

Risk factors of hypothyroidism after hemithyroidectomy

Facteurs de risque d'hypothyroïdie post hemithyroidectomie

Lina Jeridi, Emna Rejeb, Nadia Romdhane, Imen Zoghlemi, Safa Nefzaoui, Ines Hriga, Chiraz M'barek

University of Tunis El Manar, Faculty of Medicine of Tunis, Otorhinolaryngology Head Neck department, Habib Thameur Hospital, Tunis, Tunisia.

ABSTRACT

Introduction: Hemithyroidectomy has been increasingly applied in patients with thyroid diseases. Although patients are expected to maintain normal thyroid function after hemithyroidectomy, some patients may develop hypothyroidism, which requires thyroid-hormone substitution.

Our aim was to identify the risk factors of postoperative hypothyroidism after hemithyroidectomy.

Methods: We conducted a retrospective, analytical and descriptive study including all patients who underwent hemithyroidectomy between 2017 and 2022, with a minimum follow up of 12 months.

Hypothyroidism was defined as a postoperative serum thyroid-stimulating hormone (TSH) level higher than 5 mIU/L. Collected and analyzed data included age, sex, personal history of hyperthyroidism, family history of thyroid pathology, preoperative and postoperative TSH, nodule size, side and volume of resected and remaining lobes and definitive histological diagnosis.

Results: A total of 190 patients were included. Mean age of patients was 45.95 years [13;79]. The sex ratio (M/F) was 0.091. Of the 190 patients studied, 30 (15.79%) developed hypothyroidism after surgery. Among these patients 2 cases showed signs of clinical hypothyroidism such as constipation and asthenia. The mean duration of diagnosis after surgery was 3.75 months [1;12]. The personal history of hyperthyroidism, preoperative TSH greater than 1.9, remaining lobe volume less than 3.8 cm³ and the presence of lymphocytic thyroiditis on definitive pathological examination were associated with a significantly increased risk of hypothyroidism after Hemithyroidectomy ($p < 0.01$).

Conclusion: Preoperative TSH level greater than 1.9, remaining lobe volume less than 3.8 cm³ and the presence of lymphocytic thyroiditis on pathological examination justify postoperative TSH monitoring up to 12 months after surgery.

Key words: hemithyroidectomy, surgery, hypothyroidism, postoperative, incidence, risk factors.

RÉSUMÉ

Introduction : L'hémithyroidectomie est une chirurgie fréquente en otorhinolaryngologie et chirurgie cervico-faciale. L'hypothyroïdie représente une des complications postopératoire nécessitant une supplémentation en hormones thyroïdiennes.

Notre objectif était d'identifier les facteurs de risque d'hypothyroïdie postopératoire après une hémithyroidectomie.

Méthodes : Nous avons mené une étude rétrospective, analytique et descriptive incluant tous les patients ayant eu une hémithyroidectomie entre 2017 et 2022, avec un suivi minimum de 12 mois. L'hypothyroïdie a été définie par un taux sérique postopératoire de TSH supérieur à 5 mIU/L. Les données collectées et analysées comprenaient l'âge, le sexe, les antécédents personnels d'hyperthyroïdie, les antécédents familiaux de pathologie thyroïdienne, la TSH préopératoire et postopératoire, la taille du nodule, le côté et le volume des lobes réséqués et restants, ainsi que le diagnostic histologique définitif.

Résultats : Au total, 190 patients ont été inclus. L'âge moyen des patients était de 45,95 ans [13 ; 79]. Le sex-ratio était de 0,091. Parmi les 190 patients étudiés, 30 (15,79%) ont développé une hypothyroïdie après la chirurgie. Parmi ces patients, 2 cas ont présenté des signes d'hypothyroïdie clinique à type de constipation et d'asthénie. La durée moyenne du diagnostic après chirurgie était de 3,75 mois [1 ; 12]. Les antécédents personnels d'hyperthyroïdie, une TSH préopératoire supérieure à 1,9, un volume de lobe restant inférieur à 3,8 cm³ et la présence d'une thyroïdite lymphocytaire à l'examen pathologique définitif ont été associés à un risque significativement accru d'hypothyroïdie après hémithyroidectomie ($p < 0,01$).

Conclusion : Les antécédents personnels d'hyperthyroïdie, taux de TSH préopératoire supérieur à 1,9, volume du lobe restant inférieur à 3,8 cm³ et la présence d'une thyroïdite lymphocytaire à l'examen anatomopathologique justifient une surveillance postopératoire de la TSH jusqu'à 12 mois après la chirurgie.

