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Occult Lymph Node Metastases Increase Locoregional Recurrence in Differentiated Thyroid Carcinoma

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Objectives: The impact of occult lymph node metastasis (OLNM) on locoregional recurrence (LRR) and survival in patients with N0 differentiated thyroid carcinoma is unclear, because no large study has been carried out. A retrospective study was conducted in our department to assess the influence of OLNM.

Methods: We included 201 patients treated by prophylactic neck dissection for N0 differentiated thyroid carcinoma between 1974 and 2006. The incidence of OLNM and predictive factors for recurrence and survival were assessed.

Results: The incidence of OLNM was 20%. Necks were involved at levels VI, III, II, IV, V, and I, in decreasing order of frequency. After a mean follow-up of 9 years, the rate of LRR was 8.9% and the rate of distant metastasis was 3.4%. An age of greater than 55 years and the presence of OLNM were predictive factors for LRR. An age of greater than 55 years and the presence of LRR were predictive factors for distant metastasis. The presence of distant metastasis was the only factor that significantly and independently influenced the disease-specific survival.

Conclusions: We found that OLNM occurred in only 20% of N0 patients. The presence and especially the number of OLNMs on neck dissection were major risk factors for LRR in this study, but did not affect the disease-specific survival.

Key Words: N0 neck, neck dissection, papillary carcinoma, predictive factor, thyroid neoplasm.

INTRODUCTION

Differentiated thyroid cancer (DTC), including papillary and follicular thyroid cancer, has an excellent prognosis.[1] Paradoxically, cervical lymph node metastases are frequently found at diagnosis.[2] When metastasis is diagnosed before operation by palpation and/or ultrasound, treatment of these lymph nodes is straightforward and is based on neck dissection to improve locoregional control and mortality rates.[1,3-5] Thus, neck dissection is currently performed by most surgeons in N+ cases.[6-8] The treatment of occult lymph node metastasis (OLNM) is more controversial. The ability of neck dissection to provide better staging of the disease and its likely benefit on locoregional control must be balanced against the increase in morbidity.[9-11] This retrospective study was carried out to analyze the results of surgical neck management of differentiated papillary carcinoma in terms of lymph node involvement and the influence on locoregional control and survival.

PATIENTS AND METHODS

Patients. The medical records of 631 patients who underwent surgery for thyroid cancer at Rennes University Hospital between January 1974 and December 2006 were reviewed. Inclusion criteria were histologically proven papillary or follicular thyroid cancer treated by lymph node dissection, tumor size of greater than 10 mm, and no evidence of lymph node involvement on clinical examination and ultrasound imaging (after 1985). Patients with massive extrathyroid extension (T4) or distant metastases (M1) were excluded so that lymph node involvement and its effects on survival and recurrence could be determined independently from these negative predictive factors.[5,12-15] Overall, 201 patients were selected (Table 1). The male-to-female ratio was 0.30 to 1, and the mean age at diagnosis was 40.7 years (range, 12 to 78 years). The mean length of follow-up was 9 years.

Surgical Procedure. The initial treatment was thyroidectomy with frozen section biopsy. In the case of a positive frozen section during surgery, a total thyroidectomy with lateral neck dissection of ipsilateral levels II, III, IV, and V was routinely performed. Examination of the central compartment for metastatic lymph nodes was carried out systematically. If suspect lymph nodes were found, both cen-

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TABLE 1. PATIENT CHARACTERISTICS, SURGICAL PROCEDURES, AND TUMOR CHARACTERISTICS

