

Differentiated Thyroid Cancer: a Stage Adapted Approach to the Treatment of Regional Lymph Node Metastases

J.F. HAMMING,* C.J.H. VAN DE VELDE,* G.J. FLEUREN† and B.M. GOSLINGS‡

Departments of *Surgery, †Pathology and ‡Endocrinology, University Hospital, Leiden, The Netherlands

Abstract—The controversy in the management of regional lymph nodes in patients with differentiated thyroid cancer is discussed on the basis of a review of the literature. Since no prospective studies have yet compared limited dissections ('node picking') with more extensive dissections [(modified) radical neck dissection], a retrospective analysis was performed using two patient groups in which patients were managed differently with regard to the preoperative diagnosis and treatment of regional lymph node metastases. Only patients with proven lymph node metastases were included in the study. Because of selection methods necessary to create comparable patient groups, only 83 patients could be included in the analysis. There was no difference in survival or recurrence rate in either group, although recurrences occurred less frequently in the explored side of the neck after MRND (3.9% vs. 6.3%). More postoperative morbidity was found in the patients who had been subjected to a more extensive search for and treatment of lymph node metastases. Because of the relatively small number of patients only the difference in occurrence of accessory nerve palsies reached statistical significance ($P = 0.05$).

It is advocated that only in the case of papillary carcinoma with limited lymph node involvement node picking is the procedure of choice. In all other cases a modified radical neck dissection should be standard treatment.

INTRODUCTION

THE surgical management of differentiated thyroid cancer is not only controversial with regard to the surgery of the thyroid gland itself; the management of the regional lymph nodes is also subject to discussion. The biological behaviour of differentiated thyroid cancer and its lymph node metastases is more benign than that of other malignant head and neck tumours. In particular, papillary carcinoma mostly exhibits quite indolent behaviour. The presence of regional lymph node metastases of this latter type does not seem to be related to prognosis. Because of this the classical radical neck dissection is now out of practice as standard procedure. Nevertheless extensive lymph node surgery (MRND) is still performed in combination with total thyroidectomy. Only in experienced hands can these operations be performed with minimal morbidity [1].

Table 1. Options of lymph node surgery in patients with differentiated thyroid cancer

NP*

NP or MRND† depending on extent of lymph node involvement

MRND if macroscopical involved

MRND after positive biopsies

MRND electively

*Node picking.

†Modified radical neck dissection.

Unfortunately, there are no adequate comparative data providing evidence as to the preferred type of neck dissection. In Table 1 the options of lymph node surgery in differentiated thyroid cancer are shown. Other possibilities are not recommended. Prospective randomized trials concerning the treatment of patients with differentiated thyroid cancer are not available, because of the low incidence of these tumours and their relatively indolent biological behaviour. It is very difficult to compare the results of different retrospective studies. We analysed the value of extensive dissections for regional lymph node metastases of differentiated thyroid

Requests for reprints: C.J.H. van de Velde, Department of Surgery, University Hospital Leiden, PO Box 9600, 2300 RC Leiden, The Netherlands.

Abbreviations used: NP: node picking; MRND: modified radical neck dissection; RND: (classical) radical neck dissection; CD: 'conservative dissection'; ED: 'extensive dissection'.

cancer by comparing the results of two types of surgical treatment of patients with differentiated thyroid cancer performed in two institutes in two comparable groups of patients.

