The Effect of Conventional Open Thyroidectomy on Clinical Results and Respiratory Function Tests in Multinodular Goitre

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AIM: The primary aim of our study was to measure the effect of conventional open thyroidectomy performed for patients with multinodular goiter (MNG) on pulmonary volumes measured with respiratory function tests independent from surgical indications. A secondary aim was to determine whether there was a significant improvement in the complaints due to obstructive symptoms after MNG surgeries.
METHODS: This study was conducted between October 2020 and June 2022. Patients who were hospitalized to undergo surgery for giant multinodular goiter were prospectively included in the study. Patients were questioned about complaints of pressure, hoarseness, dyspnea, sleep apnea, snoring, and dysphagia before the surgery and during the follow-up 6 months after surgery. In addition, pulmonary function tests were performed preoperatively, 48 hours after surgery and 6 months after surgery. Forced expiratory volume in 0.5 seconds forced expiratory volume in 1 second and forced vital capacity values in pulmonary function test (PFT) measurements were recorded.
RESULTS: A total of 55 patients, 42 females and 13 males, mean age 49.54 ± 13.6 years, were included in the study. Although there was a significant decrease in clinical symptoms caused by the thyroid volume within 6 months in patients who were operated for giant MNG there was no significant change in pulmonary function tests. There was a positive correlation between the thyroid volume and nodule weight in patients with MNG.
CONCLUSIONS: Our results suggest that it is not necessary to follow up with patients without obstructive findings in preoperative pulmonary function tests with pulmonary function tests in the postoperative period.

Keywords: total thyroidectomy; multinodular goiter; pulmonary function tests

Introduction

Cases of goiters that reach large sizes are common, particularly in areas with endemic iodine deficiency [1]. Depending upon the size and growth rate of the thyroid tissue, respiratory problems that occur in the preoperative period and can continue in the postoperative period, especially in the large airways, causing the risk of obstruction and the feeling of pressure due to the mass effect and airway infiltration [1]. Thyroid dysfunctions affect all organ systems and are associated with poor quality of life and increased morbidity in the long term. One of the most prominent of these problems is their impact on the respiratory system [2].
Although the incidence of benign goiter causing acute airway obstruction is around 0.6%, the diagnosis of upper airway obstruction caused by goiter may also be in the late period. This is because multinodular goiter has the potential for progressive and insidious growth and may remain asymptomatic in patients up to compression that may occur in 70% of the trachea. Particularly dyspnea and obstructive symptoms are indications for goiter surgery [3].

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Compressive symptoms due to multinodular goiter (MNG) caused by the mass effect of goiter tissue may manifest particularly with dyspnea and dysphagia. Sleep apnea with respiratory symptoms, snoring, and shortness of breath develops due to partial pressure on the tracheal tissue from different points. Hoarseness may be due to compression of the recurrent laryngeal nerve. MNG may also occur with vocal cord paralysis on very rare occasions, but this usually occurs in malignancies [4].

Surgical procedures have a crucial place among the treatments used for patients with MNG. Today, the main indications for thyroidectomy surgery are malignancy (68%), compression symptoms (20.7%) and hyperthyroidism (9.7%). Thyroidectomy is performed in 50% of patients and hemithyroidectomy in 35% of patients [5]. Failure to perform preoperative spirometry evaluations in the majority of patients undergoing goiter surgery may cause physicians to overlook clinically incontrovertible symptoms [6]. As more than three-quarters of the surgeries done for goiter are thyroidectomy or hemithyroidectomy [7], it might be stated that a relatively radical attitude about the extent of resection in benign thyroid lesions still exists. In addition, the total number of thyroid surgeries performed due to benign goiter continues to decrease significantly [8].

It is a matter of curiosity whether there is a symptomatic change that might be evaluated in favor of obstruction in the postoperative period in all thyroidectomy cases.

The aim of our study was to measure the effect of conventional open thyroidectomy on lung volumes measured by pulmonary function tests regardless of surgical indication in MNG patients with clinical symptoms related to thyroid volume but without obstructive findings in respiratory function tests. A secondary aim was to determine whether patients with MNG without obstructive findings in preoperative pulmonary function tests should be followed up with pulmonary function tests in the postoperative period.

