

Hypothyroidism After Hemithyroidectomy: Incidence, Risk Factors, Natural History and Management

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1. Introduction

Thyroid lobectomy or hemithyroidectomy is considered an adequate treatment for several thyroid diseases such as large benign nodules, follicular neoplasm, and some suspected malignancies. Thyroid lobectomy theoretically preserves sufficient functioning native thyroid tissue for patients to keep euthyroid status postoperatively without the need for thyroid hormone replacement. Still, it is known that some patients who have undergone hemithyroidectomy will require thyroid hormone replacement because they have developed hypothyroidism, which is commonly diagnosed as a result of elevated levels of thyroid-stimulating hormone (TSH). Currently, the incidence and risk of hypothyroidism in patients undergoing partial thyroidectomy remains unclear. Several studies about thyroid function after hemithyroidectomy for benign thyroid disease have been published. The reported incidence of hypothyroidism ranges from 5% to 49%, with most between 15-30%. The incidence rates vary widely depending on the follow-up period and on how hypothyroidism is defined by authors. These variations have led to our interest in defining uniform criteria for diagnosis and treatment of postoperative hypothyroidism, thereby identifying patients at the greatest risk of requiring long-term thyroid hormone replacement.

Hypothyroidism after hemithyroidectomy remains an unpredictable complication. Several results have pointed to the degree of lymphocytic infiltration within the thyroid gland and the amount of thyroid remnant as possible predictors of hypothyroidism. Other reports about risk factors for hypothyroidism have indicated links to the preoperative TSH level, anti-TPO antibodies, multinodular goiter, and preoperative thyrotoxicosis. However, definite risk factors for development of hypothyroidism after hemithyroidectomy have yet to be completely characterized.

Patients with symptomatic hypothyroidism such as weight gain, fatigue, generalized edema, muscle pain and lethargy warrant treatment, as do patients with mild disease and medical comorbidities. Of late, some authors have advocated thyroxine replacement for all patients undergoing hemithyroidectomy to prevent progression of multi-nodular changes in the contralateral lobe, but others have asserted that it should not be necessary to prescribe thyroxine replacement for all patients. Patients who develop chronic hypothyroidism after

hemithyroidectomy may require life-long thyroxine replacement, as well as routine laboratory tests. The side effects of long-term thyroid hormone replacement have included arrhythmias, osteopenia, changes of lipid metabolism, and mood changes. Early diagnosis of the subclinical state, followed by treatment of symptomatic hypothyroidism should be priorities.

The risk of postoperative hypothyroidism after thyroid lobectomy is not negligible and should not be overlooked. Careful monitoring for patients who may develop hypothyroidism will improve patient care. At present, there is no universal algorithm for monitoring postoperative residual thyroid function in patients who have undergone hemithyroidectomy. In most patients, the follow-up is dependent on the discretion of the physician in charge based on clinical suspicion or the development of definite symptoms. From a practical viewpoint, only select patients at risk of developing hypothyroidism after partial thyroidectomy have been followed on a regular schedule.

In this chapter, we evaluate the incidence, natural history, and risk factors for hypothyroidism in patients undergoing thyroid lobectomy, and we review postoperative thyroid hormone replacement. We also aim to clarify a uniform monitoring and follow-up protocol for patients after hemithyroidectomy.

2. Hypothyroidism after hemithyroidectomy

2.1 Definition of hypothyroidism

Thyroid hormones are essential regulators of metabolism and transport, and thyroid hormone deficiencies of any cause result in hypothyroidism. Hypothyroidism may be primary, i.e., resulting from a defect in the thyroid gland itself, or secondary, i.e., resulting from a TSH deficiency related to pituitary or hypothalamic disease. Although there is no universally accepted definition of normal thyroid function, thyroid function assays have indicated that a TSH concentration of 4.5 uIU/L is the upper limit of normal (Surks et al., 2004; Hollowell et al., 2002).

Thyroid hormone deficiency affects nearly all organs and functions in the human body (Laurberg et al., 2005). The changes induced by hypothyroidism include the slowing and lowering of processes, which may mimic the alterations associated with aging. Symptoms and signs of hypothyroidism differ according to the severity and duration of the thyroid deficiency, the age of the patient, and the occurrence of other systemic diseases. Early symptoms of hypothyroidism are often nonspecific and insidious in onset and can include fatigue, lethargy, constipation, cold intolerance, muscle stiffness and cramping, carpal tunnel syndrome, decreased libido, depression, hair loss, menstrual irregularity, menorrhagia, and infertility. With little functional thyroid reserve, the severity of hypothyroidism can progress to a clinical picture of myxedema. At this stage, patients appear bored, depressed, and hypokinetic, with a hoarse voice, dull, expressionless faces, sparse hair, and a large tongue. The skin is cool to the touch, dry, and rough, with facial and periorbital puffiness and often generalized edema. Fluid may collect in various parts of the body, and pleural effusion, pericardial effusion, and ascites are common. On physical examination or chest X-ray, the cardiac silhouette may appear enlarged, due to chamber dilatation or pericardial effusion. Constipation is common, due to slowed gastrointestinal motility, and a dynamic ileus may cause megacolon or intestinal obstruction. A psychiatric

syndrome (“myxedema madness”) has been described, and neurologic findings include a delayed or hung-up relaxation phase of deep tendon reflexes, muscle weakness, and ataxia (Wartofsky et al., 2006).

