

Oncologic Results of Completion Thyroidectomy and Secondary Prophylactic Lymph Node Dissection in the Management of Differentiated Thyroid Cancer

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Abstract

The management of differentiated thyroid cancer consists of a total thyroidectomy and cervical lymph node dissection (LND). However, certain patients do not receive this treatment for their first surgery, with a second operation being planned for a completion thyroidectomy and LND. The present study was undertaken to evaluate the morbidity and oncologic results of this two-stage strategy. All patients treated in two surgical stages from January 1992 to June 2009 were included in this study.

A total of 140 patients were included in the analysis. None received a diagnosis of cancer before or during the first surgery. The initial treatment involved 29 total thyroidectomies and 111 lobectomies. All patients had differentiated thyroid cancer. At the second surgery, 111 lobectomies and 140 LND were performed. Morbidity included one haematoma, 30 hypoparathyroidism (six definitive), and 13 nerve palsies (six definitive), while 14 microcarcinomas were diagnosed. In total, 12 patients suffered from lymph node metastases and 24 residual diseases. After a mean follow-up of 59.8 months, four patients had metastases and three elevated thyroglobulin levels, while 133 were disease free. Completion thyroidectomy should be performed on account of the incidence of second cancers, thus allowing for radioactive iodine therapy to be performed. Secondary prophylactic LND has a significant morbidity, which calls into question its routine recommendation.

Keywords: Differentiated thyroid carcinoma; Completion thyroidectomy; Cervical lymph node dissection; Morbidity; Surgery

Introduction

In France, a total thyroidectomy is recommended for the treatment of differentiated thyroid carcinoma (DTC) diagnosed at the pre- or preoperative stage [1]. This recommendation is in line with the European and American thyroid guidelines [2,3]. However, when suspicious macroscopic cervical lymph nodes are identified during preoperative work-up or during surgery, a lymph node dissection (LND) and total thyroidectomy are recommended due to the favourable impact on survival and loco-regional recurrence rates in high- and low-risk patients, respectively. Nonetheless, prophylactic LND associated with a total thyroidectomy remains controversial. No prospective study has yet established the benefits of prophylactic LND with regard to the risks of recurrence and mortality related to the DTC. Furthermore, the majority of clinicians consider that radioiodine ablation therapy should only be used in selective patients (*i.e.*, patients with metastasis, incomplete tumour resection, or high-risk patients based on the pTNM classification or well-established criteria), because the radioiodine is aimed both at ablating normal remnants and treating known or suspected persistent neoplastic foci or residual lymph node metastases [4].

At our institutions, when the diagnosis of DTC was unknown prior to surgery, a total thyroidectomy was recommended for bilateral nodular thyroid pathologies, possibly with an intraoperative histological frozen-section analysis. This algorithm was also carried out when a lobectomy was performed for a unilateral nodule. However, the frozen sections failed to reveal malignancy in a large number of patients, with such cases leading to a possible delay in the definitive management of patients. These patients would undergo a second operation involving

a completion thyroidectomy and central compartment LND when the pathology from the initial operation determined the DTC to exceed 1 cm. Thereafter, these patients would continue with radioactive iodine therapy. According to some authors, LND must be conducted, as node invasion may be associated with a greater risk of loco-regional recurrence with a negative impact on survival [5]. For others, this surgery should not be performed when the carcinoma is not confirmed, as the morbidity associated with negative LND may be high without any impact on repetition and survival [6].

For patients diagnosed with DTC after the initial operation, we performed a systematic LND with completion thyroidectomy. The aim of the study was therefore to evaluate the morbidity and oncologic results of a second elective procedure for the planned completion of a previously unilateral or subtotal thyroidectomy with LND in a group of patients presenting DTC, which was diagnosed at the final histological examination of the first surgical procedure.

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Number of patients (%)	140
Male	38 (27.1%)
Female	102 (72.9%)
Mean age (years)	42 (range 15-71)
First surgical procedure	
Lobectomy	111 (79.3%)
Total thyroidectomy	29 (20.7%)
Pathologic finding at first procedure	
Papillary	62 (44.3%)
Papillary follicular	43 (30.7%)
Follicular	23 (16.4%)
Hürthle cells	12 (8.6%)
Initial tumour size	24.7 mm (range 1-75)
Multifocality	14 (10%)
T classifications*	
T1	51 (36.4%)
T2	71 (50.7%)
T3	17 (12.1%)
T4	1 (0.8%)
Tumour capsule invasion	49 (35%)
Non-encapsulated tumour	21 (15%)
Pathologic finding at second procedure	
Contrast carcinoma (n=111)	14
Multifocality (n=111)	2
Node positives	12

Table 1: Characteristics of patients undergoing two-stage procedures.

