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**ИММУНОЛОГИК ХАВФНИ СТРАТИФИКАЦИЯЛАШ ВА ОПЕРАЦИЯДАН ОЛДИНГИ ПЛАЗМАФЕРЕЗ АСОСИДА ТОКСИК БЎҚОҚНИ ЖАРРОҲЛИК ДАВОЛАШНИ КОМПЛЕКС ОПТИМАЛЛАШТИРИШ**

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**КОМПЛЕКСНАЯ ОПТИМИЗАЦИЯ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ТОКСИЧЕСКОГО ЗОБА НА ОСНОВЕ ИММУНОЛОГИЧЕСКОЙ СТРАТИФИКАЦИИ РИСКА И ПРЕДОПЕРАЦИОННОГО ПЛАЗМАФЕРЕЗА**

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**Резюме.** Мақолада токсик бўқоқ шаклларини таъхислаш ва жарроҳлик йўли билан даволаш бўйича кенгайтирилган илмий таҳлил келтирилган. Тадқиқот 2005–2024 йилларда Самарқанд давлат тиббиёт университети клиникаси ва 1-сон шаҳар клиник шифохонаси жарроҳлик бўлимларида текширилган ва операция қилинган 498 нафар токсик бўқоқли беморлар клиник материалига асосланган. Диффуз токсик бўқоқ 204 нафар, аралаш токсик бўқоқ 159 нафар, тугунли токсик бўқоқ 114 нафар, қайталанган операциядан кейинги токсик бўқоқ 21 нафар беморда аниқланган. Тиреотроп гормон рецепторларига қарши антителалар даражасига асосланган ҳолда операция ҳажмини дифференциал танлаш зарурлиги асосланган. Оғир тиреотоксикоз, тиреостатик терапияга чидамлилик ёки уни кўтара олмаслик ҳолатларида операция олди плазмаферезининг аҳамияти алоҳида ёритилган. Комплекс ёндашув операциядан кейинги тиреотоксик криз хавфини камайтириш, субтотал резекциядан кейин қайталаниш эҳтимолини пасайтириш ва узоқ муддатли натижаларни яхшилаш имконини берган.

**Калит сўзлар:** токсик бўқоқ, диффуз токсик бўқоқ, тиреотоксикоз, тиреоидэктомия, қалқонсимон безнинг субтотал резекцияси, ТТГ рецепторларига антителалар, плазмаферез, Грейвс касаллиги, эндокрин жарроҳлик.

**Abstract.** The article presents an expanded scientific analysis of the diagnosis and surgical treatment of toxic forms of goiter. The study is based on the clinical material of 498 patients with toxic goiter who underwent examination and surgical treatment from 2005 to 2024 at the surgical departments of the Samarkand State Medical University clinic and City Clinical Hospital No. 1. Diffuse toxic goiter was diagnosed in 204 patients, mixed toxic goiter in 159 patients, nodular toxic goiter in 114 patients, and recurrent postoperative toxic goiter in 21 patients. The article substantiates the importance of differentiated selection of the operative volume based on the level of antibodies to thyroid-stimulating hormone receptors. Particular attention is paid to the role of plasmapheresis in preoperative preparation of patients with severe thyrotoxicosis, intolerance or resistance to antithyroid therapy. The proposed comprehensive approach made it possible to reduce the risk of postoperative thyrotoxic crisis, minimize recurrence after subtotal thyroid resection, and improve long-term clinical outcomes. The obtained data confirm that immunological risk stratification, precise thyroid surgery, and individualized preoperative preparation are key components of safe and effective endocrine surgery in patients with toxic goiter.

**Keywords:** toxic goiter, diffuse toxic goiter, thyrotoxicosis, thyroidectomy, subtotal thyroid resection, antibodies to TSH receptors, plasmapheresis, Graves' disease, endocrine surgery.

**Introduction and relevance.** Toxic forms of goiter remain one of the most clinically significant problems in endocrine surgery because they combine a high prevalence of thyroid pathology, severe systemic manifestations of thyrotoxicosis, and a considerable risk of cardiovascular, neurological, metabolic and ophthalmological complications. International guidelines emphasize that the treatment of thyrotoxicosis must be based on accurate etiological diagnosis and on careful selection among antithyroid drugs, radioactive iodine therapy and surgery [8, 13]. In regions where radioactive iodine therapy is limited or where patients present with large goiters, recurrent disease, nodular transformation or medication intolerance, surgical treatment continues to play a central role [1, 3, 6].

