Incidence of Regional Recurrence Guiding Radicality in Differentiated Thyroid Carcinoma

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Abstract. Total thyroidectomy has become the routine procedure for treatment of differentiated thyroid carcinoma. However, the necessity of unilateral or bilateral neck dissection is far less standardized. Our usual procedure has been to perform a routine neck dissection in T4 tumors and in all other tumor stages only in the presence of positive diagnostic or intraoperative findings. The results concerning regional tumor recurrence in cervical lymph nodes subsequent to thyroidectomy are studied and discussed. Between April 1986 and December 1992 a group of 252 patients were operated on for differentiated thyroid carcinoma (DTC) (176 papillary, 76 follicular). Postoperative treatment included radioiodine therapy as a rule in all patients more than stage T1, and follow-up encompassed thyroglobulin measurements, cervical ultrasonography, and radioiodine scintigraphy. After a mean follow-up of 6.9 years, 77 (31%) of the patients underwent reoperation because of regional tumor recurrence [46 of 176 (26%) papillary, 31 of 76 (41%) follicular]. In papillary thyroid cancer a significant difference could be demonstrated between patients with thyroidectomy only versus thyroidectomy plus neck dissection in all tumor stages (T2, 13 of 29 (45%) versus 1 of 34 (3%); T3, 10 of 13 (77%) versus 4 of 11 (36%); T4, 6 of 8 (75%) versus 6 of 18 (33%) ($p < 0.0001$). Similar results could be achieved for follicular thyroid cancer, showing statistical significance with regard to operative procedure ($p < 0.009$). Our experience demonstrates a positive correlation of regional tumor recurrence with increasing tumor stage for both histologic tumor types. The high rate of regional recurrence justifies a more radical approach, including neck dissection at the initial operation. The impact on survival, however, must be proved by further evaluation.

Differentiated thyroid carcinomas (DTCs) are tumors with a favorable prognosis and long survival. Thus it is difficult to define the optimal strategy of treatment unless a long follow-up of at least 10 to 20 years is available. Since the 1970s total thyroidectomy has become the routine procedure for treatment of differentiated thyroid carcinoma (papillary, follicular) in Germany. Additional neck dissection—if necessary according to evidence of metastatic spread into regional lymph nodes—has been the procedure of choice. It has proved to be an effective tool for controlling the disease with regard to cure by radicality along with postoperative adjuvant therapy with radioiodine and detection of tumor recurrence by monitoring serum thyroglobulin [1–6].

Attempts to define certain low risk groups among patients with DTC led to several prognostic scoring systems established by the American Joint Commission (AJC) [7], Cady et al. (AMES) [8], Hay et al. (AGES) [9], and the European Thyroid Association

(EORTC) [10]. They allow rather precise classification and stratification into low or high risk groups concerning prognosis and outcome. Patients with small (< 1.5 cm) encapsulated papillary tumors or microinvasive follicular tumors under the age of 45 years were found to have an excellent prognosis and thus could be treated adequately by limited radical resection (i.e., lobectomy, or hemithyroidectomy).

Prophylactic lymphadenectomy of the lateral compartments is controversial [11–16]. Criteria that influence the intraoperative decision to extend the operation beyond thyroidectomy alone are preoperative localization of regional tumor spread by diagnostic imaging or histologically proved lymph node metastases [17]. Scoring schemes are not helpful in intraoperative decision-making because they are partly based on the postoperative histopathologic workup, including exact staging and grading of the tumor, and thus do not allow one to decide on the appropriate extent of surgery intraoperatively.

The grading of thyroid tumors is difficult and contains a high variance depending on the examining pathologist. Therefore the revised World Health Organization (WHO) classification of thyroid tumors does not recommend grading DTCs (papillary, follicular, medullary) any more [18]. The high rate of regional recurrence of papillary and follicular thyroid carcinomas prompted us to investigate whether use of thyroidectomy only or extension of the operation to include neck dissection has any influence on regional tumor relapse.

Methods

Patients

All patients who had been operated on for DTC (papillary, follicular) between April 1986 and December 1992 with a known follow-up were included in this study. Patients were documented on a computerized database with 97 single factors per patient, including preoperative diagnostics, operative details and complications, pathohistologic workup, and follow-up. The documentation was standardized using a numerical code to simplify the analysis of patient data. Stepwise logistic regression was deemed appropriate for multivariate analysis including prognostic factors

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Table 1. Clinical data from patients with differentiated thyroid carcinoma.