	All Patients		pN– Cases		pN+ Cases		
Characteristics	*No.*	*%*	*No.*	*%*	*No.*	*%*	*p*
No. of patients	201	100	161	80	40	20	
Male	48	24	38	24	10	25	0.85
Female	153	76	123	76	30	75	
Mean age (y)	40.7		42.3		34.5		0.002
Age <45 years	124	62	93	58	31	77	0.026
Age ≥45 years	77	38	68	42	9	23	
Papillary type	165	82	126	78	39	98	0.005
Follicular type	36	18	35	22	1	2	
Tumor size ≤20 mm	109/184	59	85/149	57	24/35	69	0.2
Tumor size >20-40 mm	63/184	34	52/149	35	11/35	31	
Tumor size >40 mm	12/184	7	12/149	8	0/35	0	
T1	102	54	84	57	18	50	0.05
T2	61	33	52	33	9	25	
T3	24	13	15	10	9	25	
Tx	14		10		4		
Plurifocality	60	30	42	26	18	45	0.019
Bilaterality	41	20	28	17	13	32	0.034
Extracapsular extension	14	7	5	3	9	23	<0.001
Angio-invasion	52	26	37	23	15	38	0.061
Presence of tumor capsule	126/169	75	111/139	79	15/30	50	0.001
Effraction of tumor capsule	70/126	56	58/111	52	12/15	80	0.536
Total thyroidectomy	195	97					
Lobectomy	6	3					
^{131}I thyroid ablation therapy	171	85					
Mean follow-up (y)	9						
Range of follow-ups (y)	0-33						

tral compartments were dissected. In the case of a bilateral or isthmic tumor, a bilateral neck dissection was performed in the same way. If malignancy was confirmed by histologic examination, the thyroidectomy was completed and associated with ipsilateral neck dissection from levels II to V. Examination of the central compartment was also performed. In patients with a tumor less than 10 mm in size, no neck dissection was performed at our institution. Most procedures were performed by the senior author (G.L.C.). Because of the large number of surgeons employed during the study period, other surgical treatments were occasionally performed, including lobectomy, selective neck dissection, prophylactic central and lateral neck dissection, no lateral neck dissection, level Ib dissection, and exclusive central neck dissection. The patients were divided into 3 groups according to their lymph node dissection status: group 1, with prophylactic central and lateral lymph node dissection; group 2, with central exploration and lateral lymph node dissection; and group 3, with any other dissection methods.

Radioiodine Treatment. Treatment with iodine 131 (^{131}I; mean activity, 98.6 mCi) was given to 171 patients (85%) after withdrawal of thyroid hormone treatment, at an interval of 4 to 6 weeks after surgery. A whole-body scan was performed 2 to 5 days after ^{131}I administration. The whole-body scan results were considered abnormal when foci were visible.

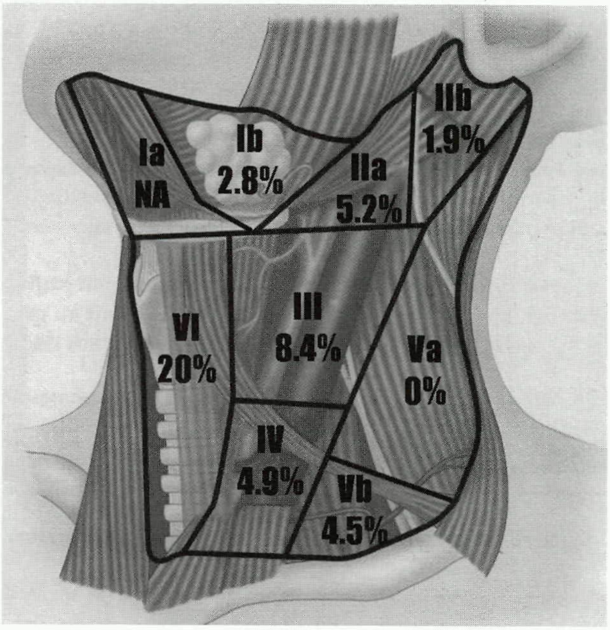
Surgical Complications. Details of surgical complications were obtained from the patients' medical records and separated into two periods: 1) early complications, arising in the first 6 months after surgery; and 2) late complications, arising or persisting 6 months after surgery.

Follow-Up. Regular clinical, biological, and imaging follow-up was performed. This included the thyroid-stimulating hormone level and the thyroglobulin level with or without thyroid-stimulating hormone stimulation. Cervical ultrasonography was performed regularly, accompanied, if necessary, by a ^{131}I whole-body scan, a computed tomography (CT) scan, magnetic resonance imaging, or fine-needle biopsy.

