Thyroid Function After Unilateral Total Lobectomy

Risk Factors for Postoperative Hypothyroidism

Dorival De Carlucci Jr, MD; Marcos Roberto Tavares, MD; Marcos Takeo Obara, MD; Leandro Augusto Liporoni Martins, MD; Flávio Carneiro Hojaij, MD; Claudio Roberto Cernea, MD

Objective: To evaluate the incidence of postoperative hypothyroidism among patients who underwent unilateral total lobectomy and identify related factors.

Design: Retrospective medical record analysis.

Setting: Oncological center and private clinic.

Patients: From March 1996 to July 2005, 228 euthyroid patients underwent unilateral total lobectomy for benign diseases; 168 had all the information required for inclusion in this study.

Main Outcome Measures: Serum levels of thyrotropin and antithyroidal antibodies were assessed, as well as ultrasonographic evaluation of the remaining thyroid lobe and review of all histological specimens, with emphasis on lymphocytic infiltration. Hypothyroidism was defined as thyrotropin level greater than 5.5 mU/L.

Results: Most patients were female (88%), with a median (range) age of 45 (16-72) years. Hypothyroidism occurred in 61 cases (32.8%), during a median follow-up period of 29 months (range, 6-108 months). Statistically related factors included higher preoperative thyrotropin levels (2.1 mU/L among hypothyroid patients vs 1.2 mU/L in euthyroid patients; \( P < .001 \)), smaller thyroid remnant volume (3.9 mL vs 6.0 mL, respectively; \( P = .003 \)); right vs left lobectomy (\( P = .006 \)), and higher thyroperoxidase antibody serum levels (\( P = .009 \)).

Conclusions: Postoperative hypothyroidism appeared in 32.8% of the cases in this series, especially among patients with elevated preoperative thyrotropin and postoperative thyroperoxidase antibody levels, after right lobectomy and when a smaller thyroid remnant was left. After confirmation with larger prospective series, these results may support the indication for early postoperative hormone supplementation in these instances.

Thyroidectomy is often performed to exclude the possibility of malignancy. Although the use of needle biopsy as a preoperative diagnostic tool has reduced the number of operations, most solitary nodules that are removed surgically are benign on histological section analysis. The occurrence of hypothyroidism after hemithyroidectomy affects postoperative outcome and quality of life. The objectives of this study were to verify the frequency of postoperative hypothyroidism in a series of consecutive patients who underwent hemithyroidectomy and to identify potential clinical and surgical risk factors.

**METHODS**

**PATIENTS**

During the 9-year period from March 1996 to July 2005, 228 patients who underwent primary surgery for nontoxic goiter at the Brazilian Institute for Cancer Control, São Paulo, Brazil, and from the authors' private clinic have been retrospectively studied. Collected data included age, sex, preoperative and postoperative serum thyrotropin and free thyroxine levels, presence of thyroid antibodies (antithyroglobulin and antithyroperoxidase), surgical indication, final pathologic results, and length of follow-up. Forty-two patients were excluded: 18 patients were receiving thyroid hormone therapy with levotiroxine preoperatively; 10 had subclinical preoperative hypothyroidism detected by thyrotropin levels greater than 5.5 mU/L; and 14 patients did not have enough data available. A total of 186 patients included in the study; 163 (87.6%) were female, with a median (range) age of 45 (16-72) years. This study was approved by the institutional review board of the Brazilian Institute for Cancer Control.

**EXAMINATIONS**

The laboratory evaluation of the thyroid function, determined by the levels of free thyroxine, ranged from 0.7 to 1.70 ng/dL (to convert to picomoles per liter, multiply by 12.871) by radioimmunoassay; thyrotropin ranged from 0.35 to 5.5 mU/L. Thyroglobulin antibody and thyroperoxidase antibody levels were considered positive when they were higher than 35 U/mL. These tests were performed preoperatively and postoperatively, 4 to 8 weeks after surgery.

Surgical indications were laringotracheal deviation caused by large goiters and suspicion of malignancy. All patients underwent hemithyroidectomies, which comprised total resection of 1 lobe and of the isthmus. Only cases with benign disease were included in this study. The size of the remnant thyroid tissue was determined by ultrasonographic examination after surgery and was correlated with the body mass index.

Final pathologic results were divided into adenoma and adenomatous goiter. The histologic slide reports from all patients were reviewed by 3 senior pathologists (which included M.T.O. and L.A.L.M.) to evaluate the presence of associated focal or diffuse lymphocytic thyroiditis by a semiquantitative analysis, as previously described. The density of lymphocytic aggregation was semiquantitatively graded (grade 0 for the absence of aggregates of lymphocytes; grade I, 1-3 aggregates per slide; grade II, 4-8 aggregates per slide; and grade III, >8 aggregates per slide). Grade IV was reserved for Hashimoto disease. Another semiquantitative analysis was performed, considering the intensity of lymphocytic follicles, with grades of 0 for absence, 1 for minor quantity, II for moderate, and III for increased amount of lymphoid follicles.

