LONG-TERM RESULTS OF SURGICAL TREATMENT IN PATIENTS WITH TOXIC GOITER AND SEVERE THYROTOXICOSIS

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Received 19 Dec 2019, Corrections received 07 Jan 2020, Accepted 12 Febr 2020
https://doi.org/10.31688/ABMU.2020.55.1.08

ABSTRACT

Introduction. The surgical treatment of goiter with severe thyrotoxicosis may lead to an improvement of the general condition of the patient, and amelioration of the clinical manifestations of thyrotoxic cardiomyopathy.

The aim of the study was to evaluate the long-term results of surgical treatment in patients with toxic goiter and severe thyrotoxicosis, including the study of changes in cardiac activity and the level of physical activity.

Materials and methods. The study was conducted in 123 patients with toxic goiter and severe thyrotoxicosis treated surgically. The duration of thyrotoxicosis ranged from 18 to 74 months. Before the surgical treatment and one year after it, structural and functional changes of the heart were studied by echocardiography and electrocardiogram, and physical activity according to the six-minute walk test. The long-term effects of surgery were evaluated by clinical, laboratory, and instrumental methods.

RéSUMÉ

Résultats à long terme du traitement chirurgical des patients atteints d’une goitre toxique et d’une thyrotoxique grave

Introduction. Le résultat du traitement chirurgical du goitre atteint d’une thyrotoxicose sévère peut être une amélioration de l’état général et de l’activité physique, une diminution ou l’élimination des manifestations cliniques de la cardiomyopathie thyrotoxique.

Le but de l’étude. Étudier les résultats à long terme du traitement chirurgical des patients atteints de goître toxique avec une thyrotoxicose sévère, et aussi des changements de l’activité cardiaque et de l’activité physique.

Matériaux et méthodes. L’étude a été menée chez 123 patients atteints de goître toxique avec une thyrotoxicose sévère traités chirurgicalement. La durée de la thyrotoxicose variait de 18 à 74 mois. Avant le...
treatment were considered good, satisfactory, unsatisfactory and ineffective.

**Results.** The results of surgical treatment depend on the severity of the manifestations of thyrotoxic cardiomyopathy. Good and satisfactory results were obtained in 44.7% cases, unsatisfactory results in 32.5% and ineffective treatment was found in 22.8% cases.

**Conclusions.** The surgical treatment of patients with toxic goiter and severe thyrotoxicosis allows eliminating thyrotoxicosis and in some patients the rhythm disorders, reducing the intensity of clinical manifestations of thyrotoxic cardiomyopathy and improving the capacity of physical activity.

**Keywords:** toxic goiter, severe thyrotoxicosis, surgical treatment, long-term results.

**List of abbreviations:**
- TG – toxic goiter
- BGD – Basedow-Graves’ disease
- NTG – nodular toxic goiter
- MTG – mixed toxic goiter
- TT – thyrotoxicosis
- HF – heart failure
- AF – atrial fibrillation
- ECG – electrocardiography
- 6 MWT – six-minute walk test

**Introduction**

Long-term results of surgical treatment in patients with toxic goiter (TO) are evaluated by general surgical complications (postoperative bleeding, infiltration, suppuration), specific complications (laryngeal nerve injuries, phonation disorders and postoperative hypoparathyroidism), thyroid residual function, relapses of goiter and thyrotoxicosis (TT)\(^1\)\(^-\)\(^3\).

The result of surgical treatment (thyroidectomy) in TT, with full compensation of postoperative hypothyroidism with thyroxine preparations, can be an improvement of the general condition and physical activity capacity (effective treatment) or improvement may not occur, it remains at the level before surgery and/or worsens (ineffective treatment).

Because of ineffective treatment, life prognosis is impeded\(^4\), secondary to complications of TG, including atrial fibrillation (AF)\(^5\), heart failure (HF)\(^6\), structural and functional changes in the heart muscle\(^7\)\(^-\)\(^11\).

