

MODERN PRINCIPLES OF SURGERY TREATMENT OF PATIENTS WITH NODULAR GOITER

Magomedov M.M.

orcid.org/0000-0002-3335-525x

Osmanov O.M.

orcid.org/0000-0002-6000-2425

Osmanov O.M.¹, Magomedov M.M.²

¹State Budgetary Institution of Healthcare "Clinical City Hospital №67", Moscow, Russia

²Federal State Budgetary Educational Institution of Higher Education «Dagestan state medical university», Department of surgery, faculty of advanced training and professional retraining of specialists with the course of endoscopic surgery, Makhachkala, Republic of Dagestan, Russia

Abstract

Purpose of the study. To justify and confirm the differentiated approach to choosing the volume of surgical intervention in benign nodular goiter. **Materials and methods.** A prospective analysis of 180 patients who underwent thyroid surgery was performed; 11 (6.1%) were men and 169 (93.9%) were women aged 20-65 years. The duration of the patients' disease was 8 months to 12 years. All patients with benign non-toxic goiter underwent a thorough evaluation of changes in the level of thyroid hormones in serum, ultrasound of the thyroid gland, and aspiration biopsy of the thyroid gland. **Results.** In laboratory studies, a high level of malignancy is observed in patients with higher levels of TSH and antibodies, TG and antibodies, TPO. There were no significant differences in the values of T3 and T4. In the ultrasound study, the average and maximum diameter of malignant nodes were significantly smaller than that of benign ones (1.99 ± 1.88 cm; $p < 0.001$). The difference between surgical procedures described as subtotal, total, and hemi-thyroidectomy was statistically significant. In 128 (71.1%) patients nodes were located in one lobe, 68 (37.8%) patients had multiple nodes, and 52 (28.9%) had solitary nodes in one of the thyroid lobes. Intraoperatively, 68 (37.7%) patients underwent cytomorphological examination of removed thyroid tissue. Hemithyroidectomy was performed in only 57 (31.6%) patients. Subtotal thyroidectomy was performed in 78 (43.3%) patients, and total thyroidectomy was performed in 45 (25%) patients. With the development of hematoma, one patient was re-operated after total thyroidectomy. Hypoparathyroidism was diagnosed in 2 (4.4%) patients after thyroidectomy, and in 1 (1.3%) patient after subtotal thyroidectomy. 3 patients had transient laryngeal paresis after thyroidectomy. Hypothyroidism developed in 14 (24.6%) patients after hemithyroidectomy, in 50 (64.1%) patients after subtotal thyroidectomy and in 45 (100%) after thyroidectomy. **Conclusion.** The decision of surgical intervention should be differentiated with respect to the choice of surgical intervention tactics.

Keywords

thyroidectomy, subtotal thyroidectomy, hemithyroidectomy, hypothyroidism, hypoparathyroidism

Түйінді зобпен аурытын науқастарды хирургиялық емдеудің заманауи принциптері

Osmanov O.M.¹, Магомедов М.М.²

¹МБДСМ №67 Қалалық клиникалық аурухана, Мәскеу қ., Ресей

²ФМББМ ЖО «Дагестан мемлекеттік медицина университеті», Эндоскопиялық хирургия курсы бар ҚҚД және БАФ хирургия кафедрасы, Махачкала қ., Дағыстан Республикасы, Ресей

