

CHANGES IN THE VULNERABILITY OF CLINICAL MANIFESTATIONS OF THYROTOXIC CARDIOMYOPATHY AS INDICATORS OF REMOTE RESULTS OF SURGICAL TREATMENT IN PATIENTS WITH TOXIC GOITER

Oleksandr V. SHIDLOVSKYI¹, Mykhailo I. SHEREMET^{3✉}, Viktor O. SHIDLOVSKYI¹, Petro O. GERASYMCHUK¹, Dmytro V. OSADCHUK¹, Andriy J. HOSPODARSKYI¹, Andrii V. CHORNOMYDZ¹, Viktoriia V. KRAVTSIV², Nina P. TKACHUK², Oleksandr V. BILOOKYI²

¹ Horbachevsky Ternopil State Medical University, Surgery department, Ternopil, Ukraine

² Bukovinian Medical University, Surgery Department No1, Chernivtsi, Ukraine

³ Lviv Regional Clinical Diagnostic and Treatment Cardiologic Center, Lviv, Ukraine

Received 22 Feb 2018, Accepted 29 Apr 2018

ABSTRACT

The aim of the work – improvement of the evaluation method of remote results of surgical treatment in patients with toxic goiter, taking into account the changes in the severity of clinical manifestations of thyrotoxic cardiomyopathy

Materials and methods. The research was conducted in 150 patients operated for toxic goiter of moderate severity (48) and severe (102). The method of estimation of remote results of surgical treatment, taking into account the regression of signs of thyrotoxic cardiomyopathy and gradation and division into good, satisfactory, unsatisfactory and ineffective treatment, was developed.

Results and discussion. A good remote outcome of surgical treatment of thyrotoxicosis was achieved in 26 (54.2 %) patients with moderate thyrotoxicosis and in 9 (8.8%) patients with severe thyrotoxicosis, satisfactory in 21 (43.7 %) and 36 (35, 3%) cases

RÉSUMÉ

Changements dans la vulnérabilité des manifestations cliniques de la cardiomyopathie thyrotoxisique en tant qu'indices des résultats lointains du traitement chirurgical des patients avec du goître toxique

L'objectif de la recherche est d'améliorer les techniques d'évaluation des résultats à long terme du traitement chirurgical des patients atteints de goître toxique, en tenant compte des variations de la complexité des manifestations cliniques de la cardiomyopathie thyrotoxisique.

Les matériaux et les méthodes. La recherche a été faite chez 150 patients opérés pour un goître toxique dans les formes modérées (48) et sévères (102). On a élaboré les techniques d'évaluation des résultats à long terme du traitement chirurgical, prenant en compte la régression des signes de la cardiomyopathie thyrotoxisique et la gradation ainsi que la division

✉ Corresponding author:

M.I. SHEREMET
Surgery Department No1 of BSMU
Address: 58018 Chernovtsy, Holovna str., 191, Ukraine
email: mihayl71@gmail.com;
phone 0956064607

respectively and unsatisfactory – in 1 (2.0 %) and 33 (32.4 %). Ineffective surgical treatment was recognized in 24 (23.5 %) patients. Unsuccessful results and ineffective surgical treatment of toxic goiter were found in patients with severe heart rate rhythm disorders, structural and functional changes in the cardiac muscle and functional classes II and III.

Conclusions. Long-term results of surgical treatment of patients with toxic goiter are determined by the severity of thyrotoxic cardiomyopathy. In cases of severe thyrotoxicosis, the question of the need for surgical treatment should be put in the development of severe heart rhythm disorders and structural and functional changes in the heart muscle.

Keywords: thyrotoxicosis; surgical treatment; long-term results.

INTRODUCTION

Long-term results of surgical treatment of patients with toxic goiter (TG) are evaluated for general-surgical complications (bleeding, infiltration, suppuration), specific complications (trauma of the laryngeal nerves, phonation disorders, hypoparathyroidism), thyroid function, goiter relapse and thyrotoxicosis (TT)¹⁻³.

However, it is known that surgically cured TT with full compensation of postoperative hypothyroidism with thyroxine drugs may not improve the life expectancy, and even cause its deterioration due to complications of toxic goiter at the time of treatment, such as atrial fibrillation (AF), heart failure (HF), structural and functional changes in the heart muscle, which in the remote period after the surgical intervention will not undergo reversible changes. After treatment of TT and euthyroidism achieving, recovery of sinus rhythm occurs only in 19% of patients with AF⁴. The structural-functional changes in the cardiac muscle and changes in cardiac activity, in particular the rhythmicity of cardiac contractions, are the reasons for the increase of mortality rate in this cohort of patients with embolism of the brain vessels, 1.2-1.4 times compared with the general population^{5,6}. In this regard, it is obvious that in

en traitement efficace, satisfaisant, insatisfaisant et inefficace.

