Langenbecks Arch Surg (2007) 392:685–691
DOI 10.1007/s00423-007-0201-6

ORIGINAL ARTICLE

Reoperative surgery for thyroid disease

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Received: 23 November 2006 / Accepted: 8 May 2007 / Published online: 26 June 2007

Abstract
Background and aims Reoperative surgery for thyroid disease is rare. However, it is sometimes indicated for nodular recurrence after partial surgery for initially benign thyroid disease or for a completion total thyroidectomy when a final diagnosis of well-differentiated thyroid cancer (WDTC) is confirmed on a permanent section of a partially removed thyroid gland. This surgery can expose the patient to postoperative complications such as recurrent laryngeal nerve (RLN) palsy or hypoparathyroidism. The aims of our study were to describe the population subjected to reoperative thyroid surgery and to evaluate postoperative morbidity to find the risk factor.
Patients and methods The present study is a retrospective analysis of our experience with completion thyroidectomy: 685 consecutive patients underwent this procedure in a 14-year period, for a recurrent uninodular (85 patients) or multinodular (333 patients) goiter, recurrent thyrotoxicosis (42 patients), or a completion thyroidectomy for WDTC after partial resection of the thyroid gland (225 patients). The operative technique was standardized with identification of the RLN and parathyroid glands before removal of the thyroid gland. L-Thyroxin treatment was started the day after surgery. Postoperative rates of suffocating hematoma, wound infection, RLN palsy, hypoparathyroidism, and persistence or recurrence of hyperthyroidism were studied and compared to the same parameters in patients who underwent primary bilateral thyroid gland resection during the same period.
Results The transient morbidity rate was 8%, with 5% hypoparathyroidism, 1.2% RLN palsy, 0.9% suffocating hematoma, and 0.2% wound infection. These results were higher than those from cases of primary thyroid resection for bilateral disease. Within the secondary surgery group, postoperative complications depended on the mean weight of the resected thyroid gland, hyperthyroidism, and the bilaterality of thyroid exploration during the previous surgery. The permanent morbidity rate was 3.8%, including 1.5% RLN palsy and 2.5% hypoparathyroidism. Permanent complication rates were higher than those for primary thyroid resection. Incidental carcinoma was found in 92 patients (13%): 10% (42 of 418) in patients with recurrent euthyroid nodular disease, 7% (3 of 42) in patients with recurrent hyperthyroidism, and 21% (47 of 225) in patients who underwent a completion thyroidectomy for cancer.
Conclusion Because reoperative thyroid surgery can lead to potential complications, especially permanent RLN palsy or hypoparathyroidism, it should be reserved for patients who need it. The importance of respecting specific technical rules should be emphasized.

Keywords Thyroid surgery · Reoperative · Reccurent nerve palsy · Hypoparathyroidism · Reccurent goiter

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Introduction

Reoperative surgery for thyroid disease is rare. It is indicated in case of nodular recurrence after partial surgery for initially benign thyroid disease or for a completion total

thyroidectomy when a final diagnosis of well-differentiated thyroid cancer (WDTC) is confirmed on a permanent section of a partially removed thyroid gland. Unfortunately, this procedure is linked to increased morbidity because of recurrent laryngeal nerve (RLN) injury and hypoparathyroidism [1–3]. Complications arise as a result of strong adhesions and a distorted anatomy after the previous neck exploration. The aims of our study were to describe the population subjected to reoperative thyroid surgery, to analyze the results of surgery, and to evaluate postoperative morbidity in 685 patients operated on over a 14-year period in a single center. These results were compared with 5,104 patients who underwent bilateral primary thyroid surgery during the same period.