Materials and Methods

After the approval of the clinical research ethics committee of Nigde Omer Halisdemir University Faculty of Medicine, no. 2020/34, was obtained, and patients who were hospitalized for surgery for MNG in the general surgery clinic were prospectively included in the study. This study was conducted between October 2020 and June 2022. The entire study was carried out in accordance with the principles of the Helsinki Declaration. All patients were informed of the work plan in detail and informed patient voluntary consent was obtained to ensure that their data were recorded during thyroidectomy. Inclusion criteria were as follows: patients in the Society of Anesthesia (ASA) physical status class (I–III), between the ages of 18–77, those who signed the informed voluntary consent form, and those who were scheduled for operation due to MNG with or without suspected malignancy on fine needle aspiration biopsy (FNAB). Exclusion criteria were as follows: pregnant patients, those with lung disease, those who had had esophageal surgery, those who had had any neck surgery, those who had thyroid and parathyroid surgery before, those who are morbidly obese, those with any psychiatric disease, those who drink alcohol, those with chronic obstructive pulmonary disease, those with asthma, those with retrosternal goiter and those who developed complications such as permanent or temporary hypocalcemia, laryngeal nerve damage, abscess, hematoma, fistula formation and reoperation. All patients underwent fine needle aspiration biopsy (FNAB) before surgery. Sixty-nine patients were included in the study. Five patients with suspected malignancy and cytological results showing malignancy (Bethesda category 5–6) were classified according to the Bethesda pathological examination system and FNAB results were not included in the study. All patients were intubated with direct laryngoscopes and Cormack-Lehane classifications were performed. Two patients with Cormack-Lehane grade 4 were not included in the study. In addition, the following patients were excluded: 2 patients with malignancy identified by surgical pathology, 1 patient due to hematoma, 1 patient due to permanent hypocalcemia and 3 patients due to seroma. Statistical analysis was performed on the data of the remaining 55 patients.

Surgical Technique

A single surgeon with approximately 14 years of experience in endocrine surgery performed all of the operations (H.B.). Intern surgeons were not allowed in the operations. The operation was started by performing a transverse Kocher incision. Thyroid loot was reached between sternohyoid muscles. The thyroid tissue was mobilized by separating it from the surrounding structures by sharp blunt dissection, and the upper and lower pole arteries and veins and other vascular structures were found one by one, then connected and cut. Intraoperative neuromonitoring was used in all operations. The superior laryngeal nerves were identified and isolated during the upper pole dissection, and the recurrent laryngeal nerves in the middle and lower pole dissection. During dissection, all thyroid tissue, including the cyst, was removed. Attention was paid to the protection of the parathyroid gland. No energy device was used in thyroid tissue dissection and no perioperative complications were observed. After surgical removal of the nodules or nodules, the weights of the specimens were measured.

If the calcium (Ca) level measured 6 hours after surgery was below 8 mg/dL, 1-2 ampoules of calcium gluconate (94 or 188 mg elemental Ca) were diluted with 50–100 mL of 5% dextrose and administered as an intravenous (IV) infusion over 5–10 minutes. All patients did intermittent breathing exercises with intermittent steam inhalation and balloon blowing for one hour during the first 24 hours, starting from the first postoperative hour. After discharge, all patients went to the endocrine clinic for postoperative replacement therapy with Levothyroxine. A clinical and biochemical euthyroid state was achieved starting with a mean dose of Levothyroxine sodium 100–150 mcg/day, according to the blood thyroid hormone levels on the 7th and 30th days postoperatively.

Preoperative Ca, phosphorus, T3, T4, and thyroid stimulating hormone (TSH) levels of all patients were measured. Age, height, weight and body mass index (BMI) were recorded. Thyroid volumes and nodule weights were measured, and patients were ensured to be euthyroid in the preoperative period.

In the discussion with the patients before the operation and at the control examinations six months after the operation; pressure sensation, hoarseness, shortness of breath, sleep apnea, snoring and dysphagia were asked and the results were marked as present or absent. In addition, three pulmonary function tests (PFTs) were applied to the patients 24 hours before the operation, 48 hours after the operation, and in the control evaluations six months after the operation. Easy on-PC Spirometry system brand spirometry device in our outpatient clinic was used to evaluate respiratory functions. On the participants, the respiratory function test was performed by experienced personnel in a closed environment without any chemicals, in a sitting position, using a nose clip. Forced expiratory volume in 0.5 seconds (FEV0.5), forced expiratory volume in 1 second (FEV1),

Table 1. Patient characteristics and clinical data.

