ORIGINAL ARTICLE

# Is hemithyroidectomy a rational management for benign nodular goitre?

## A Multicentre Retrospective Single Group Study

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## ABSTRACT

Background: The incidence and potential risk factors for the recurrence of benign nodular goitre after unilateral thyroidectomy are not clearly defined. The aim of this study was to assess the rate of progression of nodular goitre in the contralateral thyroid lobe and of hypothyroidism requiring replacement therapy after unilateral thyroid lobectomy for benign nodular goitre.

Patients and Methods: Patients who underwent hemithyroidectomy for benign nodular goitre between 2000 and 2009 were included in the study. The primary outcome of this study was the reoperation rate for recurrent goitre, the rate of progression of nodular goitre and the rate of hypothyroidism requiring L-T4 replacement therapy. Clinical factors that have an effect on progression were further analysed.

Results: 259 patients were included for study. Progression of the nodular goitre in the remnant lobe was observed in 32% (n = 83) of the patients. However, over time, only 2% of these 83 patients underwent contralateral hemithyroidectomy due to this progression. Fifty-six (22%) patients required L-thyroxin replacement due to persistent hypothyroidism after hemithyroidectomy. The factors shown to affect progression of nodular goitre were advanced age, preoperative hyperthyroidism, preoperative diagnosis of toxic nodular goitre and the presence of surgical indication for a toxic goitre causing hyperthyroidism and a definitive pathological diagnosis of nodular hyperplasia.

Conclusion: There was a progression of the nodular goitre in the remnant lobe in about one-third of the patients who underwent hemithyroidectomy. However, only 2% of these patients underwent complementary contralateral hemithyroidectomy due to clinical progression in 31 months of follow-up.

## KEYWORDS

Benign nodular goitre, hemithyroidectomy, hypothyroidism, recurrence

## INTRODUCTION

Benign nodular goitre is the most common endocrine disorder, especially in countries where iodine deficiency is endemic.[1] Surgery is the common method for the treatment of benign nodular goitre, whereas radioactive iodine is considered a good treatment option as well.[2] The optimal operative strategy for treating benign nodular goitre remains controversial. Factors affecting the extent of resection are mostly the risk of postoperative hypothyroidism and rate of surgical complications.[3-9] Hemithyroidectomy is the basic surgical procedure for benign nodular goitre restricted to one lobe. In patients who have undergone hemithyroidectomy, there is a

potential for a progression of the disease in the remnant lobe.[3] The incidence and potential risk factors for the development of such progression after hemithyroidectomy are not clearly defined.[6-8]

Management of benign nodular goitre is surgical if it is symptomatic, or fine needle aspiration biopsy turns out to be suspicious for malignancy. Patients with nodules other than these can be followed up. Therefore, multiple nodules in both lobes should not lead to bilateral surgery if the nodules on one side are asymptomatic and benign. This prevents 70-80% of patients from having permanent hypothyroidism.[3]

The aim of this retrospective study was to assess the rate of reoperation of the remnant thyroid lobe in patients living in an iodine-deficient region who had undergone unilateral hemithyroidectomy for benign nodular goitre.

## PATIENTS AND METHODS

### Study design and setting

The study was planned as a multicentre, retrospective, single-arm cohort study (TESSG-TINOTA Study).

### Patients

Patients who underwent surgery at a tertiary referral hospital with an endocrine surgery unit between 2000 and 2009 were included in the study. All patients who had undergone hemithyroidectomy for whom a preoperative fine needle aspiration biopsy had shown a benign goitre were included in the study. Hemithyroidectomy was defined as a thyroid lobectomy and isthmusectomy with preservation of the contralateral thyroid lobe.

### Ethics

The Marmara University School of Medicine Research Ethics Committee approved the study protocol. Study variables were retrieved from prospectively collected data at each institution's archives. A retrospective chart review was done from consecutive series of patients operated during the study period. Patients who were included in the study were operated on by the same surgeon at each single institution. Only patients older than 18 years were included in the study. We excluded patients who turned out to have cancer after the final pathological results/observations, whose preoperative thyroid function tests and neck ultrasonography results were not available, who were known to be pregnant or lactating, who had previously undergone more than one thyroid operation or who were not available for follow-up after the initial thyroidectomy.