Mots clés : hémithyroidectomie, chirurgie, hypothyroïdie, postopératoire, incidence, facteurs de risque.

Correspondance

Lina Jeridi

University of Tunis El Manar, Faculty of Medicine of Tunis, Otorhinolaryngology Head Neck department, Habib Thameur Hospital, Tunis, Tunisia.

Email: jeridi.lina@yahoo.com

INTRODUCTION

Hemithyroidectomy is a common surgical procedure performed in otolaryngology, often undertaken to address various thyroid conditions. While surgery is generally considered routine, it is associated with a range of potential complications that can manifest in the short, medium, and long term. One of the most frequently encountered postoperative complications is hypothyroidism.

Despite the prevalence of this issue, postoperative hypothyroidism following hemithyroidectomy remains unpredictable (1). The incidence of this condition varies widely in the literature, with reported rates ranging from 0% to 60% (2,3). This variability can be attributed to differences in postoperative follow-up practices and the lack of a standardized definition of hypothyroidism.

In order to provide individualized follow-up for patients who have undergone hemithyroidectomy, patients with a high risk of postoperative hypothyroidism should be identified. Some studies have considered the prognostic value of different factors such as age, preoperative TSH level and remaining thyroid volume and histopathological thyroiditis (4,5).

Objective: The aim of this study was to identify the risk factors associated with the development of hypothyroidism following hemithyroidectomy and to determine which patients require more intensive monitoring of thyroid function

METHODS

We conducted a single-center, observational, descriptive, analytical, and retrospective study over a period of six years, from January 1, 2017, to December 31, 2022. Hemithyroidectomy was defined as unilateral thyroid lobectomy with or without isthmectomy, while preserving the contralateral lobe.

We included patients who had not undergone previous thyroid surgery and received a benign histological diagnosis postoperatively. We excluded patients who underwent surgery and were lost to follow-up before the minimum setback, patients lost from sight and incomplete or unexploitable medical records. Patient records were compiled from the registry of individuals who underwent surgery.

The normal range of TSH in our Hospital laboratory is [0.3 – 5.6].

postoperative TSH measurements were taken at one month, 3 months, 6 months and one year postoperatively. In order to identify risk factors of postoperative hypothyroidism, we used the ROC curve to determine the preoperative TSH threshold value and the mean volume of the remaining lobe with the best ratio between specificity and sensitivity.

The volume of the remaining lobe has been calculated according to the following formula: $V = l \times H \times E \times 0.5$, with l equal to the width, H equal to the height and E equal to the thickness of the lobe.

In the descriptive part of the study, we collected various

parameters for each included patient, including background information (age, sex, medical history of hyperthyroidism), preoperative and postoperative TSH levels, definitive histopathological findings, volume of the remaining lobe, the delay between surgery and the onset of postoperative hypothyroidism, and the maintenance dose of thyroxine. All patients were assessed after a minimum follow-up period of 12 months.

For the analytical component of the study, we categorized patients into two groups based on their postoperative outcomes: Group 1, consisting of patients who did not develop hypothyroidism after surgery, and Group 2, comprising patients who developed documented hypothyroidism following the procedure.

Statistical analysis was done using SPSS. We performed the Chi-square test for qualitative variables and the Student test for quantitative variables. The Mann-Whitney test was used for nonparametric variables.

A p-value <0.05 was considered statistically significant.

RESULTS

From 2017 to 2022, 190 patients underwent hemithyroidectomy and met the inclusion criteria of the study. Mean age of patients was 45.95 years [13 ;79] and the sex ratio was 0.09. Among the 190 patients, 8 patients had preoperative hyperthyroidism. The mean preoperative TSH level was 2.75 ($\pm$ 14.79). Anatomopathological examination revealed vesicular adenoma in 135 patients (71%) , Oncocytic adenoma in 35 patients (18.4%) and lymphocytic thyroiditis in 20 patients (10.5 %). The average length of follow-up was 1.3 years [1;6].

Among the 190 patients retained, 30 patients (15.7%) developed hypothyroidism after hemithyroidectomy. The average time to onset of this complication was estimated at 3.75 months [1;12] (figure 1). Hypothyroidism was subclinical in 93.3% of cases as only two patients had signs of clinical hypothyroidism such as constipation and asthenia. Mean postoperative TSH level in patients who developed hypothyroidism after surgery was 11.98 mIU/L with normal FT4 in all cases. The average dose of L-thyroxine was 67 micrograms [25 ;100].