Les résultats et la discussion. Un bon résultat à long terme du traitement chirurgical de la thyrotoxicose a été acquis chez 26 (54,2%) patients souffrant de thyrotoxicose modérée et 9 (8,8%) patients atteints de thyrotoxicose sévère, un résultat satisfaisant en 21 (43,7%) et 36 (35,3%) cas et insatisfaisant – en 1 (2,0%) et 33 (32,4%) cas. Le traitement chirurgical inefficace a été défini chez 24 (23,5%) patients. Les résultats insatisfaisants et le traitement chirurgical inefficace du goitre toxique ont été découverts chez les patients avec des troubles sévères du rythme de la contraction du coeur, des changements structurels et fonctionnels dans le muscle cardiaque et de la classe fonctionnelle II et III.

Conclusions. Les résultats à long terme du traitement chirurgical des patients atteints de goitre toxique sont déterminés par la complexité de la cardiomyopathie thyrotoxique. En cas de la thyrotoxicose sévère, la question sur la nécessité d'un traitement chirurgical doit être mise en présence des troubles sévères du rythme de l'activité cardiaque et des changements structurels et fonctionnels du muscle cardiaque.

Mots-clés: thyrotoxicose, traitement chirurgical, résultats à long terme.

assessing the long-term results of surgical treatment of patients with TG, variants of thyrotoxic cardiomyopathy (TTCMP) after sustained euthyroidism should be taken into account. Given the literature data, one can distinguish the following: a complete regression of clinical and paraclinical manifestations of thyrotoxic cardiomyopathy and the restoration of physical activity and working capacity; asymptomatic myocardial dysfunction, which is diagnosed by echocardiography, and restriction of physical activity and working capacity; persistence of clinical and paraclinical signs of thyrotoxic cardiomyopathy and disability (rhythm disorders, hypertrophy of the myocardium, HF, dilatation of heart chambers).⁷⁻¹⁵

THE AIM OF THE STUDY – improvement of the evaluation method of remote results of surgical treatment of patients with toxic goiter, taking into account changes in the severity of clinical manifestations of thyrotoxic cardiomyopathy.

MATERIALS AND METHODS

The research was conducted in 150 patients with toxic goiter. The study was conducted in the Surgical Clinic of Emergency Hospital in Ternopil, Ukraine, between 2012–2017. Moderate thyrotoxicosis was

found in 48 patients and severe – in 102 patients, aged from 21 to 74 years. Duration of thyrotoxicosis ranged from 24 to 74 months. Indications for surgical treatment were relapse of thyrotoxicosis despite adequate thyroid therapy, the presence of complications of thyrotoxicosis, in particular heart failure and heart rhythm disorders. The causes of thyrotoxicosis were: Graves-Basedow's disease (93), nodular toxic goiter (47), mixed toxic goiter (10).

Changes in the functional class (FC) of patients with heart failure were evaluated according to the criteria of the six-minute walk test, according to the recommendations of the Ukrainian Association of Cardiologists⁷. Disturbances of cardiac rhythmic activity were studied according to the indicators of daily ECG monitoring. Structural changes in the heart muscle, in particular the ejection fraction (EF), left ventricle end-diastolic and end-systolic diameters, left ventricular myocardial mass index and left atrium diameter – by echocardiography. The studies were conducted after preoperative preparation (drug euthyroidism) and one year after the surgical treatment of thyrotoxicosis. The operation of choice was thyroidectomy.

Data on severity and functional class of heart failure after preoperative preparation are presented in Table 1.

In the group of patients with moderate thyrotoxicosis after preoperative preparation, there were 8 (16.6 %) patients with supraventricular extrasystoles. Among 102 patients with severe thyrotoxicosis, in 77 (75.5 %) cases heart rhythm disorders were diagnosed. Among them, supraventricular extrasystoles were found in 18 (23.3 %), paroxysmal atrial fibrillation – in 19 (24.7 %) and persistent/permanent atrial fibrillation – in 40 (52.0 %) patients.