Materials and Methods

Patients

This retrospective study was conducted in two tertiary university hospitals (Angers and Nantes, France) between January 1992 and June 2010. The study included all DTC patients undergoing a completion thyroidectomy or LND after initial surgery because of an indeterminate diagnosis on fine-needle aspiration (FNA) biopsy and intraoperative frozen section.

Clinicopathological factors

The rates of reoperative complications and oncologic results were assessed. Definitive complication was defined as complications lasting for more than 6 months.

Statistical analysis

The comparison of two qualitative variables was performed using the Chi-squared test. A value of $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

In total, 140 patients met the inclusion criteria for our study, comprising 38 men (27.1%) and 102 women (72.9%). The mean age was 42 years, with a range of 15 to 71 years (Table 1).

First surgical procedure

The following diagnoses were made prior to the first surgical procedure: non-functioning “cold” nodule in 54 cases (38.6%), hyperfunctioning “hot” nodule in 6 cases (4.3%), multinodular goiter in 48 cases (34.2%), Grave’s disease in one case (0.8%) and other in 31 cases (22.1%). Regarding the preoperative assessment, FNA was performed in 114 patients (81.4%), with the results being indeterminate in 32 cases, adenoma in 32, cellular atypia in 14, micro-follicular structure in 17, Hurtle cells in 16, carcinoma in two, and thyroiditis

in one. The initial intervention involved a hemithyroidectomy for 111 patients, while 29 underwent a total thyroidectomy for bilateral nodular disease. During the initial operation, frozen section was performed in 118 patients (84.3%). This analysis resulted in the diagnosis of a possible benign lesion in 61 cases, possible malignant lesion in 14, and benign lesion in 42, while for 22 patients, the frozen section was inconclusive or not performed. No postoperative complications were observed in 126 patients (90%), while morbidity following the first surgery involved five temporary recurrent nerve palsies (3.6%) and nine temporary cases of hypocalcaemia (6.4%). These complications occurred in relation to nine hemithyroidectomies (recurrent nerve palsies in five patients and hypoparathyroidism in four), and five total thyroidectomies (hypoparathyroidism in five patients). The mean size of the tumour was of 24.72 mm (range 1-75 mm). According to the TNM classification (Table 2), the median T was 2, with 51 cases of T1 (36.4%), 71 of T2 (50.7%), 17 of T3 (12.1%), and one of T4 (0.8%). The diagnosis of cancer was determined following the final histological study, with 62 classic papillary cancers (44.3%), 43 papillary-follicular carcinomas (30.7%), 23 follicular carcinomas (16.4%), and 12 Hürthle cell (oncocyctic) carcinomas (8.6%). There was no evidence of necrosis in 120 cases. The tumour was encapsulated in 68 cases and not encapsulated in 21, while there was a disruption of the capsule in 45 tumours. Thyroid capsule invasion was found in four cases. Venous invasion was observed in 33 patients, lymphatic invasion in four, and both venous and lymphatic invasion in one. Lastly, 91 patients had no evidence of invasion.

Second surgical procedure

On average, the second surgical procedure was performed 5.6 months after the initial operation (range: 1 day - 120 months). Overall, 111 patients underwent a completion thyroidectomy. One recurrent nerve was identified in 62 cases, while both were identified in 74 cases and neither in four. Parathyroid glands were not visible in 49 cases, although in the remaining patients, at least one was identified. A central LND (level VI) was carried out in 101 patients, while 12 lymph node samplings were performed during the second surgical procedure. In total, 100 patients underwent a unilateral lateral LND (levels III and IV) and 14 a bilateral lateral LND, while two had a lateral lymph node sampling. The lateral LND (levels III and IV) was performed in a prophylactic manner.

In 72 patients (64.9%) undergoing a completion thyroidectomy, nothing was discovered in the remaining part of the thyroid. In the other 39 patients (35.1%), we found 14 benign lesions, 11 thyroiditis, and 14 papillary microcarcinomas (< 10 mm). The average number of nodes examined was 14.5 (range: 1-44). Twelve patients had lymph node metastases, involving seven central node metastases, two lateral node metastases, and three with both central and lateral node metastases. For patients undergoing LND, the mean number of metastases was 0.11 and 0.18 in the lateral and central nodes, respectively. Regarding the histological findings for the second procedure, 24 patients showed residual disease, comprising 12 in the thyroid, 10 in the nodes, and two in both the thyroid and nodes.

T1: Tumor ≤ 2 cm
T2: 2 cm < tumor ≤ 4 cm
T3: > 4 cm
T4: extra- thyroid extension

UICC International Union Against Cancer. TNM Classification of Malignant Tumors. 7th edition, 2009

Table 2: Clinical classification T for DTC.