Gender	No.	Age (years)	Initial + completion	Recurrent operation
Papillary				
Women	119	43	91 (76%)	28 (24%)
Men	57	48	39 (68%)	18 (32%)
Total	176	43.6	130 (74%)	46 (26%)
Follicular				
Women	53	54	33 (62%)	20 (38%)
Men	23	53	12 (52%)	11 (48%)
Total	76	53.7	45 (59%)	31 (41%)

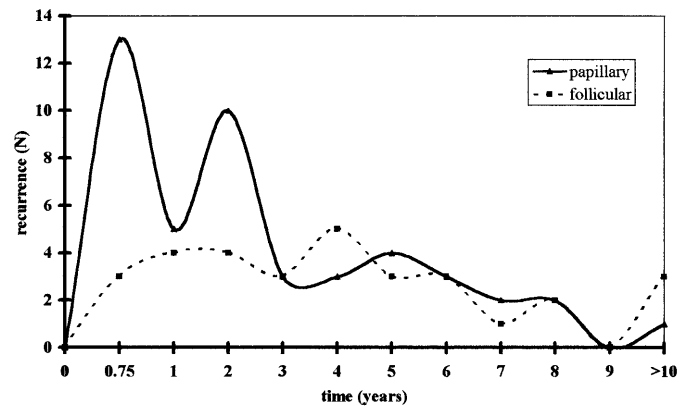**Fig. 1.** Correlation of tumor recurrence over time.

available at the time of operation (age, sex, T stage) with regard to recurrence.

Operation

Preoperative diagnosis of DTC included cervical ultrasonography and thyroid scans in all patients. The results were obtained from various examiners and institutions, as not all of the patients had their primary diagnosis and therapy in our institution.

Our standard approach to DTC was total thyroidectomy including dissection of the central lymph nodes (paratracheal, suprathyroidal, infrathyroidal), and these patients comprised group 1. Additional neck dissection of the lateral neck compartment was performed when tumor spread into these regional lymph nodes was suspected or proved by preoperative diagnostic imaging or histologic workup (group 2).

The lateral compartment includes the jugular lymph nodes reaching from the carotid artery to the trapezoid muscle and from the subclavian vein to the hypoglossic nerve [19]. Neck dissection is defined as the systematic removal of lymph nodes and fatty tissue belonging to this compartment. This procedure is performed by a transverse collar incision, as for thyroidectomy but prolonged laterocranially along the sternocleidomastoid muscle. Limited radical resection (i.e., lobectomy) was indicated for occult thyroid tumors comprising small encapsulated papillary tumors < 1 cm in size and microinvasive follicular tumors < 1 cm. According to these criteria a completion thyroidectomy was performed in all tumors that are more than stage T1 with less than total thyroidectomy at the initial operation; completion was defined by reoperation less than 6 months after the initial operation for thyroid cancer. In terms of radicality, initial operations and completing operations were considered together for further analysis and termed primary operation. Postoperative radioiodine treatment was performed on all papillary and follicular tumors more than T1 and in node-positive disease. Criteria for reoperation were gross regional recurrent disease, ^{131}I uptake of more than 10%, or no or insufficient radioiodine uptake. Regional recurrence is defined as lymph node involvement of the lateral neck compartment detected more than 6 months after the primary operation. True local recurrences in the thyroid bed mostly associated with infiltration of the trachea or esophagus were excluded, as they are known to have a poor chance of radical and curative resection and bear considerable operative morbidity.

Follow-up

Postoperative follow-up encompassed cervical ultrasonography, radioiodine scintigraphy, and serum thyroglobulin measurements. In case of questionable results or findings, computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET) were employed additionally.

Results

A total of 252 patients have been operated on for differentiated thyroid carcinoma including 176 patients with papillary and 76 patients with follicular thyroid carcinoma. The mean age of patients with papillary thyroid cancer was 43.6 years, with 119 women (43 years) and 57 men (48 years); and for follicular thyroid cancer the mean age was 53.7 years, with 53 women (54 years) and 23 men (53 years) (Table 1).