Criteria for Locoregional Recurrence. Locoregional recurrence (LRR) was suspected on routine follow-up by clinical or ultrasound examination and/or high levels of serum thyroglobulin and/or results of imaging. We defined LRR as evidence of local or regional disease that persisted or recurred after completion of the initial treatment. The LRR was confirmed by a fine-needle aspiration cytology diagnosis or a combination of clinical (suspicious node in terms of size or consistency), imaging (ultrasound, CT scan, ^{131}I whole-body scan, positron emission tomography using 18-F-fluoro-deoxy-D-glucose), and biological (thyroglobulin level of more than 1 ng/mL under thyroid-stimulating hormone stimulation achieved either by thyroid hormone withdrawal or administration of Thyrogen) parameters. In patients who underwent an exploratory neck dissection for suspicion of recurrence, LRR was confirmed histologically.

Criteria for Complete Remission. Complete remission was defined as a thyroglobulin level of less than 1 ng/mL (under thyroid-stimulating hormone stimulation achieved either by thyroid hormone withdrawal or by administration of Thyrogen) and either a ^{131}I whole-body scan showing no residual thyroid tissue or an ultrasound examination with normal findings.

Statistical Analysis. The characteristics of the patients were compared by use of Fisher's exact test, Student's parametric *t*-test, or the Mann-Whitney nonparametric test, as appropriate. The time to LRR was calculated from the date of thyroid surgery to the date of first recurrence, the date of last examination, or January 1, 2008 (time of data collection). The cumulative probability of LRR was calculated as 1 minus the probability of surviving without developing a recurrence, estimated according to the Kaplan-Meier method. Rates were compared between groups by use of the log-rank test. The 95% confidence interval for each rate was estimated. A prognosis factor analysis was performed by use of the logistic regression model, with LRR as the dependent variable. The result was expressed as a hazard ratio (HR) and the corresponding 95% confidence interval. The independent variables were gender, age at diagnosis (less than or equal to 55 versus greater than 55 years), tumor size (less than or equal to 20 mm versus greater than 20 to 40 mm versus greater than 40 mm), histologic type (papillary versus follicular), multifocality, bilaterality, extracapsular spread, presence of a tumor capsule, rupture of a tumor capsule, vascular invasion, T stage (based on the TNM AJCC staging system), lymph node involvement, number of OLNMs (0 versus 1 to 5 versus more than 5), location of lymph node metastases (central versus lateral), and presence of distant metastases. Statistical significance was defined at a p level of less than 0.05. Disease-specific survival was defined as the time from initial diagnosis to death by disease progression. All data were collected in Excel (Microsoft for Windows, release 2007) and analyzed with SPSS software (SPSS Inc for Windows).



Distribution of occult lymph node metastases. (Figure background is reprinted, with permission, from Brasnu D, Laccourreye O, Hans S, Ménard M, De Monès E, Behm E. La chirurgie conservatrice des cancers du larynx et du pharynx. Paris, France: Amplifon, 2005:39.)

RESULTS

Tumor Characteristics. The characteristics of the patients, the surgical procedures, and the pathological characteristics of the tumors are summarized in Table 1. Eighty-two percent of the tumors were papillary carcinomas. A total thyroidectomy was performed in 97% of the patients. Surgery was followed by ^{131}I thyroid ablation in 85% of the patients. Microscopic extracapsular invasion was found in 7% of patients. Data regarding the presence of a tumor capsule and tumor size were available for 169 and 184 patients, respectively.

Lymph Node Involvement. The rate of OLNM was 20% (n = 40). The Figure shows the distribution of lymph node involvement. The levels most frequently involved were levels VI and III, with 20% and 8.4% of nodes involved, respectively. No OLNM was found in level Va.

