Risk Factors for the Development of Hypothyroidism After Hemithyroidectomy

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Objectives: To assess the incidence of hypothyroidism after hemithyroidectomy and to identify risk factors for the development of hypothyroidism.

Design: Retrospective analysis.

Setting: A tertiary care academic medical center.

Patients: The study included 90 patients who underwent a hemithyroidectomy from 1999 to 2004.

Main Outcome Measures: Hypothyroidism was defined as a serum thyrotropin level greater than 6.0 mIU/L at least 8 weeks after hemithyroidectomy. All patients were analyzed for age, sex, surgical indications, preoperative and postoperative thyrotropin levels, weight of resected specimen, final pathologic analysis, and length of follow-up. Multivariate analysis was performed to identify multiple risk factors for the development of hypothyroidism.

Results: The final pathologic analysis demonstrated 49 follicular adenomas, 17 cases of Hashimoto thyroiditis, 10 multinodular goiters, and 14 other abnormalities. The overall incidence of the development of hypothyroidism after hemithyroidectomy was 27% (24 of 90 patients). When the groups were broken down by pathologic diagnosis, the incidence of hypothyroidism developing during follow-up among the Hashimoto thyroiditis and multinodular goiter groups was 59% and 50%, respectively. Also, the patients who developed hypothyroidism were noted to have statistically significant higher preoperative serum thyrotropin levels (3.15 mIU/L vs 1.95 mIU/L; P < .001) than those who remained euthyroid. There was no relationship between age, sex, or weight of the resected tissue and the subsequent risk of hypothyroidism.

Conclusions: The overall incidence of posthemithyroidectomy hypothyroidism was 27%, and the majority of cases developed in the first 6 to 12 months after surgery. Risk factors for the development of hypothyroidism include pathologic diagnosis (Hashimoto thyroiditis and multinodular goiter) as well as a high-normal serum thyrotropin level. Routine monitoring of serum thyrotropin levels should be performed in all patients who undergo a hemithyroidectomy.

Arch Otolaryngol Head Neck Surg. 2006;132:36-38

The incidence and risk factors for the development of hypothyroidism after hemithyroidectomy remain unclear. Several studies have demonstrated an incidence of postthyroidectomy hypothyroidism ranging from 5.0% to 41.9% among patients who undergo partial thyroid surgery.1-11 Previously, it was a common practice to prescribe suppressive doses of levothyroxine sodium after hemithyroidectomy. The assumption was that the suppression of the hypothalamic-pituitary axis would reduce the risk of abnormalities developing in the contralateral thyroid remnant. More recently, the routine use of levothyroxine after hemithyroidectomy has fallen out of favor owing to questions regarding the efficacy of thyroid suppression for preventing the development of nodules in the remaining contralateral thyroid lobe. In addition to the concerns regarding the efficacy of thyroid suppression, levothyroxine therapy has been associated with significant adverse effects, including atrial fibrillation and bone calcium loss (particularly in postmenopausal women). Therefore, our objectives were to assess the incidence of posthemithyroidectomy hypothyroidism and to identify risk factors for the development of hypothyroidism.

METHODS

We performed a retrospective analysis of all cases involving patients who underwent a hemithyroidectomy under the care of 2 surgeons (F.R.M. and R.A.O.) from 1999 to 2004. Institutional review board approval was obtained for the project. A hemithyroidectomy was defined as a total hemi thyroidectomy and isthmusectomy with preservation of the contralateral thyroid lobe. To be eli-
gible for analysis, the patients had to meet the following criteria: (1) hemithyroidectomy under the supervision of the 2 attending surgeons; (2) euthyroid preoperative status as reflected in normal thyrotropin levels before surgery; (3) no previous radiation therapy to the cervical region; (4) no empirical use of thyroid hormone therapy after surgery; (5) age older than 18 years; and (6) assessment of thyroid function with a serum thyrotropin test at least 8 to 10 weeks after surgery. Serum thyrotropin levels were subsequently assessed every 3 to 4 months. The reference range for normal serum thyrotropin levels in our study was 0.4 to 6.0 mIU/L. Thyrotropin values higher than 6.0 mIU/L resulted in a diagnosis of hypothyroidism, and in most cases, the patients involved were started on a regimen of thyroid hormone therapy.