Of these patients 117 (46.4%) underwent one operation only, including 37 patients with a limited radical resection and 58 (23%) with a completing operation; 77 (30.6%) patients were operated on for recurrent disease. A total of 180 patients (71.4%) had the initial operation in our institution; the others were referred for a completion or recurrence operation. In terms of our radical approach to thyroid cancer, the initial operations and completing operations were analyzed together and were referred to as primary operation. Thus 130 of 176 patients (74%) with papillary thyroid cancer had a primary operation and 46 (26%) had reoperative surgery for regional recurrent disease. Of the 76 patients with follicular thyroid cancer, 31 (41%) suffered from regional tumor relapse (Table 1). The mean follow-up was 6.9 years (median 6.0 years). The average duration between initial operation and reoperation for tumor recurrence was 3.5 years for papillary cancer and 4.3 years for follicular cancer. More than half of the patients presented with recurrent disease within the first 3 years after the initial operation (Fig. 1).

In 43 (17%) patients distant metastases were verified during the course of the disease: 18 (10%) were from papillary tumors (six of which were known at the time of operation), and 25 (33%) from follicular tumors (with five existing preoperatively) (Table 2). Distant metastatic spread showed a strong correlation to age: 12 of 16 (78%) patients with papillary cancer and 19 of 25 (76%) patients with follicular tumors were over 45 years of age. Nineteen

Table 2. Distant metastases in differentiated thyroid cancer.

	Papillary		Follicular	
Stage	No.	%	No.	%
T1	2/51	4	1/11	9
T2	6/67	9	5/23	22
T3	3/24	13	4/14	9
T4	5/26	19	10/21	48
Tx[a]	2/8	25	5/7	71
Total	18/176	10	25/76	33

[a]Tx: unknown T stage.

Table 3. Limited radical operation and tumor recurrence in papillary and follicular thyroid carcinoma.

Patient age (years)	Papillary thyroid carcinoma		Follicular thyroid carcinoma	
	T1/rec	> T1/rec	T1/rec	> T1/rec
< 45	11/0	3/0	3/0	1/1
> 45	12/0	1/0	5/1 (20%)	5/2 (40%)
Total	23/0	4/0	8/1 (13%)	6/3 (50%)

Rec: recurrence.

patients (7.5%) died during follow-up, with ten of the deaths tumor-related (3.9%).

In 15 patients the initial tumor stage based on the size of the primary tumor was not known (TX), so they were excluded from further analysis.

Limited Radical Resection

A limited radical resection was performed in 41 patients with 27 papillary carcinomas and 14 follicular carcinomas. There were few exceptions to our standard procedure, with T1 tumors seen in four patients with papillary cancers and in six with follicular cancer. The reason for the limited resection was either a primary operation outside our institution or high operative risk and advanced age. Tumor did not recur in 23 patients with papillary T1 tumors or in 4 patients with tumor size > 1 cm. One of eight patients with a small (< 1 cm) follicular tumor and three of six patients with large tumors had tumor relapse later in the course of the disease (Table 3).

Radical Resection

Of the 252 patients, 77 (30.6%) were operated once or several times for regional recurrence. The overall rate of tumor recurrence was 26% for papillary thyroid cancer (PTC) and 41% for follicular thyroid carcinoma (FTC), with an increasing rate at advanced tumor stages for both tumor types (PTC, $p < 0.0001$; FTC, $p < 0.004$) (Table 4). For both histologic tumor types there is neither a significant difference in tumor recurrence between the low risk group (< 45 years of age) and the high risk group (> 45 years): PTC < 45 years, 22 of 91 (24%); PTC > 45 years, 24 of 85 (28%); FTC < 45 years, 10 of 26 (38%); FTC > 45 years, 21 of 50 (42%). Neither was there a significant difference with regard to sex. When subdividing papillary tumors into the tumor stages T3 and T4 a tendency for worse prognosis with increasing age can be seen (Table 5).

Table 4. Multivariate analysis with stepwise linear logistic regression.

Parameter	Coefficient	Standard error	Relative risk	p
PTC				
T stage	1.867	0.521	6.47	< 0.0001
Operation	2.321	0.524	10.20	< 0.0001
FTC				
T stage	1.864	0.690	6.45	< 0.004
Operation	1.894	0.795	6.64	< 0.009

PTC: papillary thyroid cancer; FTC: follicular thyroid cancer.