The tests of evaluation of remote results were changes in the general condition of patients, structural and functional disorders of the myocardium, FC of patients with heart failure, heart rhythm disorders. According to the conducted researches on the analysis of remote results of surgical treatment of thyrotoxicosis, these results were good, satisfactory, unsatisfactory, or the treatment was considered ineffective. A good result was considered when patients noticed a significant improvement in the general condition, or some of them felt healthy, FC of patients with heart failure improved, prior to surgery, cardiac rhythm disorders were not present, and indicators of systolic and diastolic function of the heart at echocardiography were normal.

The results have been considered satisfactory when patients noticed an improvement of the general condition. At the same time, physical activity did not improve and was limited, the severity of FC in patients with heart failure did not change, the six

minute walk test distance increased by > 15 m and was not less than 370 m. The evident structural and functional changes in the heart muscle before surgical treatment decreased. Cardiac disorders improved: they disappeared and were not registered, or the persistent/ permanent form of atrial fibrillation changed to paroxysmal, and paroxysmal atrial fibrillation disappeared or changed to supraventricular extrasystoles. An unsatisfactory result was considered when patients noticed improvement in general condition and physical activity, and cardiac disorders by type of paroxysmal or prolonged persistent/ permanent form of atrial fibrillation, structural and functional changes in the heart, FC of patients with heart failure remained unchanged. Ineffective treatment was considered when patients did not notice an improvement in the general condition, and the preoperative physical activity disturbances, structural-functional heart disorders, cardiac rate, FC of patients with heart failure in the remote postoperative period did not change.

Statistical processing of the obtained research results was carried out according to the software package Statsoft STATISTICA. It was conducted using parametric and non-parametric methods. In assessing the difference between the quantitative indicators between the groups, Student's criterion was used. The difference was considered to be significant at $p < 0.05$.

RESULTS AND DISCUSSION

Among 48 patients with moderate thyrotoxicosis, 26 patients, one year after the surgical treatment of thyrotoxicosis, assessed their condition as good, and did not complain. Compared with the indicators before surgery, the length of the six minutes' walk distance increased to 13–37 meters ($p < 0.05$), and the amount of oxygen consumption to 0.7–1.5 ml/kg/min ($p < 0.05$). In terms of the six minutes' walk distance, the functional class was estimated as FC I. In 13 patients, before the surgery, FC was FC I and remained the same after the surgery. In other 13 patients, FC II evident before the surgery changed to FC I. In this case, the diastolic and systolic functions of the heart also became normal. The remote outcome of surgical thyrotoxicosis treatment in these patients was estimated to be good.

22 patients noted an improvement of the general condition, although they did not consider themselves healthy. The travelled test distance after the operation increased to 15–21 m and was within the limits of the FC II, that is, compared with the data before the operation, the severity of the FC did not change (Table 2).

In 7 patients, supraventricular extrasystoles disappeared and changed to the correct sinus rhythm,

and in one patient it remained unchanged. The results of the echocardiography indicated a return to the normal limits of the left ventricle end-diastolic and end-systolic diameters ($p < 0.05$). The reduction of the left ventricular myocardial mass index and left atrium diameter was also reliable. The ejection fraction returned to normal ($p < 0.05$), (Table 3). According to these indicators, the remote result is estimated to be satisfactory.

In one female patient, the severity of FC (FC II) and the cardiac rhythm disorders after surgery did

not change. At the same time, she had low figures of the distance covered, ejection fraction, marked changes in the structural and functional characteristics of the heart muscle, which were manifested by an increase of the left ventricular myocardial mass index, left ventricle end-diastolic diameter, left ventricle end-systolic diameter and atrium diameter. The remote outcome of the treatment of this patient was considered unsatisfactory (Tables 2, 3).

In cases of severe thyrotoxicosis one year after the surgical treatment of thyrotoxicosis, 9 patients

Table 1. Cardiac insufficiency in patients with toxic goiter after preoperative preparation.

Heart failure severity	Groups of patients with severity of thyrotoxicosis		Total
	Moderate (n=48)	Severe (n=102)	
Heart failure I, FC I	13 (27.1 %)	-	13 (8.7 %)
Heart failure IIA, FC II	35 (72.9 %)	78 (76.5 %)	113 (75.3 %)
Heart failure IIIB, FC III	-	24 (23.5 %)	24 (16.0 %)
Total	48 (32.0 %)	102 (68.0 %)	150 (100 %)

Table 2. Long-term results of surgical treatment of patients with moderate thyrotoxicosis and their characteristics by six minutes' walk test.