Аңдатпа

Зерттеу мақсаты. Қатерсіз түйінді жемсау кезіндегі отаның көлемін анықтауды таңдаудағы дифференциалды тәсілдемені негіздеу және бекіту. **Материалдар мен әдістер.** Қалқанша безіне ота жасатқан 180 науқасқа проспективті талдау жүргізілді. Оның ішінде – 20-65 жас аралығындағы 11 (6,1%) ер адамдар және 169 (93,9%) әйелдер. Науқастардың ауру ұзақтығы – 8 айдан 12 жылға дейін. Қатерсіз токсикалық емес жемсауы бар науқастардың барлығы қан сарысуындағы ҚБ гормондары деңгейінің өзгерістерін мұқият бағалаудан, қалқанша безінің УДЗ-сынан, қалқанша безінің аспирациялық биопсиясынан өтті. **Нәтижелер:** Зертханалық зерттеу кезінде қатерліліктің жоғары деңгейі ТТГ және АТ, ТГ және АТ, ТПО жоғары деңгейі бар науқастарда байқалды. Т3 және Т4 мөңдерінде нақты айырмашылық анықталған жоқ. УДЗ зерттеу кезінде қатерсіз түйіндерге қарағанда, қатерлі түйіндердің орташа және макси-малды диаметрі едәуір аз болды ($1,99 \pm 1,88$ см; $p < 0,001$). Субтоталды, тоталды және гемитиреоидэктомия ретінде сипатталған хирургиялық шаралар арасындағы айырмашылық статистикалық маңызды болды. Науқастардың 128-інде (71,1%) түйіндер бір бөлікте, науқастардың 68-інде (37,8%) көптеген түйіндер болған, ал 52 (28,9%) науқаста қалқанша безінің бір бөлігінде жеке түйіндер болды. Интраоперациялық кезеңде 68 (37,7%) науқастың қалқанша бездерінің жойылған тіндеріне цитоморфологиялық зерттеу жүргізілді. 57 (31,6%) науқасқа гемитиреоидэктомия жасалды. 78 (43,3%) науқасқа субтоталды тиреоидэктомия, ал 45 (25%) науқасқа тоталды тиреоидэктомия орындалды. Гематоманың дамуына байланысты тоталды тиреоидэктомиядан кейін бір науқасқа, гипопаратиреоз тиреоидэктомиядан кейін 2 (4,4%) науқасқа, субтоталды тиреоидэктомиядан кейін 1 (1,3%) науқасқа қайтадан операция жасалды. 3 науқаста тиреоидэктомиядан кейін көмейдің транзиторлық жарасы пайда болды. Гемитиреоидэктомиядан кейін 14 (24,6%), субтоталды тиреоидэктомиядан кейін 50 (64,1%) және тиреоидэктомиядан кейін 45 (100%) науқаста гипотиреоз дамыды. **Қорытынды.** Оталық араласудың шешімі отаның тактикасын таңдауға қатысты саралануы тиіс.

Түйін сөздер

тиреоидэктомия, субтоталды тиреоидэктомия, гемитиреоидэктомия, гипотиреоз, гипопаратиреоз

Современные принципы хирургического лечения больных с узловым зобом

Османов О.М.¹, Магомедов М.М.²

¹ГБУЗ Городская клиническая больница №67, г. Москва, Россия

²ФГБОУ ВО «Дагестанский государственный медицинский университет», кафедра хирургии ФПК и