Variables	Value*
Sex	
Male (n)	13
Female (n)	42
Age (years)	49.54 ± 13.6
Height (cm)	162.2 ± 9.33
Weigh (kg)	79.02 ± 11.47
BMI (kg/m^2)	30.17 ± 4.75
Thyroid Volume (cm)	171.23 ± 35.39
Nodule Weight (gr)	74.14 ± 67.31
Ca (mg/dL)	8.55 ± 0.55

*All values are reported as mean ± unless otherwise indicated.
BMI, body mass index; Ca, calcium.

and forced vital capacity (FVC) were measured for each patient during PFT. At each time of the measurements, at least three measurements were made for each participant and the best values obtained from the patient were included in the study.

Statistical Analysis

For the determination of the sample size, the G power test was used. Based on the study titled "Pulmonary function profile in patients with benign goiters without symptoms of respiratory compromise and the early effect of thyroidectomy" by Pradeep PV *et al.* [9], when the type error amount was 0.05, the strength of the test was 0.95, the impact power was 0.5, the minimum sample width required in both groups was calculated as 45 in equal groups.

Statistical analyses were performed using the "SPSS for Windows version 22.0" package programme (SPSS Inc., Armonk, NY, USA). Numerical variables were summarized with mean ± standard deviation. The normality of numerical variables was examined by the kolmogorov smirnov test. In dependent samples to compare the variables with normal distribution between groups, *T*-test was used. For the variables where the normality assumption was not met, the Wilcoxon test was used. The changes in the values such as type, age, weight, thyroid volume, and nodule weight over time and between the groups were calculated as mean and standard deviation. To evaluate the statistically significant differences between categorical variables, the Mc-Nemar test was used. In the comparison of multiple groups, the Annova and Wilcoxon marked rows test was applied in repeated samples. Pearson or Spearman correlation analysis was performed to evaluate the correlation between the groups. A p-value < 0.05 was considered statistically significant.

Results

The study evaluated 55 patients. Of these patients 13 (23.64 %) were male, and 42 (76.36 %) were female. The mean age of the patients was 49.54 ± 13.60 years, with an age range

Table 2. Changes in clinical symptoms of patients undergoing total thyroidectomy.

Symptoms	Preoperative	Postoperative 6th month	p
Pressure feeling			
No	23	49	0.000
Yes	32	6	
Hoarseness			
No	45	52	0.065
Yes	10	3	
Dyspnea			
No	21	48	0.000
Yes	34	7	
Dysphagia			
No	28	48	0.001
Yes	27	7	
Sleep Apnea			
No	31	49	0.000
Yes	24	6	

McNemar's Test.

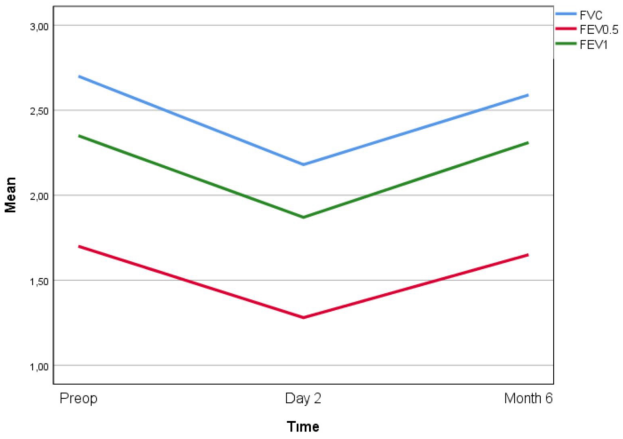

Fig. 1. Changes in pulmonary function tests before and after total thyroidectomy. FVC, forced vital capacity; FEV 0.5, forced expiratory volume in 0.5 seconds; FEV1, forced expiratory volume in 1 second.