A serum thyrotropin level greater than 6.0 mIU/L was selected to include the patients who would be clearly hypothyroid based on serologic test results and clinical symptoms. Also, an elevated thyrotropin level (>4.5 mIU/L) can indicate the early development of subclinical hypothyroidism and warrants careful follow-up.

All patients who met the above eligibility criteria for entrance into the study were assessed for age, sex, surgical indications, preoperative and postoperative serum thyrotropin levels, weight (in grams) of resected thyroid tissue, final findings of histologic analysis of the hemithyroidectomy specimen, and length of follow-up. Kaplan-Meier survival analysis was used to compare the diagnosis and survival times by sex until the thyrotropin level was greater than 6.0 mIU/L. Cox proportional hazards survival analysis was performed to assess age, sex, pathologic diagnosis, and preoperative thyrotropin levels on the time to failure (hypothyroidism or thyrotropin level >6.0 mIU/L). Groups were compared using an analysis of variance and percentage in each sex with χ² contingency table analysis.

### RESULTS

Ninety patients (73 women and 17 men; mean age, 45 years) met the eligibility criteria for entrance into the study. Thirty-seven patients were not eligible for analysis: 18 who underwent hemithyroidectomy with laryngectomy and postoperative radiation therapy, 8 who were hypothyroid or hyperthyroid before surgery, 5 who had inadequate follow-up data, and 6 who began empirical suppressive levothyroxine therapy 6 weeks after surgery. The final pathologic analysis of the 90 eligible cases revealed 49 follicular adenomas (54%), 17 cases of Hashimoto thyroiditis (19%), 10 multinodular goiters (11%), and 14 other pathologic diagnoses (16%). The “other pathologic diagnoses” category included 4 cases of papillary thyroid cancer (all <1 cm), 2 colloid cysts of the thyroid, 2 benign follicular cell neoplasms (benign), 2 intrathyroidal parathyroid adenomas, 2 cases of subacute thyroiditis, 1 case of mycobacteria of the thyroid, and 1 sarcoid of the thyroid.

<table>
<thead>
<tr>
<th>Final Pathologic Analysis</th>
<th>No. (%) of Patients With Hypothyroidism*</th>
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</thead>
<tbody>
<tr>
<td>Follicular adenoma (n = 49)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Hashimoto thyroiditis (n = 17)</td>
<td>10 (59)</td>
</tr>
<tr>
<td>Multinodular goiter (n = 10)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Other pathologic diagnoses (n = 14)</td>
<td>2 (14)</td>
</tr>
</tbody>
</table>

*Postoperative hypothyroidism was defined as a serum thyrotropin level greater than 6.0 mIU/L at least 6 weeks after surgery.

The overall incidence of the development of posthemithyroidectomy hypothyroidism was 27% (24 of 90 patients).

There were no significant differences in sex in terms of the risk for the development of postoperative hypothyroidism (22 [30%] of 73 women and 2 [12%] of 17 men) (Wilcoxon test, *P* = .12; χ² = 2.4, *P* = .12). The preoperative thyrotropin level was significantly different among the patients who developed posthemithyroidectomy hypothyroidism compared with those who remained euthyroid during the postoperative period. The mean preoperative thyrotropin level was significantly higher in the patients who developed hypothyroidism (*n* = 24) than in the patients who remained euthyroid (*n* = 66) (mean ± SD, 3.15 mIU/L ± 1.14 vs 1.95 mIU/L ± 0.92; *P* < .001). When the groups were broken down based on pathologic category, the preoperative thyrotropin levels were significantly different among the patients with Hashimoto thyroiditis (3.3 mIU/L), follicular adenoma (2.0 mIU/L), multinodular goiter (1.9 mIU/L), and other pathologic diagnoses (2.1 mIU/L) (*P* < .001). The Cox proportional hazards survival analysis demonstrated a significant relationship of preoperative thyrotropin levels (*P* < .001) and age (*P* < .03) in the time to develop hypothyroidism. An increased preoperative thyrotropin level increased the hazard rate (3.06). The mean ± SD follow-up period for the study group was 12.4 ± 3.2 months (range, 3-24 months). As a group, the mean time to failure (thyrotropin, >6.0 mIU/L) was 6.6 months; more than 75% of the cases of hypothyroidism developed within the first 9 months. In patients with more than 12 months of follow-up, there were no cases of late hypothyroidism.