The influence of age, sex, T stage, and operation on tumor relapse was analyzed. "T stage" compares stage T2 with T3 + T4 in PTC and T2 + T3 with T4 in FTC. "Operation" compares thyroidectomy with thyroidectomy plus neck dissection. Independent from other factors T stage and operation are highly significant indicators of tumor relapse.

Table 5. Tumor recurrence in papillary and follicular thyroid carcinoma according to tumor stage.

Stage and age (years)	Papillary			Follicular		
	No.	Rec	Total rec	No.	Rec	Total rec
T1						
< 45	29	4 (14%)	5/51 (10%)	4	1 (25%)	2/11 (18%)
> 45	22	1 (5%)		7	1 (14%)	
T2						
< 45	31	7 (23%)	14/67 (21%)	9	2 (22%)	5/23 (22%)
> 45	36	7 (19%)		14	3 (21%)	
T3						
< 45	16	7 (44%)	14/24 (58%)	5	2 (40%)	5/14 (36%)
> 45	8	7 (88%)		9	3 (33%)	
T4						
< 45	10	3 (30%)	12/26 (46%)	6	4 (67%)	14/21 (67%)
> 45	16	9 (56%)		15	10 (67%)	
Tx						
< 45	5	1 (20%)	1/8 (13%)	2	1 (50%)	5/7 (71%)
> 45	3	0 (0%)		5	4 (80%)	
Total	176	46 (26%)		76	31 (41%)	

Rec: tumor recurrence; Tx: unknown T stage.

The analysis of papillary thyroid carcinomas treated with thyroidectomy alone (group 1) versus thyroidectomy plus neck dissection (group 2) shows a significant difference with regard to regional tumor recurrence (group 1, 30 of 59 (51%) versus group 2, 15 of 82 (18%) ($p < 0.0001$) (Table 4). Within the subgroups T1 through T4 a difference in T2 to T4 tumors is seen that is statistically significant ($p < 0.0001$) (Table 4). The further subdivision of risk groups by age and sex demonstrates no significant difference. The histopathologic evaluation of neck-dissected patients shows a high rate of positive lymph nodes at all tumor stages. Combining the recurrences after thyroidectomy alone with obvious occult lymph node involvement at the time of initial operation and positive findings in reoperated neck-dissected patients, the overall rate of node-positive patients is 66% with a high proportion at all tumor stages (Table 6).

The overall rate of lymph node involvement in follicular thyroid cancer is 64% (35 of 55) (Table 7). It increases with advancing tumor stage from 33% at T1 to 90% at T4. The comparison of operative procedures demonstrates a difference of regional recurrence at all tumor stages ($p < 0.009$) (Table 4). There is no difference with regard to age and sex.

Table 6. Correlation of tumor recurrence with tumor stage and operation in papillary thyroid carcinoma.

Stage and age (years)	No.	TX only		TX + neck dissection			
		No.	Rec	No.	Rec	LN+	LN+
T1							
< 45	18	4	1 (25%)	14	3 (21%)	12 (86%)	13/18 (72%)
> 45	10	5	0 (0%)	5	1 (20%)	4 (80%)	4/10 (40%)
Total	28	9	1 (11%)	19	4 (21%)	16 (84%)	17/28 (61%)
T2							
< 45	28	13	7 (54%)	15	0 (0%)	9 (60%)	16/28 (57%)
> 45	35	16	6 (38%)	19	1 (5%)	11 (58%)	17/35 (49%)
Total	63	29	13 (45%)	34	1 (3%)	20 (59%)	33/63 (52%)
T3							
< 45	16	7	4 (57%)	9	3 (33%)	9 (100%)	13/16 (81%)
> 45	8	6	6 (100%)	2	1 (50%)	2 (100%)	8/8 (100%)
Total	24	13	10 (77%)	11	4 (36%)	11 (100%)	21/24 (88%)
T4							
< 45	10	1	0 (0%)	9	3 (33%)	9 (100%)	9/10 (90%)
> 45	16	7	6 (86%)	9	3 (33%)	7 (78%)	13/16 (81%)
Total	26	8	6 (75%)	18	6 (33%)	16 (89%)	22/26 (85%)
Total	141	59	30 (51%)	82	15 (18%)	63 (77%)	93/141 (66%)

TX: thyroidectomy; Rec: recurrence; LN+: lymph node positive.

