Original Article

Hypothyroidism after Hemithyroidectomy in Non-Hashimoto's Thyroiditis

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Objective: To evaluate the incidence and identify predictive factor of hypothyroidism after hemithyroidectomy in non-Hashimoto's thyroiditis.

Materials and Methods: A retrospective study was conducted between May 2013 and May 2017 in 66 patients that underwent hemithyroidectomy for benign non-Hashimoto's thyroiditis thyroid diseases. SPSS (v20.0) was used to analyze the data. A p-value lower than 0.05 was considered statistically significant.

Results: There were 66 patients, with a predominance of women (87.9%), and the mean age was 48.7 years. The majority of histological reports were adenomatous nodule or nodular goiter in 63 patients (95.5%). The three remaining patients had adenoma. Seven patients (10.6%) developed hypothyroidism. Levothyroxine was prescribed in three patients who developed overt hypothyroidism and four patients who complained about hormone decreasing symptoms. The mean follow-up period was 12 weeks. In univariate analysis, preoperative thyroid-stimulating hormone (TSH) level of 1.20 mIU/L or more (OR 10.1, 95% CI 1.14 to 89.45) was the predictor for postoperative hypothyroidism. Other factors included sex, age, preoperative free T4 level, size and weight of surgical specimen, cystic degeneration on histology, and pathological diagnosis were not established as predictive factors.

Conclusion: In benign non-Hashimoto's thyroiditis thyroid disease, patients who had preoperative TSH level of 1.20 mIU/L or more were considered as high risk for post-hemithyroidectomy thyroid hormone depletion. Clinical symptoms associated hypothyroidism should be observed carefully in patients with this TSH level cut point. In addition, postoperative monitoring for hypothyroidism should be started at 12 weeks.

Keywords: Hypothyroidism, Hemithyroidectomy, Thyroidectomy, Lymphocytic thyroiditis, Hashimoto's thyroiditis

J Med Assoc Thai 2019;102(1):57-61
Website: http://www.jmatonline.com

Hemithyroidectomy (HTx) combined with removal of isthmus and pyramidal lobe is a procedure for treating benign thyroid disease, cytologically intermediated thyroid nodule, and a selected case of thyroid cancer[1-3]. In general, the rate of surgical complications including inferior and/or superior laryngeal nerves injuries, surgical wound infection, and local hematoma are less frequent in HTx compared with total thyroidectomy (TTx)[4-6]. However, hypothyroidism after HTx is common. The prevalence was reported in the range from 10% to 55.8%[3,5,7]. High preoperative serum thyroid-stimulating hormone (TSH) level and presentation of lymphocytic infiltration on histopathological study (compatible with Hashimoto's thyroiditis) are good predictive factors for predicting postoperative hypothyroidism[7-11]. However, the predictive factors of postoperative hypothyroidism in patients diagnosed other benign thyroid diseases apart from Hashimoto's thyroiditis has not been well studied.

Therefore, the aim of the present study was to evaluate the incidence and predictive factors of hypothyroidism after HTx in Thai patients lived in northern Thailand previously classified as an endemic area of iodine deficiency by WHO[12].

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Materials and Methods

All clinical and laboratory data of patients received thyroidectomy for treating thyroid diseases

How to cite this article: Srivanitchapoom C. Hypothyroidism after Hemithyroidectomy in Non-Hashimoto's Thyroiditis. J Med Assoc Thai 2019;102:57-61.

at the department of otolaryngology, Phayao Hospital, Thailand between May 2013 and May 2017 were reviewed. Patients underwent TTx or completed thyroid lobectomy, lacked of pre- and/or postoperative data of thyroid function tests, and histopathologically confirmed the diagnosis of thyroid cancer or chronic lymphocytic thyroiditis were excluded. Patients underwent HTx with pathologically confirmed the diagnosis of other thyroid diseases apart from cancer and chronic lymphocytic thyroiditis were included. All patients were scheduled to do postoperative follow-up at 2 and 10 weeks post HTx. The aim of 2-week follow-up was to evaluate the complications at surgical site, clinical signs/symptoms associated with thyroid hormone deficiency, and reporting the histopathological result. The histopathological data included size of tumor, weight of the specimen, and histopathological findings of the specimen leading to final diagnosis were collected. The purpose of 10-week follow-up was to evaluate the thyroid functions including TSH and free thyroxine (FT4) level. However, if patients presented any clinical signs/symptoms of hypothyroidism, blood test for evaluating thyroid functions would be performed earlier. According to patients' socio-economic problems, some of them were unable to return for follow-up visits on time; therefore, a few weeks delayed after usual follow-up schedule was permitted.

