B-ENT, 2005, **2**, 67-72

Completion thyroidectomy after the unexpected diagnosis of thyroid cancer

B. Dewil, B. Van Damme**, V. Vander Poorten*, P. Delaere* and F. Debruyne**

*Department of Otorhinolaryngology, Head and Neck Surgery, and **Department of Pathology, University Hospitals Leuven, Belgium

Key-words. Thyroid cancer; completion thyroidectomy; hypocalcaemia; laryngeal nerve injury

Abstract. *Completion thyroidectomy after the unexpected diagnosis of thyroid cancer.* The optimal surgical management of well-differentiated thyroid cancer (DTC) remains a controversial topic. Preoperative and peroperative investigations quite frequently fail to detect thyroid cancer in cold nodules, and only postoperative histological examination reveals malignancy. In these cases many physicians perform a completion thyroidectomy. Others recommend a conservative approach with close follow-up because of the increased risk of complications after re-operation.
In our department, routine management includes completion thyroidectomy once the histopathological report concludes that there is carcinoma, except in cases of papillary carcinoma measuring less than 1 cm. The aim of our study was to determine the incidence of contralateral malignancy and of complications after completion thyroidectomy.
We reviewed the records of 29 patients – 25 women and 4 men – who all underwent completion thyroidectomy because of an unexpected diagnosis of DTC.
Residual malignancy was found in 12 patients (41.4%) after completion thyroidectomy. In ten patients (34.5%) the malignancy was localised in the contralateral lobe and two patients (6.9%) had lymph node metastases. Postoperative transient hypocalcaemia (< 8.0 mg/dl) occurred in five patients (17.2%) and permanent hypocalcaemia (lasting longer than 6 months) was a feature in two patients. One patient suffered transient laryngeal nerve injury occurred in one patient and there were no permanent lesions.
In conclusion, we found residual DTC in 41.4% of patients undergoing reintervention. Because of the rather low re-operation rate, we prefer to perform a completion thyroidectomy to remove potential occult malignancy and to allow for postoperative ^{131}I-treatment in all patients with a diagnosis of malignancy in their thyroid lobectomy specimen, with the exception of papillary carcinoma < 1 cm.

Introduction

Preoperative fine needle aspiration (FNA) and the intraoperative frozen section (FS) examination of thyroid masses often fail to detect differentiated thyroid carcinoma, especially follicular carcinoma.[1-5]

When postoperative histological examination reveals unexpected malignancy, we are faced with the problem of the optimal management of the thyroid remnant.

The consensus among surgeons is that completion thyroidectomy or an initial total thyroidectomy is advisable in high-risk patients and large tumours,[6,7] and that lobectomy is indicated for small papillary carcinomas measuring less than 1 cm and micro-invasive follicular carcinomas measuring less than 4 cm.[6-8]

By contrast, the optimal management of DTC in low-risk patients with follicular carcinoma and papillary carcinoma measuring 1-4 cm remains a controversial area.

In short, the discussion is whether lobectomy is preferable to completion thyroidectomy and whether the fear of complications should take precedence over the fear of contralateral disease and recurrence.

In our department, at the University Hospitals of Leuven, we routinely perform completion thyroidectomy after the unexpected diagnosis of DTC, except for papillary carcinomas measuring less than 1 cm.

The goal of our study was to evaluate this approach by examining the frequency of malignancy in residual thyroid tissue and in the cervical lymph nodes after completion thyroidectomy. We also examined the complication rate for hypoparathyroidism and recurrent laryngeal nerve injury (RLN) after the initial surgery and completion thyroidectomy.

Presented at the scientific meeting of the Royal Belgian Society for Ear, Nose, Throat, Head and Neck Surgery on 7 February 2004.