After medical or surgical treatment of TT and the achievement of euthyroidism, sinus rhythm is restored in 19.66% of the patients who had AF\(^12\). Functional and structural changes of the heart in case of thyrotoxicosis, in particular AF, are the cause of the increase in mortality from embolism in these patients, 1.2–1.4 times compared to the general population\(^13\)\(^-\)\(^16\).

traitement chirurgical et un an après, les modifications structurelles et fonctionnelles du cœur ont été étudiées selon les indicateurs de l’échocardiographie et de l’ECG, l’activité physique selon le test de marche de six minutes. Les effets à long terme du traitement ont été évalués par les gradations développées: bons résultats, satisfaisants, insatisfaisants et traitement inefficace.

**Résultats.** Les résultats du traitement chirurgical dépendent de la gravité des manifestations de la cardiomyopathie thyréotoxique. De bons et satisfaisants résultats ont été obtenus dans 44.7% des cas, un résultat insatisfaisant dans 32.5% et un traitement inefficace a été trouvé dans 22.8% des cas.

**Conclusions.** Il est établi que le traitement chirurgical des patients atteints de goître toxique avec une thyréotoxicoïde sévère permet d’éliminer la thyréotoxicoïde et chez certains patients – les troubles de l’activité cardiaque rythmique, réduisant l’intensité des manifestations cliniques de la cardiomyopathie thyréotoxique, améliorant l’activité physique et l’activité générale.

**Mots-clés:** goître toxique, thyrotoxicoïde sévère, traitement chirurgical, résultats à long terme.

**The objective of the study** was to evaluate the long-term results of surgical treatment in patients with toxic goiter and severe thyrotoxicosis, including changes in cardiac activity and physical activity capacity.

**Materials and methods**

The study was conducted in 123 surgically treated patients with severe TG, admitted in the surgical department of Ternopil City Municipal Hospital No1, Ukraine, from May 5, 2003 to August 17, 2018. The age of the patients ranged from 21 to 74 years. The duration of TT ranged from 18 to 74 months. Indications for surgical treatment were frequent relapses of TT, progression of thyrotoxic cardiomyopathy on the background of thyrostatic therapy, with the development of heart rhythm disorders and heart failure. Thyrotoxicosis was caused by Basedow-Graves’ disease (BGD) (82 cases), nodular toxic goiter (NTG) (29 cases), and mixed toxic goiter (MTG) (12 cases) (Table 1).

All the patients underwent general clinical examination, ultrasonography, determination of the level of thyroid-stimulating hormone (TSH), free thyroxine (\(T_4\)), antibodies to TSH receptors and thyroperoxidase antibody (AbTPO), electrocardiogram (ECG), daily Holter ECG. Ultrasonography was performed in the mode 2D; the results were evaluated in comparison...
with the average standards presented in the guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Research. Changes in the severity and functional class of HF were evaluated according to the criteria of the 6MWT. At the same time, the changes in heart rate and respiratory movements per minute were calculated not in absolute terms, but as a percentage of increase: 100% indicators were taken before the test.

Criteria for inclusion in the study: patients with BGD, nodular and mixed toxic goiter with severe thyrotoxicosis with recurrent course and ineffective drug treatment, heart failure NYHA class II, III.

Exclusion criteria – patients with BGD, nodular and mixed toxic goiter with severe thyrotoxicosis, recurrent course and ineffective medical treatment, NYHA class IV.

The patients were evaluated upon admission, after achieving medical euthyroidism, and one year after the surgical treatment. To analyze the long-term results of surgical treatment, the data obtained one year after surgery were compared with preoperative data.

Drug treatment before surgery consisted in antithyroid drugs, in doses that ensured the achievement of euthyroidism, and β-blockers. In individual cases, symptomatic therapy was also used. Treatment of patients with AF was carried out according to the algorithmic approach of the treatment of AF in hyperthyroidism of the European Society of Cardiology (ESC) 2016.