The clinical course of diffuse toxic goiter is determined by autoimmune stimulation of the thyroid gland. Antibodies to thyroid-stimulating hormone receptors activate follicular cells, increase the synthesis of thyroxine and triiodothyronine, and maintain a persistent hypermetabolic state. Prolonged thyrotoxicosis affects the myocardium, bone tissue, skeletal muscles, nervous system and eyes, and may lead to atrial fibrillation, heart failure, thyrotoxic myopathy, osteoporosis and endocrine ophthalmopathy [9, 13]. Therefore, the therapeutic goal is not limited to normalization of thyroid hormones; it also includes prevention of irreversible systemic complications and preservation of long-term quality of life.

Although antithyroid drugs are widely used as initial therapy, relapse after drug withdrawal remains a frequent problem, particularly in patients with high immunological activity, large gland volume, long disease duration and repeated exacerbations. The literature indicates that total thyroidectomy almost eliminates recurrence, whereas subtotal thyroid resection may preserve some thyroid function but carries a risk of recurrent thyrotoxicosis [2, 4, 12]. This creates the need for a differentiated approach that identifies patients for whom organ-preserving surgery is acceptable and those for whom radical thyroidectomy is more justified.

Preoperative preparation is another unresolved issue. Surgery performed in decompensated thyrotoxicosis is associated with a high risk of thyrotoxic crisis, arrhythmias and hemodynamic instability. Standard preparation with thionamides requires time and may be impossible in patients with severe drug reactions, hepatotoxicity, agranulocytosis or resistance. Recent studies and clinical experience support therapeutic plasma exchange as an effective bridge to surgery in selected patients with severe thyrotoxicosis, especially when rapid hormonal stabilization is required [10, 15].

For Uzbekistan and other iodine-endemic regions, optimization of surgical treatment for toxic goiter has special practical importance. Local studies

have demonstrated the significance of long-term follow-up, relapse analysis, preoperative diagnostic stratification and the use of plasmapheresis in severe forms of the disease [1, 2, 3, 4, 15]. In this context, the development of a comprehensive strategy that combines immunological risk assessment, rational choice of surgical volume, precision operative technique and individualized preoperative preparation is a scientifically justified and clinically relevant task.

**Aim of the study.** The aim of the study was to improve the long-term results of surgical treatment of patients with toxic goiter by developing and implementing a comprehensive approach to determining the operative volume, improving surgical technique and optimizing preoperative preparation.

**Materials and methods.** The study was performed at the Department of General Surgery of Samarkand State Medical University on the basis of the surgical departments of the Samarkand State Medical University clinic and City Clinical Hospital No. 1. The clinical material included exactly 498 patients with toxic goiter who were examined and surgically treated during the period from 2005 to 2024.

The age of patients ranged from 18 to 77 years, with a mean age of  $47.2 \pm 13.7$  years. According to the nosological structure, diffuse toxic goiter was diagnosed in 204 patients, mixed toxic goiter in 159, nodular toxic goiter in 114 and recurrent postoperative toxic goiter in 21. The duration of disease before surgery ranged from 4 months to 29 years, with a mean duration of  $5.8 \pm 4.6$  years. Recurrent disease during conservative treatment was found in 445 patients, and 283 of them had two or more relapses.

All patients underwent a comprehensive clinical, laboratory and instrumental examination. Clinical assessment included analysis of complaints, duration of disease, previous antithyroid therapy, signs of compression, manifestations of thyrotoxicosis and its complications. Laboratory diagnostics included the measurement of free thyroxine, free triiodothyronine, thyroid-stimulating hormone, antibodies to thyroid peroxidase and antibodies to thyroid-stimulating hormone receptors. The level of antibodies to thyroid-stimulating hormone receptors was used as a key prognostic marker for choosing the operative volume in patients with diffuse toxic goiter.