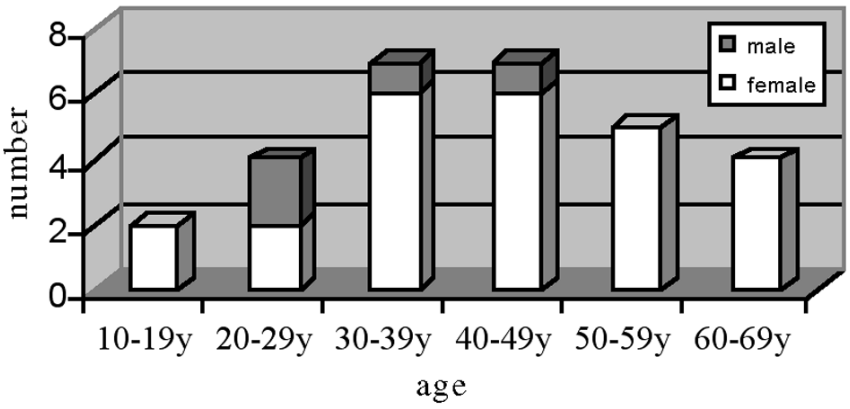

Figure 1
Distribution of age and gender

Materials and methods

The medical records of 29 patients who underwent completion thyroidectomy for DTC at the University Hospitals of Leuven from 1985-2004 were reviewed retrospectively. They were selected from 480 patients treated for thyroid cancer in our department between 1985 and 2004. They had all undergone earlier thyroid lobectomies for cold nodules. Postoperative pathologic examination showed malignancy, so completion thyroidectomy was performed. Patients with a papillary carcinoma measuring less than 1 cm were not re-operated.

The 29 patients (25 women, 4 men) had an average age of 41.9 years (range: 15-69 years) (Figure 1). Twenty-five patients were evaluated preoperatively with thyroid ultrasound and 27 with 99mTc-pertechnetate scintigraphy. FNA was performed in 19 patients.

The initial thyroid operation consisted of a unilateral lobectomy in 24 patients (in two cases combined with enucleation in the contralateral lobe and in one case combined with a parathyroidectomy). Subtotal thyroidectomy was performed in three patients and isthmectomy in two patients. Intraoperative frozen section was performed in 20 patients, but was not conclusive for malignancy in the peroperative setting.

The second operation consisted of a completion thyroidectomy with exploration of the cervical lymph nodes. Seven patients underwent cervical lymph node resections (unilateral in two patients and bilateral in 5 cases).

Completion thyroidectomy was performed through the original low-collar incision, usually with excision of the previous scar. Dissection of the overlying skin and platysma with horizontal section of the strap muscles followed. The RLN, the external branch of the laryngeal superior nerve and the parathyroid glands were found and preserved. Resection of the thyroid remnant and exploration of the cervical nodes took place.

After both operations, all patients underwent nasopharyngolaryngoscopy (NPL) during the first postoperative visit to evaluate vocal cord function. Serum calcium levels were measured and monitored after both interventions.

Hypoparathyroidism was classified as either transient or permanent. Serum calcium levels of less than 8.0 mg/dl not requiring prolonged calcium or calcitriol supplementation were defined as transient hypoparathyroidism. Permanent hypoparathyroidism was defined as hypocalcaemia requiring supplemental calcium or vitamin D for more than 6 months. Transient recurrent laryngeal nerve injury was defined as hypofunction of a vocal cord determined by NPL. Hypofunction of a vocal cord lasting more than 6 months was defined as permanent RLN damage.

Our patients were divided into low-, intermediate- and high-risk groups using to the criteria of the Memorial Sloan-Kettering Cancer Centre (MSKCC). The low-risk group consisted of low-risk patients (under the age of 45) with a low-risk tumour (< 4 cm, papillary carcinoma, no distant metastasis) and the high-risk group consisted of high-risk patients (above the age of 45) with a high-risk tumour (> 4 cm, follicular carcinoma or high-grade tumour, distant metastasis). The intermediate-risk group consisted of two categories: low-risk patients with a high-risk tumour or high-risk patients with a low-risk tumour.

Results

In all patients, the indication for initial surgery was a benign or slightly suspectthyroid neoplasm. In 18 cases, thyroid ultrasound and computed tomography (CT) showed a single nodule; in 2 cases, several unilateral nodules were found; and in 9 patients the thyroid gland was multinodular (Table 1).