of 22.00 and 77.00 years. The mean BMI was 79.02 kg/m^2. All patients who underwent thyroidectomy were euthyroid before the operation. The patients' mean thyroid volume was determined to be 171.23 cm, their mean nodule weight was found to be 74.14 g, and their mean Ca level was 8.55. Postoperatively, 6 (10.9%) of the patients developed clinical findings related to hypocalcemia, such as tingling and itching in the hands and face. It was observed that the blood calcium levels of these patients were 7–7.5 mg/dL. Ca infusion (10 mL 10% calcium gluconate diluted in 100 mL 5% dextrose was administered intravenously in 5–10 minutes) was administered to patients with clinical signs of hypocalcemia for 1 day. The clinical findings of hypocalcemia of the patients resolved and oral Ca maintenance therapy was administered for the next 7 days. By the 10th and 30th post-

Table 3. Respiratory function tests of patients who underwent total thyroidectomy.

Dependent variable	*Mean* ± SD	Dependent variable	*Mean* ± SD	*p*
PRED FVC	3.10 ± 0.78	PRE FVC	2.63 ± 0.80	0.000
PRED FEV1	2.64 ± 0.75	PRE FEV1	2.36 ± 0.77	0.017
PRE FEV0.5/FVC%	63.74 ± 12.07	POST2 FEV0.5/FVC%	58.03 ± 15.91	0.009
POST2 FEV0.5/FVC%	58.03 ± 15.91	POST6 FEV0.5/FVC%	62.27 ± 10.31	0.190
POST6 FEV0.5/FVC%	62.27 ± 10.31	PRE FEV0.5/FVC%	63.74 ± 12.07	1.000
PRE FEV1/FVC%	88.71 ± 6.96	POST2 FEV1/FVC%	83.69 ± 15.37	0.420
POST2 FEV1/FVC%	83.69 ± 15.37	POST6 FEV1/FVC%	90.43 ± 6.47	0.008
POST6 FEV1/FVC%	90.43 ± 6.47	PRE FEV1/FVC%	88.71 ± 6.96	0.360

PRED, Predict; PRE, Preoperative; POST2, Postoperative 2nd day; POST6, Postoperative 6nd month; FVC, forced vital capacity; FEV0.5, forced expiratory volume in 0.5 seconds; FEV1, forced expiratory volume 1 second; SD, Standard deviation. Analysis of variance (ANOVA) Test in Repeated Measures.

Table 4. Correlation analysis.

Variables	Thyroid volume		Nodule volume	
	r	*p*	r	*p*
NODULE WEIGHT	0.398	0.002	-	-
PRE FEV0.5/FVC%	–0.272	0.043	0.06	0.965
POST2 FEV0.5/FVC%	0.13	0.926	–0.09	0.949
POST6 FEV0.5/FVC%	–0.115	0.420	0.40	0.752
PRE FEV1/FVC%	–0.204	0.132	–0.22	0.873
POST2 FEV1/FVC%	0.58	0.672	–0.17	0.206
PRE FVC	–0.05	0.974	0.155	0.276

PRE, Preoperative; POST, Postoperative; FEEV0.5, forced expiratory volume in 0.5 seconds; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity. ^{r}, Spearman Correlation Analysis.

operative days, these patients showed no laboratory or clinical signs of hypocalcemia. Although some patients did not receive Ca maintenance therapy, no laboratory or clinical findings of hypocalcemia were found in his controls following days and 6 months. The patient's serum Ca levels at 6 months ranged from 8.8 to 10 mg/dL. It was decided that these patients had transient hypocalcemia. Permanent hypocalcemia did not develop in any of the patients (Table 1).

At the 6-month follow-up, physical and laryngeal examination (under vocal cord control) revealed no permanent recurrent laryngeal nerve injuries. In the discussions with the patients at the end of 6 months after surgery, there was a statistically significant decrease in the complaints of pressure sensation, shortness of breath, snoring, night apnea, and difficulty in swallowing ($p < 0.01$). There was no statistically significant change in hoarseness ($p > 0.05$) (Table 2).

The FVC values measured in the preoperative period were significantly lower than the predicted FVC values ($p = 0.000$). FEV0.5 values measured in the preoperative period were significantly lower than the predicted FEV0.5 values ($p = 0.001$). When the FEV0.5/FVC value, measured preoperatively, and the FEV0.5/FVC value, measured on postoperative day 2 were compared, the value on postoperative day 2 was found to be statistically significantly lower ($p < 0.01$). When the FEV0.5/FVC values of the patients in the sixth month were compared with the values preoperatively and postoperative day 2, there was no statistically significant difference ($p > 0.05$) (Table 3).