Instrumental examination included ultrasound assessment of thyroid volume, parenchymal structure and nodular changes. When nodules were detected, ultrasound-guided fine-needle aspiration biopsy was performed. Electrocardiography and echocardiography were used to assess cardiovascular complications, especially tachyarrhythmias and heart failure. Computed tomography of the neck and mediastinum was used when retrosternal goiter or compression syndrome was suspected.

Preoperative preparation was directed toward achieving euthyroidism or at least stable clinical

compensation. Standard preparation included thiamazole therapy in individually selected doses under hormonal control. In 47 patients with severe thyrotoxicosis, intolerance or resistance to antithyroid therapy, plasmapheresis was used. Each session removed 700–1200 ml of plasma, and the number of procedures ranged from 3 to 5 with an interval of 48–72 hours.

The surgical volume was selected according to the form of toxic goiter, the level of antibodies to thyroid-stimulating hormone receptors, the presence of nodular transformation and cytological data. In diffuse toxic goiter with receptor antibody levels below 1.5 U/L, subtotal thyroid resection was performed. When receptor antibodies were 1.5 U/L or higher, thyroidectomy was indicated. In nodular, mixed and recurrent toxic goiter, thyroidectomy was performed because of the higher risk of persistent or recurrent disease.

**Results.** The clinical manifestations of thyrotoxicosis were typical and reflected systemic hormonal excess. Palpitations were observed in 462 patients, increased sweating in 423, weight loss in 391, emotional lability in 372 and tremor in 345. Tachycardia with a heart rate above 100 beats per minute was detected in 412 patients, whereas atrial fibrillation was diagnosed in 63 patients. Ophthalmopathy of varying severity was present mainly in patients with diffuse toxic goiter.

The severity of thyrotoxicosis was mild in 123 patients, moderate in 271 and severe in 104. Among patients with severe thyrotoxicosis, 47 had intolerance or resistance to antithyroid therapy and therefore required plasmapheresis as a method of rapid preoperative stabilization. After plasmapheresis, heart rate decreased from  $128 \pm 14$  to  $92 \pm 8$  beats per minute, free T4 decreased from  $47.3 \pm 9.6$  to  $23.8 \pm 5.1$

pmol/L, and free T3 decreased from  $15.7 \pm 4.2$  to  $7.4 \pm 1.9$  pmol/L.

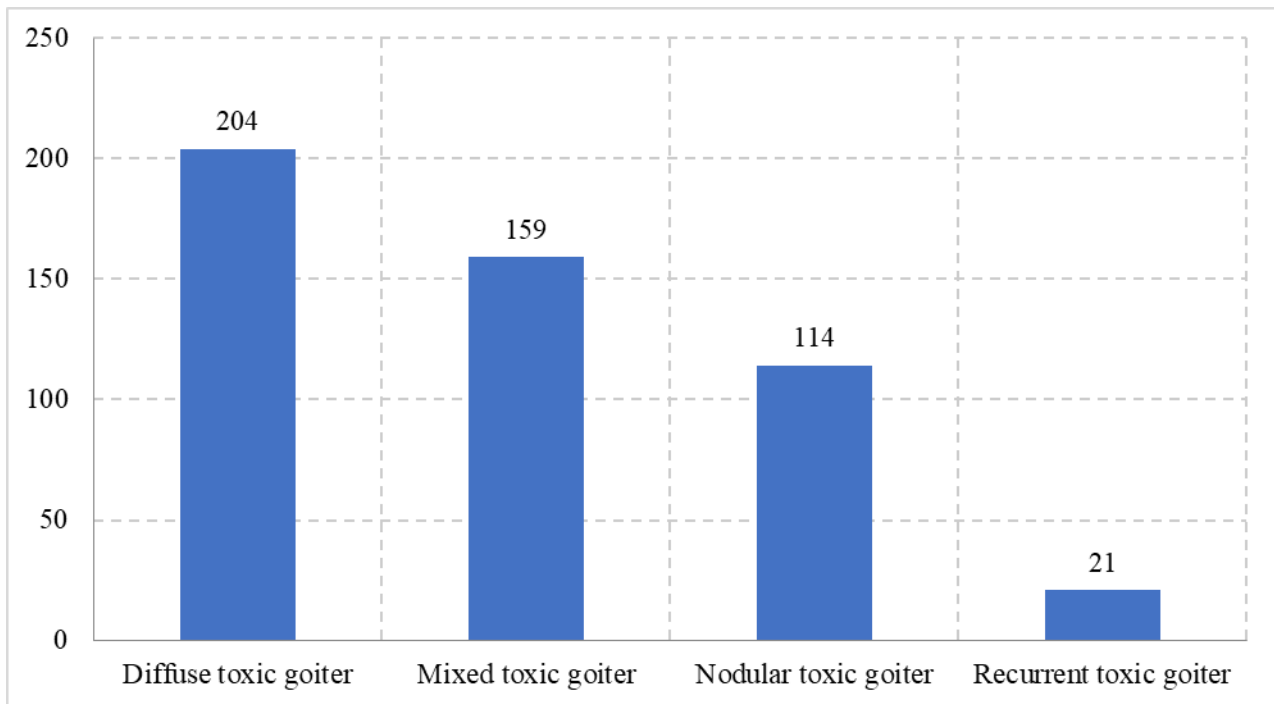
Surgical treatment was performed in all 498 patients. Thyroidectomy was performed in 312 patients and subtotal thyroid resection in 186. Early postoperative complications were registered in 34 patients, which accounted for 6.8% of the total cohort. Transient hypocalcemia developed in 23 patients, persistent hypoparathyroidism in 3, transient recurrent laryngeal nerve paresis in 8, persistent recurrent laryngeal nerve paresis in 2 and postoperative hematoma requiring revision in 3 patients. Importantly, no thyrotoxic crisis occurred among patients who underwent plasmapheresis before surgery.