Hypothyroidism can be classified as subclinical or overt (clinical), with the latter defined as abnormal serum TSH and free T4 concentrations, or as the development of hypothyroidism symptoms. Subclinical hypothyroidism is a mild degree of biochemical abnormality, characterized by increased serum TSH and T4 estimates within the laboratory reference range (Wartofsky et al., 2006). Although the cause and clinical abnormalities observed in individuals with subclinical hypothyroidism do not differ from those with overt hypothyroidism, including high TSH and low T4 concentrations, the former is milder. Either form of hypothyroidism, however, is a potential consequence of hemithyroidectomy and has a substantial impact on postoperative patient outcomes and quality of life. Hypothyroidism occurring soon after thyroid surgery or radioiodine therapy may normalize spontaneously after some months. In these patients, partial substitution therapy or control for some months before therapy is appropriate. This chapter focuses only on overt or subclinical hypothyroidism following hemithyroidectomy.

2.2 Incidence

Hemithyroidectomy, defined as the complete removal of the unilateral lobe, isthmus and where present, the pyramidal lobe of the thyroid, is a relatively common procedure for a variety of thyroid pathologies. Hemithyroidectomy is commonly indicated for patients with large benign tumors causing compressive symptoms or cosmetic concerns, as well as for toxic nodules. It is also indicated for patients with follicular lesions classified as “indeterminate” thyroid nodules to exclude thyroid carcinoma, as long as these nodules do not show any clinical features of malignancy other than in fine needle aspiration cytology (FNAC) results. Thyroid lobectomy is performed in patients with indeterminate nodules because 20-30% of nodules harbor thyroid malignancy. Hemithyroidectomy and central compartment lymph node dissection (CCND) are also usually performed on patients in Korea and Japan with papillary thyroid microcarcinoma (PTMC) (Tomoda et al., 2011). The worldwide incidence of PTMC has increased significantly, probably due to more frequent use of thyroid ultrasonography (US) as an essential part of initial health examinations. Although total thyroidectomy is the most common standard operation for thyroid cancers, hemithyroidectomy rather than total thyroidectomy may be preferred for low risk patients with PTMC to eliminate the risks of permanent hypocalcemia and bilateral recurrent and superior laryngeal nerve palsy associated with total thyroidectomy. In addition, hemithyroidectomy theoretically leaves sufficient functioning native thyroid tissue for the patient to remain euthyroid without the need for thyroid hormone replacement.

Several studies have evaluated thyroid function after hemithyroidectomy for benign thyroid disease. The reported incidence of hypothyroidism after hemithyroidectomy has been found to vary from 5.0% to 49%, with most studies reporting a range of 15-30% (Wormald et al., 2008; Chu et al., 2011; Su et al, 2009; Spanheimer et al, 2011). This disparity in results is partially due to differences in their definition of hypothyroidism and to differences in length of follow-up. Hypothyroidism, both clinical and subclinical, is a potential consequence of hemithyroidectomy and has been associated with a number of adverse clinical outcomes. However, hypothyroidism after hemithyroidectomy is an under-reported or under-

recognized complication, with patients most often monitored only for a short time postoperatively. Table 1 summarizes the incidence of hypothyroidism after hemithyroidectomy.

Author (year)	Patients (n)	Time for TSH measurement to determine postoperative hypothyroidism	Definition of postoperative hypothyroidism	Incidence (overt or subclinical) (%)
McHenry, et al. (2000)	71	At least 5 weeks after operation	Serum TSH>3.59 μ IU/L	Total: 25/71 (35%) (Overt: 9/71 (12.7%) Subclinical: 16/71 (22.5%))
Miller, et al. (2006)	90	At least 8-10 weeks after surgery	Serum TSH>6.0mIU/L	Total: 24/90 (27%)
Seiberling, et al. (2007)	58	At least 6 weeks after surgery	Serum TSH>4.0 μ IU/ml	Total: 14/58 (24.1%)
Koh, et al. (2008)	136	1,2, & 6 months after surgery	Serum TSH>4.0 μ IU/ml	Total: 58/136 (42.6%) (Overt: 11/136 (8.1%) Subclinical: 47/136 (34.6%))
Wormald, et al. (2008)	82	3,6,& 12 months after surgery	Serum TSH>4.5 μ IU/L	Total: 15/82 (18.3%) Overt: 5/82 (6.1%) Subclinical: 10/82(12.2%)
Moon, et al. (2008)	101	2 months, and every 2-3 months (more than 1 year) after surgery	Serum TSH>4.7 μ IU/L	Total: 37/101 (36.6%)
De Carlucci Jr, et al. (2008)	168	4 to 8 weeks after surgery	Serum TSH>5.5mIU/L	Total: 61/186 (32.8%)
Su, et al. (2009)	294	At least 3 months after surgery	Serum TSH>4.0mIU/L	Total: 32/294 (10.9%)
Stoll, et al. (2009)	547	6 to 8 weeks after surgery	Serum TSH>4.82 μ IU/mL	Total: 78/547 (14.3%)
Spanheimer, et al. (2011)	71	6 weeks after surgery	Serum TSH>4.20 μ IU/mL	Total: 24/71 (33.8%)
Tomoda, et al. (2011)	233	At least 4-6 weeks, and 3 months after surgery	Serum TSH>5.0mIU/l	Total: 57/233 (24.4%)
Johner, et al. (2011)	117	6 weeks(or 3 months), 6 months & 12 months after surgery	Serum TSH>5.5 μ IU/L	Total: 21.6% (Permanent: 7.8%)
Chu, et al. (2011)	263	2 weeks, 3 months, 6 months, and yearly after surgery	Serum TSH>5.5mIU/L	Total: 38/263 (14.4%)

Table 1. Incidence of posthemithyroidectomy hypothyroidism

Recently, however, Johner et al (2011) reported that the overall incidence of early postoperative hypothyroidism was 21.6%, with the incidence of permanent hypothyroidism only 7.8%. In addition to showing that the incidence of hypothyroidism following hemithyroidectomy is low, this study showed that a significant proportion of individuals who become biochemically hypothyroid (asymptomatic) demonstrate only a transient elevation in their TSH levels. The low incidence of sustained hypothyroidism supports the adoption of a watch-and-wait approach in patients with biochemical hypothyroidism after hemithyroidectomy. Previously, it was common practice to prescribe suppressive doses of thyroxine after hemithyroidectomy, but it is now thought that the remaining thyroid lobe may compensate. Since the pituitary-thyroid axis must adapt after hemithyroidectomy, serial TSH measurements after surgery will identify only those individuals who remain biochemically hypothyroid or become symptomatic and therefore require treatment with thyroid hormone. This will spare a significant number of patients the need for, and potential risks of, long-term thyroid hormone replacement therapy.