Locoregional Recurrence. Eighteen patients (8.9%) developed at least 1 LRR (Table 2), 1 patient presented with 2 consecutive recurrences, and 2 patients had 3. The mean time to relapse was 5.6 years (range, 0.4 to 21 years). The median time to relapse was 1.1 year. Eight of the 18 patients (44%) had LRR within 12 months after diagnosis. Ten of the

TABLE 2. CHARACTERISTICS OF PATIENTS WITH LOCOREGIONAL RECURRENCE

			*Initial Presentation and Treatment**					*Locoregional Recurrence*			*Distant Metastases*		*Outcome*	
Pt No.	*Sex*	*Age (y)*	*Thyroid Tumor Location*	*Histologic Type*	*Dissection*	*Location of LNM*	*No. of Nodes Involved/ Removed*	*Time Since Diagnosis (y)*	*Location*	*Diagnosis*	*Location*	*Time Since Diagnosis (y)*	*Time Since Diagnosis (y)*	*Status*
1	F	64	Uni	Fol	S Bil			17.8	C	Hist			25	Dead-rel
2	F	58	Uni	Fol	L Ipsi			21.3	L Ipsi	Imag	L	20	24	Dead-rel
3	M	32	Uni	Pap	L Ipsi			18.2	C Con	Hist			21	DF
4	F	35	≈Bil	Pap	L+C Bil	L Ipsi	5/24	9.4	C Ipsi	Hist			20	DF
5	F	19	≈Bil	Pap	S Bil	L Bil + C Ipsi	9/9	0.4	L+C Ipsi	Hist	L	0.5	14	DF
6	F	31	Uni	Pap	L Ipsi			1.1	C Ipsi	Imag			18	RD (Tg)
7	F	13	≈Bil	Pap	C Ipsi	C Ipsi	NA	1.3	L Ipsi	Hist			5	RD (Tg)
8	M	13	Uni	Pap	L+C Ipsi	C Ipsi	3/12	0.5	C Ipsi	Hist			15	DF
9	F	46	Uni	Pap	L+C Ipsi	L+C Ipsi	3/11	0.6	C	Imag			13	DF
10	F	19	≈Bil	Pap	L Ipsi	L+C Ipsi	4/8	0.9	C	Imag			5	DF
11	M	52	Uni	Fol	S Ipsi			21.3	C	Hist	L	21	22	Dead-rel
12	F	73	Uni	Pap	C Ipsi	C Ipsi	NA	1.0	NA	Hist	L	1	5	DF
13	M	62	Uni	Fol	L Bil			2.8	C Con	Hist	L	10	21	AD (lung)
14	F	24	Uni	Pap	L+C Ipsi			0.7	C Ipsi	Imag			7	RD (Tg)
15	F	30	Uni	Pap	L Ipsi			0.6	NA	Imag			7	RD (Tg)
16	F	22	Uni	Pap	L Ipsi	L Ipsi	1/25	1.4	C	Hist			4	DF
17	F	61	Uni	Pap	L Ipsi	L Ipsi	2/33	0.6	C Con	Imag			4	DF
18	F	78	Uni	Pap	L+C Ipsi	L+C Ipsi	5/8	0.7	L Ipsi	Hist	L	2	2	AD (lung)

LNM — lymph node metastasis; Uni — unilateral; Fol — follicular; S — selective; Bil — bilateral; C — central; Hist — histologic; Dead-rel — tumor-related death; L — lateral; Ipsi — ipsilateral to tumor; Imag — imaging; Pap — papillary; Con — contralateral to tumor; DF — disease-free; ≈Bil — bilateral but clinically unilateral; RD (Tg) — residual disease according to elevated thyroglobulin level; NA — not available; AD — active disease.

*All 18 patients had ^{131}I ablation.

18 cases with LRR were initially pN+ on histologic examination of neck dissections. The central compartment was involved in 3 patients, the lateral compartment in 3, and both in 4. All 18 patients were given postoperative radioiodine ablation after initial surgery. Locoregional recurrence was suspected on whole-body scans performed after the first (n = 13) or second (n = 5) therapeutic administration of ^{131}I. Locoregional recurrence was diagnosed by lymphadenectomy in 11 patients and by imaging in 7. In the latter, whole-body scans allowed the diagnosis in 5 patients, and ultrasonography, in 2. All patients had a high serum thyroglobulin level.

The LRR was localized in the level previously treated in 5 patients and in levels left untreated by initial selective neck dissection in 8 patients. One patient had neck recurrence in both treated and untreated levels. The data were missing for 4 patients. At the last follow-up, with a median follow-up time of 14 years, 9 of the 18 patients were considered disease-free, 2 had distant metastatic disease (diagnosed by CT or whole-body scans), 4 had biological disease (isolated significantly high level of serum thyroglobulin), and 3 had died (all with follicular thyroid cancer).