**RESULTS**

Postoperative hypothyroidism was defined as thyrotropin levels above 5.3 mU/L at the first postoperative evaluation, 4 to 8 weeks later.

A paired t test and Pearson χ² test were used. P < .05 was considered statistically significant. Multivariate analysis was performed, with logistic regression corrected by the Hosmer-Lemeshow test, to determine the odds ratio for postoperative hypothyroidism.

The most frequent indication for thyroidectomy was suspicion of malignancy in 116 cases (62.4%). The most common pathologic diagnosis was adenomatous goiter in 81.1% of the cases. The left side of the thyroid gland was removed in 100 of 186 surgical procedures (53.8%).

The overall prevalence of postoperative hypothyroidism was 32.8% (61 of 186 cases), with a median follow-up period of 29 months (range, 6-108 months). No statistical correlation was observed between hypothyroidism and sex, age, the indication of operation, or the final pathology report.

Preoperative thyrotropin levels were statistically significantly higher in the group with postoperative hypothyroidism than in the euthyroid group. The mean thyrotropin level in the hypothyroid group was 2.1 mU/L compared with 1.2 mU/L in the euthyroid group (P < .001). When the preoperative thyrotropin levels were between 2.0 and 5.5 mU/L, 79.1% of the patients had laboratory evidence of postoperative hypothyroidism, whereas among cases with preoperative levels greater than 2.0 mU/L, only 37.2% had hypothyroidism (P < .001).

Ultrasonographic examination revealed a mean volume of 3.9 mL of the remnant thyroid tissue in the hypothyroid group compared with 5.0 mL in the euthyroid group (P = .003). In the hypothyroid group, 61.0% of the individuals had residual thyroid volume of 4.0 mL or smaller (Table).

The overall prevalence of thyroperoxidase antibodies was 15.8%. It was higher among cases with postoperative hypothyroidism compared with the euthyroid group (61.1% vs 38.8%, respectively; P = .009). The thyroglobulin antibody analysis showed no statistically significant difference.

Considering the side of the operation, 60.8% of the euthyroid patients had their left thyroid lobe surgically removed. The right lobe was removed significantly more often (61.1% vs 38.8%, respectively; P = .04).

Table. Risk Factors for Postoperative Hypothyroidism

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hypothyroid, % (n = 61)</th>
<th>Euthyroid, % (n = 125)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>91.8</td>
<td>85.6</td>
<td>.23</td>
</tr>
<tr>
<td>Suspicion of malignancy</td>
<td>55.7</td>
<td>65.6</td>
<td>.19</td>
</tr>
<tr>
<td>Thyrotropin level &gt; 2.0 mU/L, preoperatively</td>
<td>79.1</td>
<td>37.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Right lobectomy</td>
<td>60.7</td>
<td>39.2</td>
<td>.006</td>
</tr>
<tr>
<td>Remnant thyroid volume ≤ 4.0 mL</td>
<td>61.0</td>
<td>41.0</td>
<td>.04</td>
</tr>
<tr>
<td>Thyroperoxidase antibody positive</td>
<td>61.1</td>
<td>38.8</td>
<td>.009</td>
</tr>
</tbody>
</table>

REPRINTED ARCH OTOLARYNGOL HEAD NECK SURG/VOL 134 (NO. 10), OCT 2008 WWW.ARCHOTO.COM

©2008 American Medical Association. All rights reserved.
removed. Conversely, 60.7% of hypothyroid cases underwent a right lobectomy, and the difference was statistically significant (P = .006) (Table). These findings seem to be related to residual thyroid volume; in the euthyroid group this volume was larger than 4.0 mL in 71.4% of the left lobectomy cases and 4.0 mL or smaller in 58.8% of the right lobectomy cases (P = .006). This difference was not significant in the hypothyroid group (P = .57).

The semiquantitative analysis of the lymphocytic infiltration showed no statistically significant difference between the 2 groups of patients. In hypothyroid cases, grades II and III lymphoid follicles were noted in 9.8% and 11.8%, respectively, compared with 8.3% and 6.5%, respectively, in the euthyroid group (P = .23).

There was a clear association between serum positive thyroid antibodies and intensity of lymphocytic infiltration (P < .001) (Figure). The risk for postoperative hypothyroidism was 7.1 times higher when preoperative thyrotropin level was higher than 2.0 mU/L (odds ratio, 7.14; 95% confidence interval, 2.5-20.3; P < .001). The influence of the laterality of the excised thyroid lobe was confirmed when all cases with a residual volume larger than 4.0 mL were compared: right thyroid lobectomy was associated with a 7.8-fold increased risk for postoperative hypothyroidism compared with left lobectomy (odds ratio, 7.8; 95% confidence interval, 2.0-30.4; P = .003).