ППС с курсом эндоскопической хирургии, г. Махачкала, Республика Дагестан, Россия

Аннотация

Цель исследования. Обосновать и подтвердить дифференцированный подход к выбору объема оперативного вмешательства при доброкачественном узловом зобе. **Материалы и методы.** Проведен проспективный анализ 180 пациентов, перенесших операцию на щитовидной железе. Из них – 11 (6,1%) мужчин и 169 (93,9%), женщин в возрасте от 20 до 65 лет. Продолжительность заболевания пациентов от 8 месяцев до 12 лет. Все пациенты с доброкачественным нетоксическим зобом прошли тщательную оценку с изменением уровня гормонов ЩЖ, в сыворотке крови, УЗИ щитовидной железы, аспирационная биопсия щитовидной железы. **Результаты.** При лабораторном исследовании высокий уровень злокачественности наблюдается у пациентов с более высоким уровнем ТТГ и АТ, ТГ и АТ, ТПО. Достоверных различий в значениях Т3 и Т4 не было выявлено. УЗИ исследовании средний и максимальный диаметр злокачественных узлов было достоверно меньше, чем у доброкачественных ($1,99 \pm 1,88$ см; $p < 0,001$). Разница между хирургическими процедурами, описанными как субтотальная, тотальная и гемитиреоидэктомия, была статистически значимой. У 128 (71,1%) пациентов узлы располагались в одной доле, у 68 (37,8%) пациентов узлы были множественные, а 52 (28,9%) – солитарные узлы в одной из долей щитовидной железы. Интраоперационно у 68 (37,7%) проводилась цитоморфологическое исследование удаленной ткани щитовидной железы. Гемитиреоидэктомия была выполнена всего 57 (31,6%) пациентам. Субтотальная тиреоидэктомия выполнена 78 (43,3%) пациентам, а тотальная тиреоидэктомия была выполнена у 45 (25%) пациентов. С развитием гематомы повторно была оперирована одна больная после тотальной тиреоидэктомии, у пациентов после тиреоидэктомии гипопаратиреоз у 2 (4,4%), а после субтотальной тиреоидэктомии 1 (1,3%). У 3 пациентов после тиреоидэктомии транзиторийный парез гортани. Гипотиреоз развился после гемитиреоидэктомии у 14 (24,6%), субтотальной тиреоидэктомии 50 (64,1%) и тиреоидэктомии 45 (100%). **Заключение.** Решение оперативного вмешательства должно быть дифференцированным относительно выбора тактики оперативного вмешательства.

Ключевые слова

тиреоидэктомия, субтотальная тиреоидэктомия, гемитиреоидэктомия, гипотериоз, гипопаратиреоз

Introduction

In recent years, there has been an increase in thyroid diseases, including nodular goiter. Dagestan is an endemic region where nodules are detected in most patients with thyroid pathology. The frequency of nodular non-toxic goiter among other thyroid diseases ranges from 25 to 62% [1, 2, 3, 4]. Recently, surgery for a benign goiter has been recognized as an acceptable and safe treatment method that has a low surgical risk and mortality. Despite improvements in the diagnosis and treatment of thyroid diseases over the past two decades, the literature remains controversial as to which method is best for a benign disease [2]. Previously, subtotal thyroidectomy for multiple goiter was considered a gold standard treatment, which was due to a decrease in complications related to the laryngeal nerve and parathyroid gland and a decrease in the need for lifelong hormone replacement therapy [3, 4, 5]. However, it is widely known that with long-term follow-up after subtotal thyroidectomy in multi-nodular goiter an increase in the frequency of relapses to 78% should be expected [5, 7]. Meanwhile, it is well known that repeated surgery for a receding nodular goiter results in increased damage to the laryngeal nerve and parathyroid gland compared to the original approach to the surgery. Although many clinics have changed their surgical strategy in favor of thyroidectomy, sub-

total thyroidectomy still appears to be the preferred option in every-day practice [6].

At the same time, the issue of choosing the volume of surgical intervention in patients with non-toxic goiter has not been completely resolved and requires further study [6, 7, 8, 9, 10].

Purpose of the study

To justify and confirm the differentiated approach to choosing the volume of surgical intervention in benign nodular goiter.

Material and methods

A prospective analysis of 180 patients who underwent thyroid surgery for nodular and multi-nodal non-toxic goiter at the Republican Clinical Hospital and Clinical City Hospital № 67 in Moscow was performed.

11 (6.1%) were men and 169 (93.9%) were women aged 20-65 years. The duration of the patients' disease was 8 months to 12 years.

All clinical and pathological data were prospectively entered into a computer database from medical records. We extracted data on gender, age, the composition of thyroid disease and the frequency of postoperative complications. The ethics Committee of Dagestan State Medical University approved this study, and all patients signed an informed consent.

Criteria for exclusion from the study:

1. a case of a malignant disease diagnosed before surgery;
2. the suspicion of malignancy before surgery;
3. those who have previously had thyroid surgery;
4. patients receiving treatment.

A reasonable criterion for including patients for surgery was ultrasound and fine needle aspiration biopsy with the exception of malignancy. After excluding 8 patients from the study, the main group was formed.