**Long-term outcomes and prognostic significance of receptor antibodies.** Long-term results were assessed in 471 patients, representing 94.6% of the total cohort. The follow-up period ranged from 6 months to 15 years, with a mean duration of  $4.7 \pm 3.2$  years. Recurrence of thyrotoxicosis was detected in 27 patients, corresponding to 5.7% of the followed cohort. All recurrences occurred after subtotal thyroid resection, while no recurrence was registered after thyroidectomy.

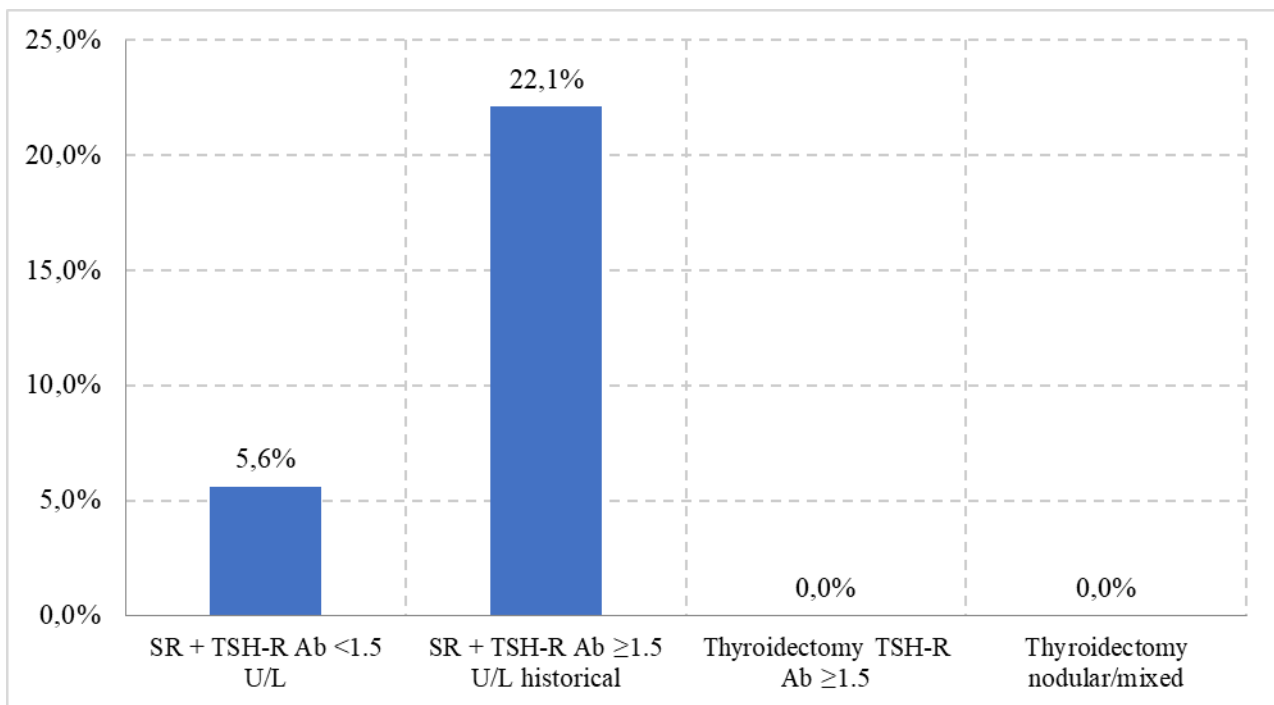
The most important predictor of recurrence was the preoperative level of antibodies to thyroid-stimulating hormone receptors. In patients with diffuse toxic goiter and antibody levels below 1.5 U/L who underwent subtotal resection, recurrence developed in 4 of 72 followed patients, or 5.6%. In the historical group with antibody levels of 1.5 U/L or higher who underwent subtotal resection, recurrence developed in 23 of 104 patients, or 22.1%. This indicates that subtotal resection in the setting of persistent autoimmune stimulation substantially increases the risk of recurrent thyrotoxicosis.