2.3 Natural history

TSH is important for pathologic thyroid growth, and elevated serum TSH may contribute to the development of recurrent nodular or diffuse thyroid enlargement. The efficacy of administering TSH-suppressive doses of thyroxine to prevent thyroid nodule recurrence after surgery has not been determined. Most studies that reported a beneficial effect of suppressive therapy in reducing recurrent nodular thyroid disease after thyroidectomy have been from areas of iodine deficiency, whereas most studies that found no benefit of suppressive therapy have been from iodine-sufficient areas (McHenry & Slusarczyk, 2000).

Hypothyroidism is now one of the most common morbidities observed after hemithyroidectomy. Most patients will continue to have normal thyroid function after hemithyroidectomy, although some will have mildly elevated TSH during the perioperative period that may normalize without pharmacologic intervention due to compensation by the remaining thyroid lobe. This may be characterized by both an increase in serum TSH concentration and an augmented release of TSH in response to TRH signaling (Lombardi et al, 1983) (Campion et al., 1995), adaptive mechanisms that may persist for 12-18 months after surgery. Animal experiments have shown that serum TSH concentration declines initially, subsequently returning to normal with compensatory hypertrophy of the remaining thyroid lobe followed by a significant elevation in serum TSH for as long as 5 months after surgery (Clark et al., 1976). Compensatory hypertrophy of the remaining thyroid lobe has been observed histologically following hemithyroidectomy (Marine et al., 1926).

Some patients with symptomatic hypothyroidism require treatment, as do patients with mild hypothyroidism and medical comorbidities. The physiological and clinical signs of hypothyroidism are generally completely reversed by appropriate thyroid hormone replacement treatment. Some physicians therefore advocate thyroxine replacement to prevent progression of multinodular changes in the contralateral lobe, whereas others prescribe thyroxine replacement for all patients after hemithyroidectomy. The possibility of compensatory hypertrophy of the residual lobe should be balanced by the need for close follow-up of patients with borderline thyroid reserves, and the potential for deterioration at times of physiological stress and progression of underlying thyroiditis. Routine thyroxine

replacement may be recommended, rather than close follow-up monitoring, for some post-hemithyroidectomy patients with risk factors, such as elevated thyroid antibody concentrations or histologic evidence of autoimmune thyroiditis (Su et al., 2009). In contrast, other researchers have reported that elevated serum TSH concentration alone may not justify the initiation of thyroid hormone replacement, since nearly 70% of individuals who developed biochemical (asymptomatic) hypothyroidism during the early postoperative period after hemithyroidectomy recovered normal thyroid function without pharmacologic intervention (Johner et al., 2011). Therefore, determination of the true indication is important prior to initiating thyroid hormone replacement therapy.

A small number of patients who develop hypothyroidism after thyroid lobectomy require life-long thyroid hormone replacement, as well as routine laboratory examinations and medical adjustments. Furthermore, chronic thyroxine therapy may be associated with adverse effects, including arrhythmias (atrial fibrillation) or loss of calcium from the bones resulting in osteopenia or osteoporosis. High serum cholesterol concentrations may result in cardiac sclerosis with all its complications, suggesting that hormone replacement therapy be delayed. Thus, an increased ability to recognize which patients are most at risk for developing hypothyroidism will improve patient care. Although closer monitoring or earlier initiation of thyroid hormone replacement therapy may be advisable for these high-risk patients, no specific TSH concentration alone is indicative of increased risk of permanent or overt hypothyroidism, suggesting that transient biochemical hypothyroidism be closely monitored rather than routinely treated. Accurate detection and diagnosis of sustained hypothyroidism after thyroid surgery is also important to avoid its associated morbidity and mortality (Johner et al., 2011).

2.4 Risk factors

Among the factors found to predict hypothyroidism after hemithyroidectomy are patient age, sex, preoperative TSH concentration, the presence of anti-thyroid antibodies, autoimmune thyroiditis in the excised lobe, and volume of remnant thyroid bed. Although these factors are also important in determining treatment plans for patients with thyroid disease, the correlation between risk factors and onset of hypothyroidism remains unclear. Table 2 shows a summary of risk factors that predict hypothyroidism after hemithyroidectomy.