Distant Metastases. Seven patients (3.4%) developed 8 distant metastases during the study: pulmonary metastases in 7 cases (88%) and bone metastasis in 1 case (12%). Thyroid ablation with ^{131}I was given to all patients. One patient received external radiotherapy and appeared to be disease-free at the 5-year follow-up. One patient received chemotherapy and died 22 years after the initial surgery. At the last update, 3 patients (43%) had died, 2 patients (28.5%) were disease-free, and 2 patients (28.5%) had distant metastases. One patient had pulmonary and bone metastases and died 15 years after initial treatment.

Disease-Specific Survival. Disease-related death occurred in 5 of the 201 patients with a mean follow-up of 9 years. The rates of 10-year and 20-year disease-specific survival were 99.5% and 97.4%, respectively.

Surgical Complications. Two thirds of the patients (65%) had no early complications of surgery (Table 3). The most frequent complication in this

TABLE 3. SURGICAL COMPLICATIONS AFTER NECK DISSECTION

Complications	*Early (%)*	*Late (%)*
None	65.0	70.7
Hematoma	4.2	NA
Hypoparathyroidism	11.5	4.2
Laryngeal nerve palsy	3.3	2.1
Ramus marginalis palsy	4.2	NA
Abscess	1.9	NA
Hypertrophic and keloid scars	NA	8.9
Shoulder dysfunction	NA	7.8
Other	9.9	6.3

NA — not available.

period was hypoparathyroidism (11.5%). Laryngeal nerve palsy was present in 3.3%.

Nearly three quarters of patients (70.7%) had no late complications of surgery. Hypoparathyroidism and laryngeal nerve palsy persisted in 4.2% and 2.1% of patients, respectively. Hypertrophic and keloid scars were the most frequent complication (8.9%). Shoulder dysfunction was found in 7.8% of patients after neck dissection.

Prognostic Factors. On univariate analysis (log-rank test), OLNM was the only variable that was significantly correlated with an increased probability of LRR ($p < 0.001$). On multivariate analysis, age of greater than 55 years (HR, 3.46) and the number of OLNMs significantly increased the risk of recurrence (Table 4). If 1 to 5 OLNMs were present, the relative risk was 8-fold higher. If more than 5 OLNMs were present, the risk was 17.2-fold higher.

On univariate analysis, 3 variables correlated significantly with an increased probability of distant metastases: age of greater than 55 years ($p < 0.001$), the presence of OLNM ($p = 0.037$), and the presence of LRR ($p < 0.001$). On multivariate analysis, age of greater than 55 years (HR, 5.64) and the presence of LRR (HR, 27.64) significantly increased the risk of distant metastases (Table 4).

On univariate analysis, 6 variables correlated significantly with an increased mortality rate: age of greater than 55 years ($p = 0.004$), papillary histology ($p = 0.045$), tumor size of at least 30 mm ($p < 0.001$), T3 stage ($p = 0.01$), presence of LRR ($p = 0.01$), and presence of distant metastases ($p < 0.001$). On multivariate analysis, the only risk factor that influenced the mortality rate was the presence of distant metastases (HR, 36; Table 4).

The prognostic factors for hypoparathyroidism and laryngeal palsy are summarized in Table 5. Central compartment dissection significantly increased the rate of early hypoparathyroidism, but did not influence the rate of late hypoparathyroidism or laryngeal palsy.

TABLE 4. PREDICTIVE FACTORS IN MULTIVARIATE ANALYSIS

Variable	*Hazard Ratio*	*95% CI*	*p*
For locoregional recurrence			
Age			
≤55 y	1		
>55 y	3.46	1.12 to 10.71	0.031
Lymph node metastasis			
0	1		
1-5	8.00	2.38 to 26.88	0.001
>5	17.20	3.27 to 90.58	0.001
For distant metastases			
Age			
≤55 y	1		
>55 y	5.64	1.04 to 30.48	0.045
Locoregional recurrence			
No	1		
Yes	27.64	3.10 to 246.80	0.003
For death			
Distant metastases			
No	1		
Yes	36.00	3.5 to 374.00	<0.001

CI — confidence interval.