According to recommendations and 6MWT test results, patients were divided into two groups: with HF NYHA class II (95 patients) and HF NYHA class III (28 patients). The group of patients with HF NYHA class II included 61 patients (74.4%) with BGD, 24 patients (32.8%) with NTG and 10 patients (33.3%) with MTG. Correspondingly, HF NYHA class III and BGD was encountered in 21 patients (25.6%), NTG in 5 patients (17.2%), MTG in 2 patients (16.7%).

In the group of patients with HF NYHA class II, the changes in the parameters of the past 6MWT distance were in the range from 324 to 425 m. The distance travelled by an individual depends on his physical activity capacity, which, in turn, is determined by the severity of functional and structural changes in the heart. Considering this, to study the effects of functional and structural changes in the heart on long-term results of surgical treatment of TG, according to the 6MWT distance, the first group of patients (with HF NYHA class II) was divided into three subgroups. The first subgroup included 12 patients who walked more than 395 m, the second one included 19 patients who walked a distance ranging from 381 to 390 m, and the third – 64 patients, who walked from 324 to 374 m. In patients of the second group, the distance travelled at 6MWT was less than 300 meters.

The long-term results were assessed by changes in the general condition of the patients, the severity and functional class of heart failure, structural and functional alterations of the heart, and the cardiac rhythm. According to the recommendations of the European Society of Cardiology, the long-term results of surgical treatment of patients with goiter and TT were considered as good, satisfactory, unsatisfactory results and ineffective treatment.

A good result was considered when patients noted a significant improvement in the general condition or felt healthy. The 6MWT distance travelled was at least 425 m. The functional class of heart failure improved, cardiac rhythm disorders were not determined and systolic and diastolic functions of the heart (by echocardiography) were normal.

When patients noted an improvement of the general condition, a satisfactory result was considered. At the same time, the severity and functional class of heart failure did not change, the 6MWT
RESULTS AND DISCUSSION

Ukraine dated February 13, 2006.

ics provisions of the Ministry of Public Health of
ments and norms of ICH GLP (2002), typical eth-
requirements of the Statute of Ukrainian Association
reference values.

of euthyroidism, with the level of TSH within the
described with thyroxine in doses that ensured the state
Thyroidectomy was the method of choice. In the
were surgically treated, under general anesthesia.
in order to achieve euthyroidism, the patients
the difference was considered significant at \( p<0.05 \).

Statistical processing of the results was per-
formed with Statssoft STATISTICA software package,
using parametric and nonparametric methods. When
assessing the difference in quantitative indicators be-
tween the groups, the Student’s criterion was applied.
The difference was considered significant at \( p<0.05 \).

After preoperative preparation, performed in order to achieve euthyroidism, the patients
were surgically treated, under general anesthesia. Thyroidectomy was the method of choice. In the
postoperative period, replacement therapy was pre-
scribed with thyroxine in doses that ensured the state
of euthyroidism, with the level of TSH within the
reference values.

The study was performed according to the re-
quirements of the Statute of Ukrainian Association
for Bioethics and the GCP norms (1992), require-
ments and norms of ICH GLP (2002), typical ethics
provisions of the Ministry of Public Health of
Ukraine dated February 13, 2006.

RESULTS AND DISCUSSION

The study has shown that a decrease of the
6MWT distance was combined with an increase in
the age of patients and the duration of TG disease.
Thus, in the first subgroup, the age of patients and
the duration of the disease were the lowest, and the
average distance walked was the highest. In other sub-
groups, the age of patients and the duration of the
disease increased and were the largest in the fourth
subgroup (Table 2), and the distance walked, re-
spectively, decreased.

Studies have shown that in response to exercise,
compared to the physiological norms, in the select-
ed subgroups of patients, the distance travelled by
6MWT decreased, and the values of oxygen consump-
tion and tachycardia decreased. The rate of increase
in heart rate also decreased, and tachypnea and Borg
scores increased (see Tables 2, 3). A simultaneous
decline in the increase in heart rate and aggravation
of tachypnea are signs of poor exercise tolerance and
progression of the severity of heart failure. In such
cases, the heart muscle has no reserve to increase
the heart rate and ensure adequate blood supply, and
increasing hypoxia compensates for tachypnea.