Author (year)	Incidence of posthemithyroidectomy hypothyroidism	Risk factors (Postoperative hypothyroidism vs. Euthyroid state)
McHenry, et al. (2000)	35%	Higher preoperative serum TSH level ($\mu\text{IU/L}$) (1.94 ± 1.00 vs. 1.10 ± 0.74)
Miller, et al. (2006)	27%	Hashimoto's thyroiditis, multinodular goiter, higher preoperative serum TSH level (mIU/L) (3.15 ± 1.14 vs. 1.95 ± 0.92)
Seiberling, et al. (2007)	24.1%	Higher preoperative serum TSH level ($\mu\text{IU/ml}$) (2.39 vs. 1.07), chronic inflammation (lymphocytic thyroiditis or Hashimoto's thyroiditis) (50.0% vs. 6.8%)

Author (year)	Incidence of posthemithyroidectomy hypothyroidism	Risk factors (Postoperative hypothyroidism vs. Euthyroid state)
Koh, et al. (2008)	42.6%	Higher preoperative serum TSH level ($\mu\text{U/ml}$) (2.15 ± 1.30 vs. 1.29 ± 0.9), preoperative microsomal Ab, thyroglobulin Ab, higher grade of lymphocytic infiltration of resected thyroid gland
Wormald, et al. (2008)	18.3%	Higher preoperative serum TSH level ($\mu\text{IU/L}$) (>1.6 vs. <1.6), higher grade of lymphocytic infiltration of resected thyroid gland
Moon, et al. (2008)	36.6%	Higher preoperative serum TSH level ($\mu\text{IU/L}$) (2.46 ± 1.16 vs. 1.22 ± 0.89), BSA-adjusted remnant thyroid volume (2.73 ± 1.34 vs. 3.48 ± 1.50)
De Carlucci Jr, et al. (2008)	32.8%	Higher preoperative serum TSH level (mU/L) (2.1 vs. 1.2), smaller remnant thyroid volume (mL) (3.9 vs. 6.0), right vs. left lobectomy, higher thyroperoxidase antibody serum levels
Su, et al. (2009)	10.9%	High-normal preoperative serum TSH level; TSH $2.5\text{--}4.0\text{mIU/L}$ (%) (18.8 vs. 3.8), thyroiditis in histology (%) (46.8 vs. 11.8), elevated thyroid antibodies levels (%) (47.8 vs. 11.5)
Stoll, et al. (2009)	14.3%	Higher preoperative serum TSH level ($\mu\text{IU/ml}$) (2.12 vs. 1.35), lower mean free T4 (ng/dL) (1.03 vs. 1.34), Hashimoto's thyroiditis
Spanheimer, et al. (2011)	33.8%	Thyroiditis on surgical pathology
Tomoda, et al. (2011)	24.4%	Higher preoperative serum TSH level (mIU/l) (2.73 ± 1.36 vs. 1.24 ± 0.82), older age (years) (56.2 ± 13 vs. 48.97 ± 15)
Johner, et al. (2011)	21.6%	Higher preoperative serum TSH level, high degree of lymphocytic infiltration, high degree of germinal center formation
Chu, et al. (2011)	14.4%	Older age, higher preoperative serum TSH level, longer follow-up period, more frequent thyroiditis on histology, lighter resected tissue weight, positive antimicrosomal antibodies. * By multivariate analysis, only resected tissue weight, and concomitant thyroiditis on histology turned out to be independent predicting factors.

Table 2. Risk factors for predicting posthemithyroidectomy hypothyroidism

Some known risk factors can be determined only after surgery, such as lymphocytic infiltration, associated thyroiditis, and the weight of the resected gland, whereas others, such as preoperative TSH concentration, age, and presence of thyroid autoantibody, are known preoperatively. In addition, the remnant thyroid volume may be easily measured from preoperative US. Because most patients scheduled for hemithyroidectomy due to thyroid nodules are evaluated by thyroid US, the remnant thyroid volume could be easily determined, allowing the surgeon to decide whether to perform a diagnostic hemithyroidectomy.

2.4.1 Elevated preoperative TSH concentration

Preoperative TSH concentration is significantly associated with postoperative hypothyroidism. In addition, studies using a TSH cutoff value, such as >1.6 or >2.0 uIU/mL, have found that patients with elevated TSH are 7-10 times more likely to develop hypothyroidism after surgery. Thus, “normally elevated” preoperative TSH >1.5 uIU/mL, especially when combined with lower preoperative T4 concentrations or specific antibodies, may indicate a potentially increased risk of hypothyroidism after hemithyroidectomy, allowing appropriate preoperative counseling of patients (Table 2).

2.4.2 Degree of chronic inflammation and autoimmune disease

2.4.2.1 Hashimoto’s thyroiditis and presence of autoantibodies

Thyroiditis is also associated with postoperative hypothyroidism. Hashimoto’s thyroiditis is an inflammatory disease that is the most common cause of hypothyroidism. Moreover, Hashimoto’s thyroiditis has been found to significantly increase the need for thyroid hormone supplementation following hemithyroidectomy. Patients diagnosed with Hashimoto’s thyroiditis were found to be almost four times more likely to develop hypothyroidism after hemithyroidectomy (Stoll et al., 2009). Hashimoto’s thyroiditis is also characterized by intense lymphocytic infiltration of the thyroid and the presence of thyroid autoantibodies. Moreover, several types of autoimmune thyroiditis are closely associated with circulating thyroid autoantibodies such as microsomal Ab and thyroglobulin Ab (Seiberling et al, 2007). The presence of thyroid autoantibodies was found to strongly correlate with post-hemithyroidectomy hypothyroidism. Similar relationships have been observed among Hashimoto’s thyroiditis, autoimmune thyroiditis, the degree of lymphocytic infiltration, the presence of chronic inflammation, or detectable thyroid autoantibodies and the occurrence of hypothyroidism after hemithyroidectomy. The association among Hashimoto’s thyroiditis, a “normal elevated” TSH concentration, a low free T4 concentration, and thyroid autoantibodies is likely due to the underlying pathologic disease process. In addition, preoperatively measured thyroid autoantibodies may predict postoperative hypothyroidism.