Remote results, number of patients	Statistical factors	Age (years)	Disease duration (months)	Test distance (meters)		VO ₂ of the test (ml/kg/min)	
				1	2	1	2
Good	M	41.6	34.2	451	468	18.6	19.5
n=26	±m	4.38	3.89	2.79	2.81 ²	0.15	0.07 ²
Satisfactory	M	54.4	50.7	391.3	407	16.9	17.5
n=21	±m	2.58 ¹	2.28 ¹	0.82 ¹	1.91 ^{1,2}	0.02 ¹	0.07 ^{1,2}
Unsatisfactory	-	73	62	387	392	16.7	16.9
n=1							

Note. Here and in the table 3-5: 1 - on the background of drug euthyroidism; 2 - one year after the surgical treatment of thyrotoxicosis. The changes are significant ($p < 0.05$):¹ - in comparison with the results of the previous subgroup, ² - in comparison with the indicators on the background of drug euthyroidism.

Table 3. Indices of structural and functional rearrangement of the left half of the heart in patients with moderate thyrotoxicosis according to remote results of treatment.

Remote results, number of patients	Statistical figures	Ejection fraction, %		left ventricle end-diastolic diameter, mm		left ventricle end-systolic diameter, mm		left ventricular myocardial mass index, g/m ²		atrium diameter, mm	
		1	2	1	2	1	2	1	2	1	2
Good	M	59.5	55.3	49.5	46.5	30.5	30.6	106.2	96.8	36.2	33.5
n=26	±m	0.37	0.26	0.18	0.17 ²	0.14	0.16	0.24	0.27 ²	0.29	0.23
Satisfactory	M	53.2	52.7	50.2	46.8	30.8	30.3	118.4	102.2	40.1	35.2
n=21	±m	0.33 ¹	0.29	0.28	0.22	0.18	0.17	0.23 ¹	0.22 ^{1,2}	0.18 ¹	0.15 ^{1,2}
Unsatisfactory		46	48	55	52	32	31	119	114	39	38
n=1											

Note. Here and in the table 3-5: 1 - on the background of drug euthyroidism; 2 - one year after the surgical treatment of thyrotoxicosis. The changes are significant ($p < 0.05$):¹ - in comparison with the results of the previous subgroup, ² - in comparison with the indicators on the background of drug euthyroidism.

out of 102 evaluated their condition as good, did not complain and considered themselves healthy. The length of the distance covered increased with 35–67 m ($P < 0.05$), and the amount of oxygen consumption increased to 0.9–1.5 ml/kg/min ($P < 0.05$). The severity of FC in patients with heart failure changed from FC II to FC I. The indicators of the structural and functional status of the cardiac muscle normalized. The age of these patients and the duration of thyrotoxicosis among all patients with thyrotoxicosis were the smallest. According to these indicators, the remote result is considered as a good one. (Tables 4, 5).

36 patients were referred to improve their general condition. Some of them limited physical activity due to fatigue and shortness of breath. The length of the distance covered increased with 15–22 m ($P < 0.05$) and ranged from 370 to 398 meters. The amount of oxygen consumed increased, but changes are not reliable. FC of patients with heart failure according to six minutes' walk test data did not change. The heart rhythm disorders, present in 20 patients before surgery, of which 15 supraventricular extrasystoles, changed to sinus rhythm; among 5 cases of paroxysmal atrial fibrillation, 2 cases changed to sinus rhythm and 3 remained with supraventricular extrasystoles. Reliable changes also occurred in the figures of systolic and diastolic heart function evaluation: ejection fraction, left ventricle end-diastolic diameter, left ventricular myocardial mass index and left atrium diameter increased. Taking into account the changes of the studied figures in the remote postoperative period, the remote outcome of treatment in these patients was regarded as satisfactory (Tables 4, 5).

A mild improvement in the general condition was noted in 33 patients. They, as well as before surgery, were disturbed by shortness of breath and fatigue during physical activity. The six minutes' walk test distance increased to 2–12 m ($P > 0.05$), and an increase in the amount of oxygen consumption was also unreliable. Cardiac rhythm disorders before surgery (in 3 patients – supraventricular extrasystoles, 14 patients – paroxysmal atrial fibrillation, and 16 patients – persistent/ permanent atrial fibrillation), in remote period after surgical treatment did not change. There were no reliable changes in the values of systolic and diastolic functions of the heart, although there was a tendency to their improvement (Table 4, 5). The results of treatment of these patients were considered unsatisfactory.