In the study period, one year after the surgical
treatment, the indices of 6MWT test compared with
the previous data significantly increased in the first
and second subgroups, which was reflected in the im-
provement of the general condition of the patients.
Patients of the third subgroup and the second group
did not present significant changes in the studied pa-
rameters (Tables 2, 3). The general condition of the
patients of the third subgroup slightly improved, and
in the patients of the second group, it remained un-
changed.

After preoperative preparation, patients in both
groups revealed structural and functional changes
in the heart. The ejection fraction was not changed
in patients of the first subgroup, but in the second
and third subgroups and in the cases of the second
subgroup it decreased (\( p<0.05 \)). The final diastolic size
of the left ventricle in patients of the second and third
subgroups and the second group increased (\( p<0.05 \)).
The same pattern of changes also applied to the final
systolic size of the left ventricle. The index of muscle
mass of the left ventricle increased: in patients of the
first subgroup, the changes were not significant and
in the second and third subgroups the increase was
significant (\( pp<0.05 \)). In patients of the second group,
this indicator was within or below the normal value.
The diameter of the left atrium in patients of all sub-
groups was larger than normal: it increased signifi-
cantly from 38.20±0.16 to 45.70±0.22 mm (\( p<0.05 \)).
Such dynamics of changes in echocardiography of
the left heart indicate the severity and progression
of heart failure against the background of thyrotoxic
cardiomyopathy (Table 4).

One year after surgical treatment, the structural
and functional indicators of cardiac activity in the
patients of the first, second and third subgroups
(\( p<0.05 \)) improved compared to the previous data
and did not change significantly in the patients of
the second group. Similar changes in structural and
functional indicators of cardiac activity in the treat-
ment of thyrotoxicosis were revealed by Sviridenko et
al\textsuperscript{25} and Oliveros-Ruiz et al\textsuperscript{26}.

Thus, EF in patients of the first subgroup de-
creased, and in patients of the second and third
subgroups increased (\( p<0.05 \)) and did not change in
patients of the second group. Indicators of the final
diastolic and systolic dimensions of the left ventricle
(\( p<0.05 \)) significantly decreased (Table 4).
After drug preparation for surgery, cardiac ar-
rhythmias in patients of the first subgroup were
represented by supraventricular (9) and ventricular
earlystoles (3), which were not detected one year
after the surgical treatment. In patients of the second
subgroup, supraventricular extrasystoles – in 10 cases
and ventricular extrasystoles – in 5 patients, atrial
fibrillation in 4 patients: with normal heart rate (3)
and rapid heart rate (1), after medical preparation.
One year after surgery, 4 patients had no rhythm ab-
normalities, 4 patients had single extrasystoles, and
2 paired extrasystoles. Frequent (about 1000 extrasys-
toles per day) ventricular extrasystoles in 4 patients
changed individually (less than 22 extrasystoles per
day). In 2 of 4 patients with atrial fibrillation, the sinus rhythm recovered, in one patient tachycardia changed to normo-cardia (Tables 5, 6), and in the other 2 patients it did not change.

Patients of the third subgroup, before surgery, had heart rhythm disorders in the form of extrasystoles, atrial fibrillation and atrial flutter. Extrasystoles were noted in 22 patients: supraventricular in 15 patients and frequent solitary ventricular extrabeats in 7 patients. From the supraventricular extrasystoles, 9 patients had frequent isolated extrasystoles, 3 patients paired extrasystoles, and 3 patients with bigeminy and trigeminy. Atrial fibrillation was diagnosed in 37 patients, and atrial flutter in 5 patients. One year after surgery, changes in cardiac rhythm disorders occurred over a wide range: frequent single supraventricular and ventricular extrasystoles disappeared; paired supraventricular extrasystoles in 2 patients disappeared, and one patient presented frequent single extrasystole; bigeminy in one patient disappeared, and in 2 patients switched to frequent single extrasystoles. The changes in the rhythm of patients with atrial fibrillation with rapid heart rate were as follows: in 31 cases it changed to normo-cardia, and in 6 cases it remained unchanged. Atrial flutter in 3 of 5 patients changed to atrial fibrillation, but did not change in two patients.

