World J Surg (2008) 32:2503–2508
DOI 10.1007/s00268-008-9717-3

World Journal of Surgery

Thyrotropin Level and Thyroid Volume for Prediction of Hypothyroidism Following Hemithyroidectomy in an Asian Patient Cohort

Hyeong-Gon Moon · Eun-Jung Jung · Soon-Tae Park · Tae Sik Jung · Chi-Young Jeong · Young-Tae Ju · Young-Joon Lee · Soon-Chan Hong · Sang-Kyung Choi · Woo-Song Ha

Published online: 30 August 2008
© Société Internationale de Chirurgie 2008

Abstract
Background As more patients undergo diagnostic thyroid surgery, the development of posthemithyroidectomy hypothyroidism is becoming a major concern. We hypothesized that the preoperative thyrotropin (thyroid-stimulating hormone, TSH) level and ultrasonographically measured thyroid volume, both commonly available in thyroid nodule patients, may predict the development of posthemithyroidectomy hypothyroidism.
Method Among the 132 patients who underwent hemithyroidectomy from January 2004 to January 2006, a total of 101 patients who were followed for more than a year were included in the analysis.
Results Biochemical hypothyroidism developed in 37 patients (36.6%). Patients who developed postoperative hypothyroidism showed higher TSH levels ($P < 0.001$) and smaller remnant thyroid volumes ($P = 0.014$). Logistic regression analysis showed that the TSH level and remnant thyroid volume were independent predictors of posthemithyroidectomy hypothyroidism ($P < 0.001$ and $P = 0.04$, respectively). A risk scoring system using these two factors 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.
Conclusions Patients with a high preoperative TSH level and small thyroid volume are at high risk of developing hypothyroidism following hemithyroidectomy. Potential risk of postoperative hypothyroidism should be discussed with these patients when thyroid surgery is being considered for a diagnostic purpose.

H.-G. Moon · E.-J. Jung · S.-T. Park (✉) · C.-Y. Jeong · Y.-T. Ju · Y.-J. Lee · S.-C. Hong · S.-K. Choi · W.-S. Ha
Department of Surgery, Gyeongsang National University Hospital, 90 Chilam-dong, Jinju, Gyeongsangnam-do 660-702, South Korea
e-mail: moonhgsurgi@gmail.com

H.-G. Moon · E.-J. Jung · S.-T. Park · C.-Y. Jeong · Y.-T. Ju · Y.-J. Lee · S.-C. Hong · S.-K. Choi · W.-S. Ha
Department of Surgical Oncology, Gyeongnam Regional Cancer Center, Jinju, Korea

T. S. Jung
Department of Endocrinology, School of Medicine, Gyeongsang National University, Jinju, Korea

Introduction

Thyroid nodules are a common clinical problem [1, 2], and their incidence is increasing probably because of more frequent use of thyroid ultrasonography as an essential part of the initial thyroid examination [3, 4]. The main concern with the newly found thyroid nodules is the possibility of malignancy. Fine-needle aspiration (FNA) is the standard diagnostic method for evaluating thyroid nodules [2, 5, 6], and recently the use of high-frequency ultrasonography (USG) has been found to help predict malignancy in selected patients [7–10]. Unfortunately, even FNA, currently the most effective diagnostic method, yields indeterminate results in up to 20% of all aspirations, which bear a 20% risk of malignancy; and these indeterminate cases often lead to thyroid surgery (usually hemithyroidectomy) for diagnostic purposes [2, 5, 6].

In the past, most patients received thyrotropin (thyroid-stimulating hormone, TSH)-suppression therapy after hemithyroidectomy to prevent the recurrence of thyroid nodules [11]. The common practice of prescribing L-thyroxine to hemithyroidectomized patients has veiled the incidence of hypothyroidism, and the assessment of surgical complications after hemithyroidectomy has mainly focused on nerve injury and hypoparathyroidism [12, 13]. Recently, routine TSH-suppression therapy has fallen out of favor owing to its questionable efficacy and associated side effects [11, 14], leaving hypothyroidism as the most common complication after hemithyroidectomy. The reported incidence of hypothyroidism after hemithyroidectomy is 18% to 35% [15–18].

