Original article

Factors associated with hypothyroidism following hemithyroidectomy: a prospective study

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Objective To assess the incidence of post-operative hypothyroidism after hemithyroidectomy in the Thai population living in the northern region of Thailand and to analyze factors associated with hypothyroidism following hemithyroidectomy.

Methods A prospective study was conducted at Chiang Mai University Hospital, Thailand, of patients who had thyroid nodules and who were scheduled for a hemithyroidectomy between September 2010 and April 2012. Patients were divided into a euthyroid group and a hypothyroid group. Demographic data, pre- and post-operative thyroid function tests, resected side, weight, and pathological diagnosis of resected thyroids were analyzed.

Results Of the 50 cases, 11 patients who had documented malignancy and required total thyroidectomy and those who were lost to follow up were excluded. The study included 39 cases (7 males and 32 females) age 19 to 71 years (average 46.9±13.8 years). Left and right hemithyroidectomies were done in 25 and 14 patients, respectively. Pathology reports on the patients indicated adenomatous goiter (66.6%), follicular adenoma (20.5%), colloid cyst (5.1%), Hurthle cell adenoma (2.6%), chronic lymphocytic thyroiditis (2.6%), and nodular goiter with lymphocytic thyroiditis (2.6%). Eight cases (20.5%) had developed hypothyroidism at eight to ten weeks postoperatively. The pre-operative TSH level of the hypothyroid group was normal, but significantly lower than in the euthyroid group (p =0.009). Age, pre-operative free T4 and free T3, weight, and resected side were not significantly different between the two groups. More male patients than females developed post-operative hypothyroidism (42.9% VS 15.6%), although the difference was not statistically significant.

Conclusions As one-fifth of the hemithyroidectomy patients developed hypothyroidism within eight to ten weeks post-operatively, clinicians should be alert for post-operative hypothyroidism and provide prompt treatment, particularly in patients with a pre-operative high normal TSH level. **Chiang Mai Medical Journal 2017;56(4):195-201.**

Keywords: hemithyroidectomy, hypothyroidism, high normal pre-operative TSH level

Introduction

Thyroid nodules are a common problem in general practice affecting five percent of the women and one percent of the men in iodine deficiency areas (1), especially in the northern region of Thailand. Ninety-five percent of thyroid nodules are benign (2), and hemithyroidectomy

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is a standard treatment for unilateral benign thyroid nodules.

Hypothyroidism is a common complication following hemithyroidectomy. Symptoms of hypothyroidism include weight gain, fatigue, tinnitus, nausea, edema, hoarseness, dry skin, and depression–symptoms that affect the quality of life. The incidence of hypothyroidism after hemi-thyroidectomy has been reported to be 10.9 to 36.6% (3-14).

A previous study mentioned that thyroid hormone replacement therapy after hemithyroidectomy could prevent the re-growth of benign thyroid tumors, reduce the risk of malignant transformation, and reduce the risk of post-operative hypothyroidism (15). However, subsequent studies have reported that the trend toward providing thyroid hormone replacement therapy after hemithyroidectomy had decined (5,6,8,9) due to a lack of evidence supporting the efficacy of thyroid hormone therapy in reducing the development of contralateral thyroid nodules (9). In addition, excessive thyroid hormone may cause other side effects such as atrial fibrillation and, in postmenopausal women, osteoporosis (8).

From the medical records of Chiang Mai University Hospital, during the period of this study an average of 416 patients per year presented with thyroid nodules in the outpatient department, and seventy of those patients underwent a thyroidectomy. During that period, a post-operative thyroid function test was not routinely done following a hemithyroidectomy at Chiang Mai University Hospital.

Objectives

The objectives of this study were to assess the incidence of post-operative hypothyroidism after a hemithyroidectomy at Chiang Mai University Hospital, and to study associated factors of post-operative hypothyroid patients.