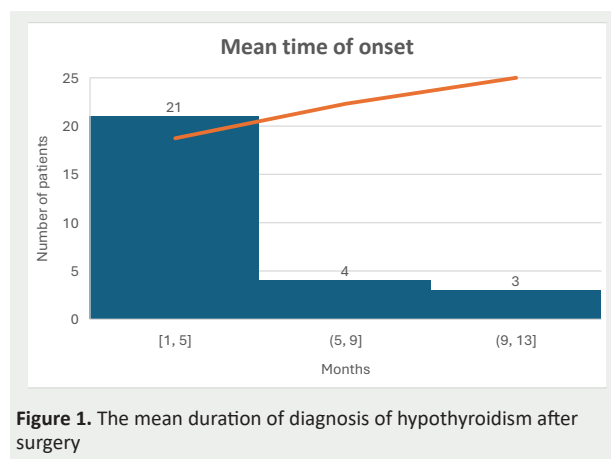


Figure 1. The mean duration of diagnosis of hypothyroidism after surgery

In order to determine the predictive factors of hypothyroidism, a comparative analysis of the demographic, TSH level and pathologic data in the two

groups of patients was conducted. The comparative study is shown in Table 1.

Table 1. Comparison of studied factors between the two groups of patients

Studied factors	Euthyroid group (n=160)	Hypothyroidism group (n=30)	P value
Mean age (years-old)	45.7	46.9	0.65
Sex ratio (H/F)	0.1 (14/144)	0 (0/30)	0.08
Medical history of hyperthyroidism	1.9%	16.7%	0.003
Mean preoperative TSH levels (mUI/L)	1.5 ($\pm$ 0.9)	2.4 ($\pm$ 1.5)	<0.001
Average size of thyroid nodules	37.3mm ($\pm$ 12.7)	33.6 ($\pm$ 11.9)	0.136
Side of lobectomy			
Right	51.2%	40%	0.351
Left	48.8%	60%	
The average volume of the operated lobe	22.8 ($\pm$ 18.7)	15.7 ($\pm$ 8.8)	0.12
Mean volume of the remaining lobe	5.8 ($\pm$ 5.3)	4.2 ($\pm$ 3.7)	0.001
Nodularity of the remaining lobe			
Nodular	89.4%	83.3%	0.354
Anodular	10.6%	16.7%	
Anatomopathological examination			
lymphocytic thyroiditis	5.6%	36.6%	< 0.001
Vesicular adenoma	25%	70%	<0.001
Oncocytic adenoma	15.6%	33.3%	0.037

The threshold value for the preoperative TSH level with the best sensitivity/specificity ratio was 1.97 mUI/L, with 78.1% sensitivity and 63.3% specificity.

The threshold value for remaining lobe volume with the best sensitivity/specificity ratio was 3.8 cm³, with sensitivity of 40% and specificity of 25.6 %.

In multivariate analysis, preoperatively TSH level > 1.9 (OR=6.47, [2.62;15.98], p <0.0001) and lymphocytic thyroiditis (OR=8.88, [2.94;26.82], p= 0.0001) were associated with higher rates of Hypothyroidism after surgery.

DISCUSSION

The main finding of our study is that a preoperative TSH level higher than 1.9 mUI/L and the presence of lymphocytic thyroiditis were associated with higher rates of Hypothyroidism after surgery. In fact, several studies have examined risk factors of hypothyroidism after hemithyroidectomy as this procedure has been increasingly applied in patients with thyroid diseases.

Although patients are expected to maintain normal thyroid function after lobectomy, some patients develop hypothyroidism, which requires thyroid-hormone substitution.

In our study, 15.7 % of patients developed hypothyroidism

after surgery. Hypothyroidism was subclinical in 93.3% of cases, two patients showed symptoms of clinical hypothyroidism such as asthenia and constipation. A meta-analysis including 51 studies Li & al concluded to a pooled risk of 29.9% (3). In this meta-analysis the risk varies from 0.6% to 60%. A second meta-analysis and systematic review including 32 studies conducted by Verloop & al. showed that the risk ranges from 0% to 43% (6). This disparity is due to different TSH thresholds, duration of patient follow-up, and type of benign thyroid pathologies present in the population being studied (7).

The mean time between surgery and diagnosis of hypothyroidism was 3.7 months with an interval of 1 month to 12 months which suggest an occurrence in the early postoperative period. TSH measurement at 1 month, 3 months, 6 months and 12 months post-operatively is necessary to detect hypothyroidism in at-risk patients(4). Abraham & al.(8) showed a mean time to hypothyroidism 6.6 months while Ahn et al. showed a mean time of 4.3 months(9). Most studies showed that hypothyroidism occurred within 12 months which recommends a postoperative monitoring period of up to 12 months(1,9–11).