We hypothesized that the capacity of remnant thyroid tissue to attain the euthyroid state depends on both qualitative and quantitative aspects of the thyroid gland, which are reflected in the preoperative TSH level and remnant thyroid volume, respectively. The aim of this study was to determine the risk factors of posthemithyroidectomy hypothyroidism using preoperatively available clinical information, including the preoperative TSH level and thyroid volume. We also sought to establish a risk scoring system that can predict posthemithyroidectomy hypothyroidism before deciding to perform diagnostic hemithyroidectomy.

Patients and methods

We conducted a retrospective review of medical records of all patients undergoing hemithyroidectomy from January 2004 to January 2006. Hemithyroidectomy is defined as total unilateral lobectomy plus isthmusectomy [15]. Patients were excluded from the study if they: (1) were preoperatively on thyroid hormone for preexisting hypothyroidism or to prevent nodule growth; (2) had suspicious clinical or USG features of thyroiditis; (3) were on medications known to cause hypothyroidism; (4) later underwent completion thyroidectomy; (5) did not undergo preoperative USG; or (6) were not followed for more than a year. This study was approved by the institutional review board of the institution, and was conducted according to the principles of the Helsinki declaration.

Patients' medical records were reviewed for age, sex, preoperative thyroid function tests including TSH, height and weight at the time of surgery, and final histologic diagnosis. The normal range of TSH in our institution during the study period was 0.17 to 4.7 μIU/L. A postoperative thyroid function test was performed 2 months after the surgery in all patients. All included patients were followed for more than a year, and their thyroid function was evaluated every 2 to 3 months during the follow-up period.

The remnant thyroid volume was measured from the preoperative USG images. Preoperative USG was performed by thyroid radiologists using a commercially available real-time ultrasonographic scanner (SONOLINE Antares; Siemens, Munich, Germany) with a high-frequency linear transducer (>7.5 MHz). The volume (V) of the remnant lobe was calculated using the following equation [19].

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

Because thyroid volume is positively correlated with the body surface area (BSA) [20], we estimated the BSA-adjusted remnant thyroid volume by calculating the remnant thyroid volume/BSA ratio. BSA was calculated by the Mosteller formula.

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

The statistical significance of the difference between hypothyroid and euthyroid patients was analyzed using Student's t-test for continuous variables and the chi-squared test for nominal variables. Pearson's correlation coefficient was calculated to examine the correlation between variables and the degree of hypothyroidism. Variables showing statistical significance or a borderline statistical relation ($P < 0.2$) and variables having a reported association with posthemithyroidectomy hypothyroidism were entered into logistic regression analysis. Backward stepwise selection with a likelihood ratio test was used for logistic regression analysis. The probability of posthemithyroidectomy hypothyroidism was calculated based on the results of logistic regression analysis. A risk scoring system was created using the independent predictive factors; and the highest score of each variable was determined by its β regression coefficient. The area under the receiver operating characteristic (ROC) curve was used to compare the accuracy of the risk model to predict postsurgical hypothyroidism. Values of $P < 0.05$ were considered statistically significant.

Results

From 2004 to 2006, a total of 132 patients underwent hemithyroidectomy in our institution. After excluding 31 patients based on the aforementioned criteria, 101 patients were included in the analysis. The most common reason for exclusion was the lack of preoperative USG ($n = 24$). Two patients (one with minimally invasive follicular carcinoma and one with medullary carcinoma) underwent completion thyroidectomy and were excluded from the analysis. Both patients showed "follicular neoplasm" during preoperative FNA and "benign follicular neoplasm" on intraoperative frozen section. Follow-up thyroid function tests were not available for the remaining five patients.

The patients' mean ± sd age was 47.5 ± 12.7 years; and 76 patients (75.2%) were women. The final pathologic diagnosis was benign thyroid nodules in 63 patients (37 nodular goiters, 21 follicular adenomas, 3 Hurthle cell adenomas, 2 cysts) and malignant nodules in 38 patients (36 papillary microcarcinomas, 2 minimally invasive follicular carcinomas). Papillary microcarcinoma was diagnosed before surgery in 30 patients; the remaining 6 patients had only suspicious cytologic findings, although the final histologic examination confirmed the diagnosis of papillary microcarcinomas. None of the microcarcinoma diagnoses were results of incidental findings in the resected specimens.