### Outcomes

The primary outcome was the number of patients who underwent secondary surgery for thyroid disease (complementary contralateral lobectomy). Secondary outcomes were the progression rate (increase in size and number of nodules or appearance of new nodules in the remnant lobe), the number of patients with postoperative hypothyroidism who required thyroxin treatment, the indications for contralateral lobectomy and the factors that predicted progression rate.

### Data

Factors which were assessed for disease progression included the following: patient's age at the time of surgery, gender, number of nodules and the diameter of the largest nodule in the removed lobe, the number of nodules in the remnant lobe and the diameter of the largest, the functional status of the thyroid gland, final histopathological findings, indications for surgery, previous exposure to ionising radiation, having a family history of thyroid cancer, serum anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) levels and length of follow-up.

Progression was defined as the need for complementary contralateral lobectomy or the appearance of new nodules, or an increase in size of the nodules in the remnant lobe of at least 3 mm.

A positive family history was defined as the occurrence of thyroid cancer (any type) for any first-degree relative. Previous radiation exposure was defined as any occupational exposure to radiation, accidental exposure to environmental radiation or receiving any radiation as a form of medical treatment.

Having high titres of any or both antibodies (against TPO and Tg) in the serum was regarded as thyroid autoimmunity regardless of pathology assessment.

Serum TSH, free T3, free T4, anti-TPO, anti-Tg calcium levels and neck ultrasonography results were retrieved from the database. Current permanent use of L-thyroxin was noted. Also, indications for the complementary contralateral lobectomy surgery, final histopathology and operative complications were recorded.

### Statistical analysis

Statistical analyses were done by the SPSS software package (version 11.0). A two-tailed chi-square or a Fisher's exact test were used to compare categorical variables, whereas independent two-sample t-tests were used for continuous variables. Continuous variables were given as mean (± standard deviation; SD). A logistic regression test was used to analyse the independent factors for progression. Factors which were found to be significant in the univariate analysis were tested by multivariate analysis in order to find independent factors. All statistical tests were two-sided and a p value of less than 0.05 was considered significant.

## RESULTS

A total of 259 patients from nine tertiary endocrine surgery units in Turkey, who had undergone hemithyroidectomy between November 2000 and December 2009, were included in the study. The mean age of the patients was 48 years and 75% were female. Of the patients, 60 (23%) had overt hyperthyroidism and 12 (5%) patients had elevated levels of at least one of two thyroid antibodies. Two patients had a family history of thyroid surgery. No patients had a history of previous radiation to the neck. Most patients (n = 195; 75%) had no nodules in the remnant lobe as a preoperative ultrasonography finding. The mean size of the largest nodule in the remnant lobe was 9.3 ± 5.3 mm for patients with at least one nodule left in situ after the hemithyroidectomy (*table 1*).

The most common indications for surgical treatment were hyperthyroidism (n = 66; 25%) and compression of a solitary normo-active nodule (n = 65, 25%; *table 2*). The most common findings were nodular hyperplasia and colloid nodules (n = 176; 68%). The mean follow-up time was 31 (25.5; *table 3*) months within the range of 6-126 months.

Fifty-six (22%) patients received L- thyroxin supplementation due to permanent hypothyroidism after the initial hemithyroidectomy. Anti-TPO and/or anti-Tg titres (autoimmunity) were not found to be predictive for hypothyroidism requiring supplementation after surgery (*table 4*).

Progression of nodular goitre was observed in 83 (32%) patients. New nodules developed in 77 (30%) patients. The median number of newly developed nodules was 3.5 (1-6). In patients with at least one nodule left in the remnant lobe, the nodules were enlarged in 54 (21%) patients. The median increase in size was 8 (3-18) mm. Only five (2%) patients underwent complementary contralateral hemithyroidectomy due to progression of nodular goitre. The mean follow-up period in patients with progression