PATIENTS AND METHODS

The results of the treatment regimens of two major referral centres in the Netherlands were compared.* Total thyroidectomy was the treatment of choice for differentiated thyroid cancer in both institutes. However, the lymph node metastases were treated in two different ways. In the University Hospital Leiden the central neck was carefully inspected and only suspicious lymph nodes were removed; secondly, only clinically involved lymph nodes in the lateral neck were removed: node picking (NP). If uptake was visible on the postoperative scan (made after injection of 1 mCi ^{131}I), patients received an ablation dose of 75 mCi ^{131}I . This group was designated as CD ('conservative dissection'). In the Netherlands Cancer Institute Antoni van Leeuwenhoekhuis dissection of the neck was performed and the pre- and paratracheal lymph nodes and those in the tracheoesophageal groove were removed [2]. During operation, biopsies were also taken from the lymph nodes lying along the lower part of the internal jugular vein and sent for frozen section. When these contained tumour metastases, a MRND was performed. An ablation dose of ^{131}I was only given, when the residual uptake of ^{131}I was more than 3.5%. This group was designated as ED ('extensive dissection'). In both institutes patients underwent preoperative as well as postoperative indirect laryngoscopies to evaluate the mobility of the vocal cords. Hypoparathyroidism was diagnosed on the basis of serum calcium levels (below 2.20 mmol/l). Patients treated in the period from 1960 to 1980 were screened ($n = 280$). From this group only patients who underwent a neck dissection as described above were selected. Patients whose tumour stage could not be evaluated, who had tumour recurrence before treatment was completed or who had non-radical operations were excluded. Finally 83 patients were available for study: 32 in the CD group and 51 patients in the ED group. All histological slides were examined following the WHO criteria [3]. The minimum follow-up period was 4 years and the maximum was 26 years with an average of 14 years.

RESULTS

The comparability of the two patient groups was judged on the basis of four risk factors related to survival: age, sex, histology and tumour stage. In Table 2 the results are summarized: the two patient groups were comparable with regard to these risk

Table 2. Patients and risk factors

Neck dissection*	CD		ED	
	%	(n)	%	(n)
Patients		32		51
Risk factors				
Younger than 40 years	59	(19)	63	(32)
Female	66	(21)	63	(32)
Papillary carcinoma	97	(31)	96	(50)
pT4†	25	(8)	29	(15)
N3†	22	(7)	17	(8)

*CD = 'conservative dissection'; ED = 'extensive dissection'.

†Tumour growth beyond the capsule of the thyroid or lymph nodes respectively.

Table 3. Neck recurrence after surgical treatment

No. of recurrences	Neck dissection*		ED	
	%	(n)	%	(n)
Total	9.4	(3/32)	9.8	(5/51)
Explored side	6.3	(2/32)	3.9	(2/51)

*CD = 'conservative dissection'; ED = 'extensive dissection'.

factors. Regional recurrences in the neck occurred in the same percentage of patients in both groups (Table 3). However, in the ED group this occurred less frequently in the explored area of the neck (3.9% vs. 6.3%), although this difference was not significant. None of the patients in either group died from regional recurrences: in the CD group one patient still has evidence of disease and in the ED group one patient died within 2 years after diagnosis as a result of extensive lung metastases of papillary carcinoma. The postoperative morbidity of the neck dissections as performed in the two institutes is summarized in Table 4. In the ED group, two patients had permanent accidental unilateral recurrent laryngeal nerve palsies; no such lesions were observed in any patients in the CD group. No bilateral lesions occurred in either group. Other complications were observed more often in the ED group than in the CD group. The higher incidence of hypoparathyroidism in the ED group is most likely due to the elective dissection of the tracheoesophageal groove and not to the MRND of the lateral neck. Palsy of the accessory and facial nerve as a result of routine MRND was more frequent in the ED group; this difference was only significant for the palsies of the accessory nerve.

DISCUSSION

For decades the surgical management of differentiated thyroid cancer is a topic that challenges interested physicians. Mostly the debates concern the extent of removal of thyroid tissue. The optimum treatment of lymph node metastases of differentiated thyroid cancer is not yet established and is more

*To be published elsewhere in depth.