The reason for surgical intervention was tracheal compression syndrome and dysphagia in 108 patients (57.4%). Of these patients, 29 (26.8%) had a cervical and retrosternal arrangement of nodes. Fine needle aspiration biopsy (TAB) is an effective method that should be preferred as first-line diagnostic procedure as it gives the most accurate results for suspicious thyroid nodes detected by ultrasound. In our study, when evaluating thyroid nodes, it showed sensitivity of 65- 88%, specificity of 86% and 5% of false negative results.

Cytological evaluation of patients who underwent a fine needle aspiration biopsy revealed benign cytology in 98 patients, suspicious cytology of thyroid carcinoma in 8 patients, follicular adenoma in 32 patients, and insufficient cytology for diagnosis in 31 patients. 8 patients were excluded from the study as a malignant disease.

In 128 (71.1%) patients, nodes were located in one lobe of the thyroid gland. 68 (37.8%) patients had multiple nodes, and 52 (28.9%) had solitary nodes in one of the thyroid lobes. During the surgical intervention, a cytomorphological assessment was performed in 68 (37.7%) samples of the thyroid tissue. The study of surgery outcome lasted 6 months to 5 years and was conducted on the basis of examination of patients, study of thyroid status by ELISA, thyroid ultrasound was performed using the ultrasound scanner "AlocaSSD-3000" with a linear phased antenna transducer with frequency of 7.5 MHz. Serum (TSH), free triiodothyronine (T3), and free thyroxine (T4) were analyzed in the laboratory and determined using a chemiluminescent analyzer RocheCodalE601 (Switzerland) and a matched set.

The collected data was analyzed using the SPSS software (version 20; SPSS Inc.). Quantitative data were expressed as an average $SD \pm$ standard deviation

and qualitative data were reported by frequency (%). For interference analysis, we used the exact Fischer test and Chi-square to compare qualitative data in the frequency distribution. Based on the results of the Kolmogorov-Smirnov test, which shows the normality of the data distribution, independent t-test samples were used to compare quantitative data for each gender. Logistic regression was used to assess the association of factors such as gender, age, body mass index (BMI), medical history, type of surgery, indications for surgery, the experience of the surgeon, and the frequency of post-operative early and late complications. Thus, the values for the 95% confidence interval and the odds ratio were obtained. The significance level ($p < 0.05$) was taken into account for all analyses.

Results

Surgical intervention was performed depending on the composition and spread of the pathological process, the results of preoperative (fine needle aspiration biopsy) performed under the control of ultrasound. During the operation thyroid tissue was removed using intraoperative cytophotometry.

At the nodal lesion of one lobe, hemithyroidectomy was carried out with removal of isthmus. Hemithyroidectomy was performed with visual control of the recurrent laryngeal nerve and extracapsular ligation of the thyroid artery tributaries. The thyroid artery was not ligated to preserve blood flow to the parathyroid gland. Only 57 (31.6%) patients underwent such operations. If there were small nodes in the other lobe, the subtotal removal of that lobe was performed. Thyroidectomy was performed for multinodular goiter and adenoma of both lobes.

Subtotal thyroidectomy was performed according to the method of O. V. Nikolaev in 78 (43.3%) patients with the colloid goiter with the preservation of a clinically significant volume of tissue of the thyroid residue (more than 3 cm³), in the absence of clinical and morphological data indicating the presence of thyroid cancer. Thyroidectomy was performed in 45 (25%) patients.

There was a significant difference between the groups of surgical patients ($p < 0.05$).

The composition and volume of surgical intervention for benign thyroid diseases are presented in table 1.

Table 1.

Volume and composition of surgical intervention in nodular goiter of benign origin

№	Volume of surgical intervention	n= 180	
		Quant.	%
1.	Hemithyroidectomy	57	32,0
2.	Subtotal thyroidectomy	78	43,3
3.	Total thyroidectomy	45	25
Total		180	100

Complications of various thyroid operations and the frequency of postoperative complications were compared between patients with different approaches. There was no lethality in the postoperative period. A serious complication requiring re-opening of the operative wound occurred only in a 57 year-old patient who underwent a thyroidectomy with a modified neck dissection with the development of a hematoma. In patients who underwent radical treatment (thyroidectomy) hypocalcemia (levels less than 2.1 mmol/l) was observed in 2 (4.4%), and in 1 (1.2%) after subtotal thyroidectomy.