Table 7. Correlation of tumor recurrence with tumor stage and operation in follicular thyroid carcinoma.

Stage and age (years)	No.	TX only		TX + neck dissection			
		No.	Rec	No.	Rec	LN+	LN+
T1							
< 45	1	1	1 (100%)				1/1 (100%)
> 45	2	2	0 (0%)				0/2 (0%)
Total	3	3	1 (33%)				1/3 (33%)
T2							
< 45	9	8	2 (25%)	1	0 (0%)	1 (100%)	3/9 (33%)
> 45	12	6	2 (33%)	6	1 (17%)	4 (67%)	6/12 (50%)
Total	21	14	4 (29%)	7	1 (14%)	5 (71%)	9/21 (43%)
T3							
< 45	4	2	0 (0%)	2	1 (50%)	2 (100%)	2/4 (50%)
> 45	7	4	2 (50%)	3	0 (0%)	3 (100%)	5/7 (71%)
Total	11	6	2 (33%)	5	1 (20%)	5 (100%)	7/11 (64%)
T4							
< 45	6	4	4 (100%)	2	0 (0%)	2 (100%)	6/6 (100%)
> 45	14	10	8 (80%)	4	1 (25%)	4 (100%)	12/14 (86%)
Total	20	14	12 (86%)	6	1 (17%)	6 (100%)	18/20 (90%)
Total	55	37	19 (51%)	18	3 (17%)	16 (89%)	35/55 (64%)

TX: thyroidectomy; Rec: recurrence; LN+: lymph node positive.

Complications

Fourteen patients (5.6%) had persistent laryngeal nerve palsy: Four occurred after completion thyroidectomy and two after reoperation for recurrent disease. Four of the nerves were sacrificed intentionally for reasons of radicality; one was due to tumor growth. Bilateral laryngeal nerve palsy was observed in three patients who had had previous external operations. Persistent hypoparathyroidism was seen in seven patients (2.8%). Accessory and phrenic nerve palsy were observed in one patient each; one case of cervical plexus irritation, one Horner syndrome, and three chyle leaks occurred after reoperation (Table 8).

Discussion

The extent of removal of thyroid tissue in patients with DTC has been a controversial subject over the years [20–26]. The effect of limited radical resections versus total resection of the thyroid gland on intrathyroidal tumor recurrence is debatable. In Germany total thyroidectomy has evolved to be the preferred procedure for thyroid cancer in most surgical departments and particularly in specialized centers [27]. At our institution total thyroidectomy was the standard procedure for manifest papillary and follicular tumors. Limited surgical radicality was indicated only for small encapsulated papillary tumors and small microinvasive follicular carcinomas. The radical strategy provides excellent conditions for follow-up of patients. Thyroglobulin monitoring becomes a sensitive tool for detecting recurrence in athyroid patients [6]. Postoperative ablation of thyroid remnants by radioactive iodine with unnecessary, high doses (3–6 GBq) can be avoided [4]. Thus ^{131}I total body scans and radioiodine treatment are excellent instruments for controlling the disease. ^{131}I total body scans are performed routinely on all our patients with tumors larger than T1 or with node-positive disease [28].

This strategy guarantees reliable staging, with misclassification of the primary tumor stage occurring infrequently. Moreover, the high sensitivity of postoperative follow-up might explain the high rate of detected regional tumor recurrence in our patients (77 of 252, 30.6%), which is surprising for follicular carcinoma [papillary, 46 of 176 (26%); follicular, 31 of 76 (41%)]. Other series report regional recurrences in 6% to 9% of patients [13–15].

Iodine deficiency, which is common in Germany, might play a role, as it is known to induce aggressive tumor growth and conversion to anaplastic carcinoma. Dedifferentiation of thyroid tumors during the course of the disease was observed in about one-third of the patients and is described in detail elsewhere [29].

Lymph node involvement is frequent in DTC, particularly in papillary tumors; but its impact on survival remains questionable [30, 31]. Our study shows a high rate of involved regional lymph nodes at all stages and both histologic tumor types, with an overall incidence of 66% in PTC and 64% in FTC.

