

Hemithyroidectomy for Unilateral Thyroid Disease

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Rezumat

Hemithyroidectomy în patologia tiroidiană unilaterală

Scop: de a identifica ratele de recurență și de apariție a hipotiroidismului după hemithyroidectomy pentru boală nodulară tiroidiană unilaterală, precum și avantajele acesteia comparativ cu rezecțiile radicale bilaterale.

Metode: Cincizeci de pacienți supuși lobectomiei tiroidiene pentru patologie tiroidiană unilaterală au fost incluși în studiu. Urmărirea a constat în măsurarea funcției tiroidiene prin teste hormonale în prima lună și apoi la fiecare 3 luni și control ecografic anual postoperator. Recurența, definită ca cel puțin un nodul cu diametrul de 5 mm sau mai mare la nivelul lobului restant, și nevoia de tratament postoperator cu tiroxină au fost analizate, precum și relația dintre acestea și tratamentul medical preoperator, rezultatele histologice, numărul și diametrul nodulilor tiroidieni, durata perioadei de urmărire.

Rezultate: Incidența recurențelor după hemithyroidectomy a fost de 12% după o perioadă medie de urmărire de 25,2 luni (limite 10-43), în timp ce incidența hipotiroidismului clinic necesitând terapie de substituție cu tiroxină a fost de 8%. Sexul, vârsta, tratamentul substitutiv sau supresiv preoperator, evaluarea histologică, prezența nodulilor multipli și diametrul acestora nu au fost factori predictivi pentru recurențe sau pentru necesitatea administrării de tiroxină.

Concluzii: Hemithyroidectomy în patologia tiroidiană unilaterală prezintă o rată moderată de recurență, rate scăzute de apariție a

hipotiroidismului și complicații postoperatorii rare, cu perioadă scurtă de spitalizare.

Cuvinte cheie: patologie tiroidiană benignă, hemithyroidectomy, hipotiroidism, recurență, glandă tiroidă

Abstract

Aim: To identify rates of recurrence and hypothyroidism after hemithyroidectomy for unilateral nodular thyroid diseases and its advantages over bilateral radical resections.

Methods: Fifty patients who underwent thyroid lobectomy with unilateral thyroid disease were included. Follow-up with thyroid function tests on the first month and then once every three months, as well as ultrasonography controls once a year were performed postoperatively. Recurrence, which was accepted as at least one nodule with a diameter of 5 mm on the remnant lobe, and the need for postoperative thyroxine therapy were analysed, along with the relation of both with preoperative medical therapy, histological results, numbers and diameters of thyroid nodules, follow-up duration.

Results: The incidence of recurrent disease after hemithyroidectomy was 12% after a mean follow-up time of 25.2 months (range, 10-43) while the incidence of clinical hypothyroidism which needs thyroxine therapy was 8%. Gender, age, substitutive and suppressive therapy before operation, histological evaluation, the presence of multiple nodules and diameter of nodules were predictive of neither recurrence nor postoperative thyroxine therapy.

Conclusion: Hemithyroidectomy for unilateral thyroid disease has a moderate rate of recurrence, low rates of hypothyroidism and rare postoperative complications, with short hospital stay.

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Key words: benign thyroid disease, hemithyroidectomy, hypothyroidism, recurrence, thyroid gland

Introduction

Thyroid nodules are common, as 4-10 % of the US population have palpable nodules with female predominance (6.4% versus 1.6%, Framingham population-based study) (1). This nodule prevalence may be tenfold higher when nodule detection is performed by ultrasound and according to autopsy data it is approximately 50% (2,3). Despite this high prevalence only 2% of nodules were found to have occult carcinoma (4). However the extent of the surgery for thyroid nodules, especially with monolobar expression, is controversial. It has been generally accepted that a pathologic process of the thyroid involves the whole gland. Total thyroidectomy is considered as the treatment of choice for multinodular goiter in most experienced centers (5-7). However, hemithyroidectomy for thyroid pathologies of one lobe is a favorable procedure with low complication rates (8). Besides, the necessity of postoperative life-long thyroxine therapy with its insidious side effects is significantly lower in hemithyroidectomy than the other more extensive surgical procedures of the thyroid such as subtotal, near total and total thyroidectomy (9,10). On the other hand, recurrence after hemithyroidectomy represents the major problem, but reoperation for recurrent disease is rather low. In addition, hemithyroidectomy studies are generally retrospective and the assessment of the contralateral lobe may not have been done with meticulous care, which would be responsible for high recurrence rates.