2.4.2.2 Degree of lymphocytic infiltration

Lymphocytic infiltrate into the thyroid gland has been found to decrease thyroid function, and a semiquantitative analysis of this infiltrate usually reflects the risk of hypothyroidism. The degree of lymphocytic infiltration, graded on a scale of 0-IV, into the resected thyroid lobe may aid in predicting the development of hypothyroidism in post-hemithyroidectomy patients (Koh et al, 2008). An extensive review of histopathologic data, which assessed whether the degree of lymphocytic infiltration and germinal center formation within the

thyroid lobe could accurately predict the development of postoperative hypothyroidism, found that when inflammation was graded based on the extent of lymphocytic infiltration (graded 0-3) and the frequency of germinal centers was qualitatively assessed as a histologic measure of immunologic activation (graded 0-3), most patients with lymphocytic infiltration or germinal center formation in the resected thyroid lobe are at increased risk for post-hemithyroidectomy hypothyroidism (Johner et al, 2011). Other studies have assessed the relationship between postoperative pathologic findings and risk of developing hypothyroidism, but, since these findings were detected after surgery, they could not be used to determine the need for postoperative thyroidectomy.

Taken together, these findings indicate that Hashimoto's thyroiditis and other risk factors, such as lymphocytic infiltration and the presence of autoantibodies, significantly increase the risks for developing postoperative hypothyroidism after thyroid lobectomy. Preoperative evaluation is therefore important in counseling patients about a possible future need for thyroid hormone replacement therapy.

2.4.3 Amount of remnant thyroid gland

One of the major risk factors for hypothyroidism after hemithyroidectomy is the amount of remnant thyroid gland. Small remnant thyroid volume has been recognized as a risk factor for hypothyroidism (De Carlucci Jr et al., 2008). Remnant thyroid volumes can be measured on preoperative US images and can be calculated using the equation (Miccoli et al., 2006):

$$\text{Volume} = \text{length} \times \text{width} \times \text{depth} \times \pi / 6.$$

Patients who developed post-hemithyroidectomy hypothyroidism were found to have a significant smaller body surface area (BSA)-adjusted remnant thyroid volume than patients who remained euthyroid (Moon et al, 2008). Another predictive factor may be BSA-adjusted remnant thyroid volume, determined by calculating remnant thyroid volume/BSA ratio. BSA can be calculated using the Mosteller formula:

$$\text{BSA} = \sqrt{(\text{height} \times \text{weight} / 3600)}.$$

2.4.4 Risk scoring systems

Risk-scoring systems that can predict hypothyroidism after hemithyroidectomy are summarized in Table 3.

Having a valid model predictive of postoperative hypothyroidism is also useful when making follow-up plans for patients undergoing hemithyroidectomy. Most surgeons recommend regular postoperative visits to the clinic, although some counsel their patients to visit only when surgery-related symptoms develop.

A unique risk-scoring system that can predict hypothyroidism after hemithyroidectomy was recently described (Tomoda et al, 2011). In this system, risk scores are calculated as the sum of a patient's age and preoperative TSH concentration. The rates of hypothyroidism in patients with risk scores of 0, 1, 2, and 3 were found to be 3%, 20%, 39%, and 70%, respectively, suggesting that the potential risk of postoperative hypothyroidism should be discussed with patients before surgery based on this scoring system.

Author (year)	Number of patients	Risk scoring system
Moon, et al. (2008)	101	Risk scoring system using two independent risk predictors (TSH level and BSA-adjusted remnant thyroid volume) was created based on the results of logistic regression analyses. The incidences of hypothyroidism were 5.3%, 12.1%, 51.7%, and 85.0% according to the risk scores of 0,1,2, and 3, respectively.
Stoll, et al. (2009)	547	When stratified into 3 groups based on their preoperative TSH measurement (≤ 1.5 , 1.51-2.5, and $\geq 2.51\mu\text{IU/mL}$), the rate of hypothyroidism increased significantly at each level (13.5%, 20.5%, and 41.3%, respectively)
Tomoda, et al. (2011)	233	A risk-scoring system was calculated by summing the score of risk factors such as preoperative TSH level (<1 , 1-2.49, and $\geq 2.5\mu\text{IU/ml}$) and patient's age (<55 , and ≥ 55 year). The incidences of hypothyroidism were 3, 20, 39, and 70% according to the risk scores of 0, 1, 2 and 3, respectively.
Johner, et al. (2011)	117	Assessment of the histologic scoring criteria for thyroid lymphocytic infiltration (score 0-3), and germinal centers (score 0-3) as well as classification of TSH levels (<5.5 , 5.5-6.9, 7-14.9, and $\geq 15\mu\text{IU/L}$) can predict potential risks associated with long-term thyroid hormone replacement therapy.

Table 3. Risk scoring system in posthemithyroidectomy hypothyroidism

An alternative risk-scoring system using two factors, TSH concentration and remnant thyroid volume, was based on the results of logistic regression analyses (Moon et al, 2008). This score system was developed using independently predictive factors, with the highest score of each variable determined by its β regression coefficient. Logistic regression analysis was used to derive an equation that calculates the probability (P) of developing hypothyroidism after hemithyroidectomy:

$$P = 1 / (1 + e^{-(-1.325 + 1.191 * \text{preoperative TSH} - 0.435 * \text{remnant thyroid volume})})$$

The incidences of hypothyroidism in patients with risk scores of 0, 1, 2, and 3 were found to be 5.3%, 12.1%, 51.7%, and 85.0%, respectively, with the model having an overall accuracy in predicting post-hemithyroidectomy hypothyroidism of about 77.2%.

In summary, elevated preoperative TSH concentration, Hashimoto's thyroiditis, small remnant thyroid volume, and/or advanced age are associated with increased risk of developing hypothyroidism and a greater likelihood of requiring thyroid hormone supplementation after hemithyroidectomy. Patient counseling on the need for hormone replacement should therefore be based on these factors.