Patients and methods

From 1991 to 2004, 8,657 patients underwent 9,017 surgical procedures for thyroid disease in our institution. Eight thousand one hundred and seventy-one primary and 846 secondary surgical procedures were carried out. One hundred and sixty-one cervical recurrences (nodal or non-nodal) of thyroid carcinoma after total thyroidectomy were excluded from the study because of specific issues. In the remaining 685 patients, the most frequent indication for reoperation was a history of partial thyroidectomy for benign disease with a recurrent uninodular (85 patients) or multinodular (333 patients) goiter. Forty-two patients were diagnosed with recurrent thyrotoxicosis, including two toxic adenoma, 20 toxic multinodular goiters, and 20 cases of Grave's disease; in these patients, the indication for surgery was compression, suspected malignancy, or recurrent hyperthyroidism impervious to iodine therapy or antithyroid drugs. Two hundred and twenty-five patients were referred for a completion total thyroidectomy because of a final diagnosis of WDTC after finding malignancy in a thyroid lobectomy or isthmectomy. Justification for performing a completion thyroidectomy in these patients included the following: age$<$70 years, tumor size$\geq$5 mm, multifocality, follicular carcinoma, some variants of papillary carcinoma (follicular, tall-cell, and columnar-cell variants), extrathyroidal extension, lymph node metastasis, and distant metastasis. A completion thyroidectomy was performed as soon as possible after establishing the definitive diagnosis, with no restriction on timing.

Vocal cord mobility was assessed via indirect laryngoscopy before carrying out secondary surgery on all patients. It was repeated after reoperation in patients with dyspnea, hoarseness, or loss of voice quality. A completion total thyroidectomy was always performed, except in cases of preoperative RLN palsy on the side opposite that of the proposed secondary thyroidectomy. In such cases, a small remnant of thyroid tissue (2 g) was left in contact with the functional RLN.

The 685 patients referred for reoperation were compared with 5,104 patients who underwent primary bilateral resection of the thyroid during the same period. All information relating to patient characteristics, operative procedures, pathology, and complications was recorded prospectively.

The operative technique has already been described [4]: dissection was started laterally by dividing the infrahyoid muscles to avoid the fibrous tissue around the thyroid remnant when the lobe had been partially removed during previous surgery. If the lobe to be resected had not been disturbed at prior operation, we went through the infrahyoid muscles to avoid fibrosis around the anterior face of the trachea. The first step was ligation of the superior thyroid vessels with special attention being paid to the superior parathyroid gland and the external branch of the superior laryngeal nerve. Then, the RLN was clearly identified in the lower part of the neck and traced very carefully along its cervical course. The inferior parathyroid gland was preserved when it was located far from the thyroid lobe. Any parathyroid gland that could not be salvaged because of its anatomic location was minced and placed in a sternocleidomastoid muscle. Collagen pads were left in the thyroid bed, and until 2000, suction drainages were left in place. From that time, the cervicotomy was closed without drainage. In case of a completion thyroidectomy for cancer, patients with lymph node metastasis diagnosed before or during surgery had a modified radical neck dissection, including resection of lymph nodes of the central compartment around the trachea (compartment VI) and those around the jugular vein extending from the carotid sheath to the trapezoid muscle and from the subclavian vein to the hypoglossal nerve (compartments II and IV) [5]. In patients with bilateral lymph node metastasis, modified neck dissection was bilateral. If metastasis was unilateral, modified neck dissection was performed on the affected side with limited lymph node excision on the other side. For patients with macroscopically normal lymph nodes, a limited lymph node excision was performed with blind sampling medially, behind the sternal notch, and laterally, between the carotid sheath and trapezoid muscle.

If the postoperative course was uneventful, the patient was discharged from the hospital on postoperative day (POD) 2. When RLN palsy was diagnosed on postoperative indirect laryngoscopy, a trial of speech therapy was started during the first week and continued over several months for a course of 30 treatments. RLN palsy was considered permanent if there was no proof of recovery using laryngoscopy within 6 months of surgery. The serum calcium concentration was assessed on POD1 and repeated on POD2 if the first result was less than 2 mmol/l.

Symptomatic hypocalcemia was defined as a calcemia of less than 2 mmol/l with overt manifestations, such as anxiety, carpopedal spasms, or tingling or numbness of the extremities. Asymptomatic patients with a calcemia under 1.9 mmol/l on POD1 were included in the hypocalcemic group and treated. Patients who became symptomatic after POD2 had a calcemia measurement; if it was under 2 mmol/l, they were also included in the hypocalcemic group. Hypoparathyroidism was transient if the patient required an oral calcium supplement for less than 6 months. It was permanent if the patient required an oral calcium supplement and vitamin D for 6 months or more with a plasma parathyroid hormone level below 8 pg/ml. Postoperative complications observed in patients who were lost from the long-term follow-up (>6 months) were considered permanent. Postoperative L-thyroxin therapy was started on POD1 and then adjusted according to hormonal assays.

