Abstract. Background: Prospective randomized studies aimed at evaluating the different therapeutic protocols for the treatment of papillary or follicular carcinoma are lacking at the moment. Although total thyroidectomy is widely accepted, indication to locoregional lymphadenectomy is strongly debated. Materials and Methods: Fifty-four patients with papillary or follicular thyroid carcinoma (45 papillary and 9 follicular) underwent functional evaluation of the gland before intervention, FNAB included. Surgical management was carried out as follows: 41 total thyroidectomy, 6 lobectomy with further totalization in 5, 6 total thyroidectomy plus central compartment lymphadenectomy and 1 left laterocervical lymphadenectomy (papillary carcinoma, treated elsewhere through total thyroidectomy plus central and right laterocervical lymphadenectomy). All operated patients were submitted to whole body scintigraphy and treated thereafter by radiometabolic therapy and chronic hormone suppressive therapy. Results: Fifty-one patients are currently alive, 3 died from non-related causes; surgical complications included 1 permanent impairment of inferior laryngeal nerve function and 1 case of hypoparathyroidism. The follow-up was from 1 to 139 months. Discussion: The optimal treatment of lymph node metastases, especially for papillary carcinomas, has not yet been defined. Two trends are evident concerning lymphadenectomy: the first one suggests routine lymphadenectomy, the second supports lymphadenectomy by necessity. In follicular carcinoma lymphadenectomy is recommended only in the presence of clinical evidence of lymph node involvement. Occult differentiated carcinoma does not require any further treatment of lymph nodes. Conclusion: Considering the high efficacy of radiometabolic treatment after total thyroidectomy combined with chronic TSH inhibition through L-tyrosine administration, lymphadenectomy is suggested only by necessity.

Papillary and follicular carcinomas represent the greater portion of thyroid malignant tumors; thyroid cancers are rare (about 1% of all malignant neoplasms), however an increase in their incidence has been observed during the last decade (1, 2). A uniform therapeutic strategy is not available, due to the lack of prospective randomized studies which would allow the evaluation of different therapeutic protocols; as well, current systems of prognostic evaluation offer limited accuracy and reliability (3-8). Extension of parenchymal exeresis, lymph node clearance and radiometabolic therapy are still the object of discussion regarding their effects on cumulative survival and/or local recurrence (5-13): this is particularly true for those patients in whom a clear-cut lymph node involvement or distant metastases are not demonstrated through the preoperative diagnostic procedures (7). Total thyroidectomy followed by radiometabolic therapy is widely accepted; whereas the indication for lymphadenectomy is strongly debated (6, 7, 14-18). With regard to the latter, the available data are conflicting: significant variations are reported in the incidence of lymph node involvement and as well as in the percentage of mortality and/or recurrence in N+ cases. As a consequence, opinions about the results of routine vs by necessity lymphadenectomy and its beneficial effects in MO cases are conflicting too (6, 7, 13, 17, 18); on the other hand, trends exist for occult carcinomas and for M+ cases (5-7, 9, 19).

The aim of the present study was to evaluate whether routine lymphadenectomy offers any real advantage in terms of survival and of disease-free interval.

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Key Words: Papillary thyroid carcinoma, follicular thyroid carcinoma, lymphadenectomy.
Materials and Methods

Among all thyroid cancer patients treated in our Department from January 1989 through October 2002, 54 patients, treated by the same surgeon and followed-up by the same team, were enrolled. There were 49 females (90.8%) and 5 males (9.2%); the age ranged from 20 to 83 years (mean 47.8 years): 35 patients were under 45 years and 19 were 45 years old or more. The pathological diagnosis was: papillary carcinoma 45, follicular carcinoma 9. Preoperative study included in all patients indirect laryngoscopy, blood assay for Ca, Mg, P, FT3, FT4, PTH and FNAB. Out of 54 FNAB procedures (53 thyroid lesions, one lymph node lesion), papillary carcinoma was diagnosed in 36 instances (33 uninodeal thyroid lesions, 2 multinodal thyroid lesions, 1 lymph node lesion) and follicular proliferation in 18. Recently, the FNAB retrieved material was submitted to Galectin-3 test in 3 cases (folllicular carcinoma 2, papillary carcinoma 1). Surgical management consisted of the following: total thyroidectomy 41 (37 papillary, 4 follicular); lobectomy 6 (2 papillary, 4 follicular) with further totalization in 5, one patient having refused reoperation; total thyroidectomy plus central compartment lymphadenectomy 6 (4 papillary, 2 follicular); one left laterocervical lymphadenectomy (papillary carcinoma, treated elsewhere through total thyroidectomy plus central and right laterocervical lymphadenectomy).