Scintigraphy showed a cold nodule in 25 cases and a hot nodule in 2 cases. The result was

Table 1

Initial presentation form

Clinical, ultrasound scan and CT	**number**
solitary nodule	18
multiple nodules unilateral	2
multinodular bilateral	9
99mTc-pertechnetate scintigraphy	**number**
cold thyroid nodule	25
hot thyroid nodule	2
unknown	1

Table 2

Result frozen section after initial surgery

Result frozen section (FS)	**number**
no malignancy (negative FS)	14
Hashimoto thyroiditis	1
Hürthle cell adenoma	1
follicular hyperplasia (no malignancy)	1
follicular adenoma	1
adenoma with lymphoid infiltration	1
oxyphilic carcinoma,suspicious for malignancy	1
FS not possible because of calcifications	1
No FS executed	8

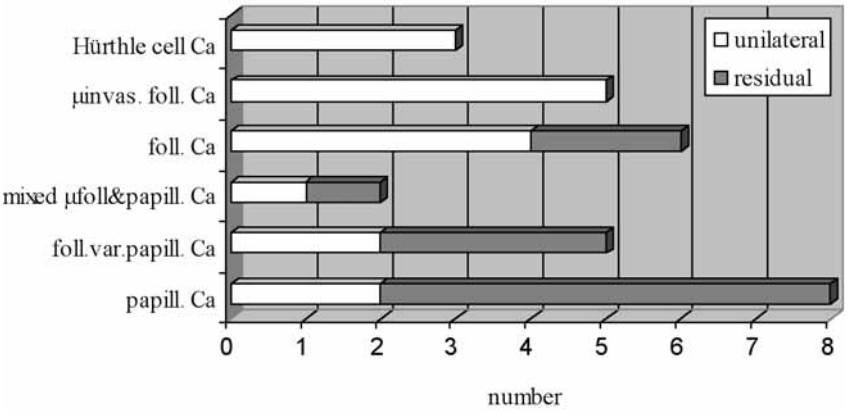

Figure 2

Pathology results after initial and second surgery: no malignancy versus residual malignancy.

Legend: Hürthle cell Ca= Hürthle cell carcinoma; µinvas. foll. Ca= micro-invasive follicular carcinoma; foll. Ca= follicular carcinoma; mixed µfoll&papill. Ca= mixed microfollicular and papillary carcinoma; foll.var.papill. Ca= follicular variant of papillary carcinoma; papill. Ca= papillary carcinoma

unknown in one patient. Preoperative FNA showed follicular neoplasia in most patients, without cellular morphological anomalies in 7 patients, with mild to moderate cellular anomalies (nuclear atypism and numerous mitoses) in 3 patients and with severe cellular anomalies in 2 cases. In the other patients, the degree of atypism was not further specified. FNA was not performed in 9 patients. Peroperative FS was performed in 20 patients during the first operation, but was not conclusive of malignancy (Table 2). This included the patients with mild to moderate or severe cellular anomalies.

Pathologic examination after the initial resection showed malignancy in all cases. Papillary carcinoma was found in 8 patients (27.6%), the follicular variant of papillary carcinoma in 5 patients (17.2%), and mixed microfollicular and papillary carcinoma in 2 patients (6.9%). Follicular carcinoma was present in 6 patients (20.7%) and micro-invasive follicular carcinoma in 5 cases (17.2%). Hürthle cell carcinoma was found in 3 patients (10.3%). The mean serum calcium level after initial surgery was 9.08 mg/dl. One patient had transient calcium levels lower than 8.0 mg/dl and 2 patients (6.9%) had a transient RLN palsy. Completion thyroidectomy was performed on average 43.9 days after the initial surgery (median: 34 days).

Definitive pathologic examination after completion thyroidectomy and lymph node exploration showed residual malignancy in 12 patients (41.4%), see Figure 2. Malignancy was found in the contralateral lobe in 10 patients (34.5%) and 2 patients had lymph node metastases. The residual malignancy was papillary carcinoma in 9 patients (30.6%): papillary carcinoma in 4 patients (13.8%), follicular variant of papillary carcinoma in 3 patients (10.3%) and papillary lymph node metastases in 2 patients (6.9%). Two patients with follicular carcinoma after the first operation had a residual follicular malignancy and one had a mixed microfollicular and papillary carcinoma.

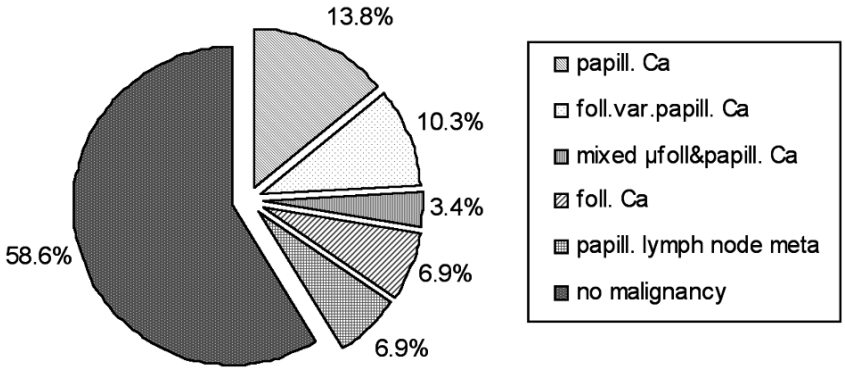

Figure 3
Pathology (%) after completion thyroidectomy

Table 3
Complication rates after primary surgery and after completion thyroidectomy