**Table 1.** *Demographic features and preoperative ultrasonography findings of patients*

| | Patients with progression (n = 83) | Patients without progression (n = 176) | Total (n = 259) | P |
|---|---|---|---|---|
| **Sex** | | | | **0.54** |
| • Female | 65 (78%) | 130 (74%) | 195 (75%) | |
| • Male | 18 (22%) | 46 (26%) | 64 (25%) | |
| **Age, mean (SD)** | 47.9 (10.7) | 40.8 (12.2) | 43.1 (12.2) | **0.0001** |
| **Operated lobe** | | | | **0.94** |
| **Number of nodules, n(%)** | | | | |
| • 0 | 0 (0%) | 0 (0%) | 0(0%) | |
| • 1 | 52 (63%) | 124 (70%) | 176(68%) | |
| • 2 | 16 (19%) | 25 (14%) | 41(16%) | |
| • More than 2 | 15 (18%) | 26 (15%) | 41(16%) | |
| **Remnant lobe** | | | | **0.27** |
| **Number of nodules, n(%)** | | | | |
| • 0 | 59 (71%) | 136 (77%) | 195(75%) | |
| • 1 | 13 (16%) | 16 (9%) | 29 (12%) | |
| • 2 | 6 (7%) | 15 (9%) | 21 (8%) | |
| • More than 2 | 5 (6%) | 9 (5%) | 14 (5%) | |
| **Size of nodule, mean, mm(SD)** | 10.7 (6.9) | 8.5(4) | 9.3 (5.3) | **0.1** |
| **Pre-op function of thyroid, n(%)** | | | | **0.0001** |
| • Euthyroid | 45 (54%) | 149 (85%) | 194 (75%) | |
| • Hyperthyroid | 36 (43%) | 24 (13%) | 60 (23%) | |
| • Hypothyroid | 2 (3%) | 3 (2%) | 5 (2%) | |
| **Autoimmunity, n(%)** | | | | **0.058** |
| • No | 75 (90%) | 170 (97%) | 245 (95%) | |
| • Yes | 7 (9%) | 5 (3%) | 12 (5%) | |
| • Unknown | 1 (1%) | 1 (1%) | 2 (%) | |
| **Family history, n(%)** | | | | **1.0** |
| • No | 83 (100%) | 173 (98%) | 256 (99%) | |
| • Yes | 0 (0%) | 2 (2%) | 2 (1%) | |
| • Unknown | 0 (0%) | 1 (1%) | 1 (0.3%) | |
| **History of RT to neck, n(%)** | | | | **1.0** |
| • No | 83 (100%) | 175 (100%) | 258 (100%) | |
| • Yes | 0 (0%) | 0 (0%) | 0 (0%) | |
| • Unknown | 0 (0%) | 1 (1%) | 1 (0.3%) | |

**SD = standard deviation; RT = radiation treatment.**

**Table 2.** *Preoperative diagnosis and surgical indications*

| | Total progression n = 259 | Patients without progression n = 176 | Patients with progression n = 83 | p |
|---|---|---|---|---|
| **Preop diagnosis; *n (%)*** | | | | 0.0001 |
| • Solitary euthyroid nodule | 115 (44) | 88 (50) | 27 (32) | |
| • Unilateral euthyroid MNG | 33 (13) | 16 (9) | 17 (21) | |
| • Bilateral euthyroid MNG | 33 (13) | 29 (16) | 4 (5) | |
| • Solitary toxic nodule | 50 (18) | 24 (14) | 26 (31) | |
| • Unilateral toxic MNG | 7 (3) | 3 (2) | 4 (5) | |
| • Bilateral toxic MNG | 4 (2) | 1 | 3 (4) | |
| • Follicular/Hurthle cell neoplasm | 17 (7) | 15 (9) | 2 (2) | |
| **Surgical indications; *n (%)*** | | | | 0.0001 |
| • Compression | 65 (25) | 52 (30) | 13 (16) | |
| • Hyperthyroidism | 66 (25) | 29 (16) | 37 (45) | |
| • Suspicious FNAB | 52 (20) | 45 (26) | 7 (8) | |
| • Insufficient FNAB | 35 (14) | 23 (13) | 12 (14) | |
| • Asymptomatic | 33 (13) | 23 (13) | 10 (12) | |
| • Other | 8 (3) | 4 (2) | 4 (5) | |