**Table 1.** Key clinical and surgical characteristics of the study cohort

Indicator	Value	Clinical interpretation
Total number of patients	498	Large single-center endocrine surgery cohort
Diffuse toxic goiter	204 (41.0%)	Main autoimmune form requiring antibody-based stratification
Mixed toxic goiter	159 (31.9%)	Combination of diffuse hyperfunction and nodular transformation
Nodular toxic goiter	114 (22.9%)	Predominantly surgical indication due to autonomous nodules
Recurrent postoperative toxic goiter	21 (4.2%)	High-risk group requiring radical removal of residual tissue
Patients treated with thyroidectomy	312 (62.7%)	Radical operation associated with absence of recurrence in follow-up
Patients treated with subtotal resection	186 (37.3%)	Organ-preserving operation acceptable in low immunological risk
Patients treated with plasmapheresis	47 (9.4%)	Severe thyrotoxicosis with drug intolerance or resistance
Follow-up cohort	471 (94.6%)	Long-term follow-up from 6 months to 15 years



**Fig. 1.** Distribution of patients by toxic goiter form in the study cohort



**Fig. 2.** Long-term recurrence of thyrotoxicosis by surgical strategy

Correlation analysis demonstrated a strong direct relationship between the level of antibodies to thyroid-stimulating hormone receptors and recurrence risk. The Pearson correlation coefficient was 0.715, and ROC analysis showed an area under the curve of 0.863. The threshold of 1.5 U/L provided a sensitivity of 85.2% and a specificity of 79.6% for predicting recurrence. Therefore, the receptor antibody level can be considered not only a diagnostic marker of Graves' disease activity, but also a practical surgical stratification criterion.

**Discussion.** The presented data support the concept that surgical treatment of toxic goiter should not be based only on thyroid size or the surgeon's preference. The biological activity of the disease, expressed by the level of antibodies to thyroid-stimulating hormone receptors, must be integrated into operative planning. Patients with low antibody activity may benefit from subtotal thyroid resection, whereas patients with high antibody activity require thyroidectomy to prevent recurrence.

The role of thyroidectomy has increased during the last decades because modern endocrine surgery

allows safe radical removal of the thyroid gland when recurrent laryngeal nerves and parathyroid glands are reliably visualized. The low rate of permanent complications in the present cohort demonstrates that the risk of surgery can be minimized by precision technique, careful hemostasis and preservation of parathyroid blood supply. In this context, lifelong levothyroxine replacement after thyroidectomy should be considered an acceptable and predictable consequence compared with recurrent thyrotoxicosis, repeated operations and cardiovascular complications.