Intraoperative microscopy was not a routine procedure; in 18 cases of uninodeal pathology (52 out 54), in which preoperative diagnosis was unclear, lobectomy was performed followed by peroperative microscopy on macroscopically normal parenchyma. The patient was advised that a total thyroidectomy would be performed in case of macro- or microfoculal hyperplasia.

Thyroid hormones and thyreoglobulin were assayed 30 days p.o. All operated patients were submitted to whole body scintigraphy 45 days p.o. and thereafter treated by radiometabolic therapy and chronic TSH-suppressive therapy.

Our follow-up protocols included: cervical and whole body scintigraphy after 1, 3 and 5 years and thence for every 5 years; thyroid hormones and thyreoglobulin assay every three months for the first year and successively every six months; neck ultrasonography every six months for the first year and successively every year; chest X-ray every year in case of follicular cancer.

Results

Of the 54 resected neoplastic lesions, there were 30 T1 (all papillary), 15 T2 (7 papillary, 8 follicular) and 9 T4 (7 papillary, 2 follicular). Lymphadenectomy in 8 cases resulted in 5 N1 and 3 N0 (all papillary). Surgical complications after 59 operative procedures (including 5 reoperations to complete the thyroid exeresis) included: 4 impairment of inferior laryngeal nerve function (6.8%), permanent in one case (1.7%); 2 cases of hypothyroidism (3.4%), permanent in one (1.7%). Fifty-two out of 54 patients (96.2%) were regularly followed-up from 1 to 139 months. Fifty patients are currently alive and free from disease: 3 died from non-related causes.

Discussion

The optimal treatment of lymph node metastases, especially for papillary carcinoma, has not yet been defined (19-22).
the submandibular gland, the internal jugular vein and the internal accessory nerve. The modified procedure would imply reduced morbidity without any significant difference regarding local recurrence and survival (13,23,24,27). Other authors (15,18,21,28) perform lymphadenectomy only when lymph node involvement is demonstrated, relying on some studies (12,19) according to which subclinical metastases do not influence the prognosis provided surgery is followed by radiometabolic therapy. Finally, some authors (21) perform a sampling of central compartment lymph nodes, resorting to lymphadenectomy in case of positive pathological examination.

Follicular carcinoma. Lymph node involvement in follicular carcinoma is rarer than in papillary carcinoma (8-13%) (29). However it has been demonstrated that, even if a bad prognosis is mainly correlated with distant metastases, lymph node involvement indicates a more aggressive behaviour and could be correlated with a higher rate of local recurrence and reduced survival (7,8,30). Most authors suggest total thyroidectomy and regional lymphadenectomy in case of demonstrated lymph node involvement (29). Prospective studies on this topic are lacking.

Occult carcinoma. It is widely accepted that occult differentiated thyroid carcinoma does not require any further treatment of lymph nodes (7,31).

Conclusion

In conclusion, the lack of knowledge regarding the biological behaviour of the different types of differentiated cancer of the thyroid, as well as the lack of prospective randomized studies, do not allow a reliable comparison between the different therapeutic strategies found in the literature.

Two trends are evident concerning lymphadenectomy. The first one suggests routine lymphadenectomy, more or less extensively, with the aim of more radical oncologic treatment. It relies on: (a) a careful stage estimation, often not achievable preoperatively, involving however an undue overtreatment for some groups of patients; (b) the low morbidity of such a procedure, not superior to that related to simple thyroidectomy, at least with experienced surgeons, while reoperation implies higher morbidity; (c) the reduction of the amount of tissue where radioiodine may be potentially fixed, thus ameliorating the effects of radiometabolic therapy. The second trend supports lymphadenectomy only if there is clinical evidence of lymph node involvement, relying on the consideration that only clinical metastases have prognostic significance, albeit not influencing cumulative survival. It is justified by the low aggressiveness of these cancers and by the similarity in survival to patients submitted to lymphadenectomy. Moreover, radical lymphadenectomy, even if modified, implies some morbidity, consequently doubts exist about its routine use. There is no evidence about the advantages of clearing lymph nodes without clinical metastatic involvement; control of subclinical metastases may be obtained in 80% of the cases through radiometabolic therapy. The latter is strongly recommended, both in patients submitted to lymphadenectomy and in those submitted only to thyroidectomy. As well there is complete agreement about the lifelong administration of hormone-suppressive drugs to prevent any TSH-dependent proliferation.

Our protocol in follicular or papillary thyroid cancer implies total thyroidectomy, lymphadenectomy only by necessity, post-operative radiometabolic treatment and chronic TSH inhibition through L-tyrosine administration.

References