In our study, neither age nor sex was correlated with hypothyroidism after surgery. Although several studies concur with our findings (1,2,9). Advanced age and female sex have been reported as a risk factor for hypothyroidism (3,6,12).

Preoperative hyperthyroidism was significantly correlated with the risk of postoperative hypothyroidism in our study. Kaya & al. (13) have reported in their study that permanent hypothyroidism requiring L-thyroxine treatment was observed in 31% of patients operated for toxic nodules. These results show that patients with preoperative hyperthyroidism are more likely to develop postoperative hypothyroidism.

Our results showed that high preoperative TSH level was significantly correlated with the occurrence of hypothyroidism. The TSH value which had the best sensitivity/specificity ratio was 1.97 mUI/L. Cutoff values of preoperative TSH range between 1.7 and 3 mUI/L, mentioned in various studies (10,12,14,15). A higher preoperative TSH level usually indicates a preoperative deficiency in thyroid reserve function(3).

Also, the volume of the remaining lobe was correlated with the risk of hypothyroidism after surgery in our series. The threshold value for remaining lobe volume with the best sensitivity/specificity ratio was 3.8 cm³, with sensitivity of 40% and specificity of 25.6 %. Many studies have shown that remnant thyroid volume is an independent predictor of hypothyroidism after hemithyroidectomy (6,16,17). Lang & al. (17) showed that a remnant volume smaller than 3.2 cm³ is correlated with more than 50% risk (54.2%) for the development of biochemical hypothyroidism after a hemithyroidectomy. These findings are in line with our results.

Lymphocytic thyroiditis is the main risk factor on which most studies agree. In fact, the inflammatory and destructive phenomena of the thyroid parenchyma can compromise the compensatory role of the remaining lobe (6,7). Lymphocytic infiltration is a histopathological

diagnosis that influences post-operative follow-up. It cannot be preoperative predicting factor. The meta-analysis conducted by Verloop & al. has shown that a positive ATPO antibody level predicts the risk of preoperative hypothyroidism (6). In our series, this level was not measured systematically, so its influence could not be studied.

Levothyroxine treatment should be considered in cases of subclinical hypothyroidism with TSH > 10 mIU/L. In the case of mild subclinical hypothyroidism, a wait-and-see strategy is recommended to see if the thyroid levels are normalized. However, patients with cardiovascular risk and subclinical hypothyroidism levothyroxine treatment may be considered (18). In addition Treatment must take into consideration the patient's fragility, particularly in elderly patients (19).

McHenry & al. showed that in patients with a functioning residual lobe of the thyroid gland, the mean dosage of L-T4 required to normalize serum TSH levels was 1.3 mcg/kg/d (20). Buehler & al. showed that the average dose needed to maintain euthyroidism was 1.05 mcg/kg/d(21). A TSH assess were performed after 6-8 weeks with adjustment of the Levothyroxine dose to maintain TSH levels within the normal range.

After reviewing the literature, there is no well-established consensus regarding the management of hypothyroidism after surgery, which depends on the TSH level, clinical symptoms and the patient's background. This is why it is important to identify patients at risk to prevent complications.

The strengths of our study are that it deals with an important subject. Indeed, risk factors for hypothyroidism after hemithyroidectomy need to be finely assessed, since it is a frequent surgical treatment for a wide range of unilateral thyroid pathologies. In addition, we included a significant number of patients. While limitations of our study are the retrospective and monocentric aspect of the study but also the fact that we were unable to assess whether hypothyroidism was transitory or permanent.

CONCLUSION

Hypothyroidism after hemithyroidectomy is not a rare complication. Our study shows that preoperative TSH level greater than 1.9, remaining lobe volume less than 3.8 cm3 and the presence of lymphocytic thyroiditis are associated with higher risk of hypothyroidism. A minimum follow-up and TSH monitoring up to 12 months after surgery is necessary to detect hypothyroidism, which in most cases is subclinical.