Methods

This prospective study, covering the period from September 2010 through April 2012, recruited the patients age more than 18 years old who had undergone a hemithyroidectomy in the Department of Otolaryngology, Chiang Mai University Hospital. Patients whose pathology reports indicated malignancy and those who later underwent a complete thyroidectomy were excluded. Ethical approval was granted by the Hospital Ethics Committee. Patient demographics recorded include age, sex, pre-operative thyroid function test results, size of thyroid gland, and history of previous thyroid hormone replacement. After the hemithyroidectomy was completed, specimens were sent to the pathologists at the Department of Pathology, Chiang Mai University Hospital. A post-operative evaluation of the patients was done at 8 to 10 weeks after surgery using clinical assessment and the thyroid function test. Additional blood exams for levels of thyroid peroxidase antibody (anti-TPO) and thyroglobulin antibody (anti-TG) were done in patients with any one of the following conditions: (1) post-operative hypothyroidism, (2) Hashimoto's thyroiditis confirmed by pathology, or (3) lymphocytic infiltration in the thyroid specimens. All blood specimens (thyroid function test, anti-TPO, anti-TG) were analyzed by the pathology laboratory of Chiang Mai University Hospital.

The normal range of serum thyroid stimulating hormone (TSH) was set at 0.27-4.20 ng/dL, free T4 (FT4) at 0.90-1.70 ng/dL, and free T3 (FT3) at 0.18-0.46 ng/dL. Post-operative hypothyroidism was defined as serum TSH levels above the normal range at eight to ten weeks after hemithyroidectomy. Hypothyroidism was classified into two categories: (1) subclinical hypothyroidism, defined as a high TSH level but normal FT4 and FT3 levels, and (2) true hypothyroidism, defined as a high TSH level with low FT4 and FT3 levels.

The calculated sample size was 38 patients. The incidence of hypothyroidism is shown as a percentage. Factors potentially associated with hypothyroidism were statistically analyzed using the Chi-square test for qualitative data and the t-test or the Mann-Whitney U test for quantitative data. Statistical significance was set at $p < 0.05$.

Results

From September 2010 through April 2012, 50 patients underwent a hemithyroidectomy. Eleven patients were excluded from the study: five patients had a malignancy, and six patients missed their appointment for the post-operative thyroid function test. The remaining 39 patients were included in this study (32 females, 7 males), mean age 46.9±13.8 years (range 19-71 years). A left hemithyroidectomy was done in 25 patients and a right hemithyroidectomy in 14 patients. Thirteen of the patients had received thyroid hormone suppression

therapy prior to surgery, but the therapy was discontinued at least three months before surgery, and the results of the pre-operative thyroid function test were euthyroid.

Findings in the pathology reports included adenomatous goiter (66.6%), follicular adenoma (20.5%), colloid cyst (5.1%), Hurthle cell adenoma (2.6%), chronic lymphocytic thyroiditis (2.6%), and nodular goiter with lymphocytic thyroiditis (2.6%).

Eight of 39 patients (20.5%) developed post-operative hypothyroidism (3 males and 5 females). Six were subclinical hypothyroidism and two were true hypothyroidism. The pathology report findings included nodular/multinodular/adenomatous goiter (75.0%), follicular adenoma (12.5%) and nodular goiter with lymphocytic thyroiditis (12.5%). However, none of these patients had signs or symptoms of hypothyroidism at 8 to 10 weeks postoperatively. The data of the post-operative hypothyroid patients is shown in Tables 1 and 2.

Two patients developed true hypothyroidism post-operatively and were given thyroid hormone replacement therapy immediately. The other six patients who developed subclinical hypothyroidism were monitored by the thyroid function test every three months. If the hypothyroidism became worse or if signs and symptoms of hypothyroidism appeared, the patients were also treated by thyroid hormone replacement. At the time of the 5-month follow-up, one patient's hypothyroidism had become more severe, and one patient had developed symptoms of hypothyroidism. These two patients were treated by thyroid hormone replacement. Only one of the eight patients with subclinical hypothyroidism recovered to euthyroid status. Two subclinical hypothyroid patients with a less severe condition were followed up periodically and one patient did not come to the five-month post-operative follow-up. The pathological diagnoses of both of the patients who developed true hypothyroidism post-operatively were adenomatous goiter and nodular goiter with lymphocytic thyroiditis. Only one patient had developed true hypothyroidism with high anti-TG and anti-TPO post-operatively; their pathology reports showed nodular goiter with lymphocytic thyroiditis.