The aim of the present prospective study is to define the factors that are predictive of recurrence and hypothyroidism in patients who undergo hemithyroidectomy for diseases with monolobar expression and assess the efficacy of hemithyroidectomy for this condition.

Materials and Methods

Ethical approval was granted by the hospital's ethics committee (Ethical approval code: Diskapi Teaching and Research Hospital Ethics Committee: 01.06.2005-16/3). All the patients gave informed consent. Fifty consecutive patients who fulfilled study criteria and underwent hemithyroidectomy with a clinical diagnosis of solitary nodule or nodules of one thyroid gland from March 2005 through October 2008 were included in the study. The indications for hemithyroidectomy were nodule(s) with at least a diameter of 30 mm, toxic nodule, suspicious / non diagnostic / follicular-hurthe cell neoplasm on fine needle aspiration cytology (FNAC), and symptomatic disease. The study was based on the presence of a nodule or nodules according to preoperative ultrasound (US) examination in which FNAC was benign and intraoperative histological examination of frozen section (FS) showed non-malignant

disease. The patients with malignant FNAC or FS were excluded from the study. Recurrence and the need for postoperative thyroxine therapy were analysed and the relation of both with preoperative medical therapy, histological results, numbers and diameters of thyroid nodules, follow-up duration were explored. Postoperative complications and discharge days were also recorded.

Preoperative ultrasound examinations of the patients were done by different radiologists, but all the postoperative long-term follow up was performed by the same radiologist. The size and number of nodules in the related lobe preoperatively and in the remnant lobe postoperatively in the follow-up period were recorded. On the preoperative US evaluation the patients who had a nodule or nodules which had a minimum size of 5 mm diameter on the contralateral lobe were excluded, but heterogeneity, irregularity and pseudonodular parenchyma irregularity on the contralateral lobe were not accepted as a criteria for exclusion. After the operation all the patients were followed up with US control yearly. Recurrence on follow-up in the remnant lobe was accepted as at least one nodule with minimum 5 mm diameter.

Thyroid function was established biochemically by measurement of serum concentrations of thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4). All the patients followed up with thyroid function tests on the first month and after then once every three months postoperatively. TSH level of 4.5 μ IU/L was accepted as the upper limit of normal. The diagnosis of thyroid dysfunction and the decision of medical treatment were performed by the same endocrinologist. Patients with associated subclinical hypo-thyroidism had a high TSH level in conjunction with normal free thyroid hormone (T4 and T3) estimates. Patients with clinical hypothyroidism exhibited reduced FT4 estimates and increased TSH levels.

The surgical procedure of hemithyroidectomy (lobectomy and isthmusectomy) was performed with a short incision length (maximum 4 cm) and care was taken not to disturb the contralateral lobe that conserves the normal tissue planes.

Indications for reoperation of recurrence were the presence of a nodule bigger than 3 cm in diameter, the risk of malignancy, esthetic preference, and the presence of compressive symptoms.

Statistical software package SPSS 11.5 was used to perform all the statistical analyses. Univariate statistical analysis was conducted using student t test and a Chi-square test or Fisher's exact test where appropriate. Data is given as number of patients (%) or mean $\pm$ SD. Multivariate logistic regression was performed. $p < 0.05$ was accepted as significant.

