V, et al. Are there disadvantages in administering 131I ablation therapy in patients with differentiated thyroid carcinoma without a preablative diagnostic 131I whole-body scan? Clin Endocrinol (Oxf) 2004; 61:704-10.
53. Sherman SI, Tielens ET, Sostre S, et al. Clinical utility of posttreatment radioiodine scans in the management of patients with thyroid carcinoma. J Clin Endocrinol Metab 1994; 78:629-34.
54. Sosa JA, Bowman HM, Tielsch JM, et al. The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. Ann Surg 1998; 228:320-30.
55. Fratkin MJ, Newsome HH Jr, Sharpe AR Jr, Tatum JL. Cervical distribution of iodine 131 following total thyroidectomy for thyroid cancer. Arch Surg 1983; 118:864-7.