### COMMENT

Over the last 4 decades, a number of studies have attempted to define the incidence of hypothyroidism after hemithyroidectomy. The traditional approach had been to routinely place patients on a regimen of suppressive doses of levothyroxine after partial thyroid surgery, with the logic that this treatment would prevent the development of abnormalities in the contralateral thyroid lobe. Griffiths et al reported an 11% incidence of hypothyroidism in thyrotoxic patients undergoing hemithyroidectomy and an incidence of 6.5% in nonthyrotoxic patients. McHenry and Slusarczyk demonstrated an incidence of posthemithyroidectomy hypothyroidism of 35%. They also demonstrated that an elevated preoperative thyrotropin level was an independent risk factor for the development of hypothyroidism.

Our data are in agreement with previous reports in the literature, with a posthemithyroidectomy hypothyroidism incidence of 27% among the patients in our series. When broken down by pathologic diagnosis, the subset of patients with the highest risk for the development of hypothyroidism were those with Hashimoto thyroiditis (59%) and those with multinodular goiter (30%). This is similar to the 49.3% incidence of hypothyroidism reported by Sugino et al in a series of patients who underwent hemithyroidectomy for Graves disease. It is clear from our data that patients with ongoing thyroiditis or multinodular thyroid disease are at an increased risk of developing hypothyroidism. In addition to the...
pathologic findings, an elevated preoperative thyrotropin level was associated with an increased risk for the postoperative development of hypothyroidism. This association may reflect the abnormal function of the entire thyroid gland and/or the presence of ongoing autoimmune thyroiditis. McHenry and Slusarczyk reported similar findings, with an elevated preoperative thyrotropin level found to be significantly related to the risk of postoperative hypothyroidism. A preoperative thyrotropin level in the upper-normal reference range (>3.0-3.5 mIU/L) should alert the surgeon to the elevated risk of hypothyroidism developing in the patient in the postoperative period. An elevated thyrotropin level will develop in the vast majority of patients who become hypothyroid (>75%) within the first 6 to 9 months after they undergo hemithyroidectomy. One limitation of this retrospective study is the inability to accurately define a time frame for the development of late hypothyroidism owing to the variability in obtaining the results of postoperative thyroid function studies. While the majority of the hypothyroidism developed in our patients in the first 6 to 9 months, it certainly is possible that a portion of the population will develop late hypothyroidism in the ensuing years. In our practice, many of these patients continue long-term follow-up with their primary care physician or endocrinologist; therefore, we may not have accurate data on late hypothyroidism beyond the first 24 months. Also, while we had no late failures (>12 months after surgery), we believe that this patient population requires ongoing assessment of thyroid function, because it seems logical that some percentage of the patients may develop hypothyroidism over the ensuing years.

From a practical standpoint, our study, along with our review of the literature, suggests that all patients who undergo hemithyroidectomy should be counseled regarding the potential need for lifelong thyroid hormone therapy. The overall incidence of hypothyroidism is in the range of 20% to 45%. Patients with Hashimoto thyroiditis, multinodular goiter, and an elevated preoperative thyrotropin level are at particular risk. Our current recommendation is to obtain a postoperative thyrotropin measurement 8 to 12 weeks after surgery, followed by the measurement of thyrotropin levels at 6 months and 12 months after surgery. If the thyrotropin level is normal at 12 months, we recommend biannual determination of thyrotropin levels unless symptoms of hypothyroidism manifest.

Submitted for Publication: July 14, 2005; final revision received August 25, 2005; accepted September 1, 2005. Correspondence: Frank R. Miller, MD, Department of Otolaryngology–Head and Neck Surgery, University of Texas Health Science Center at San Antonio, Mail Code 777, 7703 Floyd Curl Dr, San Antonio, TX 78229-3900 (millerfr@uthscsa.edu).

Financial Disclosure: None.

Previous Presentation: This study was presented as a poster at the American Head and Neck Society Annual Meeting; May 15-16, 2005; Boca Raton, Fla.

REFERENCES