Results

The mean age was 42.3 ± 12.7 years with female dominance. 36 (72%) patients were female and 14 (28%) patients were male. Preoperative complaints were swelling in the neck in 25 (50%) patients, shortness of breath in 5 (10%) patients, palpitation and tremor in 13 (26%) patients and none in 7 (14%) patients. 13 (26%) patients who had toxic nodules

were treated preoperatively with antithyroid drugs. Thirty seven patients (74%) were euthyroid. The FNAC cytological examinations of the fifty patients were as follows: 82% (41/50) benign, 10% (5/50) non diagnostic, 6% (3/50) suspicious, 2% (1/50) follicular neoplasm. Hemithyroidectomy indications for patients were as follows: nodule(s) with a diameter of at least 30 mm, toxic nodule, suspicious / non diagnostic / follicular-hurthe cell neoplasm on FNAC, and symptomatic disease in 23, 13, 9, and 5 patients respectively. The patients underwent right (60%, 30/50) or left (40%, 20/50) hemithyroidectomy and had a mean follow-up of 25.2 (minimum-maximum, 10-43) months.

Postoperative complications such as hematoma, transient hypocalcaemia, permanent hypocalcaemia, and recurrent laryngeal nerve injury were seen in 0%, 4%, 0%, and 0% of patients, respectively. 30% (15/50) of patients needed suction drain catheter, while all of the remaining catheters were removed on the first postoperative day. 76% (38/50) of patients were discharged on the first postoperative day and the mean discharge interval was 1.44 ± 0.97 days. During follow-up period four patients (8%) were diagnosed with clinical and four

patients (8%) with subclinical hypothyroidism so that the incidence of total hypothyroidism was 16%. Thyroxin therapy was started in four patients with clinical hypothyroidism. None of the patients (0/50) needed reoperation in the follow-up period of 25.2 months (range, 10-43).

The incidence of recurrence was 12% (6/50) and five (5/6, 83.3%) of the recurrence nodules had diameters of 5-9 mm, of which only one (1/6, 16.7%) had a diameter equal or larger than 10 mm. Five patients had a second accompanying nodule but only one patient's second nodule had a diameter larger than 5 mm so only this patient's situation was accepted as multiple recurrence. Recurrent patients are detailed in Table 1.

The need for thyroxin therapy due to hypothyroidism was 8% (4/50). Age and gender did not affect the rates of recurrence and the need for thyroxin therapy in the event of hypothyroidism. The incidence of recurrence according to preoperative numbers and diameters of thyroid nodules, toxicity of the nodule, and resected lobe pathology, are detailed in Table 2.

The incidence of postoperative thyroxin therapy in the event of hypothyroidism according to numbers and diameters

Table 1. Preoperative and follow-up variables of six recurrent patients with their demographic characteristics

Age	Gender	Preoperative Nodule Number & Size (mm)	Nodule Function	FNAC	Resected Lobe Pathology	Recurrent Nodule Size (mm)
64	Male	One, 30x30	Toxic	Benign	Nodular hyperplasia	9x7
35	Female	One, 30x24	Nontoxic	Benign	Nodular hyperplasia	11x6
64	Female	One, 41x34	Toxic	Benign	Nodular hyperplasia	8x6
24	Female	One, 25x13	Toxic	Benign	Nodular hyperplasia	6x4
68	Male	One, 20x20	Nontoxic	Non diagnostic	Nodular hyperplasia	*6x3, 5x4
65	Female	One, 50x50	Nontoxic	Benign	Nodular hyperplasia	5x5

*multiple recurrence

Table 2. The numbers and the diameters of thyroid nodules, preoperative hormonal status of nodule, and resected lobe pathology did not have a statistical relation with the recurrence after thyroid hemithyroidectomy. Data is given as number of patients (%) or mean $\pm$ SD

	Recurrence			
Variable	n (%)	n	(%)	p value
Nodules in preoperative USG				
0-29 mm	16 (32)	2	12.5	0.635
30 mm & ↑	34 (68)	4	11.8	
Nodule number in preoperative USG				
single	41 (82)	6	14.6	0.283
multiple	9 (18)	0	0	
Preoperative nodule hormonal status				
Nontoxic	37 (74)	3	8.1	0.173
Toxic	13 (26)	3	23.1	
Resected lobe pathology				
Nodular hyperplasia	41 (82)	6	14.6	0.351
Follicular adenoma	7 (14)	0	0	
Lymphocytic thyroiditis	2 (4)	0	0	