Preoperative plasmapheresis represents an important component of the proposed strategy. The method is not intended to replace antithyroid drugs in routine cases, but it becomes highly valuable in severe thyrotoxicosis when standard therapy fails or is contraindicated. Rapid reduction of circulating thyroid hormones and immune mediators decreases cardiac stress, improves hemodynamic stability and enables surgery under safer conditions. The absence of postoperative thyrotoxic crisis among patients prepared with plasmapheresis confirms the practical value of this approach in selected high-risk patients.

Another clinically significant finding is the importance of long-term follow-up. Recurrence after subtotal resection may develop months or years after operation, especially when autoimmune stimulation persists. Therefore, postoperative monitoring must include clinical examination, thyroid hormone profile, thyroid-stimulating hormone level and ultrasound assessment of residual thyroid tissue. In patients after thyroidectomy, monitoring is aimed primarily at ensuring adequate replacement therapy and detecting hypocalcemia or voice-related complications.

The proposed comprehensive approach may be summarized as a three-level model. The first level is etiological and immunological diagnosis, including receptor antibody measurement. The second level is surgical risk stratification and selection of operative volume. The third level is individualized preoperative and postoperative management, including plasmapheresis in severe cases, precision surgery, calcium-vitamin D prophylaxis and lifelong endocrinological observation when needed.

#### **Conclusion:**

A comprehensive approach to the diagnosis and surgical treatment of toxic goiter in 498 patients demonstrated that immunological stratification, differentiated choice of operative volume and targeted preoperative preparation improve the safety and long-term effectiveness of treatment.

The level of antibodies to thyroid-stimulating hormone receptors is a prognostically significant criterion for recurrence after subtotal thyroid resection. A threshold value of 1.5 U/L can be used to identify patients who require thyroidectomy rather than organ-preserving surgery.

Subtotal thyroid resection is justified in patients with diffuse toxic goiter and low antibody activity, while thyroidectomy is indicated in patients with high antibody levels, nodular and mixed toxic goiter, and recurrent postoperative toxic goiter.

Plasmapheresis is an effective method of preoperative preparation in patients with severe thyrotoxicosis, intolerance or resistance to antithyroid therapy. Its use allows rapid clinical stabilization and prevents postoperative thyrotoxic crisis.

Precision surgical technique with visualization and preservation of recurrent laryngeal nerves and parathyroid glands ensures a low rate of permanent complications and allows thyroidectomy to be used safely when radical treatment is clinically justified.

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**КОМПЛЕКСНАЯ ОПТИМИЗАЦИЯ  
ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ ТОКСИЧЕСКОГО  
ЗОБА НА ОСНОВЕ ИММУНОЛОГИЧЕСКОЙ  
СТРАТИФИКАЦИИ РИСКА И  
ПРЕДОПЕРАЦИОННОГО ПЛАЗМАФЕРЕЗА**

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***Резюме.** В статье представлен расширенный научный анализ диагностики и хирургического лечения токсических форм зоба. Исследование основано на клиническом материале 498 больных токсическим зобом, прошедших обследование и хирургическое лечение в 2005–2024 гг. в хирургических отделениях клиники Самаркандского государственного медицинского университета и городской клинической больницы № 1. Диффузный токсический зоб был диагностирован у 204 пациентов, смешанный токсический зоб — у 159, узловой токсический зоб — у 114, рецидивный послеоперационный токсический зоб — у 21 пациента. Обосновано значение дифференцированного выбора объёма операции с учётом уровня антител к рецепторам тиреотропного гормона. Особое внимание уделено роли плазмафереза в предоперационной подготовке больных с тяжёлым тиреотоксикозом, непереносимостью или резистентностью к тиреостатической терапии. Комплексный подход позволил снизить риск тиреотоксического криза, уменьшить вероятность рецидива после субтотальной резекции и улучшить отдалённые результаты лечения.*

***Ключевые слова:** токсический зоб, диффузный токсический зоб, тиреотоксикоз, тиреоидэктомия, субтотальная резекция щитовидной железы, антитела к рецепторам ТТГ, плазмаферез, болезнь Грейвса, эндокринная хирургия.*