2.5 Postoperative thyroid hormone replacement after hemithyroidectomy

Hypothyroidism is an underappreciated sequel of hemithyroidectomy. It is most often mild and subclinical, requiring low doses of thyroid hormone to normalize serum TSH concentrations. Hypothyroidism has been reported in up to one third of euthyroid patients who undergo hemithyroidectomy. Formerly, it was common practice to routinely start patients with nodular thyroid disease on “prophylactic” TSH-suppressive doses of thyroid hormone (L-thyroxine) following hemithyroidectomy to prevent recurrence (Gharib & Mazzaferri, 1998), based on the hypothesis that suppression of the hypothalamic-pituitary axis would reduce the risk of abnormalities developing in the contralateral thyroid remnant. Thus, routine administration of L-thyroxine to hemithyroidectomy patients could be expected to decrease the incidence of hypothyroidism. More recently, however, L-thyroxine (TSH-suppression therapy) has not been routinely prescribed for all patients after hemithyroidectomy, largely due to its questionable efficacy in thyroid suppression and prevention of the development of nodules in the remaining contralateral thyroid lobe. In addition, thyroxine administration may cause subclinical hyperthyroidism, which has been associated with possible side effects including decreased bone mineral density, particularly in postmenopausal women, a three-fold increase in the incidence of atrial fibrillation, and aggravation of ischemic heart disease (Mchenry & Slusarczyk, 2000). Therefore, early detection of postoperative hypothyroidism and treatment with L-thyroxine may inhibit the development of overt hypothyroidism and its potential complications. Although administration of thyroid hormone to suppress serum TSH levels in euthyroid patients may not be of value, treatment of patients with elevated TSH is important for relieving the symptoms of hypothyroidism and may be important in reducing recurrent thyroid disease. Administration of thyroxine after hemithyroidectomy may also require long-term monitoring of thyroid function and it has not been determined how long these patients should continue on thyroxine. These problems encouraged us to investigate the frequency of hypothyroidism following hemithyroidectomy, as well as its potential risk factors and management.

The unfavorable side effects of TSH-suppressive doses of thyroid hormone are known, whereas replacement doses of thyroxine have not been associated with the adverse sequelae observed with TSH-suppressive doses of thyroxine. Patients with postoperatively elevated TSH concentrations may represent a subgroup at high risk for the development of recurrent nodular or diffuse thyroid enlargement. Normalization of serum TSH concentrations may help minimize the potential negative effects of elevated serum TSH concentrations without subjecting patients to the adverse sequelae associated with TSH-suppressive doses of L-thyroxine. Therefore, the selective use of L-thyroxine therapy for patients with elevated TSH after hemithyroidectomy may help prevent recurrent nodular or diffuse thyroid enlargement without the unnecessary administration of L-thyroxine to patients with a normal serum TSH level and exposing them to its harmful effects (McHenry and Slusarczyk, 2000).

In summary, hypothyroidism after hemithyroidectomy is usually mild and asymptomatic, and can be treated with lower than normal replacement doses of L-thyroxine to maintain serum TSH concentrations within their normal range.

2.6 Post-hemithyroidectomy follow-up guidelines

Theoretically, a single thyroid lobe should possess enough functioning thyrocytes for a patient to remain euthyroid. In fact, many surgeons and patients choose hemithyroidectomy owing to the belief that postoperative thyroid hormone therapy will not be required. However, patients with risk factors for hypothyroidism, such as severe preoperative thyroiditis, may not have sufficient thyroid tissue remaining after thyroid lobectomy. Thus, all patients who undergo hemithyroidectomy should be counseled regarding the potential need for lifelong thyroid hormone therapy.

There is no widely accepted guideline or algorithm for the monitoring of thyroid function after hemithyroidectomy, leaving hypothyroidism as the most common resulting complication. Follow-up guidelines vary widely and generally consist of a single postoperative measurement of TSH. Some patients may not be examined at all until the development of overt hypothyroidism. If thyroid dysfunction is detected, the decision to start thyroid hormone replacement therapy is usually based on the preference of the treating physician, patient symptoms, and the degree and duration of TSH elevation, rather than on evidence obtained from clinical trials. Therefore, it is important to identify those patients who are at risk of developing hypothyroidism soon after surgery so that they can be more attentively monitored using thyroid function tests. Additionally, it would be of benefit to identify risk factors predictive of the development of early hypothyroidism.

One of the difficulties in monitoring thyroid function other than thyroid hormone concentrations after hemithyroidectomy is that many symptoms of subclinical hypothyroidism are nonspecific. Although most physicians recommend regular postoperative visits, some recommend visits only when patients develop surgery-related symptoms. Although routine and continuous long-term monitoring of thyroid hormone concentrations after hemithyroidectomy is a possible solution, it is often ineffective and not cost effective due to unnecessary hospital visits. In contrast, unrecognized hypothyroidism after hemithyroidectomy may have an unfavorable effect on a patient's general health. This may inevitably result in overt hypothyroidism in some patients, increasing the risks of developing cardiovascular and/or neuropsychiatric diseases. To overcome this dilemma, preoperative risk factors for hypothyroidism after hemithyroidectomy have been formulated to identify high-risk patients. Table 4 summarizes several follow-up protocols followed after hemithyroidectomy.

In most patients, hypothyroidism after hemithyroidectomy manifests as an increased serum TSH concentration within 3-12 months after surgery. Moreover, hypothyroidism in most of these patients is rarely severe or progressive. Therefore, patients who are postoperatively euthyroid rarely go on to develop hypothyroidism, making yearly evaluations by measuring serum TSH concentrations sufficient. Thus, most thyroid function should be monitored once yearly for life (McHenry & Sulsarczyk, 2000; Miller et al., 2006).