Table 3. The numbers and the diameters of thyroid nodules, preoperative hormonal status of nodule, and resected lobe pathology did not have a statistical relation with postoperative hypothyroidism. Data is given as number of patients (%) or mean $\pm$ SD

Variable	n (%)	Thyroxine Therapy		p value
		n	(%)	
Nodule size in preoperative USG				
0-29 mm	16 (32)	2	12.5	0.38
30 mm & ↑	34 (68)	2	5.9	
Nodule number in preoperative USG				
single	41 (82)	4	9.8	0.44
multiple	9 (18)	0	0	
Preoperative nodule hormonal status				
Nontoxic	37(74)	3	8.1	0.73
Toxic	13 (26)	1	7.7	
Resected lobe pathology				
Nodular hyperplasia	41 (82)	3	7.3	0.90
Follicular adenoma	7 (14)	1	14.3	
Lymphocytic thyroiditis	2 (4)	0	0	

of thyroid nodules, preoperative toxicity of the nodule, and resected lobe pathology are detailed in Table 3.

Gender, age, preoperative toxicity of the nodule, histological evaluation, the presence of multiple nodules and diameter of nodules were not predictive for recurrence or postoperative thyroxine therapy. Only the duration of follow-up was predictive for recurrence while it was also not predictive for postoperative thyroxine therapy in univariate analysis.

In multivariate logistic regression none of the parameters (age, follow up duration, size and the number of the nodules, pathology) reached statistical significance to be independent predictors on recurrence.

Discussion

Thyroid disease recurrence in the remnant tissue after hemithyroidectomy for benign disease was the main problem which creates the preconception that pathologic processes of the thyroid involve the whole gland. This has led surgeons to perform total or near total thyroidectomy to prevent the risk of recurrence. The indications for total thyroidectomy include Graves' disease, toxic multinodular goiter, benign multinodular goiter and malignant diseases because these disorders are thought to affect the whole gland and may recur in the residual lobe (11). Indeed limited surgery such as nodular excision has very high rates of recurrence. However hemithyroidectomy with fewer complications is the basic surgical procedure for nodular goiter restricted to a lobe. Also, the unilateral hemithyroidectomy procedure which was routinely performed in this study may be a definitive treatment, as long as the histological diagnosis confirms the benignity of the lesion (11).

If the diagnosis of the hemithyroidectomy specimen is malignant, as an advantage of this procedure, completion of the thyroidectomy will be safer due to the conserved normal tissue planes of the other lobe. Besides, if low risk papillary micro carcinoma is detected in one lobe, it is commented in

a review that lobectomy with isthmusectomy (hemithyroidectomy) and central node dissection would be adequate (12). Additionally, in a review by Yasuhiro Ito and Akira Miyauchi it is suggested that most papillary carcinomas, especially papillary microcarcinoma (PMC), remain harmless and are not life threatening and the best therapeutic strategy for low risk PMC is just to follow-up (12). Papillary microcarcinoma, the most common subtype, is often identified incidentally in thyroid tissue removed for benign clinical nodules or diffuse processes (e.g., thyroiditis). In this clinical situation, over 99% are cured by simple hemithyroidectomy, which advocates this procedure (13). Furthermore, epidemiologic reports from the US showed that although the incidence of thyroid carcinoma increased between 1973–2002, its mortality has not changed during this period, indicating that the increased incidence is predominantly due to increased detection of PMC (14). We think that a considerable amount of malignant conditions may be treated with only hemithyroidectomy.