Biochemical hypothyroidism developed in 37 patients (36.6%). Demographic, clinical, and pathologic data, as well as the TSH level and BSA-adjusted remnant thyroid volume, were compared between postoperatively euthyroid and hypothyroid patients. (Table 1) Patients who developed hypothyroidism showed significantly higher preoperative TSH levels and smaller BSA-adjusted remnant thyroid volumes. The preoperative TSH level and BSA-adjusted remnant thyroid volume also showed a significant correlation with postoperative TSH levels measured 2 months after hemithyroidectomy (Pearson's correlation coefficient was 0.502 and −0.352, respectively: $P < 0.001$ for both). This result shows that both factors predict not only the occurrence but also the severity of posthemithyroidectomy hypothyroidism. However, the preoperative TSH level and BSA-adjusted remnant thyroid volume did not have significant correlation with each other (Pearson's correlation coefficient of − 0.114, $P = 0.254$) (Fig. 1).

Table 1 Comparative analysis between postoperative euthyroid and hypothyroid patients

Parameter	Euthyroid	Hypothyroid	*P*
Age	47.7 ± 11.1	47.35 ± 15.2	0.91
Female/male	45/19	31/6	0.13
Benign/malignant	43/21	20/17	0.19
BSA	1.67 ± 0.18	1.68 ± 0.17	0.93
Preoperative TSH level	1.22 ± 0.89	2.46 ± 1.16	<0.001
BSA-adjusted remnant thyroid volume	3.48 ± 1.50	2.73 ± 1.34	0.014

BSA: body surface area; TSH: thyroid-stimulating hormone

Logistic regression analysis showed that both the preoperative TSH level and the BSA-adjusted remnant thyroid volume were independent predictors of postsurgical hypothyroidism after hemithyroidectomy (Table 2). From this logistic regression analysis, we derived an equation that calculates the probability (P) of developing hypothyroidism after hemithyroidectomy.

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

The overall accuracy of the logistic regression prediction model for predicting posthemithyroidectomy hypothyroidism was 77.2%.

Subsequently, a risk scoring system to predict posthemithyroidectomy hypothyroidism using the preoperative TSH level and BSA-adjusted remnant thyroid volume was created. Considering the β regression coefficient of each variable, we assigned a highest score of 2 to preoperative TSH and a highest score of 1 to the remnant thyroid volume (Table 3). Cutoff values of each variable were determined according to the percentiles of the patients. The risk scoring system showed significant association with the development of posthemithyroidectomy hypothyroidism. Patients with scores of 0, 1, 2, and 3 developed hypothyroidism with an incidence of 5.3%, 12.1%, 51.7%, and 85.0%, respectively ($P < 0.001$, chi-squared test (Fig. 2a). Also, this simplified risk scoring system predicted posthemithyroidectomy hypothyroidism with an accuracy similar to that of the probability equation derived from the logistic regression prediction model (area under the ROC curve was 0.835 for the logistic regression prediction model and 0.849 for the risk scoring system, as seen in Figure 2b).

Discussion

We have demonstrated here that a high preoperative TSH level and a small remnant thyroid volume are independent risk factors for posthemithyroidectomy hypothyroidism.