The pituitary-thyroid axis undergoes adaptation following partial thyroidectomy, with most patients showing an increase in serum TSH at 1 month (Tomoda et al, 2011). Since most patients who will develop subclinical hypothyroidism will not do so within the first 3 months after surgery, it may be advisable to measure TSH concentration 4 weeks and 3 months after surgery. At 3 months, patients with subclinical hypothyroidism (>10 uIU/ml) may be prescribed L-thyroxine. TSH concentrations should again be measured at 6 and 12

months, and every 6 or 12 months thereafter, unless patients manifest overt symptoms of hypothyroidism.

Author (year)	Recommended follow-up protocol
McHenry, et al. (2000)	All symptomatic patients should be treated with L-T4 replacement. If it is elected not to treat asymptomatic patients, they should have a baseline serum fT4 and total T3 level measured and a yearly evaluation including measurement of serum fT4, T3, TSH levels to assess for progression to overt hypothyroidism.
Miller, et al. (2006)	Recommendation is to obtain a postoperative TSH measurement 8 to 12 weeks after surgery, followed by the measurement of TSH levels at 6 months and 12 months after surgery. If the TSH level is normal at 12 months, biannual to annual determination of TSH levels was encouraged unless symptoms of hypothyroidism manifest.
Koh, et al. (2008)	If preoperative risk factors (presence of microsomal Ab and thyroglobulin Ab, or higher degree of lymphocytic infiltration of resected thyroid gland) were present, these patients were to be follow up at least for 12 months with explanation of possibility of developing postsurgical hypothyroidism.
Wormald, et al. (2008)	Patients with risk factors (raised TSH level or lymphocytic infiltration) should undergo thyroid function tests at 3,6,12 months and annually thereafter postoperatively. In all other patients, testing of thyroid function once at 1-year is sufficient.
Moon, et al. (2008)	Frequent follow-up and thyroid function monitoring can be tailored to high-risk patients if a valid prediction model can be established in prospective studies.
Su, et al. (2009)	TSH monitoring at 6 months, 12 months, and then yearly for 2 years was recommended for asymptomatic patients. High-risk patients should have serial TSH for the first year, then yearly thereafter.
Tomoda, et al. (2011)	Postoperative TSH level should be checked 4 weeks after surgery and again 3 months. At 3 months after operation, the decision regarding prescription of levothyroxine to patients with subclinical hypothyroidism (more than 10 μ IU/ml). After 3 months after operation, the measurement of TSH levels was recommended at 6 and 12 months after surgery. If the TSH level is normal at 12 months, biannual to annual determination of TSH levels could be checked unless symptoms of hypothyroidism manifest.
Johner, et al. (2011)	To obtain a postoperative TSH measurement for all patients at 6 weeks after surgery, followed by the measurement of TSH levels at 6 and 12 months after surgery was advised. TSH level at 3 months was no longer recommended because most patients displayed marked increase in their TSH level immediately after surgery, that subsequently normalized over time.

Table 4. Recommendation protocol for follow-up after hemithyroidectomy

Another follow-up protocol recommends that all symptomatic or asymptomatic patients with hypothyroidism be treated with L-thyroxine (McHenry & Slusarczyk, 2000). If

treatment of asymptomatic patients is not preferred, serum free T4 and total triiodothyronine (T3) concentrations should be measured at baseline, followed by yearly evaluations including measurements of serum free T4, T3, and TSH to assess the progression to overt hypothyroidism.

Another recommendation is to measure TSH 8 to 12 weeks after surgery, as well as at 6 and 12 months. If TSH concentration is normal at 12 months, it should be measured every 6 to 12 months thereafter, unless patients develop symptoms of hypothyroidism (Miller et al., 2006).

A recent modification of an earlier algorithm (Johner et al, 2011) recommended that TSH be measured 6 and 12 months after hemithyroidectomy, indicating that the measurement of TSH at 3 months was no longer required because most study participants displayed marked increases in serum TSH concentration immediately after surgery, which subsequently normalized over time. This new algorithm recommended that serum TSH be measured biannually in asymptomatic patients with mild biochemical hypothyroidism (TSH 5.6-6.9 uIU/L). This follow-up schedule allows for the timely detection of biochemical hypothyroidism and appropriate surveillance for individuals managed conservatively, with an expectation of eventual return to normal thyroid function.

Although it has been suggested that all hemithyroidectomy patients be monitored for as long as possible, it may be more practical to use a selective monitoring strategy in which monitoring is dependent on the presence of risk factors.

3. Conclusion

The incidence of hypothyroidism after hemithyroidectomy is not negligible and should not be overlooked. Approximately 15-30% of patients who undergo hemithyroidectomy may have this complication, and some may need thyroid hormone replacement therapy. Risk factors such as elevated preoperative TSH levels, elevated concentrations of thyroid autoimmune antibodies, degree of thyroiditis, age, and residual thyroid volume are associated with an increased risk of hypothyroidism after hemithyroidectomy. Patients at increased risk for postoperative hypothyroidism should be made aware of their risk factors and undergo more intensive follow-up.