The hypothyroid group had a significantly higher pre-operative TSH level than the euthyroid group (p =0.009). However, there was no significant difference in age, sex, side of hemithyroidectomy, weight of resected thyroid, or pre-operative FT4 & FT3 between these two groups. Comparison of data for the euthyroid and hypothyroid groups are shown in Table 3. Male patients were more likely to develop post-operative hypothyroidism than female patients (42.9% VS 15.6%), although the difference was not significantly significant (Table 4). Nodular/multinodular/adenomatous goiter was the most common pathological finding in these two groups (Table 5)

There was only one patient in the post-operative euthyroid group with a pathology report of chronic lymphocytic thyroiditis.

Discussion

Hypothyroidism is a common complication after hemithyroidectomy, but the condition is often temporary, and usually returns to euthyroidism. A minimal decrease in thyroxine secretion results in a significant increase in TSH, the most sensitive indicator for hypothyroid screening. The half-life of thyroxine (FT4) is one week. The optimal time for measuring

Table 1. Hypothyroidism and demographic characteristics of post-operative hypothyroid patients

	(N%)
Hypothyroidism	8 (100.0)
Subclinical hypothyroidism	6 (75.0)
True hypothyroidism	2 (25.0)
Sex	
Male	3 (37.5)
Female	5 (62.5)
Side of hemithyroidectomy	
Right	4 (50.0)
Left	4 (50.0)
Pathological findings	
Nodular/multinodular/adenomatous goiter	6 (75.0)
Follicular adenoma	1 (12.5)
Nodular goiter with lymphocytic thyroiditis	1 (12.5)

Table 2. Individual data of the post-operative hypothyroid patients

Patient	Sex	Age (yrs)	Type of hypothyroidism	Pathological findings	Anti-TG	Anti-TPO	Follow-up and treatment
1	Male	57	Subclinical	Nodular goiter with cystic degeneration	Normal	Normal	Returned to euthyroidism 5 months post-operatively
2	Female	60	True	Adenomatous goiter	Normal	Normal	Thyroid hormone supplement
3	Female	53	Subclinical	Follicular adenoma	Normal	Normal	Patient failed to follow up with five-month post-operative thyroid function test
4	Male	53	Subclinical	Nodular goiter with cystic degeneration	Normal	Normal	Periodic thyroid function test due to subclinical hypothyroidism without symptoms of hypothyroidism 1 year post-operatively
5	Female	44	Subclinical	Multinodular goiter	Elevated	Normal	Subclinical hypothyroid 5 months post-operatively; thyroid hormone supplement started because symptoms of hypothyroidism developed
6	Female	63	True	Nodular goiter & lymphocytic thyroiditis	Elevated	Elevated	Thyroid hormone supplement
7	Male	46	Subclinical	Multinodular goiter with hyperplastic nodule	Normal	Normal	Subclinical hypothyroid worse at 5 months post-operatively; thyroid hormone supplement started
8	Female	31	Subclinical	Multinodular goiter with cystic change	Normal	Normal	Periodic thyroid function test due to subclinical hypothyroidism without symptoms of hypothyroidism 5 months post-operatively

Table 3. Comparison of post-operative euthyroid and hypothyroid patients

Parameter	Euthyroidism	Hypothyroidism	*p-value*
Age (years; mean ± SD)	45.9 (±14.5)	50.9 (±10.3)	0.370
Sex			0.106
Male	4 (12.9%)	3 (37.5%)	
Female	27 (87.1%)	5 (62.5%)	
Side of hemithyroidectomy			0.351
Right	10 (32.2%)	4 (50.0%)	
Left	21 (67.8%)	4 (50.0%)	
Pre-op TFT			
TSH (ng/dl; mean±SD)	1.23 (±0.61)	1.93 (±0.71)	0.009*
FT4 (ng/dL; mean±SD)	1.17 (±0.24)	1.20 (±0.26)	0.796
FT3 (ng/dL; mean±SD)	0.29 (±0.05)	0.29 (±0.05)	0.915
Post-op TFT			
TSH (ng/dL; mean±SD)	2.02 (±0.96)	7.76 (±3.04)	0.001*
FT4 (ng/dL; mean±SD)	1.10 (±0.02)	1.02 (±0.13)	0.164
FT3 (ng/dL; mean±SD)	0.60 (±0.73)	0.27 (±0.05)	0.507
Weight of resected thyroid (g.)	39.42 (±30.91)	45.38 (±25.01)	0.618