Complications	after primary surgery	after completion thyroidectomy
transient hypocalcaemia	1 (3.4%)	5 (17.2%)
permanent hypocalcaemia		2 (6.9%)
transient laryngeal nerve injury	2 (6.9%)	1 (3.4%)
permanent laryngeal nerve injury		0 (0%)

In 58.6%, or 17 patients, no residual malignancy was found after the second operation (Figure 3).

Seventy-five percent of the papillary carcinomas were bilateral. This was the case for 60% of the follicular variants of the papillary carcinoma, 50% of the mixed follicular and papillary carcinomas, and 33% of the follicular carcinomas. In our study, none of our patients with micro-invasive follicular carcinoma or Hürthle cell carcinoma had contralateral malignancy (Figure 2).

The mean serum calcium level after the completion surgery was 8.62 mg/dl. Transient hypoparathyroidism was present in 17.2% (5 patients) and permanent hypoparathyroidism in 6.9% (2 patients). One of those patients was a woman who also underwent a parathyroidectomy. One patient (3.4%) developed a transient RLN palsy after completion thyroidectomy (Table 3).

We classified our 29 patients using the MSKCC criteria. There were 10 low-risk patients, 14 intermediate-risk patients and 5 high-risk patients. There was no correlation between the risk level and the presence of contralateral malignancy.

Discussion

The management of well-differentiated thyroid cancer (DTC) and the type of surgery to be undertaken both remain controversial in the literature. The low incidence of DTC (1% of all malignancies) and the excellent prognosis for this cancer in most cases (0.5% of all cancer-related mortality) make large prospective studies almost impossible and it is therefore unlikely that this issue will be definitively resolved.[1,6,9,10]

There is general agreement that completion thyroidectomy or an initial total thyroidectomy are appropriate for high-risk patients and large tumours. Lobectomy is also considered to be sufficient for small papillary carcinomas measuring less than 1cm and micro-invasive follicular carcinomas measuring less than 4 cm without blood vessel invasion.[6,7] The optimal management of DTC in low-risk patients with follicular carcinomas and papillary carcinomas measuring between 1 and 4 cm remains controversial. There are several staging and clinical prognostic scoring systems that use patient age (above or below 40) as a major factor in the assessment of cancer mortality risk. Patients can be allocated to high-risk or low-risk categories using the AMES criteria (Age, Metastasis, Extent of tumour, Size of tumour). Other classification systems are the TNM classification, the AGES scoring system (Age, Grade, Extent, Size) and the GAMES criteria (Grade, Age, Metastasis, Extent, Size) of the Memorial Sloan-Kettering Cancer Centre (MSKCC). They are all effective in predicting cancer mortality, but do not forecast the high number of recurrences that occur in patients below 20 years of age.[6,7,11,12] Young patients, who have low mortality rates but high recurrence rates, are classified as low-risk cases by these staging systems, which some surgeons use to justify unilateral lobectomy.

These surgeons believe that procedures less aggressive than total thyroidectomy are sufficient. They argue that there is only a small risk of significant contralateral disease and that it is uncertain that the contralateral disease is clinically relevant.[13,14] They are

concerned about increased morbidity after completion thyroidectomy, with an increased risk of laryngeal nerve injury and the removal of parathyroid tissue in a previously operated neck. Some studies have found no difference in survival rate among patients treated with unilateral lobectomy and those treated with total thyroidectomy. However, different studies have shown that, in experienced hands, total thyroidectomy or completion thyroidectomy can be performed safely and with low morbidity.[9,15,16]

The two most feared complications of repeated surgery are recurrent laryngeal nerve injury and permanent hypoparathyroidism.