REFERENCES

- 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.
- Wormald R, Sheahan P, Rowley S, Rizkalla H, Toner M, Timon C. Hemithyroidectomy for benign thyroid disease: who needs follow-up for hypothyroidism? *Clin Otolaryngol*. 2008 Dec;33(6):587–91.
- Li Z, Qiu Y, Fei Y, Xing Z, Zhu J, Su A. Prevalence of and risk factors for hypothyroidism after hemithyroidectomy: a systematic review and meta-analysis. *Endocrine*. 2020 Nov;70(2):243–55.
- Cooper D, Kaur R, Ayeni FE, Eslick GD, Edirimanne S. Hypothyroidism after hemithyroidectomy: a systematic review and meta-analysis. *Thyroid Res*. 2024 Jul 8;17:18.
- Cao Z, Liu R, Wu M, Xu X, Liu Z. Risk factors for thyroid hormone replacement therapy after hemithyroidectomy and development of a predictive nomogram. *Endocrine*. 2022;76(1):85–94.
- Verloop H, Louwerens M, Schoones JW, Kievit J, Smit JWA, Dekkers OM. Risk of Hypothyroidism following Hemithyroidectomy: Systematic Review and Meta-Analysis of Prognostic Studies. *J Clin Endocrinol Metab*. 2012 Jul;97(7):2243–55.
- Johner A, Griffith OL, Walker B, Wood L, Piper H, Wilkins G, et al. Detection and Management of Hypothyroidism Following Thyroid Lobectomy: Evaluation of a Clinical Algorithm. *Ann Surg Oncol*. 2011 Sep;18(9):2548–54.
- Abraham CR, Ata A, Stain SC, Khalaf ZM, Hazimeh Y. Time to Hypothyroidism Following Hemithyroidectomy. *Cureus*. 14(12):e32837.
- Ahn D, Sohn JH, Jeon JH. Hypothyroidism Following Hemithyroidectomy: Incidence, Risk Factors, and Clinical Characteristics. *J Clin Endocrinol Metab*. 2016 Apr;101(4):1429–36.
- Chu KKW, Lang BHH. Clinicopathologic predictors for early and late biochemical hypothyroidism after hemithyroidectomy. *Am J Surg*. 2012 Apr;203(4):461–6.
- Chaabouni MA, Sellami M, Jameleddine E, Kharrat R, Thabet W, Mnejja M, et al. Predictive factors for hypothyroidy after hemithyroidectomy. *F1000Research*. 2022 Dec 21;11:1355.
- Song HS, Kim CJ, Lee S, Bae JS, Jung CK, Jang J. Risk Factors that Predict Levothyroxine Medication after Thyroid Lobectomy. *Acta Endocrinol Buchar*. 2020;16(4):454–61.
- Kaya S, Yuksek MO, Sari R, Altin O, Sikar H, Kucuk H. Is hemithyroidectomy sufficient in unilateral benign nodular goitre? *Minerva Endocrinol*. 2021 Dec;46(4):406–12.
- Tomoda C, Ito Y, Kobayashi K, Miya A, Miyauchi A. Subclinical Hypothyroidism following Hemithyroidectomy: A Simple Risk-Scoring System Using Age and Preoperative Thyrotropin Level. *ORL*. 2011;73(2):68–71.
- Park S, Jeon MJ, Song E, Oh HS, Kim M, Kwon H, et al. Clinical Features of Early and Late Postoperative Hypothyroidism After Lobectomy. *J Clin Endocrinol Metab*. 2017 Apr 1;102(4):1317–24.
- Moon H, Jung E, Park S, Jung TS, Jeong C, Ju Y, et al. Thyrotropin Level and Thyroid Volume for Prediction of Hypothyroidism Following Hemithyroidectomy in an Asian Patient Cohort. *World J Surg*. 2008 Nov;32(11):2503.
- Lang BHH, Wong CKH, Wong KP, Chu KKW, Shek TWH. Effect of Thyroid Remnant Volume on the Risk of Hypothyroidism After Hemithyroidectomy: A Prospective Study. *Ann Surg Oncol*. 2017 Jun;24(6):1525–32.
- Calissendorff J, Falhammar H. To Treat or Not to Treat Subclinical Hypothyroidism, What Is the Evidence? *Medicina (Mex)*. 2020 Jan 19;56(1):40.
- van Vliet NA, Noordam R, van Klinden JB, Westendorp RG, Bassett JD, Williams GR, et al. Thyroid Stimulating Hormone and Bone Mineral Density: Evidence From a Two-Sample Mendelian Randomization Study and a Candidate Gene Association Study. *J Bone Miner Res*. 2018 Jul 1;33(7):1318–25.
- McHenry CR, Slusarczyk SJ. Hypothyroidism following hemithyroidectomy: Incidence, risk factors, and management. *Surgery*. 2000 Dec;128(6):994–8.
- Buehler LA, Madhun NZ, Bena J, Nasr C, Scharpf J, Zhou K. Hormonal Outcomes Following Hemithyroidectomy. *Otolaryngol Neck Surg*. 2021;164(5):1011–8.