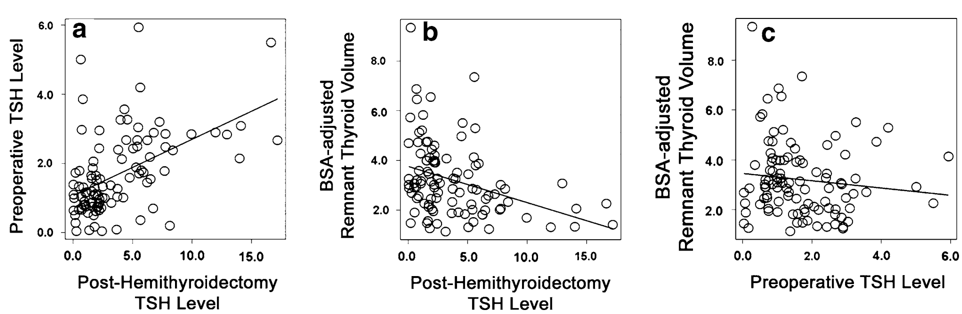

Fig. 1 Scatter diagrams of the preoperative thyroid-stimulating hormone (TSH) level and the body surface area (BSA)-adjusted remnant thyroid volume versus the postoperative TSH (**a**, **b**) and the preoperative TSH level versus the BSA-adjusted remnant thyroid volume (**c**). Posthemithyroidectomy TSH levels were measured 2 months after the surgeries

Table 2 Independent predictors of posthemithyroidectomy hypothyroidism

Predictor	LR	Standard error	95.0% CI for LR		χ^2	*P*
			Lower	Upper		
Preoperative TSH level	1.2187	0.2794	0.7113	1.8143	19.03	< 0.0001
BSA-adjusted remnant thyroid volume	−0.4510	0.2216	−0.9162	−0.0426	4.14	0.0418

LR: likelihood ratio; CI: confidence interval

Table 3 Creation of risk scoring system to predict hypothyroidism after hemithyroidectomy

Parameter	Cutoff value[a]	Risk score
Preoperative TSH level[b]	≤1 mIU/L	0
	>1 and ≤2 mIU/L	1
	>2 mIU/L	2
BSA-adjusted remnant thyroid volume[c]	>3 cm^3	0
	≤3 cm^3	1

[a] Cutoff values were determined according to the percentiles of each variable

[b] Preoperative TSH level of 1 mIU/L matched the 34th percentile and 2 mIU/L matched the 67th percentile

[c] BSA-adjusted remnant thyroid volume of 3 cm^3 matched the 51st percentile

These results are particularly interesting as both predicting factors are easily determined from the patient's clinical information in a modern endocrine practice. To our knowledge, this is the first study that shows the relation between the remnant thyroid volume and posthemithyroidectomy hypothyroidism.

Hemithyroidectomy is a commonly performed surgical procedure for patients with "indeterminate" thyroid nodules so long as the nodules do not show clinical features of malignancy other than in the FNA results [5, 6]. The rationale for performing thyroid resection for indeterminate nodules is that these nodules harbor thyroid carcinoma in up to 20% of cases [2, 6], and the main reason to perform hemithyroidectomy rather than total thyroidectomy is to preserve thyroid function and prevent nerve and parathyroid injury [13].

Several studies have looked into the risk factors of developing posthemithyroidectomy hypothyroidism (Table 4) [15–18]. They noted that some of the proposed risk factors can be determined only after surgery, whereas others can be detected during the preoperative period. Among them, the preoperative TSH level was commonly noted to have a significant relation with postoperative hypothyroidism. Similarly, in the present study, the preoperative TSH level showed significant correlation with the development and severity of posthemithyroidectomy hypothyroidism. In addition to the preoperative TSH level, our results show that patients who developed posthemithyroidectomy hypothyroidism had a significant smaller BSA-adjusted remnant thyroid volume compared to those who remained in the euthyroid state. Although the preoperative TSH level had a more significant contribution to the development of hypothyroidism, logistic regression analysis showed that the BSA-adjusted remnant thyroid volume is still an independent risk factor of posthemithyroidectomy hypothyroidism. The remnant thyroid volume can be easily measured from preoperative USG images. Because most patients with thyroid nodules undergo thyroid USG as an initial approaching step [5], the remnant thyroid volume can be easily assessed prior to the time the surgeon must make a decision about whether to perform diagnostic hemithyroidectomy.