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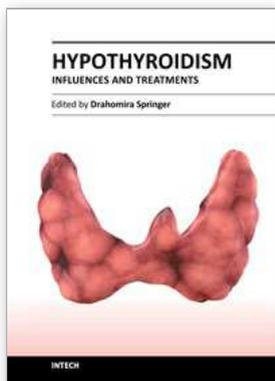
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5. References

- Campion, L.; Gallou, G. & Ruelland, A. (1995) Lipid and thyroid changes after partial thyroidectomy: guidelines for L-thyroxine therapy? *Clin Chem*, Vol.41, No.3, pp.473-474
- Chu, KK. & Lang, BH. (2011) Clinicopathologic predictors for early and late biochemical hypothyroidism after hemithyroidectomy. *Am J Surg*, Epub ahead of print. DOI:10.1016/j.amjsurg.2011.03.004

- Clark, OH; Lambert, WR. & Cavalieri, RR. (1976) Compensatory thyroid hypertrophy after hemithyroidectomy in rats. *Endocrinology*, Vol.99, No.4, pp.988-995
- De Carlucci Jr, D.; Tavares MR. & Obara, MT. (2008) Thyroid function after unilateral total lobectomy: risk factors for postoperative hypothyroidism. *Arch Otolaryngol Head Neck Surg*, Vol.134, No.10, pp.1076-1079
- Gharib, H. & Mazzaferri, EL. (1998) Thyroxine suppressive therapy in patients with nodular thyroid disease. *Ann Intern Med*, Vol.128, No.5, (March 19989), pp.386-394
- Hollowell, JG.; Staehling, NW. & Flanders, WD. (2002) Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab*, Vol.87, No.2, pp.489-499
- Johner, A.; Griffith, OL. & Walker, B. (2011) Detection and management of hypothyroidism following thyroid lobectomy: evaluation of a clinical algorithm. *Ann Surg Oncol*, Epub ahead of print. DOI 10.1245/s10434-011-1627-1
- Koh, YW.; Lee, SW. & Choi, EC. (2008) Prediction of hypothyroidism after hemithyroidectomy: a biochemical and pathological analysis. *Eur Arch Otorhinolaryngol*, Vol.265, No.4, pp.453-457
- Laurberg, P.; Andersen, S. & Bülow Pedersen, I. (2005) Hypothyroidism in the elderly: pathophysiology, diagnosis and treatment. *Drugs Aging*, Vol.22, No.1, pp.23-38
- Lombardi, G.; Panza, N. & Lupoli, G. (1983) Study of the pituitary-thyroid axis in euthyroid goiter after partial thyroidectomy. *J Endocrinol Invest*, Vol.6, No.6, pp.485-487
- Marine, D. (1926) Control of compensatory hyperplasia of the thyroid of guinea-pigs by administration of iodine. *Arch Pathol*, Vol.2, pp.829
- McHenry, CR. & Slusarczyk SJ. (2000) Hypothyroidism after hemithyroidectomy: incidence, risk factors, and management. *Surgery*, Vol.128, No.6, pp.994-998
- Miccoli, P.; Minuto, MN. & Orlandini, C. (2006) Ultrasonography estimated thyroid volume: a prospective study about its reliability. *Thyroid*, Vol.16, No.1, (January 2006), pp.37-39
- Miller, FR.; Paulson, D. & Prihoda, TJ. (2006) Risk factors for the development of hypothyroidism after hemithyroidectomy. *Arch Otolaryngol Head Neck Surg*, Vol.132, No.1, pp.36-38
- Moon, HG.; Jung, EJ. & Park, ST. (2008). Thyrotropin level and thyroid volume for prediction of hypothyroidism following hemithyroidectomy in an Asian patient cohort. *World J Surg*, Vol. 32, No.11, pp. 2503-2508
- Seiberling, KA.; Dutra, JC. & Bajaramovic, S. (2007) Hypothyroidism following hemithyroidectomy for benign nontoxic thyroid disease. *Ear Nose Throat J*, Vol.86, No.5, pp.295-299
- Spanheimer, PM.; Sugg, SL. & Lal, G. (2011) Surveillance and intervention after thyroid lobectomy. *Ann Surg Oncol*, Vol.18, No.6, pp.1729-1733
- Stoll, SJ.; Pitt, SC. & Liu, J. (2009) Thyroid hormone replacement after thyroid lobectomy. *Surgery*, Vol.146, No.4, pp.554-558
- Su, SY.; Grodski, S. & Serpell, JW. (2009) Hypothyroidism following hemithyroidectomy: a retrospective review. *Ann Surg*, Vol.250, No.6, pp.991-994
- Surks, MI.; Ortiz, E. & Daniels, GH. (2004) Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *JAMA*, Vol.291, No.2, pp.228-238

- Tomoda, C.; Ito, Y. & Kobayashi, Y. (2011) Subclinical hypothyroidism following hemithyroidectomy: a simple risk-scoring system using age and preoperative thyrotropin level. *ORL J Otorhinolaryngol Relat Spec*, Vol.73, No.2, pp.68-71
- Wartofsky, L. & Van Nostrand, D. (2006) Overt and 'subclinical' hypothyroidism in women *Obstet Gynecol Surv*, Vol.61, No.8, pp.535-4542
- Wormald, R.; Sheahan, P. & Rowley, S. (2008) Hemithyroidectomy for benign thyroid disease: who needs for follow-up for hypothyroidism? *Clin Otolaryngol*, Vol.33, No.6, pp.587-591



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Hypothyroidism is the most common thyroid disorder and it is significantly more frequent than presented - millions of people suffer from this disease without knowing it. People with this condition will have symptoms associated with slow metabolism. Estimates of subclinical hypothyroidism range between 3 to 8 %, increasing with age, whereas it more likely affects women than men. About 10% of women may have some degree of thyroid hormone deficiency. Hypothyroidism may affect lipid metabolism, neurological diseases or other clinical conditions. The book includes studies on advancements in diagnosis, regulation and replacement therapy, thyroid ultrasonography and radioiodine therapy for hypothyroidism. "Hypothyroidism - Influences and Treatments" contains many important specifications, results of scientific studies and innovations for endocrine practice.

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