**MNG = multinodular goitre; FNAB = fine needle aspiration biopsy.**

**Table 3.** *Definitive histopathology findings and follow-up period of patients*

| | Total n = 259 | Patients without progression n = 176 | Patients with progression n = 83 | p |
|---|---|---|---|---|
| **Histopathology results; *n (%)*** | | | | 0.0001 |
| • Nodular hyperplasia | 110 (43) | 57 (32) | 53 (64) | |
| • Colloidal nodule | 66 (25) | 55 (31) | 11 (13) | |
| • Follicular adenoma | 65 (25) | 49 (28) | 16 (19) | |
| • Hurthle cell adenoma | 17 (7) | 14 (8) | 3 (4) | |
| • Other | 1 | 1 (1) | 0 | |
| **Follow-up time; *month (SD)*** | **31 (25.5)** | **24.8 (20.7)** | **43.6 (29.4)** | 0.0001 |

**Table 4.** *The features of patients according to their L-T4 requirement*

| | Patients requiring no L-T4 replacement n = 203 | Patients requiring L-T4 replacement n = 56 | p |
|---|---|---|---|
| **Autoimmunity; *n (%)*** | | | 0.14 |
| • No | 194 (96) | 51 (91) | |
| • Yes | 7 (3) | 5 (9) | |
| • Unknown | 2 | 0 | |
| **Preoperative thyroid function; *n (%)*** | | | 0.003 |
| • Euthyroid | 151 (74) | 43 (77) | |
| • Hyperthyroidism | 51 (25 | 9 (16) | |
| • Hypothyroidism | 1 (1) | 4 (7) | |
| **Interval time; *month (SD)*** | **27.6 (23.5)** | **43.6 (28.9)** | 0.0001 |

of nodular goitre (43.6 months) was significantly longer than for those with no such progression (24.8 months, p = 0.0001; *table 3*).

Multivariate analysis showed that advanced age, preoperative hyperthyroidism, preoperative diagnosis of toxic nodular goitre and a definitive pathological diagnosis of nodular hyperplasia are factors which had an independent effect on the progression of nodular goitre.

## DISCUSSION

The reported recurrence rate following surgical resection for benign nodular thyroid disease varies from 0.3-80% depending on the extent of the initial surgery, the regional iodine-deficiency status and the length of follow-up.[1-10] However, surgery is the common method for the treatment of benign nodular goitre, whereas radioactive iodine is

also considered to be a reliable treatment option. The choice of surgical procedure for symptomatic benign nodular goitre is still controversial. Some surgeons prefer a hemithyroidectomy or subtotal thyroidectomy because of their lower complication rates. However, after these procedures the need to reoperate may arise due to the recurrence of symptomatic benign nodular goitre. Recently, with the advancement made in surgical techniques and increased experience, total thyroidectomy was preferred by some surgeons because of its low incidence of recurrence.[12-14] However, total thyroidectomy is associated with a potentially higher morbidity and a need for life-long thyroid hormone replacement therapy after the procedure. The advantage of hemithyroidectomy is that half of the thyroid gland remains. Therefore, most of the patients do not need to take thyroid supplements. Moreover, because the one lobe of the thyroid is untouched, there is no risk of damaging the contralateral recurrent laryngeal nerve and parathyroid glands. In this current study, most of the patients underwent surgery for unilateral disease.

Recurrent benign nodular goitre was defined as the return of the benign nodular goitre causing symptoms necessitating thyroid resection. In a study, with up to 134 months of follow-up, a higher recurrence rate (11%) in the unilateral resection group was reported when compared with the bilateral group (3%).[14] Other studies showed that the recurrence rate for benign nodular goitre in patients undergoing hemithyroidectomy is 1.2-26%, with a mean time to recurrence being 10-16 years and the recurrence rate for patients undergoing total thyroidectomy was found to be 3%. However, not all patients (especially the elderly) with recurrent symptoms required reoperation, thus the rate of reoperation was about 0.4%.[7,15] In our study, we found that out of 83 (32%) patients who had a progression of the nodular goitre only two (2%) were reoperated for recurrent benign nodular goitre. The fact that only 2% of patients underwent a reoperation is likely to be due to the short follow-up time in our study. The number of patients who would need further operation may very well increase when follow-up is extended.