Although the risk scoring system proposed in this study showed promising predictability in our cohort of patients, it

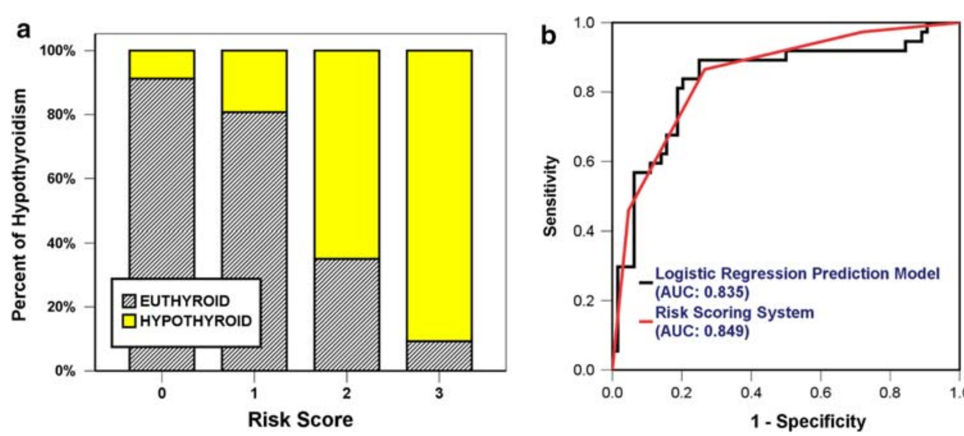

Fig. 2 (**a**) Percentages of hypothyroidism according to the risk scoring system. (**b**) Receiver operating characteristic (ROC) curve for the risk scoring system. AUC: area under the curve

Table 4 Previous studies regarding the risk factors of posthemithyroidectomy hypothyroidism

Study	Hypothyroidism	Risk factors of hypothyroidism	Factors without significant association
McHenry and Slusarczyk [15]	35% (25/71)	Preoperative TSH level	Associated thyroiditis
			Weight of resected gland
Buchanan and Lee [16]	24.1% (38/158)	Lymphocytic infiltration	
		Presence of thyroid autoantibody	
Piper et al. [17]	18% (12/66)	Lymphocytic infiltration	
		Preoperative TSH level	
Miller et al. [18]	27% (24/90)	Preoperative TSH level	Sex
		Age	
Present study	36.6% (37/101)	Preoperative TSH level	Age
		Remnant thyroid volume	Sex

has certain limitations for its prompt application in everyday practice. First, we could not perform a validation analysis in an independent patient cohort; therefore, the high predictability of our risk scoring system needs further validation before its application. Second, the cutoff values in the risk scoring system are based on the percentiles of the patients in this study. Koreans have a high level of iodine intake and excretion, mostly due to the seaweed in their diet [21]. Epidemiologic studies show that the TSH level and thyroid volume are affected by iodine intake; therefore, the cutoff values in this study should be modified in regions with different iodine intakes [22, 23].

Being able to predict the individual patient's likelihood of developing posthemithyroidectomy hypothyroidism is of value when making diagnostic and therapeutic plans for patients with thyroid nodules whose FNA results are indeterminate. The potential risk of hypothyroidism should be kept in mind especially when discussing a diagnostic hemithyroidectomy with patients who have a relatively high TSH level and small thyroid volume. Recent reports regarding the accuracy of thyroid USG in predicting malignant thyroid nodules have shown promising results [7–10]. If the indeterminate nodules in these high risk patients show USG features that strongly suggest a benign nature of the nodules, short-term follow-up with USG and repeated FNA may be a more reasonable option than proceeding directly to surgery in terms of preventing unnecessary hypothyroidism. However, avoiding diagnostic surgery merely to prevent postoperative hypothyroidism on the basis of the patient's small thyroid volume and high TSH level while the patient's nodule has certain characteristics of malignancy (e.g., nodule growth, atypical cells in FNA, suspicious USG features) is not justified. Although preserving thyroid function by avoiding unnecessary hemithyroidectomy has certain benefits, we should be careful to minimize the chance of delayed diagnosis of thyroid cancer.

Having a valid prediction model for 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 advise their patients to make future visits to the clinic only when surgery-related symptoms develop. Both follow-up policies have advantages and disadvantages. The former policy is beneficial in terms of early detection of hypothyroidism but may result in unnecessary hospital visits. On the other hand, the latter policy may be cost beneficial, but it inevitably results in overt hypothyroidism in some patients. 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.