In 3 patients, the operating period after thyroidectomy was complicated by transient laryngeal paresis with respiratory preservation. Surgical intervention performed for a benign nodular formation of the thyroid gland was confirmed by the results of histological examination of the surgical material. In a laboratory study, as shown in table 2, there were no significant differences in the values of T3 and T4 between the two groups. The prevalence of malignant diseases was 1.6% at a TSH level of less than 0.36 Mme/l, compared to 8.5% at a TSH level of 4.9 Mme/l or more ($p = 0.14$). A relatively high level of malignancy was observed in patients with higher levels of TSH.

Continuous variables are compared using the Mann-Whitney U-criteria, and categorical variables are compared using χ^2 -tests ($p < 0.05$).

Abbreviations: Ab-TG - antibody against thyroglobulin, Ab-TPO - antibody against thyroid peroxidase.

Patients with malignant nodes had positive results of Ab-TG and Ab-TPO testing more often than patients with benign nodes, as can be seen from the table 2. In an ultrasound study, the average maximum diameter of malignant nodes was significantly smaller than that of benign ones (1.99 ± 1.88 cm vs. 2.88 ± 1.91 cm, $p < 0.001$). The distribution of solitary nodes in malignant cases did not differ from that in benign ones (29.1% vs. 25.4%, $p = 0.108$).

There were no differences in eggshell calcification between the benign and malignant groups ($p > 0.05$).

91 (50.5%) patients had follicular adenomas, 5 (2.7%) patients had papillary thyroid cancer, and 3 (1.6%) patients had follicular cancer. Ultrasound examination revealed 8 cases of thyroid cancer, but surgical treatment was not included.

The analysis of postoperative intervention found that characteristic preoperative syndromes disappeared in 45% of patients. Clinical manifestations of laryngeal paresis in 3 patients resolved with conservative treatment within a year.

The results of surgical intervention and their functional results are shown in table 3.

The results of surgery for hemithyroidectomy with the manifestation of hypothyroidism were observed in 14 (24.6%) patients. Statistically significant differences in the frequency of postoperative hypothyroidism after thyroidectomy and subtotal thyroidectomy were found ($p < 0.05$).

In all patients with hypothyroidism, drug-induced euthyroidism was achieved by prescribing L-thyroxine 75 mcg per day. In patients with subtotal removal of the thyroid gland, the need for L-thyroxine was 150 mcg per day.

However, the frequency of relapse largely depended on the duration of the postoperative period. On ultrasound examination, in 8 (14%) patients after hemithyroidectomy nodules with a volume of from 0.6 to 0.9 cm³ were identified. The detection period for these nodes is up to 4 years.

In euthyroid patients after subtotal thyroidectomy, in the tissue of the thyroid residue the nodes in the volume from 0.7 to 2.5 cm³ were detected up to 5 years after surgery. In patients who initially underwent less radical hemithyroidectomy, 6 (3.3%) patients relapsed after 8 years and had to undergo a second operation to remove the remaining thyroid tissue.

Values	Benign tumor	Malignant tumor	P-value
Free T3, pmol/l	4,11 (3,93 – 5,08)	4,45 (3,98 – 5,01)	0,808
Free T4, pmol/l	14,98 (12,81 – 16,99)	15,51 (13,7 – 18,08)	0,064
TSH, Miu/l	1,19 (0,59 – 2,21)	1,65 (0,80 – 2,70)	< 0,001
Ab-TG	15	231,3	< 0,001
Ab-TPO	18,1	126,8	0,028

Table 2. Laboratory values in patients with nodular formation thyroid

№	Volume of surgical intervention	Functional state		Total, %
		Euthyroidism, %	Hypothyroidism, %	
1.	Hemithyroidectomy	47 (32,8)	14(24,6)	57
2.	Subtotal thyroidectomy	28 (35,9)	50 (64,1)	78
3.	Total thyroidectomy	–	45(100)	45
Total		75 (41,7%)	109 (60,5)	180