Number	First procedure	Second procedure
Temporary nerve paralyse	5	8
Definitive nerve paralyse	0	5
Temporary hypoparathyroidism	9	24
Definitive hypoparathyroidism	0	6

p-value for nerve paralyse = 0.18; p-value for hypoparathyroidism = 0.0003

Table 3: Postoperative morbidity for the first and second surgery.

Morbidity

There was no 30-day post-operative mortality. Furthermore, there was no recurrent laryngeal nerve palsy in 126 patients, although 10 patients developed recurrent nerve palsies, with four being definitive, while one patient developed bilateral palsy requiring a temporary tracheotomy. Two cases of superior laryngeal nerve palsy were observed. Postoperatively, 110 patients became normocalcemic, while 24 patients developed temporary hypocalcaemia and six permanent hypocalcaemia (Table 3).

Follow-up

Mean follow-up was 71.8 months (range 12-181 months). Surgery was followed by radioiodine ablation therapy in 131 patients, typically 8-12 weeks after the second operation. Among these patients, 112 received one dose of 100 MCI, 11 two doses, while five patients had three consecutive doses. During follow-up, four patients developed distant metastases (bones, lung) and three had elevated thyroglobulin levels with negative examination, while 133 were disease free.

Discussion

Histological results

In our study, the histological results for the completion thyroidectomy revealed a neoplastic lesion on the other side of the thyroid in 14 patients and nodal metastases in 12. These results are in line with previous studies, thus confirming that a total thyroidectomy should be performed to treat DTC when the tumour exceeds 1 cm or in the case of multifocal disease [7-11].

We found that 8.5% of lymph node metastases were only microscopic. The carcinogenic potential of these microscopic node metastases was previously studied and evaluated. The majority of studies suggested that microscopic lymph node metastasis had a minimal clinical impact, particularly in terms of loco-regional recurrences [12-14].

Sugitani et al. revealed that the accuracy of ultrasonographic diagnosis of central compartment lymph node metastasis had a positive predictive value of 82%, specificity of 91%, and sensitivity of only 29% [15]. However, we believe that the exploration of the central compartment during initial surgery based on preoperative ultrasound and intraoperative exploration may detect macrometastasis, which should then be dissected. Systematic prophylactic LND probably does not increase the risk of loco-regional recurrence. A total thyroidectomy alone with post-operative radioiodine ablation therapy was previously shown to improve survival and reduce local recurrence [16,17]. Some authors even advocated radioactive iodine remnant ablation as a safe, effective, and less costly alternative to completion thyroidectomy for DTC patients [18,19].

Morbidity

In our series, morbidity related to the second surgical procedure was higher than for the first, with a significantly higher rate of hypoparathyroidism (p=0.0003) and recurrent laryngeal nerve injury

(Table 3). In our study, 30 patients developed hypocalcaemia, including six permanent, while 13 patients had nerve palsies, with six being permanent. These findings are in consistent with previous studies, particularly following completion thyroidectomy and LND [20-22]. Lateral LND is known to increase morbidity, with spinal or phrenic nerve paralysis, Claude Bernard Horner syndrome, or chyle leak [20-22]. This surgical morbidity must be taken into account for the treatment of patients with DTC.

Preoperative ultrasonography

The prognostic significance of lymph node metastases remains controversial, with the extent of LND being debated. The second surgery in this region (particularly the central level VI) is more challenging, with a higher risk of complications. Consequently, preoperative cervical examination by ultrasound in addition to a definitive preoperative diagnosis of malignancy may guide the extent of surgical procedure. Preoperative ultrasounds may identify suspicious lymph nodes, with a 98% positive predictive value for the lateral compartment level II – IV. The majority of suspicious nodes have specific characteristics, including hypervascularisation, cystic forms, hypoechogenicity, irregular aspects, and absence of hilus [23]. These characteristics may be used as a basis for a systematic non-surgical approach, supported by the known preferential sites of node metastases according to the localisation of the primitive tumour [24]. Knowledge about the predictive factors of node invasion based on the initial tumour data may also help justify non-surgical treatment [25].

Conclusion

In conclusion, our results confirmed that when DTC is diagnosed following the initial surgical procedure, a total thyroidectomy is justified due to the high incidence of contralateral malignancy. However, secondary prophylactic LND was associated with significant morbidity and thus, should be cautioned against in a reoperative context. Given the high sensitivity of preoperative imaging, selective LND has a decreased morbidity during the initial operation. Overall, the indications for LND must be carefully evaluated considering the favourable long-term outcomes of patients with DTC and the authors suggest that the realization of a cervical LND has to lean on the characteristics of the primitive tumour, the study of predictive factors of lymph node invasion and the results of sonological cervical evaluation.

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