*p-value < 0.05

Table 4. Comparative data in post-operative hypothyroid patients between males and females

	Male	Female
Hypothyroid patients	3	5
Patients undergoing hemithyroidectomy	7	32
Percent	42.9	15.6

thyroid hormone is at least five times the half-life of thyroxine, i.e., five weeks post-operatively (5). This study found an incidence of post-operative hypothyroidism of 20.5%, measuring the thyroid hormone level at eight to ten weeks post-operatively; however, none of the patients had any signs or symptoms of hypothyroidism at that time. That might be because the duration of the hypothyroidism was not long enough for signs or symptoms to appear; some patients did develop signs and symptoms of hypothyroidism later. Only one patient had returned to euthyroidism by five months after surgery, and that patient had the least severe post-operative hypothyroidism.

Many studies have reported on factors associated with post-operative hypothyroidism, including high normal pre-operative TSH (4-10,12-14), lymphocytic infiltration or thyroiditis (7,8,13,14), high anti-TPO or anti-TG (10,12,13), and small residual thyroid volume (4,10) (Table 6). In this study, the post-operative hypothyroid patients had significantly higher pre-operative TSH than the euthyroid group (p =0.009) (Table 3). Other factors, including age, sex, side of hemithyroidectomy, and weight of resected thyroid gland, were not significantly different between the post-operative hypothyroid and euthyroid group.

Table 5. Pathological report of post-operative euthyroid and hypothyroid patients

Pathological report	Euthyroidism	Hypothyroidism
Nodular/multinodular/ adenomatous goiter	20	6
Follicular adenoma	7	1
Colloid cyst	2	-
Hurthle cell adenoma	1	-
Chronic lymphocytic thyroiditis	1	-
Nodular goiter with lymphocytic thyroiditis	-	1
Total	31	8

Three of seven male patients (42.9%) and five of 32 female patients (15.6%) had post-operative hypothyroidism. Among the patients who underwent hemithyroidectomy, there were 4.5 times as many females as males. Although more males than females tended to develop post-operative hypothyroidism, the difference was not statistically significant.

Nodular, multinodular, and adenomatous goiter were the most common pathological diagnoses found in both the post-operative hypothyroid and euthyroid groups, 75.0% and

Table 6. Associated factors of post-operative hypothyroidism in previous studies

Studies	High normal pre-op TSH	Lymphocytic infiltration / Thyroiditis	Small residual thyroid volume	High Anti-TPO / Anti TG
Piper HG, et al (2005)		⁄		
Moon HG, et al (2008)	⁄		⁄	
McHenry CR, et al (2000)	⁄			
Wormald R, et al (2008)	⁄	⁄		
Stoll SJ, et al (2009)	⁄	⁄		
Miller FR, et al (2006)	⁄	⁄		
Seiberling KA, et al (2007)	⁄			
DeCarlucci D, et al (2008)	⁄		⁄	⁄
Koh YW, et al (2008)	⁄	⁄		⁄
Su SY, et al (2009)	⁄	⁄		⁄
This study	⁄			

64.5%, respectively. According to Koh *et al*. (12) and Su *et al*. (13), thyroiditis and high anti-TPO and anti-TG are factors associated with post-operative hypothyroidism. In this study, we found thyroiditis in only two patients (one chronic lymphocytic thyroiditis and one nodular goiter with lymphocytic thyroiditis). One patient developed post-operative hypothyroidism with high anti-TPO and anti-TG, but another patient had normal anti-TPO and anti-TG without post-operative hypothyroidism. Thyroiditis is not common in Thailand, and there are few studies about thyroiditis in that country so the database is limited.

The post-operative hypothyroid patients were classified into two groups, subclinical hypothyroid and true hypothyroid. The true hypothyroid patients were treated immediately with thyroid hormone supplements even though they did not have any signs or symptoms of hypothyroidism. According to previous studies by Piper *et al*. (3) and McHenry *et al*. (5), serum TSH should be monitored twice a year in asymptomatic post-operative subclinical hypothyroid patients, allowing the remaining thyroid gland to return to normal function without thyroid hormone supplement. Following that advice, we monitored thyroid function every three months in the asymptomatic subclinical hypothyroid patients. If a patient developed any signs or symptoms of hypothyroidism or if the TSH tended to increase, the patient was treated with thyroid hormone supplement.