There was no statistically significant difference when the FEV1/FVC value, measured preoperatively was compared with the FEV1/FVC value, measured on postoperative day 2 ($p > 0.05$). There was also no significant difference between FEV1/FVC values at month 6 and the preoperative values ($p > 0.05$). In addition to that, when the FEV1/FVC values on postoperative day 2 were compared with the measurements at 6 months, the result at 6 months was statistically significantly higher ($p < 0.05$) (Table 3, Fig. 1).

The correlation between preoperative FEV0.5/FVC and FEV1/FVC values and thyroid volume and nodule volume measured preoperatively was evaluated. There was a weak negative correlation between the preoperative FEV0.5/FVC% and thyroid volume (r = –0.272, $p = 0.043$). Although there was a very weak negative correlation between the preoperative FEV1/FVC% and thyroid volume, there was no statistically significant difference (r = –0.204, $p = 0.132$). No correlation between thyroid nodule volume and percent FEV/FVC measurements at any measurement time was noted. There was a moderate positive correlation between thyroid volume and nodule weight measured preoperatively (r = 0.398, $p = 0.002$) (Table 4).

Discussion

Although many spirometry measurements can be made in pulmonary function tests, the American Thoracic Society recommends reporting FVC, FEV1 and FEV1/FVC values as standard, as most of them do not provide a clinical benefit in routine use [10]. Because of this, we have used these values in our study.

Pulmonary function tests are also used to determine the degree of airway obstruction of the people measured. The parameters most frequently measured for this purpose are FVC, FEV 0.5 and FEV1. These are the values obtained by calculating the ratio of difficult expiratory volume in seconds to functional vital capacity [11].

Bartsch DK *et al*. [12] stated that spirometry results in patients with benign goiter with local compressive findings were useful in determining whether or not to operate. For the detection of compressive findings, FEV1/FVC is calculated by spirometry method to determine obstructive respiratory defects. The most common causes of obstructive problems are chronic obstructive pulmonary disease and asthma. A decrease in the FEV1/FVC ratio below 80% indicates the presence of an obstructive problem in patients [13]. Although the patients in our study had clinical symptoms because of the pressure sensation, the preoperatively measured FVC and FEV1 values were significantly lower than the predicted values and the mean FEV1/FVC value was 88%.

Arikan Y *et al*. [14] claimed that the pulmonary function test results 1 month after surgery in patients who underwent surgical thyroidectomy for toxic multinodular goiter did not change compared to preoperative results. In our study, although the preoperative FEV0.5/FVC values decreased on postoperative day 2, they increased again after the 6-month period to such an extent that there was no significant difference with the preoperative values. This result suggests that; although there is a decrease in the percentage FEV/FVC value due to some decrease in patient effort in the early postoperative period after thyroidectomy, this will not be permanent.

Htun C *et al*. [15] observed that obstructive changes in the peripheral airway led to changes in the FEV1/FVC ratio. In our study, we found that there was no significant decrease in early postoperative values in terms of FEV1/FVC ratios compared to preoperative values. However, we consider the increase in these values at 6 months compared to the early postoperative period as the return to normal obstructive findings after recovery.

Bhandari L *et al*. [16] measured FVC as 3.29 ± 0.66, FEV1 as 2.88 ± 0.56, FEV1/FVC as 82.83 ± 1.09 in their measurements in 60 euthyroid patients and found no obstructive pattern. In our study, we measured these values as FVC 2.70 ± 0.84, FEV1 2.35 ± 0.76, FEV1/FVC 88.87 ± 6.91, and our results were consistent with the findings of Bhandari L *et al*. [16].

When the FEV0.5/FVC% and FEV1/FVC%values were interpreted, we observed that there was no significant increase after thyroidectomy in patients whose spirometry measurement values were not obstructive.