The reference range of serum TSH and FT4 level in the present study were 0.3 to 4.2 mIU/L and 0.58 to 1.64 ng/dl, respectively. Hypothyroidism was classified into two categories including overt and subclinical hypothyroidism. Overt hypothyroidism was defined as high TSH and low FT4 level, while subclinical hypothyroidism was defined as high TSH with normal FT4 level. Levothyroxine was given to all patients with overt hypothyroidism; however, it was also prescribed to selected patients with subclinical hypothyroidism presenting with clinical symptoms related to thyroid hormone deficiency such as fatigue and facial edema. SPSS version 20.0 was used to perform statistical analysis. All continuous data were presented as mean; unpaired t-test was used to compare two different mean. All categorical data were reported in percentages. Fisher's exact test, Chi-square test, and odds ratio (OR) with 95% confidence intervals (CI) were used to compare the data. A p-value lower than 0.05 was considered statistical significance. The present study was approved by the Research Ethics Committee of Phayao Hospital, Thailand.

Results

One hundred fifty-five patients with various thyroid diseases who were treated with thyroidectomy were included in this study. Sixty-five patients underwent TTx and the histopathological confirmed the diagnosis of malignancy, bilateral benign lesion such as multinodular goiter and chronic lymphocytic thyroiditis. Completed thyroid lobectomy was performed in 10 patients. Fourteen patients were unable to return for the 2-week follow-up postoperatively. Sixty-six patients who met the inclusion criteria were enrolled to the present study. There were 58 women and 8 men. The average age was 48.7 years (range from 20 to 72 years). The mean preoperative TSH and FT4 level were 1.36 mIU/L and 0.82 ng/dl, respectively. Histopathological reports consisted of 63 adenomatous nodule or nodular goiter (95.5%), two follicular adenomas, and one hurthle cell adenoma. The average size of tumor was 4.73 cm (range from 2.5 to 8 cm) and mean weight of surgical specimen was 31.61 g (range from 9 to 147 g). Cystic degeneration presented in surgical specimen was found in 30 of 66 specimens (45.5%). The mean duration of follow-up was 12 weeks.

Seven of 66 patients (10.6%) developed hypothyroidism (three overt, and four subclinical hypothyroidism) during the postoperative follow-up period. Three of them (one overt and two subclinical) were clinically detection of hypothyroidism at two weeks while four patients (two overt and two subclinical) developed hypothyroidism within 10 weeks postoperatively. A comparison of patients between hypothyroid and euthyroid group is shown in Table 1. There were no statistically significant difference of all parameter including sex, age, the mean preoperative TSH and FT4 level, size of tumor, weight of specimen, presentation of cystic degeneration on histopathology, and histopathological results between hypothyroid and euthyroid group. However, the mean preoperative TSH level of the hypothyroid group tended to increase as compared with euthyroid group.

In univariate analysis, preoperative TSH level of 1.20 mIU/L or more (OR 10.1, 95% CI 1.14 to 89.45, p-value 0.04) was the only predictor for postoperative hypothyroidism (Table 2). Levothyroxine was prescribed to the three patients with overt hypothyroidism who presented symptoms of hypothyroid within two to three weeks after HTx. Furthermore, four patients with subclinical hypothyroidism also received levothyroxine due to their complaint about symptoms associated with

Table 1. Patient demographic and histology data of hypothyroid and euthyroid group