Table 4. Postoperative morbidity after different neck dissection

Morbidity	Neck dissection*			
	%	CD (n)	%	ED (n)
Permanent hypoparathyroidism excluding PT4,N3	13	(4/32)	22	(11/51)
	—	—	10	(5/51)
Permanent palsy:				
recurrent laryngeal nerve	—	—	4	(2/51)
accessory nerve	6	(2/32)	25	(13/51)
facial nerve	—	—	4	(2/51)
Haemorrhage/wound infection	6	(2/32)	10	(5/51)

*CD = 'conservative dissection'; ED = 'extensive dissection'.

conservative than the treatment of lymph nodes of other head and neck malignancies for several reasons. Three important arguments for this different strategy are used. In the first place most authors do not find an adverse effect of the presence of lymph node metastases on survival [4–7]. Secondly it is uncertain whether more extensive procedures result in higher survival rates (there is no difference in survival between classical radical neck dissection (RND) and MRND [1, 7, 8]). Thirdly these extensive operations carry a substantial risk of serious postoperative morbidity [9, 10]. For most malignant head and neck tumours regional lymph node metastases are indicators of an unfavourable prognosis. In contrast to this, the prognostic significance of these metastases in patients with differentiated thyroid cancer is debatable. Papillary thyroid carcinoma tends to spread to the regional lymph nodes even in the early stages of the disease [11]. In follicular cancer, lymph node metastases are far less common and have more negative implications for prognosis. When elective dissections were performed systematically, up to 90% of all patients with papillary thyroid cancer had metastases in regional lymph nodes [1, 11]. The incidence of recurrent disease in the large number of patients without clinical evidence of lymph node metastases, who were not treated by elective neck dissection, is less than 10% [4–7]. Although some authors observe an increased rate of regional recurrence in patients with positive lymph nodes at the time of diagnosis, most of them find no adverse effect on survival [5, 6]. Others do not even find more recurrences [4, 7]. Another notable phenomenon is the fact that the incidence of lymph node involvement (mostly a sign of advanced tumour stage) is inversely proportional to age [6, 7]. Harwood *et al.* found that nodal involvement did have an adverse effect on prognosis when the patients were matched by age [12]. However, in this study 12% of the patients with nodal disease had follicular carcinoma; lymph node metastases of this type of thyroid cancer are known to behave more aggressively than those of

papillary carcinoma. The aim of a classical radical neck dissection (RND) is to remove all fatty tissue and all lymph nodes in order to either prevent the outgrowth of any microscopically present lymph node metastases (prophylactic RND) or to treat these metastases and to prevent recurrences in the area (therapeutic RND). Since the introduction of the 'modified' version of RND (MRND), most surgeons have abandoned the classical procedure for the treatment of regional lymph node metastases in patients with differentiated thyroid cancer. Also the tendency has been observed to perform a MRND instead of a RND in the treatment of other primary tumours [13]. The modification of the RND includes the preservation of one or more of the following structures (if permitted by the extent of tumour growth): the sternocleidomastoid muscle, the internal jugular vein and the accessory nerve. The submaxillary triangle is not routinely included in MRND for thyroid cancer. In experienced hands MRND can be performed with minimum postoperative morbidity and a relatively good cosmetic result (in contrast with the RND), as has been reported by Attie and others [1, 14, 15]. Most surgeons only use the MRND when the regional lymph nodes are involved. Some mainly use NP in cases of limited lymph node involvement. NP rarely is standard practice. Table 5 shows the type of treatment preferred by authorities in the field of thyroid surgery. The lymph nodes along the trachea (paratracheal) and in the tracheoesophageal groove, are the first to be involved [8, 11, 16–20]. The preferred management of these nodes is not always clear. Some surgeons routinely remove these nodes concomitant with the total thyroidectomy [1, 11, 16, 19], while others carefully inspect this area and send suspicious nodes for frozen section [8, 20, 21]; if positive, the lymph nodes are removed. Recurrences in the central neck are serious and are more difficult to treat than recurrences lateral to the carotid artery. It has never been well established which type of neck dissection leads to the better result in the treatment of patients with differentiated thyroid