DISCUSSION

In this retrospective study of 201 patients with DTC, the rate of LRR was 8.9%. The fact that almost one half of LRRs were in the year following diagnosis suggests that most patients with LRR had persistent disease rather than true recurrences. The presence of OLNM was the strongest risk factor for LRR in this study. As reported previously, age of greater than 45 years (55 years in our study) is re-

TABLE 5. INFLUENCE OF NECK DISSECTION ON HYPOPARATHYROIDISM AND LARYNGEAL PALSY

		Group 1		*Group 2*		*Group 3*	
	p	*No.*	*%*	*No.*	*%*	*No.*	*%*
Early complications*							
Hypoparathyroidism	<0.001[a,b,c]	12/41	29.3	11/128	8.6	1/25	4.0
Laryngeal palsy	0.23[d]	3/41	7.3	3/128	2.3	1/25	4.0
Late complications†							
Hypoparathyroidism	0.48[d]	3/38	7.9	4/120	3.3	1/25	4.0
Laryngeal palsy	0.27[d]	2/38	5.3	2/120	1.7	0/25	0

[a]p < 0.001 between group 1 (prophylactic central and lateral lymph node dissection) and group 2 (central exploration and lateral lymph node dissection).

[b]p < 0.001 between group 1 and group 3 (other dissection methods).

[c]p > 0.05 between groups 2 and 3.

[d]p > 0.05 between groups 1 and 2, between groups 2 and 3, and between groups 1 and 3.

*In 194 neck dissections.

†In 183 neck dissections.

lated to an increased risk of LRR.[16] In our study, age of greater than 55 years was also associated with an increased risk of distant metastases.[6,17,18]

According to our data, 20% of patients with N0 DTC have OLNM, in accordance with another French study on papillary cancer.[19] As most surgeons do not practice both central and lateral neck dissection, the rates of OLNM reported in the medical literature are subject to controversy. Asian and American studies have revealed higher rates of OLNM. Wada et al[20] reported OLNM in 61% of patients with papillary microcarcinoma, and Ito et al[6] found lateral OLNM in 64% of 1,321 patients with papillary cancer. For Attie et al,[21] the rates varied from 21% to 69%. This wide range between studies highlights the difficulty in obtaining clear data for thyroid disease. However, it is obvious that thyroid cancer in different geographic areas varies, not only with regard to genetic changes in tumor tissue (*ras*, *gsp*, *p53*, and *p21* mutations), but also clinically, in the rates of regional and distal spread and in disease course.[22]

The most frequently involved levels in our study were levels VI (central), III, IV, and II — a finding consistent with those of other studies on therapeutic neck dissection[23,24] and with the conventional anatomy of lymphatic drainage of the thyroid area. Our data clearly show that the presence of OLNM is a risk factor for LRR. In multivariate analysis, when 1 to 5 OLNMs were present, the risk of LRR was 8 times higher than when no OLNMs were found. When more than 5 OLNMs were present, the risk was multiplied by 17.2. These findings agree with those of previous studies. For Leboulleux et al,[15] the recurrence rate increased when more than 10 lymph node metastases were present. Ito et al[6] reported a decrease in the 10-year lymph node disease–free survival rate from 96.1% to 90.5% when more than 5 OLNMs were present. However, according to a study of 447 patients with papillary thyroid cancer by Bardet et al,[19] OLNM had no role in recurrence, although these authors did not distinguish according to the number of metastatic lymph nodes. A high number of OLNMs could reveal a more aggressive histologic form of the disease, as shown by Ito et al[25] in a comparison between microscopic and macroscopic lymph nodes. Other studies comparing the histologic properties of thyroid tumors with OLNM, and the numbers of OLNMs, could help to identify aggressive subgroups with a risk of LRR that could benefit from neck dissection.