In conclusion, the incidence of postoperative hypothyroidism after hemithyroidectomy is not negligible and should not be overlooked. Roughly one-third of hemithyroidectomy patients may have this consequence and might need thyroxine oral supplementation. This study suggests that the following factors are associated with an increased risk: elevated preoperative thyrotropin levels, elevated levels of thyroperoxidase antibodies, operations involving the right thyroid lobe, and residual thyroid tissue volume 4.0 mL or smaller. In these instances, a closer follow-up or even an earlier onset of oral thyroxine administration is advised. The role of lymphocytic infiltration was not clear.

Submitted for Publication: April 26, 2007; final revision received November 26, 2007; accepted December 11, 2007.

Correspondence: Dorival De Carlucci Jr, MD, Rua Padre João Manuel, 450 Room 18, Cerqueira Cesar, São Paulo 01411-001, Brazil (decarlucci@uol.com.br).

Author Contributions: Dr De Carlucci had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analy-

Hemithyroidectomy is considered an adequate treatment for benign nodules operated on because of suspected malignancy. In fact, this is presently the main indication for thyroid surgery. In the present series, the prevalence of postoperative hypothyroidism was 32.8%, which is comparable with most international series. There was a significant correlation with preoperative thyrotropin levels. It is noteworthy that, even within the normal laboratory range, there was a direct relationship between the occurrence of postoperative hypothyroidism and thyrotropin level greater than 2.0 mU/L, with a 7.1 times higher risk. This observation was confirmed by other authors and might be associated with decreased functional reserve of the thyroid gland. According to Miller et al, a preoperative thyrotropin level in the upper-normal reference range should alert the surgeon to the possibility of postoperative hypothyroidism.

Previous series including only toxic goiters pointed out the influence of the amount of remnant thyroid tissue on postoperative thyroid function. Small volume was related with hypothyroidism, but also with no risk of recurrent thyrotoxicosis. Similarly, in nontoxic goiter, the volume of the residual thyroid tissue seems to be relevant. In Brazil, there are some areas of iodine deficiency and, consequently, large multinodular goiters are common. In fact, 37.6% of the operations in the present series were indicated by compressive symptoms caused by large goiters. This finding may explain the importance of the volume of the residual thyroid tissue in this series: postoperative hypothyroidism was 6.3 times more prevalent when the volume of this remnant, evaluated by ultrasound examination, was 4.0 mL or smaller (odds ratio, 6.3; 95% confidence interval, 1.6-24.5; P = .008).

Hyperthyroidism is also related to postoperative hypothyroidism. The lymphocytic infiltrate of the thyroid gland decreases thyroid function, and a semiquantitative analysis of this infiltrate usually reflects the risk of hypothyroidism. Nevertheless, no such statistical correlation was found in the present series. The presence of thyroid antibodies has been associated with thyroiditis. In this series, the majority of patients who developed postoperative hypothyroidism presented with thyroperoxidase antibodies. Interestingly, a direct relationship between elevated thyroid antibodies and higher degrees of lymphocytic infiltration was noted.

Curiously, in the present series, hypothyroidism was statistically significantly related to the side of the surgery. More patients who had right hemithyroidectomy became hypothyroid. To our knowledge, this observation has not been previously reported, and it is somewhat difficult to understand. One possible explanation could be the difference in size of the thyroid lobes, suggested by the large series of thyroid ultrasound examinations.

In conclusion, the incidence of postoperative hypothyroidism after hemithyroidectomy is not negligible and should not be overlooked. Roughly one-third of hemithyroidectomy patients may have this consequence and might need thyroxine oral supplementation. This study suggests that the following factors are associated with an increased risk: elevated preoperative thyrotropin levels, elevated levels of thyroperoxidase antibodies, operations involving the right thyroid lobe, and residual thyroid tissue volume 4.0 mL or smaller. In these instances, a closer follow-up or even an earlier onset of oral thyroxine administration is advised. The role of lymphocytic infiltration was not clear.
sis. Study concept and design: De Carlucci and Tavares. Acquisition of data: De Carlucci, Obara, and Hojaij. Analysis and interpretation of data: De Carlucci, Tavares, Martins, Hojaij, and Cernea. Drafting of the manuscript: De Carlucci, Obara, Martins, and Cernea. Critical revision of the manuscript for important intellectual content: De Carlucci, Tavares, Hojaij, and Cernea. Administrative, technical, and material support: De Carlucci, Tavares, Hojaij, and Cernea. Statistical analysis: De Carlucci and Hojaij. Obtained funding: De Carlucci. Administrative, technical, and material support: De Carlucci, Obara, Martins, and Cernea. Study supervision: De Carlucci, Tavares, and Cernea.

Financial Disclosure: None reported.

Previous Presentation: This study was presented at the 2007 American Head & Neck Society Annual Meeting; April 28, 2007; San Diego, California.

REFERENCES