In patients of the second group, after the preoperative preparation, the most severe disorders of cardiac activity were registered (see Tables 5, 6). Atrial fibrillation with rapid heart rate was determined in 19 patients, and atrial flutter in 9 patients. One year after the surgical treatment, atrial fibrillation in one case changed from rapid heart rate to normal heart rate, and in 18 patients it remained unchanged. Atrial flutter in 3 of 5 patients changed to atrial fibrillation, but did not change in two patients.

The results were used to assess the long-term results of treatment (Table 7). A good treatment result was obtained in patients of the first subgroup, in which the 6MWT distance before surgical treatment
ranged from 395 to 408 m, and after it to more than 425 m. Accordingly, the satisfactory result was in 19 patients of the second subgroup, in which the 6MWT distance travelled before surgical treatment was in the range from 381 to 390 m, and one year after it – to more than 398 m. A satisfactory result of treatment was found in 24 patients of the third subgroup, in which the 6MWT distance travelled before surgical treatment ranged from 361 to 374 m, and one year after it to at least 385 m. An unsatisfactory result of treatment was observed in 40 patients of the third subgroup, in which the 6MWT distance travelled before surgical treatment was 327-353 m, and one year after it increased in some cases by 15-19 meters. Ineffective treatment was found in patients of the second group (Table 7).

The study showed that the surgical treatment of TT had a positive effect (good and satisfactory results) only in 52 of 123 patients (44.7%). These results are alarming about the correctness of the therapeutic strategy and indications of the surgical treatment in patients with TG.

Fierro et al. consider that factors such as patient’s age and duration of drug treatment have a significant impact on the long-term results of surgical treatment of toxic goiter, on the recovery of sinus rhythm especially. According to Biondi28, the return to sinus rhythm occurs more often in successfully treated hypothyroid patients under 50 years old with newly diagnosed heart rhythm disorders. Long-term treatment (more than 30 months) with thyrostatic drugs in TG patients and thyrotoxicosis with cardiac disorders worsens the long-term results of surgical treatment27,31.

CONCLUSIONS

The surgical treatment of patients with toxic goiter and severe thyrotoxicosis leads to positive results in 44.7% of cases: it eliminates thyrotoxicosis, reduces the intensity of clinical manifestations of thyrotoxic cardiomyopathy and improves cardiac activity, physical activity capacity and general condition of the patients. The long-term results of surgical treatment in patients with severe thyrotoxicosis depend on the duration of drug therapy for thyrotoxicosis and the age of the patients. The test for predicting the long-term results of surgical treatment in patients with toxic goiter is the length of the distance covered at the 6MWT. In patients with toxic goiter and signs of severe thyrotoxicosis, the main indication for surgical treatment is the presence of thyrotoxic cardiomyopathy with cardiac disorders.

Author contributions

Conceptualization, V.O.S. and M.I.S.; methodology, O.V.S.; software, I.M.P.; validation, G.S.K. and V.V.K.; formal analysis, O.V.S. and H.P.H.; investigation, V.V.M., V.V.T., and H.H.; resources, N.P.T.K.; data curation, A.A.P. and O.V.S.; writing – original draft preparation, O.V.S. and H.P.H.; writing – review and editing, V.O.S., O.V.S. and M.I.S.; visualization, V.V.K. and A.A.P.; supervision, G.S.K. and V.V.K.; project administration, N.P.T. All the authors read and agreed with the final version of the article.

Compliance with Ethics Requirements:

“The authors declare no conflict of interest regarding this article”

“The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study”

“No funding for this study”

Acknowledgments: none

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