Variable	Hypothyroid group	Euthyroid group	p-value
Patient, n (%)	7 (10.6)	59 (89.4)	
Sex, n			0.61
Female	6	52	
Male	1	7	
Age (year), Mean±SD	47.9±6.2	48.8±11.8	0.12
Preoperative TSH (mIU/L), Mean±SD	2.34±1.18	1.24±0.81	0.15
Preoperative FT4 (ng/dl), Mean±SD	0.83±0.12	0.82±0.16	0.44
Size of tumor (cm), Mean±SD	3.94±1.27	4.82±1.23	0.70
Weight of tumor (g), Mean±SD	30.86±28.89	31.69±26.38	0.48
Cystic degeneration, n			0.60
Present	3	27	
Absent	4	32	
Histology, n			0.71
Adenomatous nodule/nodular goiter	7	56	
Adenoma	0	3	

SD=standard deviation; TSH=thyroid-stimulating hormone; FT4=free thyroxine

Table 2. Preoperative TSH level to predict the post-operative hypothyroidism

Preoperative TSH level	OR (95% CI)	p-value
≥1.00 mIU/L	6.2 (0.70 to 54.78)	0.10
≥1.10 mIU/L	8.2 (0.92 to 72.12)	0.06
≥1.20 mIU/L	10.1 (1.14 to 89.45)	0.04

TSH=thyroid-stimulating hormone; OR=odds ratio; CI= confidence interval

thyroid hormone deficiency including fatigue and facial edema within 2, 11, and 13 weeks after HTx. The mean follow-up time was 13 weeks in the euthyroid group. While in the hypothyroid group, the mean follow-up time to detect hypothyroidism was five weeks.

Discussion

Determination of the exact prevalence of hypothyroidism after HTx is not simple. Many factors are needed to be considered such as definition of hypothyroidism, timing of the follow-up, and the variety of clinical signs and symptoms to determine hypothyroidism. However, the prevalence of hypothyroidism after HTx was reported up to 50%[4,5,7,13]. Hypothyroidism after HTx was detected in 10.6% within 10 weeks postoperatively in the present study, which was lower than previous studies. The possible explanation of this concern may be due to the exclusion criteria of the present study. The author's study excluded patient with histopathological confirmed diagnosis of chronic lymphocytic thyroiditis, which was well documented as a predictive factor of postoperative hypothyroidism.

Hypothyroidism was classified as overt and subclinical forms. From the meta-analysis[7], the included studies reported the incidence of subclinical more than overt hypothyroidism. In clinical hypothyroidism, thyroid hormone is replaced immediately while subclinical hypothyroidism is unclear. Some authors suggested to close follow-up with TSH and symptoms associated such as fatigue, weight gain, facial edema, and wait until subclinical hypothyroidism has spontaneous recovery[5,14]. In addition, many authors also mentioned the side effect of levothyroxine such as arrhythmia, cardiovascular disease, and loss of calcium in the bones resulting in osteoporosis and fracture[4,6,14]. On the other hand, Said et al[2] found hypothyroidism most likely occurred permanently. Additionally, compensated hypertrophy of the remaining thyroid lobe also developed; therefore, thyroid hormone replacement was preferred in the subclinical group[2,15,16]. Su et al[3] advocated hormone replacement when subclinical hypothyroidism presented, especially in patient who had positive antithyroid peroxidase (anti-TPO) antibody and thyroiditis on histological diagnosis. The supportive data showed thyroid function did come back in long-term follow-up at a low rate (12.5%)[3]. Ahn et al[5] suggested hormone prescription only in subclinical patient who had preoperative TSH level of 2.60 mIU/L or more and for patients 46 years or

older. According to the ATA/AACE Guidelines for Hypothyroidism in Adults, patients with TSH levels above 10 mIU/L are at increased risk for heart failure and cardiovascular mortality and should be considered for treatment with levothyroxine[17]. In patients with the TSH levels between 4.5 to 10 mIU/L, the treatment should also be considered if they have symptoms suggestive of hypothyroidism, positive TPO antibody or evidence of atherosclerotic cardiovascular disease, heart failure, or associated risk factors for these diseases[17]. In the present study, all subclinical hypothyroidism patients were encouraged for thyroid hormone replacement due to the manifestation of clinical symptoms associated with thyroid hormone deficiency.