In our study, the incidences of transient and permanent hypoparathyroidism were 17.2% (5 patients) and 6.9% (2 patients) respectively. One of these patients was a woman who also underwent a parathyroidectomy. Other studies showed an incidence of transient hypoparathyroidism of 3-17% in completion thyroidectomy.[15,17-19] Permanent hypoparathyroidism was found in 3-5%. The most feared complication is RLN injury. In our study, two patients (6.9%) had a transient RLN palsy after primary surgery; only one (3.4%) suffered this complication after completion thyroidectomy. None of our patients developed a permanent RLN palsy. In the literature, the incidence of transient palsy varies from 2.5 to 5%, with the incidence for permanent palsy varying[15,18,19] from 0 to 2.6%.

It has been stated that completion thyroidectomy should be performed either within ten days of the primary surgery or after three months to reduce the incidence of complications.[20] Recent studies, however, found no definite indications that the timing of surgery affected the rate of complications after completion thyroidectomy.[21]

In our study completion thyroidectomy was performed on average 43.9 days after the initial surgery (median: 34 days). We did not study the relation between timing and complication rates.

Most surgeons and endocrinologists advocate total or completion thyroidectomy as the standard treatment for DTC.[9] They point to the high frequency of contralateral disease as justification for total excision and to the reduction of recurrence and distal metastases. Previous studies[9,15,17,20,22] have reported frequencies for residual malignancy of 38%, 55.6% and even 88%. Pasieka *et al*.[17] found residual cervical malignancy after completion thyroidectomy in 53% of their patients: 43% in the contralateral lobe and 10% as locoregional lymph node metastases. In our study we found residual malignancy after completion thyroidectomy in 12 patients (41.4%). The malignancy was localised in the contralateral lobe in ten patients (34.5%) and lymph node metastases were found in two patients (6.9%). Another reason for the removal of all thyroid tissue is that it allows the close monitoring of serum thyroglobulin levels (in patients without thyroglobulin antibodies), which can used as a marker for recurrent disease. In addition, there is a reduced risk of residual disease becoming clinically significant or undergoing an anaplastic transformation. An important advantage of this treatment is the higher efficacy of radioactive iodine for the ablation and treatment of residual or recurrent microscopic disease.[9,15]

Although outcome and mortality may be almost identical after both types of surgery, the rate of recurrence is much higher if surgery is limited because of the high incidence of contralateral malignancy in DTC.[23] That is why many surgeons prefer performing total or completion thyroidectomy in low-risk patients also.

Other surgeons and endocrinologists have advocated the ablation of the remaining gland with radiolabelled iodine over completion surgery. This approach has many disadvantages, because multiple doses of ^{131}I are required for the ablation of large thyroid remnants. The long-term effects of high doses of ^{131}I treatment include parathyroid injury, leukaemia, temporary bone marrow suppression and pulmonary fibrosis.[15,24]

In our opinion, therefore, surgical resection remains the best way to remove the thyroid tissue.

The recent guidelines from Europe (British Thyroid Association)[6] and the USA (National Comprehensive Cancer Network)[7] also advocate completion thyroidectomy as the gold standard in patients after lobectomy for a tumour > 1 cm or, in case of metastases, recurrence or incomplete removal.

In conclusion we found residual malignancy in 41.4% of our patients after completion thyroidectomy. The complication rates in our study also suggest that completion thyroidectomy can be performed safely with minimal short-term morbidity and almost no permanent sequelae.

We think that the extent of surgery and the decision to perform completion thyroidectomy should not be based on concern about complications from a second operation. The goal of

treatment should not be limited to the reduction of mortality, but should also include the reduction of recurrence and therefore the improvement of the patient's quality of life.

That is the reason we prefer completion thyroidectomy in all patients with a diagnosis of malignancy in their thyroid specimen. The only exception is the very small papillary carcinoma <1cm.