After thyroidectomy, swallowing disorders associated with a thyroidectomy complicated by superior laryngeal nerve or recurrent laryngeal nerve paralysis is explained. However, it has been reported that thyroidectomy may lead to an improvement in swallowing difficulty and similar complaints, as well as an increase in these complaints [17]. In addition, patient satisfaction was measured as 97% in MNG patients who underwent thyroidectomy [18]. The most crucial factor affecting satisfaction is the improvement of complaints patients had preoperatively [19]. Pressure sensation, shortness of breath, and dysphagia, which affect patient satisfaction in our study, improved significantly at 6 months compared to the preoperative period.

Reiher AE *et al*. [20] claimed that thyroidectomy in MNG patients could significantly reduce the frequency of snoring and sleep apnea complaints in their study on 45 patients. In our study, among other complaints, there was a significant decrease in sleep apnea and snoring complaints in the controls in the sixth month after thyroidectomy. This result supports the findings of Reiher AE *et al*. [20].

Hoarseness is a relatively common complication of thyroidectomy and may be attributed to many factors and other such non-surgical causes as surgeon error or nerve injury during intubation. However, thyroidectomy has been reported to be a procedure with a relatively low rate of recurrent laryngeal nerve paralysis (RLNP) compared to procedures such as cervical spine surgery, mediastinal surgery, esophagectomy, and endarterectomy [21]. In our study, there was no difference at 6 months after thyroidectomy hoarseness was evaluated, which supports the findings obtained in previous studies.

Singh PK *et al*. [22] claimed that there was a strong correlation between thyroid volume, FEV1, FVC, and disease severity. In our study, we also examined the correlation between total thyroid volume and nodule volume and observed that there was a moderate positive relationship. This supports the idea that the thyroid volume also increases as the nodule weight increases. In addition, the weak positive correlation between thyroid volume and the FEV/FVC ratio measured preoperatively supports the idea that obstructive symptoms will increase as the thyroid volume increases. However, we did not find a correlation between other measurement parameters and thyroid volume.

Pradeep PV *et al*. [9] claimed that the duration of goiter and its size may be associated with a decrease in FEV1 values, so they recommended early thyroidectomy in patients with benign MNG. In our study, we could not find a significant correlation between nodule mass and preoperative and postoperative FEV/FVC rates. This suggests that the increase in nodule weight is not related to obstructive findings.

It has been reported that devascularization of the parathyroid glands especially after total thyroidectomy and early postoperative hypocalcemia after parathyroidectomy frequently occur, but are mostly temporary and rarely turn into permanent postoperative hypocalcemia persisting for more than 6 months [23]. Permanent hypocalcemia did not develop in any of our patients. However, if symptomatic hypocalcemia developed after surgery; Ca infusion was administered and blood calcium levels were monitored. In patients with persistent hypocalcemia, magnesium levels should be monitored as well. During chronic treatment, if parathyroid hormone is measured once a month and it returns to normal levels, Ca and vitamin D treatment should be discontinued

In our study, follow-up lasted 6 months, and this short follow-up is one of the limitations of our study. We performed a pulmonary function test on the patients who un-

derwent thyroidectomy 2 days after the operation. The mean hospital stay of the patients was 2 days. Since the patients were discharged on day 2, the test could not be performed later. The fact that this test was not performed later is another limitation of our study given the possibility that pain and edema-related factors can affect the test results later whereas general anesthesia and incision do so in the early period.

Conclusions

There is a significant decrease in clinical symptoms caused by thyroid volume in the 6 months period, except for hoarseness in MNG patients without obstructive findings in pulmonary function tests. Although there is a decrease in pulmonary function test results in the early postoperative period probably due to pain and edema, we think that there is no need to follow up giant MNG goiter patients who do not show obstructive findings in preoperative pulmonary function tests with pulmonary function tests in the postoperative period as there is no significant change in the tests in the 6-month period.

Availability of Data and Materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

HB, MK designed the research study. HB and MK performed the research. HB and MK analyzed the data. HB wrote the article. Both authors revised the manuscript critically for important intellectual content. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The stugy was approved by the clinical research ethics committee of Nigde Omer Halisdemir University Faculty of Medicine (no. 2020/34) and patients who were hospitalized for surgery for MNG in the general surgery clinic were prospectively included in the study. The entire study was carried out in accordance with the principles of the Helsinki Declaration. All patients were informed of the work plan in detail and informed patient voluntary consent was obtained to ensure that their data were recorded during thyroidectomy.

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Conflict of Interest

The authors declare no conflict of interest.

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