Table 5. Treatment preferences for lymph node metastases

Procedure	Author	Year of publication	Reference
NP	Farrar	1980	4
	Mazzaferri	1981	5
NP or MRND	Beahrs	1984	16
	Clark	1982	26
	Lennquist	1986	21
	Rossi	1986	6
MRND (macroscopically involved)	Crile Jr	1985	24
	Marchetta	1970	15
MRND (positive biopsies)	Block	1977	27
	Rosen	1983	31
MRND (electively)	Attie	1971	1
	Noguchi	1970	17

cancer. Mazzaferri and Young could not find a difference in recurrence rate between patients treated by NP and those treated by RND or MRND [5], but the extent of lymph node surgery was probably influenced by the extent of metastases at initial operation. McGregor *et al.* [22] found no difference between NP and (M)RND when lymph nodes were only minimally involved. In cases of extensive lymph node involvement the ultimate control of neck disease was better after (M)RND, but the overall survival was not different. Noguchi *et al.* [23] found many recurrences after conservative management (58%!) and changed to more aggressive surgery. On the other hand conservative therapy has also been described to give satisfactory results [6, 8, 24, 25]. The advantages of extensive lymph node surgery are not always evident and therefore other arguments such as postoperative morbidity gain in importance. In experienced hands MRND can be performed with very little morbidity [1, 15]; nevertheless some structures, which should be preserved in MRND such as the accessory nerve and other motor nerves, are especially at risk. Postoperative hypoparathyroidism is a well-known and serious complication of thyroidectomy and has been reported to occur in frequencies ranging from less than 1% up to more than 30%. In institutes with experienced surgeons, this figure should not exceed 3% [21, 26–28]. However, it is not always clear whether or not the paratracheal area and the tracheoesophageal groove have been explored and how this has been done (an important factor with regard to this complication). Secondary operations in previously explored areas are associated with more serious postoperative morbidity. In the light of the latter it is important to realize, that removal of involved lymph nodes is easier from areas laterally in the neck that have not yet been explored [8, 19, 29]. As mentioned before, recurrences

located centrally in the neck are more serious. Last, but not least, the extent and infiltration of tumour growth is an important factor in the preservation of structures in the neck.

In the present study the management of lymph node metastases of differentiated thyroid cancer was evaluated by analysing two comparable patient groups. Unfortunately, as a consequence of the necessary selection method, only 83 patients could be evaluated. The results suggest, that a MRND is not superior to NP combined with an ablation dose of ^{131}I . There was no significant difference in the overall regional recurrence rate between the two patient groups, although there were fewer recurrences in the explored area after MRND. After the relatively short follow-up period, no influence of the recurrences on the survival could be detected. The benefit of a routine ablative dose of ^{131}I has been disputed, but it might have some effect on occult lymph node metastases [30]. In the ED ('extensive dissection') group, where the MRND and elective dissection of lymph nodes lying in the tracheoesophageal groove was performed, the postoperative morbidity was higher. However, because of the relative small number of patients evaluated only the difference in accessory nerve palsies was statistically significant ($P = 0.05$).

Differentiated thyroid cancer has a low incidence (2–6/100,000/year). The two institutes participating in this study traditionally see more patients with thyroid cancer and thus have more experience in this field of surgery than most other hospitals in the Netherlands. It does not seem advisable that less experienced surgeons perform extensive neck dissections in patients with differentiated thyroid cancer and limited lymph node involvement. The extent of lymph node dissection depends on individual circumstances, including the type of the lesion, the extent of lymph node involvement and the surgeons'

experience and judgement. The lymph nodes in the central neck should be inspected carefully and should be removed if the presence of tumour involvement is suspected. Although this procedure jeopardizes the vascularization of the parathyroids considerably it should be performed to prevent recurrences centrally in the neck. The recurrent laryngeal nerve has already been visualized during the thy-

roidectomy and should be spared. In the case of limited nodal involvement in papillary cancer, 'node picking' is an acceptable procedure. Extensive lymph node involvement and metastases lateral to the carotid artery are preferably treated by MRND; it is also the treatment of choice in follicular cancer with lymph node involvement.

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