There was no regular schedule for post-operative follow-up[14-16]. Some studies suggested the appropriated timing for detection hypothyroidism should be around four to five life cycle of TSH, which is seven days per cycle[8,13]. Studies in 2009 and 2016 preferred postoperative schedule at four to eight weeks after HTx[6,14]. Most of the articles suggested the follow-up period be around 6 to 12 months[5,8,13] and some authors favored long duration up to two years[2,3]. In the present study, the average 12 weeks follow-up was performed and hypothyroidism was mostly detected within two to three weeks postoperatively.

The predictive factors of hypothyroidism after HTx were documented in many previous studies[5,6,9,13,14]. Demographic data that included gender and sex did not showed statistically significant difference between hypothyroid and euthyroid group in the present study, similar to the previous studies[3,7,8]. Although one study[6] reported that preoperative FT4 level could predict hypothyroidism after HTx; however, this finding was not found in the present study. In histopathological findings, various studies[3,6-8] reported no significant difference of size of the nodule and weight of the surgical specimen between hypothyroid and euthyroid group. This result was also identified in the present study. Chu and Lang postulated that the weight of the excised gland might reflect the remaining volume of the residual thyroid gland[9]. Furthermore, de Carlucci et al[10] suggested that the volume of residual thyroid gland measured by ultrasound of 4.0 ml or smaller increased chance of thyroid hormone replacement. Unfortunately, the data of residual volume of thyroid gland measured by ultrasound in the present study was not available. Pathological diagnosis of multinodular goiter was evaluated as a risk factor of hypothyroidism[15] although statistical significance was not shown in the present study.

Hashimoto's thyroiditis is another predictive factor for post-HTx hypothyroidism[2,3,6,9,11]. Hashimoto's thyroiditis is characterized by intense chronic lymphocytic infiltration of the thyroid tissue[6]. Hypothyroidism can occur during the progression of Hashimoto's thyroiditis; therefore, it is hard to make the conclusion that patients developed hypothyroidism prior to surgery due to natural course of Hashimoto's thyroiditis or developed hypothyroidism later because of surgery[7,18]. Raised serum concentration of thyroid antibodies [anti-TPO (microsomal) and anti-thyroglobulin] correlated with focal thyroiditis in thyroid tissue[18]. According to the correlation, thyroid antibodies were also statistically significant in hypothyroid group after HTx[4,9-11,13]. However, in the present study population, Hashimoto's thyroiditis was excluded.

Preoperative TSH level was established as the most important predictor[2,5,10,11]. The predictive TSH level was different in prior studies such as TSH level of 2 mIU/L or greater[5,14] or TSH level of 2.5 mIU/L or greater[3,11]. In 2013, Said et al[2] found hypothyroidism was more frequent with increasing preoperative TSH levels in every 1 mIU/L. The present study result showed TSH level of 1.2 mIU/L or greater was significantly. The mean preoperative TSH level of 1.10 mIU/L higher in hypothyroid patients was in the same range when compared with a meta-analysis (1.06 mIU/L (0.83 to 1.29) higher in hypothyroid patients)[7]. However, the preoperative TSH level of 1.2 mIU/L or higher that associated with postoperative hypothyroidism was lower than in the same meta-analysis (preoperative TSH level 2.5 mIU/L or higher). Because Hashimoto's thyroiditis was excluded from the present study and most of our patients had nodular goiter, patients with this pathologic disease should be closely monitored although they have relatively low level of preoperative TSH.

Conclusion

The incidence of hypothyroidism following HTx in benign non-Hashimoto's thyroiditis thyroid diseases was 10.6% within 10 weeks postoperative in the present study. Patient with preoperative TSH level of 1.20 mIU/L or more should be informed of having a high risk of thyroid hormone depletion after surgery. Careful follow-up of thyroid function test and clinical symptoms of hypothyroidism should be performed and started at 12 weeks after surgery in this group of patients.