The follow-up of patients was rather short, with a mean observation period of 6.9 years, but a high incidence of recurrence was seen within the first years postoperatively, as is reported in the literature [24, 28, 32]. Some of the early recurrences might be attributed to undiagnosed lymph node involvement that was present at the initial operation but which was detected only postoperatively owing to increased sensitivity of radioiodine scan in athyroid patients. Authors with an aggressive approach to thyroid cancer who perform elective lymph node dissection find metastases in regional lymph nodes in as many as 90% [33–35]. In contrast, the recurrence rate in patients not treated by neck dissection is reported to be less than 10% [14, 23]. The reason for the controversial management of lymph node dissection is the lack of reliable criteria with regard to intraoperative decisions on the appropriate extent of surgery. Prospective and randomized trials on the surgical approach do not exist. Scoring systems with excellent estimations of prognosis, such as AGES, AMES or AJC, are based on pathohistologic data, which are for the most part available only postoperatively [7–10].

Therefore we studied our patients by dividing them into two groups: those treated by thyroidectomy alone and those treated by

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Table 8. Postoperative complications.

Operation	No.	LNP	HPT	Accessory paralysis	Phrenic paralysis	Cervical plexus	Chyle leak	Horner
Primary	117	8	2	—	—	—	1	—
Completion	58	4	2	—	—	—	1	—
Recurrence	77	2	3	1	1	1	1	1
Total	252	14 (5.6%)	7 (2.8%)	1 (0.4%)	1 (0.4%)	1 (0.4%)	3 (1.2%)	1 (0.4%)

LNP: laryngeal nerve palsy; HPT: hypoparathyroidism.

thyroidectomy plus neck dissection at the primary operation. There was a certain selection in the group of neck-dissected patients due to preoperatively suspected or proved lymph node involvement, which prompted us to choose a more aggressive approach, using a modified radical neck dissection, which otherwise is not routinely performed. Classification of tumor stages was done according to tumor size and invasion of the thyroid capsule (T1–T4), which can be assessed intraoperatively in most patients.

The analysis of papillary tumors shows a significant difference in recurrence rates with regard to tumor stage and kind of operation. The relative risk increases six times when comparing stage T2 with T3 + T4 and 10 times in patients with thyroidectomy alone. The lack of a difference for T1 tumors can be explained by a negative selection of patients in group 2 (with most of the tumors having been diagnosed by previous lymph node excision) and a positive selection of patients in group 1 (with possibly overtreated encapsulated tumors). Regarding the total rate of recurrence in group 1 it can be concluded that 51% of the patients would have profited from a more extensive operation that included neck dissection. Age and sex as other prognostic factors do not show a difference within the groups. On the other hand, in group 2 only 63 of 82 patients had positive lymph nodes, leaving 19 patients (23%) with possibly unnecessary neck dissection (Table 6).

Similar results were obtained for patients with follicular thyroid cancer, showing statistical significance in tumor stage T2 + T3 versus T4 and thyroidectomy versus thyroidectomy plus neck dissection. The risk of recurrence increases by a factor of six. Surprising is the high rate of lymph node involvement, which might be an indicator of poor prognosis. Most of the patients with distant metastases (21 of 25, 84%) had positive lymph nodes, and 60% (21 of 35) of all lymph node-positive patients had distant metastases. Of the patients in group 1, 51% developed tumor recurrence, whereas only 2 (11%) patients of group 2 had no lymph node metastases in the resected specimen. Thus patient selection for the extended operation was good. Only half of the patients in group 1 had no lymph node metastases, and the other half developed lymph node metastases subsequent to the primary operation. Therefore neck dissection should be considered, particularly in patients with suspected distant metastases, in order to avoid reoperations and to improve radioiodine therapy of distant metastases [36, 37].

Radical surgery must always take into consideration the operative morbidity. Total thyroidectomy is a safe procedure with a low rate of recurrent nerve palsy (RNP) and hypoparathyroidism. Our own series revealed 14 (5.6%) laryngeal nerve palsies, 7 (2.8%) of which occurred accidentally (three during the primary operation, four at the completion thyroidectomy). Bilateral nerve damage and tracheostomy were not observed. Hypoparathyroidism was seen in seven patients (2.8%) including recurrent operations. The complication rate following neck dissection was low, with one case each of damage to the accessory and phrenic nerves, one Horner syndrome, one cervical plexus lesion, and three chyle leaks. There was no operative mortality. These data are comparable to those from the literature: There is an acceptably low morbidity rate, which can be tolerated in view of the benefit achieved by the radical operation [38, 39].