There was no improvement in the general condition after surgical treatment of thyrotoxicosis in 24 patients. In the remote postoperative period, clinical signs of heart failure, in particular shortness of breath

and fatigue almost did not change. Disturbances of heart rate, as well as before surgical treatment, were manifested as a persistent/ permanent form of atrial fibrillation. The values of ejection fraction and left ventricular myocardial mass index were small, and left ventricle end-diastolic and end-systolic diameters and left atrium diameter were increased (Table 5). The remote outcome of surgical treatment of these patients was considered as an ineffective treatment.

The evaluation of remote results of surgical treatment of patients with toxic goiter according to the developed method showed that its positive effect (good and satisfactory) was obtained in 92 (61.3 %) cases. Among them, in case of moderate thyrotoxicosis – in 47 (98.0 %) patients, and severe thyrotoxicosis – in 45 (44.1 %) (Table 6).

The conducted studies showed that the main indicators of evaluation of remote results of surgical treatment of patients with toxic goiter complicated by thyrotoxic cardiomyopathy are functional tests. It is difficult to overestimate the value of the six minutes' walk test and its indicators, such as the length of the distance covered and the amount of oxygen consumption, that objectively and reliably reflects the functional capacity of the cardiac muscle and its functional reserves. Changes in the functional class of patients with heart failure, which are a direct reflection of functional reserve of the heart, have special significance. Particular importance in evaluating long-term results should be paid to heart rate abnormalities; because atrial fibrillation is the cause of increased mortality in vascular cerebral and cardiac blood supply disorders. Considering this, atrial fibrillation, uncorrected in the postoperative period, is an indicator of delayed, ultimately surgical treatment of patients with toxic goiter, since atrial fibrillation is a consequence of profound structural and functional changes in the cardiac muscle of thyrotoxic genesis. Changes in structural and functional disorders of the cardiac muscle in the remote period after surgery are worthy of attention. This is the case for changes in the figures of the ejection fraction, left ventricular myocardial mass index, left ventricle end-diastolic and end-systolic diameters and atrium diameter.

CONCLUSIONS

The developed method of evaluation of remote results of surgical treatment of patients with toxic goiter showed the importance of taking into account their definition of the severity of structural and functional cardiac disorders of thyrotoxic genesis and the degree of their recovery after the elimination of thyrotoxicosis. Long-term results of surgical treatment

Table 4. Figures of age, disease duration and six minutes' walk test in patients with severe thyrotoxicosis depending on the remote results of treatment.

Remote results, number of patients	Statistical data	Age (years)	Disease duration (months)	Test distance (meters)		VO ₂ of the test (ml/kg/min)	
				1	2	1	2
Good n=9	M ±m	27.7 2.72	23.7 1.24	400 4.18	449 4.43 ²	16.8 0.11	18.7 0.13 ²
Satisfactory n=36	M ±m	44.3 1.92	34.4 1.53	374 1.93 ¹	391 2.72 ^{1,2}	16.2 0.08	16.8 0.08 ¹
Unsatisfactory n=33	M ±m	53.1 0.97	45.8 2.11	353 7.09 ¹	357 3.42 ¹	15.4 0.07 ¹	15.7 0.09 ¹
Ineffective treatment n=24	M ±m	65.5 1.38	45.3 2.58	287 2.82 ¹	288 1.54 ¹	13.7 0.10 ¹	13.8 0.07 ¹

Note. Here and in the table 3-5: 1 - on the background of drug euthyroidism; 2 - one year after the surgical treatment of thyrotoxicosis. The changes are significant (p < 0.05): ¹ - in comparison with the results of the previous subgroup, ² - in comparison with the indicators on the background of drug euthyroidism.

Table 5. Figures of structural and functional reconstruction of the heart in patients with severe thyrotoxicosis according to remote results of treatment.

Results of treatment, number of patients	Statistical data	Ejection fraction, %		left ventricle end-diastolic diameter, mm		left ventricle end-systolic diameter, mm		left ventricular myocardial mass index, g/m ²		left atrium diameter, mm	
		1	2	1	2	1	2	1	2	1	2
Good n=9	M ±m	55.1 0.34	55.3 0.27	49.6 0.28	46.6 0.19 ²	30.8 0.21	30.4 0.17	107.8 0.37	94.2 0.26 ²	37.8 0.17	34.8 0.29 ²
Satisfactory n=36	M ±m	49.7 0.24 ¹	52.2 0.27 ^{1,2}	51.7 0.24 ¹	48.1 0.25 ^{1,2}	31.4 0.27	30.7 0.29	120.7 0.39 ¹	105.1 0.21 ^{1,2}	41.2 0.24 ¹	36.1 0.18 ^{1,2}
Unsatisfactory n=33	M ±m	46.3 0.27 ¹	49.1 0.29	53.2 0.21	50.3 0.25	32.9 0.28	32.1 0.12	117.4 0.33	112.2 0.37 ¹	44.1 0.27	41.6 0.29 ¹
Ineffective treatment n=24	M ±m	38.7 0.17 ¹	38.6 0.18 ¹	53.9 0.31	53.8 0.17 ¹	33.7 0.31	33.8 0.33	105.7 0.28 ¹	105.4 0.24 ¹	45.4 0.23	45.2 0.21 ¹