Statistical analysis

Results are reported as median (ranges) or mean±SD. In a first analysis, the primary outcome measure was reoperative thyroid surgery. Patients who underwent a completion thyroidectomy were compared to patients who had a bilateral primary thyroidectomy using the Chi-squared test or Student's *t* test when appropriate. Univariate logistic regression was used to estimate the relationship between reoperative surgery and the following variables: sex, age, mean thyroid gland weight, pathology, and postoperative complications (transient or permanent, including RLN palsy, hypocalcemia, suffocating hematoma requiring urgent surgical drainage, superficial hematoma, and wound infection). A second analysis was only performed in patients who were reoperated on. Univariate logistic regression was used to estimate the relationship between morbidity on the one hand and the following continuous variables on the other: mean thyroid gland weight, age, and pathology. We performed a multivariate analysis including the predictive factors with significant links to morbidity in the univariate analysis; odds ratios (OR) were estimated using an unconditional logistic regression model. Significance was defined as $p<0.05$. All analyses were performed using the SAS computer software® (SAS Institute, Cary, NC).

Results

Patients who underwent primary or secondary surgery displayed similar characteristics, except for two variables: the rate of hyperthyroidism and the mean weight of the resected thyroid gland, which were higher in cases of primary thyroidectomy (Table 1). Thyroid carcinoma was found in 13% (92 of 685 patients) of the resected thyroid glands at reoperative surgery: 10% (42 of 418) in patients with recurrent euthyroid nodular disease, 7% (3 of 42) in patients with recurrent hyperthyroidism, and 21% (47 of 225) in patients who underwent a completion thyroidectomy for cancer.

Table 1 Comparison of patients who underwent primary or secondary thyroidectomy (excluding surgery for local recurrences of thyroid carcinoma)

	Secondary thyroidectomy (n=685)	Primary thyroidectomy (n=5,104)	p value
Female/male (sex ratio)	577/108 (5.3)	4,192/912 (4.6)	0.18
Mean age±SD (years)	51±14	49±14	0.49
Hyperthyroidism	42 (6%)	1,406 (28%)	<0.0001
Mean weight of the resected thyroid gland±SD (grams)	41±48	58±61	<0.0001
Associated primary hyperparathyroidism	8 (1.2%)	42 (0.8%)	0.36
Median sternotomy	3 (0.4%)	24 (0.5%)	0.91
Differentiated carcinoma	92 (13.4%)	858 (16.8%)	0.02
Lymph node metastasis	26 (3.8%)	198 (3.9%)	0.91

Table 2 Postoperative complications after bilateral thyroidectomy (5,789 patients)

	Secondary thyroidectomy (n=685)	Primary thyroidectomy (n=5,104)	p value
RLN palsy			
Transient[a]	8 (1.2%)	100 (2%)	0.15
Permanent	10 (1.5%)	23 (0.5%)	0.001
Hypocalcemia			
Transient	34 (5%)	364 (7.1%)	0.035
Permanent	17 (2.5%)	90 (1.8%)	0.19
Suffocating hematoma requiring urgent surgical drainage	6 (0.9%)	54 (1.1%)	0.66
Wound infection	1 (0.2%)	21 (0.4%)	0.51
Miscellaneous surgical complications	6 (0.9%)	13 (0.3%)	0.008
Nonsurgical complications	2 (0.3%)	37 (0.7%)	0.19
Total of complications	84	702	
Total of surgical complications	82	665	
Total of patients with at least one surgical complication[b]	81 (11.8%)	635 (12.4%)	0.65
Transient	55 (8%)	521 (10.2%)	0.07
Permanent	26 (3.8%)	114 (2.2%)	0.01

[a] Including 17 cases of bilateral RLN palsy, of which one was in the secondary thyroidectomy group (only one patient required a transient tracheotomy)

[b] Some patients had more than one complication.