References

1. Shaha AR. Controversies in the management of thyroid nodule. *Laryngoscope.* 2000;110:183-193.
2. Tyler DS, Shaha AR, Udelsman RA, *et al*. Thyroid cancer: 1999 Update. *Ann Surg Oncol.* 2000;7:376-398.
3. Caraci P, Aversa S, Mussa A, Pancani G, Ondolo C, Conticello S. Role of fine-needle aspiration biopsy and frozen-section evaluation in the surgical management of thyroid nodules. *Br J Surg.* 2002;89:797-801.
4. Cheng MS, Morgan JL, Serpell JW. Does frozen section have a role in the intraoperative management of thyroid nodules? *ANZ J Surg.* 2002;72:570-572.
5. Shemen LJ, Chess Q. Fine-needle aspiration biopsy diagnosis of follicular variant of papillary thyroid cancer: Therapeutic implications. *Otolaryngol Head Neck Surg.* 1998;119:600-602.
6. British Thyroid Association and Royal College of Physicians. Guidelines for the management of thyroid cancer in adults. *London: Royal college of Physicians (RCP).* 2002. Available at: www.british-thyroid-association.org.
7. National Comprehensive Cancer Network (NCCN). Thyroid carcinoma practice guidelines. Version 1.2001. Available at: www.nccn.org/guidelines.htm.
8. Baudin E, Travagli JP, Ropers J, *et al*. Microcarcinoma of the thyroid gland: the Gustave-Roussy Institute experience. *Cancer.* 1998;83:553-559.
9. Kupferman ME, Mandel SJ, Didonato L, Wolf P, Weber RS. Safety of completion thyroidectomy following unilateral lobectomy for well-differentiated thyroid cancer. *Laryngoscope.* 2002;112:1209-1212.
10. Vini L, Harmer C. Management of thyroid cancer. *Lancet Oncol.* 2002;3:407-414.
11. Mazzaferri EL, Kloos RT. Clinical review 128: Current approaches to primary therapy for papillary and follicular thyroid cancer. *J Clin Endocrinol Metab.* 2001;86:1447-1463.
12. Lee YM, Lo CY, Lam KY, Wan KY, Tam PK. Well-differentiated thyroid carcinoma in Hong Kong Chinese patients under 21 years of age: a 35-year experience. *J Am Coll Surg.* 2002;194:711-716.
13. Shaha AR. Thyroid cancer: extent of thyroidectomy. *Cancer Control*. 2000;7:240-245.
14. Saadi H, Kleidermacher P, Esselstyn C. Conservative management of patients with intrathyroidal well-differentiated follicular thyroid carcinoma. *Surgery.* 2001;130:30-35.
15. Chao T, Jeng L, Lin J, Chen M. Completion thyroidectomy for differentiated thyroid carcinoma. *Otolaryngol Head Neck Surg.* 1998;118:896-899.
16. Mishra A, Mishra SK. Total thyroidectomy for differentiated thyroid cancer: primary compared with completion thyroidectomy. *Eur J Surg.* 2002;168:283-287.
17. Pasieka JL, Thompson NW, McLeod MK, Burney RE, Macha M. The incidence of bilateral well-differentiated thyroid cancer found at completion thyroidectomy. *World J Surg.* 1992;16:711-716.
18. De Jong SA, Demeter JG, Lawrence AM, Paloyan E. Necessity and safety of completion thyroidectomy for differentiated thyroid carcinoma. *Surgery.* 1992;112:734-737.
19. Wax MK, Briant TD. Completion thyroidectomy in the management of well-differentiated thyroid carcinoma. *Otolaryngol Head Neck Surg.* 1992; 107:63-68.
20. Tan MP, Agarwal G, Reeve TS, Barraclough BH, Delbridge LW. Impact of timing on completion thyroidectomy for thyroid cancer. *Br J Surg.* 2002;89:802-804.
21. Auguste LJ, Attie JN. Completion thyroidectomy for initially misdiagnosed thyroid cancer. *Otolaryngol Clin North Am.* 1990;23:429-439.
22. Alzahrani AS, Al Mandil M, Chaudhary MA, Ahmed M, Mohammed GE. Frequency and predictive factors of malignancy in residual thyroid tissue and cervical lymph nodes after partial thyroidectomy for differentiated thyroid cancer. *Surgery.* 2002;131:443-449.
23. Hay ID, Grant CS, Bergstralh EJ, Thompson GB, Van Heerden JA, Goellner JR. Unilateral total lobectomy: is it sufficient surgical treatment for patients with AMES low-risk papillary thyroid carcinoma? *Surgery.* 1998;124:958-966.
24. Eroglu A, Berberoglu U, Buruk F, Yildirim E. Completion thyroidectomy for differentiated thyroid carcinoma. *J Surg Oncol.* 1995;59:261-267.

Bieke Dewil
Department of Otorhinolaryngology, Head and Neck Surgery
UZ Sint-Rafaël
Kapucijnenvoer 33
B-3000 Leuven, Belgium
E-mail: bieke.dewil@uz.kuleuven.ac.be