Hemithyroidectomy, especially for lesions with monolobar expression and cytologically defined as follicular neoplasm in which FNAC cannot distinguish between benign and malignant follicular structured neoplasms, is a good option (15). Besides, a second surgical procedure can be performed easily if the diagnosis of malignancy is confirmed by the final histological examination. This approach was defined as diagnostic hemithyroidectomy and has an advantage of completing thyroidectomy in a sterile, untouched area with low morbidity (11). The necessity for re-entry into previously operated fields presents a tenfold increase in the risk of complications (16,17). Therefore we also do not suggest digital exploration of the contralateral lobe although it has been advocated by some authors in order to make sure that no abnormality of the thyroid gland remains undetected and untreated (18,19). Additionally, hemithyroidectomy was considered as the adequate treatment for follicular and Huthle cell neoplasms with a preoperative FNAC diagnosis (20, 21).

As the focus of this study were benign thyroid nodules,

FNAC with benign characteristics or at least with non-malignant features (suspicious and non-diagnostic patients involved) were included into research. Also, intraoperative frozen section (FS), an examination which has similar diagnostic accuracy with FNAC (22-24), was accomplished for the proof of non-malignant disease. FNAC and FS were used together in this research and remarkably no malignancy was confirmed by the final histological examination of any patient (0/50), but in our opinion, routine frozen section examination is not necessary in a patient with a benign fine needle aspiration biopsy result. FNAC was generally accepted as adequate for preoperative evaluation and even for follow-up, as it has been reported that virtually all nodules (98%-99.3%) found to be benign at aspiration will remain benign if followed for 10 years (25, 26).

Reoperation after hemithyroidectomy will be necessary if the symptomatic disease recurs. However, symptomatic recurrence usually takes decades to manifest, if ever, and a remedial procedure does not significantly increase the complication rate (18). The recurrence rate for multinodular goiter in patients undergoing unilateral thyroidectomy is 1.2% to 26%, with the average time to recurrence being 10 to 16 years. For solitary thyroid nodule it was 26% at 4-year follow-up, for unilateral non-toxic goiter was 33.9% after a mean follow-up time of 79.9 months (19,27-29). The recurrence rate of this study, as for diseases with monopolar expression, after a mean follow-up of 25.2 months is 12%, which is acceptable and similar. Our study was prospective and therefore included carefully selected patients according to predetermined criteria making sure that the disease is unilateral, the contralateral lobe is meticulously searched for nodule or nodules which had a minimum size of 5 mm diameter. The lower recurrence rate is probably due to both careful selection of patients and the short follow-up period, because as the follow-up period gets longer recurrence rates statistically increase. However during this follow-up period no patient had the indication for reoperation for recurrence as it was expressed by the presence of a nodule bigger than 3 cm in diameter, the risk of malignancy, esthetic preference, and the presence of compressive symptoms (29). Bellantone et al reported the reoperation rate of hemithyroidectomy was 7.4% after a mean follow-up time of 79.9 months and the predictive factors were the resected thyroid weight, presence of multiple nodules, and the lack of postoperative hormonal therapy. Furthermore, the last two parameters were also reported as predictive factors for recurrence (29). Many factors other than the resected thyroid weight were examined in this study, none of them being found predictive of either recurrence or reoperation, but short follow-up duration should be taken into consideration.

Hemithyroidectomy may be preferred because of its lower complication rate, as hematoma, transient hypocalcaemia, permanent hypocalcaemia, and recurrent laryngeal nerve injury were seen in 0%, 4%, 0%, and 0% of patients respectively. The recurrent laryngeal nerve complication rates of hemithyroidectomy are similar with other reported series (0% to 3%) (30-33). The complication rates of hemithyroidectomy were lower than total thyroidectomy in which the incidences of hematoma were 0.4%, of permanent hypoparathyroidism 1% to

5%, and of temporary hypoparathyroidism 5%-30% (30-33). The higher complication rate associated with total thyroidectomy is expected due to the greater extent of surgery. Therefore unilateral thyroidectomy would be a good choice for monolobar expressed disease of the thyroid.