We defined progression as the need to operate on the remnant lobe, the emergence of a new nodule or an increase in the diameter of an old nodule by more than 3 mm. In this study, progression of the nodular goitre was observed in 83 (32%) patients. In all the cohort, the medial follow-up time was 31 months, the longest being 126 months.

All factors that had an independent effect on progression, except advanced age, were in accordance with previous studies, which reported that undergoing an operation at a younger age increased the incidence of recurrent benign nodular goitre. This result is consistent with the natural course of benign nodular goitre, which is typically slow-growing so that the rate of recurrence increases as time elapses after the initial operation.[3] It has also been reported that there is a linear relationship between the patient's age, thyroid volume, and nodularity, respectively, with an average increase in thyroid volume of 4.5% per year based on serial ultrasound measurements.[16]

Other authors have found that even patients who had initially undergone hemithyroidectomy for a solitary nodule were subsequently found to have multinodular disease in the resected lobe on the final pathological examination. However, in these patients reoperation was rarely necessary (3%) after a mean follow-up of 14 years.[15] In our study the reoperation rate was 2% in accordance with previously reported series.

According to our results a definitive pathological diagnosis of nodular hyperplasia was associated with a greater risk of progression. Previous studies showed that follicular adenoma has a low recurrence rate, because adenoma is considered to be a solitary disease in a normal thyroid gland, rather than a lesion that develops in a diseased thyroid gland, as usually seen in nodular hyperplasia. However, it is remarkable that many patients with a solitary hyperplastic nodule, according to the ultrasonographic findings, developed a nodular relapse or a parenchymal irregularity.

In this study, only 56 (22%) patients needed to receive L-thyroxin supplementation due to postsurgical permanent hypothyroidism. By reserving total thyroidectomy only for patients with bilaterally symptomatic benign nodular goitre, nearly 80% of patients who had undergone hemithyroidectomy avoided thyroid hormone supplementation. It is well known that most patients after thyroid lobectomy are euthyroid (60-90%) and do not require thyroid hormone replacement therapy.[17-21] However, the incidence and contributing factors for hypothyroidism after hemithyroidectomy remain uncertain. The likelihood of thyroid hormone replacement demonstrated a trend with a contralateral nodule and a significant association with thyroiditis on the basis of the pathological findings.[22] Stoll *et al.*[23] concluded that patients with preoperative TSH levels greater than 1.5 μIU/ml or low free T4 levels or Hashimoto's thyroiditis are at increased risk for permanent hypothyroidism. They recommended that these patients should be counselled and followed appropriately. Piper *et al.*[24] also showed that 18% of patients become hypothyroid after hemithyroidectomy. However, they noted that some patients who became hypothyroid became euthyroid over time, even without any supplementation.

In our study, cancer was not reported for any of the patients who had progression after hemithyroidectomy for benign nodular goitre.

From our results, it is expected that the overall recurrence rate would increase with a longer follow-up time. Having a relatively short follow-up period was the major limitation of our study, and thus we emphasise the importance of

performing a regular annual follow-up for patients after hemithyroidectomy for benign nodular goitre. Nodular hyperplasia, preoperative hyperthyroidism, preoperative diagnosis of toxic nodular goitre, surgical indication for toxic goitre causing hyperthyroidism and a definitive pathological diagnosis of nodular hyperplasia were found to be associated with progression of remnant nodules after hemithyroidectomy.

There are some limitations of our current study which might have caused selection bias. We could not provide data regarding the total number of hemithyroidectomies done in all centres for any reason. This was one of the downsides of our retrospective design. Another drawback of the present study is the missing data regarding time to progression. Also, nearly 15% of the cohort were found to have undergone surgery, although they were asymptomatic. We could not determine exactly the reason for operation in detail for these patients since we admit that asymptomatic patients do not require surgical treatment.

In conclusion, according to the results of our study the progression rate after hemithyroidectomy is as high as 31%. However, the need for secondary surgical intervention is very low. Our results suggest that patients with unilateral or bilateral benign nodular goitre with asymptomatic nodules on one side can safely undergo hemithyroidectomy.

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## DISCLOSURES

We hereby declare explicitly that we have no relationship with any third party or conflict of interest or a fund that supports our study.

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