In conclusion these data show a high rate of regional recurrence for both histologic tumor types, and the kind of operation performed is an independent factor relating to tumor relapse. Therefore the data support a more aggressive procedure for differentiated thyroid cancer with regard to dissection of the lateral cervical lymph node compartment. We recommend routine exploration of jugular lymph nodes; and if positive central lymph nodes are found, a modified radical neck dissection should be performed. Thus the rate of reoperations and complications from regional recurrences can be reduced and associated mortality avoided [40]. Whether this advantage has an effect on the outcome and survival of patients remains to be evaluated after a longer follow-up.

Résumé

La thyroïdectomie totale est devenue le procédé de choix dans le traitement du cancer différencié de la thyroïde. La nécessité d'un curage ganglionnaire uni ou bilatéral ou non, est cependant beaucoup moins standardisée. Notre procédé de choix est de faire un curage ganglionnaire systématique chez tous les patients T4 et chez tous les autres patients chez lesquels on trouve des lésions ganglionnaires soit en préopératoire soit au moment de l'intervention. Les résultats concernant la récidive régionale des ganglions cervicaux après la thyroïdectomie sont étudiées et discutées. Entre Avril 1986 et Décembre 1992, 252 patients ont été opérés pour un cancer différencié de la thyroïde (176 papillaires, 76 folliculaires). Le traitement postopératoire comprenait toujours un traitement par l'iode radioactif chez tous les patients T1 ou plus et le suivi a comporté des dosages de thyroglobuline, une échographie cervicale et une scintigraphie à l'iode radioactif. Après un suivi moyen de 6.9 ans, 77 (31%) des patients avaient eu une réintervention en raison d'une récidive tumorale papillaire (46/176 26%) ou folliculaire 31/76 41%). En ce qui concerne le cancer papillaire, on a pu mettre en évidence une différence significative entre les patients ayant eu une thyroïdectomie simple et ceux qui ont eu une thyroïdectomie associée à un curage ganglionnaire dans tous les stades (T2: 13/29 (45%) vs 1/34 (3%), T3: 10/13 (77%) vs 4/11 (36%), T4: 6/8 (75%) vs 6/18 (33%) (p < 0.0001). Des résultats similaires ont été enregistrés dans le cancer folliculaire avec une différence statistiquement significative selon le procédé chirurgical (p < 0.009). Notre expérience démontre une corrélation positive entre la récidive régionale et le stade de la tumeur dans les deux types histologiques. Le taux élevé de récidive régionale justifie une approche radicale comprenant un

curage ganglionnaire lors de l'intervention initiale. L'impact sur la survie, cependant, reste à déterminer par d'autres études.

Resumen

La tiroidectomía total se ha convertido en el procedimiento de rutina para el tratamiento del cáncer diferenciado de tiroides. Sin embargo, la necesidad de practicar disección unilateral o bilateral no ha sido estandarizada. Nuestra rutina ha sido practicar disección cervical rutinaria en los tumores T-4 y en todos los otros estadíos tumorales, sólo en presencia de un diagnóstico positivo o de hallazgos intraoperatorios. En este artículo se estudian y analizan los resultados concernientes a recurrencia tumoral regional en ganglios cervicales subsecuente a tiroidectomía. Entre abril de 1986 y diciembre de 1992 se operaron 252 pacientes por carcinoma diferenciado de tiroides (CDT) (176 papilares, 76 foliculares). El tratamiento postoperatorio incluyó terapia con radioyodo como regla general en todos los pacientes > T1 y el seguimiento incluyó determinaciones de tiroglobulina, ultrasonografía cervical y escintigrafía con radioyodo. Luego de un seguimiento medio de 6.9 años, 77 (31%) pacientes requirieron reoperación por recurrencia tumoral regional (46/176, 26%, papilar; 31/76, 41%, folicular). En el cáncer papilar se pudo demostrar una diferencia significativa entre los pacientes con tiroidectomía versus los que recibieron tiroidectomía más disección ganglionar en la totalidad de los estadíos tumorales (T2:13/29, 45%, vs. 1/34, 3%; T3: 10/13, 77%, vs. 4/11, 36%; T4: 6/8, 75%, vs. 6/18, 33%) (p < 0.0001). Similares resultados fueron logrados en los cánceres foliculares, exhibiendo significancia estadística en relación con el procedimiento operatorio (p < 0.009). Nuestra experiencia demuestra una correlación positiva entre la recurrencia tumoral y el estadío tumoral en ambos tipos de cáncer diferenciado. La alta tasa de recurrencia regional justifica un aproche más radical, incluyendo disección cervical en la operación inicial. El impacto sobre la supervivencia, sin embargo, debe ser comprobado mediante evaluación adicional.