It is likely that the risk of nodular recurrence of adenoma is theoretically low because it is considered to be a solitary disease in the normal thyroid gland, rather than a lesion that is developing in a diseased thyroid gland, as usually seen in nodular hyperplasia (19). Similarly, in our study, all the recurrences developed in the nodular hyperplasia group (%14.6, 6/41), but due to the low number of patients with follicular adenoma (%0, 0/7) and lymphocytic thyroiditis (%0, 0/2), the type of the pathology of the resected lobe did not reach statistical significance as a predictive factor ($p > 0.05$). However, it is not possible to differentiate adenoma and nodular hyperplasia preoperatively, so that the postoperative pathologic result would not help us regarding the decision of the surgical procedure.

Hypothyroidism is another well recognized complication after thyroid surgery. In this study, hypothyroidism was diagnosed as the increase of TSH level over $4.5 \mu\text{IU/L}$, which was recommended by Hollowell et al in from their National Health and Nutrition Examination Survey (NHANES III) (34). The reported incidence of hypothyroidism following hemithyroidectomy varies from 5.0% to 41.9% (35). Hypothyroidism incidence of 16% (8% clinical and 8% subclinical) in our study is also within this range. Besides the well known clinically overt complications, subclinical hypothyroidism has been associated with an increased risk of developing cardiovascular disease, neuropsychiatry symptoms and progression to overt hypothyroidism (36-39). Hypothyroidism is unavoidable after total thyroidectomy and its only practical therapy is per oral ingestion of thyroid hormone, in which long term usage is associated with side effects including arrhythmias, and osteoporosis. However, empirical use of thyroxin following hemithyroidectomy to treat hypothyroidism and to reduce the risk of abnormalities developing in the contralateral lobe has fallen out of favor (31). Therefore we advocate hemithyroidectomy for benign thyroid diseases with monolobar expression, as only four patients (8%) needed thyroxin therapy.

The aim of drain replacement after thyroid surgery is to drain off hemorrhage which would compress the air passages and produce respiratory failure (40,41). This life-threatening complication prompts the surgeon to use drains after thyroid surgery especially for the radical ones. Although postoperative complications cannot be prevented by using drains after total thyroidectomy or lobectomy for benign thyroid disorders, the drains are used routinely in most surgical centers and generally in our institution after total thyroidectomy (42). However, their usage after hemithyroidectomy is not routinely recommended (43). In the present study, the incidence of drain replacement after hemithyroidectomy was 30% (15/50), which was significantly lower than the total thyroidectomy at least in our institution. This low incidence is another advantage of hemithyroidectomy, as it is reported that the use of drains prolongs the hospital stay, increases postoperative pain and

may be associated with an increased risk of infective complications (42). Because all of the catheters were removed on the first postoperative day, hemithyroidectomy becomes promising as a day-case surgery which would have benefits for both the patients and healthcare providers.

Thyroid surgery is performed using general anesthesia by the majority of surgeons in current practice; however thyroidectomy using local anesthesia appears to be safe and applicable (44). Although local anesthesia is appropriate for all types of thyroid surgery, it may be preferred for hemithyroidectomy, which will support day-case feasibility of this procedure and thereby decrease cost. The feasibility and safety of the day-case thyroidectomy was advocated in several studies (45,46). Hemithyroidectomy may have prominent economic benefits because it is associated with shorter operation time and hospital stay, lower operative complications, lower requirements for postoperative thyroxin therapy and operation cost than other radical resections.

Conclusions

It is concluded in this study that only the duration of follow-up may be predictive for recurrence, while no other predictive factor was found for postoperative thyroxin therapy after hemithyroidectomy. The complication rate of hemithyroidectomy for unilateral thyroid disease is lower than for total thyroidectomy. The rate of recurrence is moderate and symptomatic recurrence usually takes decades to manifest, so that reoperation for recurrent disease is low. Also, the completion of the thyroidectomy will be safer due to the conserved normal tissue planes of the contralateral lobe. The decreased usage of thyroxin therapy and protection from its long term side effects are the advantages of hemithyroidectomy. Besides short incision and lower necessity for drainage for cosmetic appearance, commonly one day hospitalization and lower cost are other favorable factors. Therefore, we consider that patients with unilateral disease can safely undergo unilateral thyroidectomy. However, further studies with more numbers of patients and longer follow-up duration would be appropriate.

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