No significant difference was found in our study between the different groups according to neck dissection in terms of LRR, although LRR was more frequent in patients with selective neck dissection (group 3, 19%) than in patients with central and lateral neck dissection (group 1, 9%) or exploration and lateral neck dissection (group 2, 7%). This lack of a significant difference between neck dissection strategies was reported by Bardet et al,[19] who found no difference between cases with and without prophylactic neck dissection. This comparison was not done in our study, because our two groups were too different to be compared: 77% of patients in the group without neck dissection (data not shown) had microcarcinoma, which has an excellent prognosis and a low rate of LRR. It is clear that multicenter retrospective studies comparing different surgical strategies or prospective studies will have more appropriate methodology to answer this question. Prospective studies are difficult to perform in thyroid neoplasia, because of the low incidence of the disease and because of its good prognosis with relatively late and low LRR and mortality rates.

Thus, most studies are retrospective, and lateral and central prophylactic neck dissections are still controversial in thyroid cancer. In our series, no difference in recurrence or mortality rates was found between patients with central exploration and central dissection. A few studies, mainly retrospective, have shown a decrease in LRR with systematic central neck dissection and advocate prophylactic central neck dissection because of improved staging and reduced morbidity in second-look cases.[26,27] However, central neck dissection is responsible for more cases of permanent hypoparathyroidism and unintentional laryngeal nerve palsy.[26] In our study, group 1 was associated with a significantly higher risk of early hypoparathyroidism ($p < 0.001$) and a higher incidence of late laryngeal palsy and hypoparathyroidism (not significant) than were groups 2 and 3. The rates of LRR were similar in groups 1 and 2 (9% and 7%, respectively; not significant). According to our results, central exploration allows the same control as central neck dissection in terms of the disease, but carries less risk to the laryngeal nerve and parathyroid glands. Our results are in accordance with recommendations on DTC that stated that prophylactic central node dissection may not be necessary for noninvasive T1 or T2 papillary thyroid carcinoma and most follicular cancer, and that a close intraoperative inspection of the central compartment with compartmental dissection only in the presence of obviously involved lymph nodes is a valid option.[1]

Lateral neck dissection is less controversial. In cases of clinical lymph node metastasis, lateral neck dissection is recommended and is preferred to simple lymph node "picking."[1,27] In contrast, when no clinical lymph node metastases are present, prophylactic neck dissection of the lateral compartment is not recommended, because no benefit has been established in terms of survival or LRR. The current data do not clearly enable us to answer this question, but no statistically significant difference in LRR rates was noticed in patients with lateral neck dissection (7% and 9%) compared to patients with selective neck dissection, although the latter group presented more LRR (19%). We explain this unusually high rate of LRR in group 3, compared to the literature, by the small number of patients in this group (n = 25).

In this study, OLNM was not predictive of a higher rate of mortality, although we found that OLNM predicts LRR, LRR predicts distant metastases, and distant metastases predict mortality. This situation can be explained by sampling fluctuations due to the retrospective design of this study and the low mortality rate in our patients. Thus, the data reflect our sample, but do not reflect the general population. This is a common problem in studies of thyroid carcinomas, which are mainly of retrospective design and are rarely prospective because of the excellent survival rates and low rates of recurrence that make prospective studies very difficult to perform. To our knowledge, no study has shown the influence of OLNM on mortality.

This retrospective study has several other limitations. First, although it covers a long period of time (1974 to 2006), during which improvements in imaging may have resulted in differences in the likelihood of detecting preoperative lymph node metastases and postoperative recurrence, the vast majority of diagnoses (86%) were made after 1985, at a time in which ultrasonography was used routinely in our patients. Second, all lymph node metastases not detected before surgery were considered microscopic, including peroperative central nodes removed after positive exploration. Finally, the fact that postoperative radioiodine was administered to most, but not all, patients may have introduced a potential bias. These differences in treatment were taken into account in the multivariate analysis.

CONCLUSIONS

This study is one of the most thorough on OLNM in DTC. Occult lymph node metastasis occurs in only 20% of N0 cases, has a predictable pattern and spread, and has factors predictive of recurrence that can aid the clinician in the choice of therapy. The presence and especially the number of OLNMs on neck dissection were the major risk factors for LRR in this study.

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