In patients who underwent reoperative thyroid surgery, there were no deaths. Eighty-four early postoperative complications occurred in 81 patients (11.8%; Table 2). Fifty-one patients had symptomatic hypocalcemia requiring treatment with calcium supplements (7.4%). Oral calcium supplements and alfacalcidol were mandatory in 17 of these patients (2.5%) for 6 months and longer. They were judged to have permanent hypoparathyroidism. Eighteen patients had RLN palsy (2.6%). In ten cases (1.5%), RLN palsy was permanent. In the remaining cases, including one bilateral case, RLN palsy was transient.

When the 685 patients referred for secondary surgery were compared to the 5,104 patients who underwent primary bilateral surgery, transient hypocalcemia was found to be more frequent in primary surgery (7.1 vs 5%, OR=0.7 [95% CI 0.5–1.0]), mainly because of a high rate of hyperthyroidism in these patients (28 vs 6%). Conversely, the rate of permanent complications was significantly higher in secondary surgery (3.8 vs 2.2%, OR=1.7 [95% CI 1.1–2.7]). This result was linked to an increased risk of permanent RLN palsy (1.5 vs 0.5%, OR=3.3 [95% CI 1.6–6.9]) and a tendency for an increased risk of permanent hypocalcemia, although it did not reach significance (2.5 vs 1.8%, OR=1.4 [95% CI 0.8–2.4]). Morbidity was similar in patients who had a secondary thyroidectomy for recurrent initially benign disease or for carcinoma, except for transient hypocalcemia (Table 3). The increased rate of transient hypocalcemia in recurrent thyroid disease (6.3 vs 2.2%) was multifactorial with a heavier resected thyroid gland (47±50 vs 10±8 g), more frequent hyperthyroidism (41 of 460 patients, 8.9 vs 1 of 225 patients, 0.4%), and a higher rate of bilateral exploration during the previous surgery (120 of 460 patients, 26 vs 28 of 225 patients, 12%).

Within the secondary thyroidectomy group, significant morbidity factors were hyperthyroidism, a bilateral dissection of the thyroid gland during the previous surgery, and the weight of the resected thyroid gland (Table 4). In the multivariate analysis, the only factor that remained independent was hyperthyroidism (OR=3.6 [95% CI 1.6–8.0]). Other factors were not significant. No factors were found to significantly affect the risk of permanent postoperative complications. For transient complications, only hyperthyroidism was, again, a significant risk factor (OR=3.5 [95% CI 1.6–7.7]).

Table 3 Postoperative complications after secondary thyroidectomy (685 patients)

	Secondary thyroidectomy for initially benign disease (n=460)	Completion thyroidectomy for carcinoma (n=225)	p value
Female/male (sex ratio)	410/50 (8.2)	167/58 (2.9)	<0.0001
Mean age±SD (years)	54±12	43±14	0.06
Previous surgery: bilateral thyroid resection	120 (26%)	28 (12%)	<0.0001
Previous surgery performed in another center	433 (94%)	39 (17%)	<0.0001
Mean delay±SD (years)	17.4±10.3	0.4±1.1	<0.0001
Hyperthyroidism	41 (8.9%)	1 (0.4%)	<0.0001
Associated primary hyperparathyroidism	6 (1.3%)	2 (0.9%)	0.63
Mean weight of the resected thyroid gland±SD (grams)	47±50	10±8	<0.0001
RLN palsy			
Transient[a]	5 (1.1%)	3 (1.3%)	0.78
Permanent	8 (1.7%)	2 (0.9%)	0.38
Hypocalcemia			
Transient	29 (6.3%)	5 (2.2%)	0.02
Permanent	11 (2.4%)	6 (2.7%)	0.83
Suffocating hematoma requiring urgent surgical drainage	6 (1.3%)	0	0.19
Wound infection	1 (0.2%)	0	
Miscellaneous surgical complications	2 (0.4%)	4 (1.8%)	0.08
Nonsurgical complications	2 (0.4%)	0	
Total of complications	64	20	
Total of surgical complications	62	20	
Total of patients with at least one surgical complication[b]	61 (13.3%)	20 (8.9%)	0.1
Transient	43 (9.3%)	12 (5.3%)	0.07
Permanent	18 (3.9%)	8 (3.6%)	0.8

[a] Including one case of bilateral transient RLN palsy in a patient who underwent secondary thyroidectomy for initially benign disease
[b] Some patients had more than one complication.