Conclusions

As one-fifth of the hemithyroidectomy patients developed hypothyroidism within eight to ten weeks post-operatively, clinicians should be alert for post-operative hypothyroidism and should provide prompt treatment if signs or symptoms appear, particularly in patients with a pre-operative high normal TSH level.

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ปัจจัยที่ส่งผลต่อการเกิดภาวะฮอร์โมนไทรอยด์ต่ำ หลังการผ่าตัดต่อมไทรอยด์ข้างเดียว ในโรงพยาบาลมหาราชนครเชียงใหม่

ศณัฐธร เชาวน์ศิลป์ และ รักษ์ ตนานุวัฒน์
ภาควิชาโสต ศอ นาสิกวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ เพื่อศึกษาอุบัติการณ์และปัจจัยของการเกิดภาวะฮอร์โมนไทรอยด์ต่ำ หลังการผ่าตัดต่อมไทรอยด์ข้างเดียว ในโรงพยาบาลมหาราชนครเชียงใหม่

รูปแบบและระเบียบวิธีวิจัย เป็นการศึกษาแบบเก็บข้อมูลไปข้างหน้าในผู้ป่วยที่มีก้อนที่ต่อมไทรอยด์ ตั้งแต่อายุ 18 ปีขึ้นไป และได้รับการผ่าตัดต่อมไทรอยด์ข้างเดียว ณ แผนก หู คอ จมูก โรงพยาบาลมหาราชนครเชียงใหม่ ตั้งแต่ 1 กันยายน พ.ศ. 2553–30 เมษายน พ.ศ. 2555 โดยผู้ป่วยจะได้รับการเก็บข้อมูลทั่วไป ตรวจวัดระดับฮอร์โมนไทรอยด์ก่อนและหลังผ่าตัด และตรวจชิ้นเนื้อทางพยาธิวิทยา

ผลการศึกษา ผู้ป่วยเข้าร่วมการศึกษาทั้งหมด 39 ราย ช่วงอายุ 19-71 ปี (ค่าเฉลี่ย 46.9±13.8 ปี) พบผู้ป่วย 8 ราย (ร้อยละ 20.5) ที่มีภาวะฮอร์โมนไทรอยด์ต่ำหลังได้รับการผ่าตัดต่อมไทรอยด์ข้างเดียว โดยผู้ป่วยที่มีภาวะฮอร์โมนไทรอยด์ต่ำหลังผ่าตัดมีระดับ TSH ก่อนผ่าตัดค่อนข้างสูง (High normal pre-op TSH) กว่าผู้ป่วยที่มีภาวะฮอร์โมนไทรอยด์ปกติหลังผ่าตัดอย่างมีนัยสำคัญทางสถิติ (p =0.009) และเพศชายมีแนวโน้มที่จะเกิดภาวะฮอร์โมนไทรอยด์ต่ำหลังผ่าตัดมากกว่าเพศหญิง อย่างไรก็ตาม ไม่พบความแตกต่างกันในเรื่องของอายุ เพศ ข้างของต่อมไทรอยด์ที่ทำการผ่าตัด และน้ำหนักของต่อมไทรอยด์ที่ทำการผ่าตัดระหว่างผู้ป่วยกลุ่มที่มีภาวะฮอร์โมนไทรอยด์ปกติและมีภาวะฮอร์โมนไทรอยด์ต่ำอย่างมีนัยสำคัญทางสถิติ

สรุป การตรวจวัดระดับฮอร์โมนไทรอยด์หลังผ่าตัดที่ 8-10 สัปดาห์ ควรใช้เป็นแนวทางในการตรวจติดตามผู้ป่วยหลังผ่าตัดไทรอยด์ข้างเดียว เพื่อที่สามารถตรวจพบผู้ป่วยที่มีภาวะฮอร์โมนไทรอยด์ต่ำและให้การรักษาได้อย่างทันท่วงที ซึ่งจะส่งผลต่อคุณภาพชีวิตของผู้ป่วยในระยะยาวต่อไป **เชียงใหม่เวชสาร 2560;56(4):195-201.**

คำสำคัญ: การผ่าตัดต่อมไทรอยด์ข้างเดียว ภาวะฮอร์โมนไทรอยด์ต่ำ