Table 3. The results of surgical intervention

Discussion

There are several types of surgical interventions used in the treatment of benign thyroid diseases. However, in recent years there has been an increase in the use of radical operations, such as total thyroidectomy, and a decrease in the number of less radical operations like subtotal thyroidectomy and hemithyroidectomy. In our study, the percentage of radical thyroidectomy operations increased from 12% in 2001 to 25% in 2018. Some authors have recommended a more radical operation for a non-toxic multi-node goiter [5]. They emphasized that since the entire thyroid gland is affected, leaving behind even a small amount of tissue, the risk of pathological changes, such as a relapse that requires repeated surgery, increases. Other authors consider a high risk of relapse and a significantly higher risk of postoperative complications a similar disadvantage of non-radical treatment [16, 17].

Some studies have found that the frequency of relapses after non-radical surgery of a multi-node non-toxic goiter is very high, up to 20% [7]. However, the frequency of relapses described by various authors largely depended on the duration of the postoperative period. According to these authors, the problem of recovery after surgery is more complex. Relapse is not a problem in itself. The problem occurs when a second operation is required. Repeated operation on the thyroid gland is technically much more difficult and is associated with a higher risk of complications than the previous operation. According to the literature, repeated surgery is associated with a greater risk of damage to the laryngeal nerve and hypoparathyroidism [8]. Hormonal treatment is often discussed by opponents of radical surgery [4]. Subtotal thyroidectomy does not require hormonal treatment. Opponents of a less radical operation quickly disproved this claim [6]. They proved that the left-over thyroid tissue does not protect against hypothyroidism.

According to their research, 100% of patients after subtotal thyroidectomy require high doses of levothyroxine, up to 150 mcg per day. In our study, all patients after subtotal thyroidectomy received hormonal support in daily doses from 75 mcg to 100 mcg.

The main goal of surgical treatment of thyroid diseases should always be the most effective performance with minimal complications and frequency of relapses. The authors of less radical thyroid

surgery oppose total thyroidectomy in the treatment of benign diseases, and emphasize increased morbidity, including damage to the laryngeal nerve and parathyroid gland. They emphasize that these patients are also sentenced to life-long hormone replacement therapy [7]. Recent studies concerning relapse in benign thyroid diseases show that young age, nodular and multi-nodular goiter, family history, and inadequate surgery are the main risk factors for relapse [1, 10]. To prevent the recurrence of benign thyroid disease, a detailed preoperative assessment is required to decide on the appropriate surgical intervention. Studies have shown that l-thyroxine therapy protects against relapses and repeated operations by reducing TSH stimulation on residual tissue. Thus, there is an opinion that the addition of thyroid hormones after surgery can effectively protect patients from recurrence [11, 12]. On the other hand, according to other researchers, despite substitution therapy, long-term postoperative follow-up showed a high rate of relapses after subtotal thyroidectomy [8].

Recent studies show that the protective effect of hormone therapy is controversial [7,8].

Thus, the rate of relapses after surgery for benign thyroid diseases was 11.1%. Inadequate surgical interventions, lack of substitution therapy, presence of a multi-node goiter, young age and family history should be taken into account as predictors of relapse. The need for repeated surgery for recurrent benign nodular diseases of the thyroid gland is a serious clinical problem due to the high frequency of post-operative complications.

Conclusion

Analysis of the results of surgical treatment of benign thyroid diseases confirmed the validity of the differential approach to the choice of the volume of surgical intervention, taking into account the detection of pathology and according to ultrasound, fine needle aspiration biopsy and intraoperative cytomorphometry of the damaged thyroid tissue. Therefore, each decision regarding the choice of thyroidectomy should be made individually. In addition to absolute medical indications for more radical treatment, such as compression symptoms, goiter progression, or suspected cancer, other factors should also be considered, such as young age, concomitant diseases, and an iodine-deficient region.

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