



Differences in incidence of hypothyroidism and levothyroxine dosages in relation to right or left lobe hemithyroidectomy

- An exploratory retrospective study

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Table of contents

1	Background	3
2	Research questions and aims	4
3	Study design.....	4
4	Patients	4
4.1	Inclusion criteria.....	4
4.2	Exclusion criteria	4
5	Primary and secondary parameters.....	5
6	Methodology.....	5
6.1	Statistical analysis	5
6.1.1	Null hypothesis.....	6
6.1.2	Secondary hypotheses	6
6.1.3	Number of patients.....	6
7	Data protection	6
8	Benefit-risk assessment	6
9	References	7
10	Appendix	7
10.1	Abbreviations and acronyms:	7

1 Background

Thyroid hormones, thyroxine (T4) and triiodothyronine (T3), are produced in the follicular cells of the thyroid gland and can impact nearly every cell in the human body. They are essential to the human metabolism, influence the basal metabolic rate, bone growth, neural maturation, the body's sensitivity to catecholamines, cell development and differentiation as well as protein, fat and carbohydrate metabolism. With about 5000 µg, the thyroid is the largest storage of T4.^{1(p303)} Therefore, the maintenance of adequate thyroid hormones levels is crucial for the patient's quality of life after a hemithyroidectomy. The thyroid is constituted of a right and a left lobe as well as a connecting isthmus. In most patients, the right lobe is significantly larger than left lobe.² In a 2009 study by Ying and Yung, the right lobe was 6.8ml as opposed to the left lobe with a volume of 5.66ml.³ Although the remaining lobe adapts and continues to grow up to 30% from its original size to compensate for the loss,⁴, thyroid hormone supplementation is required in approximately 22% of all patients after thyroid lobectomy.^{5,6} In order to predict the necessity of thyroid hormone replacement therapy after hemithyroidectomy, risk factors such as a higher TSH before surgery, but also the resected thyroid volume have been identified in the past. Surprisingly, the resected thyroid volume showed significant negative correlation with postoperative TSH levels in a 2015 study by Lee et al.⁵ Previous studies aiming at optimizing post-surgery levothyroxine dosages incorporated sex, age, body surface area (BSA) and body mass index (BMI) but not if the right of left thyroid gland was resected into their calculations.^{7,8} Therefore, the study at hand aims at investigating a possible difference in levothyroxine requirements depending on the side of the resection to ensure adequate treatment.

2 Research questions and aims

- **Research Questions:** We hypothesize a possible influence of right vs left hemithyroidectomy on developing postoperative hypothyroidism as well as treatment dosage.
- **The aim** of this study is to be able to better predict the necessity, dosage and starting point of levothyroxine treatment after a hemithyroidectomy.

3 Study design

The study at hand is an exploratory retrospective study conducted on approximately 1250 patients who received a hemithyroidectomy at the Medical University of Vienna, Department of General Surgery, Division of Endocrine Surgery. A possible confounding factor is that the underlying conditions such as goiter or nodules which lead to the surgery might differ in the patients.

4 Patients

All patients who received a hemithyroidectomy at the Department of General Surgery, Division of Endocrine Surgery between 1994 and 2018 will be included in the study which are around 50 per year totalling around 1250 patients. Due to the study design, no power calculations have been conducted beforehand. However, considering similar studies^{5,6}, this sample size was deemed sufficient in order to achieve valid results and a statistical power of 0.8.

4.1 Inclusion criteria

- 18 years
- Males and females
- St.p. hemithyroidectomy

4.2 Exclusion criteria

- Radiation therapy
- Pregnancy
- Previous thyroid surgery (e.g. nodule removal surgery)

Differences in Levothyroxine requirements after hemithyroidectomy



5 Primary and secondary parameters

The occurrence of post-surgery hypothyroidism and levothyroxine dosage is the primary outcome parameter. The secondary outcome parameter is the timespan between hemithyroidectomy and the need for levothyroxine treatment.

6 Methodology

The list of patients who underwent a hemithyroidectomy will be provided by the IT4Science department via a data extraction from the RDA database. Further information necessary for the analysis (side of hemithyroidectomy, type and dosage of treatment) will be extracted from the AKH-Informationsmanagement (AKIM) at the General Hospital of Vienna (AKH), analyzed and pseudonymized by Dr. Carola Deischinger and, then, safely secured on a server at the Chiari Stoffwechsellambulanz.

6.1 Statistical analysis

The collected data will be analyzed by descriptive statistics and illustrated in SPSS (Version 22) by using graphs, tables and boxplots. All data is password protected and anonymized to ensure adequate privacy protection.

Normally distributed data will be described by calculating median, mean and standard deviation. Patient baseline characteristics will be described as percentages and frequencies for categorical variables or mean and median values and standard deviation for normally distributed continual variables. In order to ensure comparability, a Levene's Test for Equal Variances will be performed. Differences of characteristics between the groups will be analyzed by unpaired T- tests for continuous variables. Possible confounding factors such as age, sex, underlying disease and BMI will be identified and adjusted for in a multiple logistic regression model.

In order to compare the levothyroxine dosages, a parametrical test (t-test) with a significance level of $p < 0.05$ will be performed. Adequate transformations such as the Levene's Test for Equal Variances will be applied to deal with not normally distributed residues and, thus, ensure comparable variances. For illustrational purposes, bar charts, histograms and boxplots will be used.



6.1.1 Null hypothesis

H₀: The side of the resected thyroid lobe in a hemithyroidectomy does not influence the hypothyroidism occurrence and levothyroxine dosage requirements after surgery.

6.1.2 Secondary hypothesis

H₀: There are no sex differences between men and women depending on the side of the resected thyroid lobe in the occurrence of hypothyroidism and the needed levothyroxine dosage after a hemithyroidectomy.

6.1.3 Number of patients

Approximately 1250 patients

7 Data protection

Various measures will be implemented to ensure data protection and avoid unauthorized use and loss of data. Data will be stored on a secure server at the Medical University of Vienna, Chiari Stoffwechselambulanz which is password protected and kept in a locked room. Only authorized personnel have access to the Chiari Stoffwechselambulanz and the server. A full description of the technical and organizational measures can be provided on request. Data protection for this study is the responsibility of Dr. Carola Deischinger.

8 Benefit-risk assessment

Although there is no direct benefit for the patients due to the retrospective character of the study, negative side effects are not to be expected as well. Besides a possible data breach, which is minimized by pseudonymization and data protection, the patients are not at risk in any way. The results obtained in this study can be used to optimize patient care.

9 References

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10 Appendix

10.1 Abbreviations and acronyms:

BMI – Body mass index

BSA – Body surface area

SPSS - Statistical Package for the Social Sciences

Differences in Levothyroxine requirements after hemithyroidectomy