What is already known on this topic?

Hypothyroidism has been reported as a post-operative complication after HTx. The two main variables that were established as predictive factor for hypothyroidism were preoperative TSH level and Hashimoto's thyroiditis. Therefore, patients who underwent HTx and had the predictor should be considered as a high risk for levothyroixine replacement.

What this study adds?

According to exclusion of Hashimoto's thyroiditis, the preoperative TSH level established as a predictor for hypothyroidism was lower than previous studies. The mean follow-up period at 12 weeks postoperative was recommended.

Conflicts of interest

The author declares no conflict of interest.

References

1. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 2016;26:1-133.
2. Said M, Chiu V, Haigh PI. Hypothyroidism after hemithyroidectomy. World J Surg 2013;37:2839-44.
3. Su SY, Grodski S, Serpell JW. Hypothyroidism following hemithyroidectomy: a retrospective review. Ann Surg 2009;250:991-4.
4. Kandil E, Krishnan B, Noureldine SI, Yao L, Tufano RP. Hemithyroidectomy: a meta-analysis of postoperative need for hormone replacement and complications. ORL J Otorhinolaryngol Relat Spec 2013;75:6-17.
5. Ahn D, Sohn JH, Jeon JH. Hypothyroidism following hemithyroidectomy: Incidence, risk factors, and clinical characteristics. J Clin Endocrinol Metab 2016; 101:1429-36.
6. Stoll SJ, Pitt SC, Liu J, Schaefer S, Sippel RS, Chen H. Thyroid hormone replacement after thyroid lobectomy. Surgery 2009;146:554-8.
7. Verloop H, Louwerens M, Schoones JW, Kievit J, Smit JW, Dekkers OM. Risk of hypothyroidism following hemithyroidectomy: systematic review and meta-analysis of prognostic studies. J Clin Endocrinol Metab 2012;97:2243-55.
8. Beisa V, Kazanavicius D, Skrebunas A, Simutis G, Ivaska J, Strupas K. Prospective analysis of risk for hypothyroidism after hemithyroidectomy. Int J Endocrinol 2015;2015:313971.
9. Chu KK, Lang BH. Clinicopathologic predictors for early and late biochemical hypothyroidism after hemithyroidectomy. Am J Surg 2012;203:461-6.
10. De Carlucci D Jr, Tavares MR, Obara MT, Martins LA, Hojaij FC, Cernea CR. Thyroid function after unilateral total lobectomy: risk factors for postoperative hypothyroidism. Arch Otolaryngol Head Neck Surg 2008;134:1076-9.
11. Lee DY, Seok J, Jeong WJ, Ahn SH. Prediction of thyroid hormone supplementation after thyroid lobectomy. J Surg Res 2015;193:273-8.
12. WHO/UNICEF/ICCIDD. Indicators for assessing iodine deficiency disorders and their control through salt iodinization. Geneva: World Health Organization; 1994.
13. Koh YW, Lee SW, Choi EC, Lee JD, Mok JO, Kim HK, et al. Prediction of hypothyroidism after hemithyroidectomy: a biochemical and pathological analysis. Eur Arch Otorhinolaryngol 2008;265:453-7.
14. Chotigavanich C, Sureepong P, Ongard S, Eiamkul-vorapong A, Boonyaarunnate T, Chongkolwatana C, et al. Hypothyroidism after hemithyroidectomy: The incidence and risk factors. J Med Assoc Thai 2016; 99:77-83.
15. Miller FR, Paulson D, Prihoda TJ, Otto RA. Risk factors for the development of hypothyroidism after hemithyroidectomy. Arch Otolaryngol Head Neck Surg 2006;132:36-8.
16. Piper HG, Bugis SP, Wilkins GE, Walker BA, Wiseman S, Baliski CR. Detecting and defining hypothyroidism after hemithyroidectomy. Am J Surg 2005;189:587-91.
17. Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract 2012;18:988-1028.
18. Vanderpump MP. The epidemiology of thyroid disease. Br Med Bull 2011;99:39-51.