Discussion

Reoperative thyroid surgery is not an innocuous procedure, even in specialized centers. Our 3.8% permanent complications rate serves to highlight the need to choose indications with great care and to minimize this procedure with an active policy of prevention. Surgical experience and good knowledge of the normal anatomical variations of the RLN and the parathyroid glands are major factors in diminishing postoperative morbidity. These factors are necessary but not sufficient because devascularization of the parathyroid glands during the previous surgery or distorted RLN anatomy because of strong postoperative

Table 4 Morbidity factors of secondary thyroidectomy (685 patients)

	Patients with surgical complications (n=81)	Patients without surgical complications (n=604)	p value
Female/Male (sex ratio)	70/11 (6.4)	507/97 (5.2)	0.57
Mean age±SD (years)	50±13	51±14	0.65
Indication for secondary thyroid surgery: recurrent nodular disease/ completion thyroidectomy for differentiated carcinoma	61/20	399/205	0.1
Bilateral dissection of the thyroid gland on previous surgery (n=148)	25	123	0.03
Number of previous operations >1 (n=39)	7	32	0.2
Mean delay±SD (years)[a]	11.2±10.0	11.9±11.9	0.06
Hyperthyroidism (n=42)	11	31	0.003
Associated primary hyperparathyroidism (n=8)	2	6	0.25
Mean weight of the resected thyroid gland±SD (grams)	49±74	40±42	<0.0001
Differentiated thyroid carcinoma (secondary surgery; n=92)	11	81	0.97
Lymph node dissection (n=237)	22	215	0.13
Lymph node metastasis (n=26)	4	22	0.57
Median sternotomy (n=3)	1	2	0.31

[a] In case the number of previous thyroid operations >1, the delay was the time passed between the most recent surgery and completion thyroidectomy.

adhesions can impair the results. Despite these considerations and recommendations, in certain situations, a secondary thyroidectomy must be performed. Thyroid carcinoma is frequently diagnosed only after reviewing permanent histologic sections, despite improvements in preoperative fine-needle aspiration biopsy (FNAB) and in intraoperative examination of a frozen section of thyroid nodules. In this case, indications for a completion thyroidectomy are still controversial when a less than total or near-total thyroid resection has been performed. However, it has been demonstrated that contralateral disease is frequent [6], that residual disease can be a major prognosis factor because a total thyroidectomy decreases the risk of local recurrence and lymph node metastasis [7] even in low-risk carcinoma [8], and that anaplastic transformation of residual disease is possible. With a completion thyroidectomy, serum thyroglobulin levels can be monitored as a marker of recurrent disease once all tissue has been removed. The effectiveness of radioactive iodine for ablation of the remaining normal tissue or of residual microscopic disease is enhanced. For these reasons, we chose in our institution to complete thyroidectomy in all patients with thyroid carcinoma, except small and single papillary carcinomas without capsular extension or lymph node metastasis.

The purpose of our study was not to demonstrate that a completion thyroidectomy for carcinoma was useful in long-term disease control but to assess pathological features and postoperative morbidity. Contralateral carcinoma was frequent (21%), and complications occurred in 8.9% of our patients, including a 3.6% rate of permanent complications. These rates were similar in reoperative surgery for patients who had a history of partial thyroidectomy for benign disease with a recurrent uninodular or multinodular goiter and for patients with recurrent thyrotoxicosis. Hypoparathyroidism was the more frequent complication. This should serve to highlight the need to protect and preserve all visualized parathyroid glands even when a single lobectomy is performed; a quick completion thyroidectomy can be indicated even if an intraoperative frozen section wrongly concluded that the examined nodule was benign, and the recurrence of initially benign disease can indicate reoperative surgery at a distance. Another issue is the risk of RLN injury. This complication is particularly frequent in reoperative surgery with a 1.5% permanent RLN palsy rate in our series, and this rate is maybe underestimated in our study because not all patients underwent laryngoscopy after surgery. Only symptomatic patients were referred for indirect laryngoscopy, and it is well known that at least some vocal cord paralyses are asymptomatic. We think that some recommendations should be respected to decrease this complication rate. Preoperatively, direct laryngoscopy should always be performed because clinical symptoms are not always reliable for documenting RLN palsy. Bilateral RLN palsy potentially requiring a tracheostomy is possible if an RLN is no longer functioning on the side contralateral to that being reoperated on with RLN damage during a secondary thyroidectomy. Intraoperatively, RLN visualization is mandatory [9]. We choose to approach the thyroid laterally because this allows the RLN to be identified at minimal risk. Once the RLN is identified, strap muscles can be divided low in the neck, and the RLN is then followed along its course. This approach is also