Note. Here and in the table 3-5: 1 - on the background of drug euthyroidism; 2 - one year after the surgical treatment of thyrotoxicosis. The changes are significant (p < 0.05): ¹ - in comparison with the results of the previous subgroup, ² - in comparison with the indicators on the background of drug euthyroidism.

Table 6. Distribution of patients according to remote results of treatment of toxic goiter.

Results of treatment	Thyrotoxicosis severity		Total
	moderate	severe	
Good	26 (54.2 %)	9 (8.8 %)	35 (23.3 %)
Satisfactory	21 (43.8 %)	36 (35.3 %)	57 (38.0 %)
Unsatisfactory	1 (2.0 %)	33 (32.4 %)	34 (22.7 %)
Ineffective treatment		24 (23.5 %)	24 (16.0 %)

of patients with toxic goiter are determined by the severity of structural changes in the cardiac muscle and functional cardiac disorders.

In cases of severe and long-term thyrotoxicosis, the need of surgical treatment should be set as soon as possible, at least prior to the development of severe heart rhythm disorders and structural and functional changes in the heart muscle.

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“

REFERENCES

- Makarov IV, Galkin RA, Andreev MM. Long-term results and their prediction for the surgical treatment of diffuse toxic goiter. *Endocrine Surgery*. 2013;(2): 47-51 [in Russian].
- Rybachkov VV, Tevyashov AV, Rossoshanskaya EI, Kabanov EN. Evaluation of the quality of life of patients operated for thyroid nodules. *Chelovek i ego zdorovye*. 2011;(1): 72-5 [in Russian].
- Kharnas SS, Mamayeva SK. Long-term results and quality of life after surgical treatment of diffuse toxic goiter. *Endocrine Surgery*. 2008; (1): 10-14 [in Russian].
- Skvortsov VV, Fomina NG, Emelyanov DN. Modern aspects of pharmacotherapy of CHF in patients with thyrotoxic myocardial dystrophy (cardiopathy). *Doctor's Journal*. 2014;3(55): 39-47 [in Russian].
- Brandt F, Thvilum M, Almind D, et al. Morbidity before and after the diagnosis of hyperthyroidism: a nationwide register-based study. *PLoS One*. 2013;8(6): 667-711.
- Brandt F, Green A, Hegedüs L, Brix TH. A critical review and meta-analysis of the association between overt hyperthyroidism and mortality. *Eur. J. Endocrinol*. 2011;165(4): 491-7.
- Bahn Chair RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid*. 2011;21(6): 593-646.
- Oliveros-Ruiz L, Vallejo M, Canseco LFD, et al. Determinants of thyrotoxic cardiomyopathy recovery. *Biomed Research International*, 2013, 452709.
- Ertek S, Cicero AF. Hyperthyroidism and cardiovascular complications: a narrative review on the basis of pathophysiology. *Archives of Medical Sciences*, 2013, 9(5):94-952.
- Ngo ASY, Tan DCL. Thyrotoxic heart disease. *Resuscitation*, 2006, 70(2):287-290.
- Dahl P, Danzi S, Klein I. Thyrotoxic cardiac disease. *Current Heart Failure Reports*, 2008, 5(3):170-176.
- Razvi S, Jabbar A, Pingitore A, et al. Thyroid hormones and cardiovascular function and diseases. *JACC*, 2018, 71(16):1781-1796.
- Blondi B. How could we improve the increased cardiovascular mortality in patients with overt and subclinical hyperthyroidism? *European Journal of Endocrinology*, 2012, 167:295-299.
- Mourouzis I, Forini F, Pantos C, Iervasi G. Thyroid hormone and cardiac disease: from basic concepts to clinical application. *Journal of Thyroid Research*, 2011,: 958626.
- Ghandour A, Reust C. Hyperthyroidism: a stepwise approach to treatment. *J Fam Pract*, 2011, 60:388-95.