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Invited Commentary

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Simon et al. take a worthy, careful look at whether regional lymph node dissection should become a *routine* practice added to thyroidectomy for differentiated thyroid carcinoma. There are a number of questions that require answers before adopting such a practice.

1. Has the initial treatment been adequate? Although still controversial in some respects, total thyroidectomy is unassailably considered adequate as the central treatment for differentiated thyroid carcinoma. Moreover, the authors' overall management is excellent, including (a) routine central node dissection combined with total thyroidectomy; (b) lateral neck dissection when indicated for tumor size greater than T1 or pre- or intraoperative findings establishing abnormal nodes; (c) follow-up with radioactive iodine and ultrasound scans; and (d) adjuvant treatment with radioactive iodine for tumors greater than T1 size plus all node-positive patients. Criticism could be leveled at the inclusion of a number of patients who were evaluated and initially operated elsewhere. Although such inclusion increases the variability and raises questions about the adequacy of ultrasonography and initial surgery performed elsewhere, it also depicts the realism of a referral practice.

2. Are the authors assessing the appropriate endpoints? Because death from differentiated thyroid cancer is uncommon and is often delayed, this endpoint is a difficult one. Regional nodal recurrence, although a separate issue, is a reasonable endpoint from a number of standpoints (discussed subsequently).

3. Has adequate follow-up been obtained on the patient population? A mean of 6.9 years to assess nodal disease is sufficient to discover most recurrences.

4. Is regional lymph node recurrence a *real* problem? It certainly engenders significant concern on the part of patients facing reoperation plus the risk of added surgical morbidity and expense. Although the presence of metastatically involved nodes has not been shown convincingly to affect long-term survival, this issue remains in question. Nevertheless, the 31% regional nodal recurrence rate observed by the authors justifies careful attention. In contrast to some other diseases, lymphadenectomy for differentiated thyroid cancer can enhance subsequent treatment of distant metastases through the use of radioactive iodine. A key issue, however, is whether survival is affected by removal of the lymph nodes, particularly if they are subclinical and nonpalpable. As the authors point out, when prophylactic lateral node dissections have been performed, up to 90% of patients with differentiated thyroid cancer harbor at least microscopic disease in these nodes. However, even when far fewer than 90% of these patients have undergone lateral node dissection, survival has remained exceptionally good, calling into question the clinical relevance of these nodes.

5. Can the patient population under study, their assessment, management, and recommendations, be applied generally to other populations of patients with the same disease? There is at least one striking exception. The authors found a 41% frequency of metastatic lymph nodes in pure follicular carcinoma, which is extraordinarily high when compared to our and other North American experience. Perhaps as the authors suggest, the disease is different in Europe within an endemic goiter area. Yet another explanation might be that in their patients with distant metastases these associated positive nodes might equate to distant disease, analagous to positive nodes in patients with soft tissue sarcomas in other parts of the body.

6. Is the solution proposed by the authors acceptable? Clearly they have shown that routine lymphadenectomy can reduce the subsequent nodal relapse rate from 51% to 18%. Their surgically related morbidity is acceptably low. However, when considering a radical lymphadenectomy with its attendant risk, increased operative time, and cosmetic implications, particularly in patients who prove to have negative nodes, a more selective approach would be optimal. Perhaps more highly sensitive preoperative imaging studies or better intraoperative methods to assess the nodes is an option. However, the authors have developed a strong basis for their approach.

In summary, Simon et al. have evaluated their method of assessment and combined medical-surgical management of differentiated thyroid carcinoma patients and have identified a substantial problem of regional lymph node recurrence. They have proposed a reasonable, although not ideal, solution to this management problem. At the least, it should stimulate other investigators to address this important problem.