useful because it exposes the superior pole of the thyroid and preserves the superior parathyroid gland. Inferior parathyroid glands can usually be avoided with an extracapsular dissection, leaving them in situ. Half the inferior parathyroid glands are far from the thyroid gland and can easily be preserved with their vessels in the perithyroidal fat. For the other half, the glands must be swept off the thyroid capsule. Any devascularized parathyroid gland should be minced and transplanted into a sternocleidomastoid muscle [10].

Prevention is essential. For bilateral thyroid disease, surgical procedures should be limited to total or near-total thyroidectomy (leaving a remnant less than 2 g on one side). Recurrences cannot occur after total or near-total thyroidectomy for benign disease, and leaving one or two remnants more than 2 g induces recurrences and does not prevent the need for thyroxin replacement in many patients. Furthermore, if cancer is diagnosed at the final pathology, an isotopic completion thyroidectomy is possible without reoperative surgery and with an acceptable radiation dose. For thyroid disease limited to the isthmus or to one lobe, nothing less than an isthmusectomy or lobectomy and isthmusectomy should be performed. When a single lobe and isthmus have already been removed, the morbidity of a completion thyroidectomy can be minimized when the contralateral lobe has not been explored via palpation [11]. This operative exploration is useless because ultrasonography is widely performed when surgery is being considered for thyroid disease. Palpation is less accurate than ultrasonography, but if exploration is considered indispensable by the surgeon, it should be performed between the sternothyroid and sternohyoid muscles to prevent adhesions developing along the thyroid capsula [12]. Our results confirmed the higher risk of complications when previous surgery has been performed on both sides. This situation should gradually disappear if strict rules are respected to leave the normal thyroid lobe untouched, and to perform total or near-total thyroidectomy when a bilateral resection is needed.

Another major risk factor is hyperthyroidism, even controlled with antithyroid drugs at the time of surgery. This factor is already identified in primary resection of the thyroid gland because of vascularization and dense inflammation of the perithyroid tissue [13, 14]. When a treatment is discussed for recurrent hyperthyroidism after partial resection of the thyroid gland, close observation using antithyroid drugs or radioiodine therapy is preferable to surgery, except in case of large remnants inaccessible to radioiodine, the failure of antithyroid drugs or allergy, cold nodules, and strong suspicion of carcinoma on FNAB.

Factors other than hyperthyroidism and the bilaterality of the previous surgery influence postoperative morbidity. As expected, the weight of the resected thyroid gland is a risk factor. In large recurrent goiters, the anatomy of the RLN and parathyroid glands is frequently distorted, with vascularization compromised by the scar tissue and the volume of the thyroid. More surprising is the lack of influence of the delay between the two surgical procedures. In our series, the risk of complications proved similar whether a completion thyroidectomy was performed weeks or decades after primary surgery. On patients with cancer diagnosed on final pathology, completion should ideally be performed within a week, before dense adhesions occur linked to acute inflammation, but the final pathological evaluation is rarely available in that time limit. Because it has been reported that nothing is to be gained by waiting 2 or 3 months [15], secondary surgery can be performed at any time.

Reoperative thyroid surgery is rare and should, with good prevention rates, become the exception. Because reoperative thyroid surgery can result in potential complications, especially permanent RLN palsy or hypoparathyroidism, it should be reserved for patients who need it. The importance of respecting specific technical rules should be emphasized.

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