Acknowledgments The authors thank Ms. So-Young Kang from the Cancer Research Institute & Seoul National University Biomedical Informatics for her kind advice in the statistical analysis.

References

1. Hegedus L (2004) Clinical practice: the thyroid nodule. N Engl J Med 351:1764–1771
2. Mandel SJ (2004) A 64-year-old woman with a thyroid nodule. JAMA 292:2632–2642
3. Bonnema SJ, Bennedbaek FN, Ladenson PW et al (2002) Management of the nontoxic multinodular goiter: a North American survey. J Clin Endocrinol Metab 87:112–117
4. Ross DS (2002) Nonpalpable thyroid nodules: managing an epidemic. J Clin Endocrinol Metab 87:1938–1940
5. Cooper DS, Doherty GM, Haugen BR et al (2006) Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 16:109–142
6. AACE/AME Task Force on Thyroid Nodules (2006) American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocr Pract 12:63–102
7. Moon HG, Jung EJ, Park ST et al (2007) Role of ultrasonography in predicting malignancy in patients with thyroid nodules. World J Surg 31:1410–1416
8. Papini E, Guglielmi R, Bianchini A et al (2002) Risk of malignancy in nonpalpable thyroid nodules: predictive value of

ultrasound and color-Doppler features. J Clin Endocrinol Metab 87:1941–1946
9. Tae HJ, Lim DJ, Baek KH et al (2007) Diagnostic value of ultrasonography to distinguish between benign and malignant lesions in the management of thyroid nodules. Thyroid 17:461–466
10. Rago T, Scutari FS, Pinchera A et al (2007) Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. J Clin Endocrinol Metab 92:2917–2922
11. Gharib H, Mazzaferri EL (1998) Thyroxine suppressive therapy in patients with nodular thyroid disease. Ann Intern Med 128:386–394
12. Randolph GW (2003) Surgery of the thyroid and parathyroid glands. Saunders, Philadelphia
13. Rosato L, Avenia N, Bernante P et al (2004) Complications of thyroid surgery: analysis of a multicentric study on 14, 934 patients operated on in Italy over 5 years. World J Surg 28:271–276
14. Biondi B, Filetti S, Schlumberger M (2005) Thyroid-hormone therapy and thyroid cancer: a reassessment. Nat Clin Pract Endocrinol Metab 1:32–40
15. McHenry CR, Slusarczyk SJ (2000) Hypothyroidisim following hemithyroidectomy: incidence, risk factors, and management. Surgery 128:994–998
16. Buchanan MA, Lee D (2001) Thyroid auto-antibodies, lymphocytic infiltration and the development of post-operative hypothyroidism following hemithyroidectomy for non-toxic nodular goitre. J R Coll Surg Edinb 46:86–90
17. Piper HG, Bugis SP, Wilkins GE et al (2005) Detecting and defining hypothyroidism after hemithyroidectomy. Am J Surg 189:587–591
18. Miller FR, Paulson D, Prihoda TJ et al (2006) Risk factors for the development of hypothyroidism after hemithyroidectomy. Arch Otolaryngol Head Neck Surg 132:36–38
19. Miccoli P, Minuto MN, Orlandini C et al (2006) Ultrasonography estimated thyroid volume: a prospective study about its reliability. Thyroid 16:37–39
20. Gomez JM, Maravall FJ, Gomez N et al (2000) Determinants of thyroid volume as measured by ultrasonography in healthy adults randomly selected. Clin Endocrinol (Oxf) 53:629–634
21. Kim JY, Moon SJ, Kim KR et al (1998) Dietary iodine intake and urinary iodine excretion in normal Korean adults. Yonsei Med J 39:355–362
22. Laurberg P, Pedersen KM, Hreidarsson A et al (1998) Iodine intake and the pattern of thyroid disorders: a comparative epidemiological study of thyroid abnormalities in the elderly in Iceland and in Jutland, Denmark. J Clin Endocrinol Metab 83:765–769
23. Zimmermann MB, Ito Y, Hess SY et al (2005) High thyroid volume in children with excess dietary iodine intakes. Am J Clin Nutr 81:840–844