



# ECHOCARDIOGRAPHIC EVALUATION OF CARDIAC FUNCTION IN FEMALE PATIENTS WITH THYROID DISORDERS

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## ABSTRACT

The aim of this study was to assess echocardiographic changes in female patients with untreated dysfunctional thyroid states and whether the therapy aimed to normalize the thyroid dysfunction could lead to improvement in cardiac systolic and diastolic function. The study included 90 female subjects who performed control of thyroid hormonal status at the Institute of Nuclear Medicine at the University of Sarajevo Clinics Centre and who previously were untreated for the thyroid functional disorders. The study sample was divided in three groups based on the thyroid hormones levels: a) hyperthyroid group (n= 30) b) hypothyroid group (n=30) and c) eu-thyroid (control). Echocardiography measurements were performed on commercially available *Toshiba, SSH 140*.

Before the therapy no statistically significant differences in the peak early and late mitral inflow velocities (E/A) values between the study groups was observed, but the mean left ventricular ejection fraction (LVEF) in hypothyroid group was significantly lower (58,30±1,05) compared to control (64,96±0,71) and hyperthyroid group (64,69±1,31) (p<0,001). In hypothyroid group we found significant increase in mean LVEF (58,30±1,05 vs. 64,95±0,86, p<0,01) and E/A (1,06±0,07 vs. 1,17±0,08 ; p=0,01) values after the normalization of thyroid hormone status. Thyroid dysfunctional states were not associated with impaired diastolic function, probably due to the short duration of thyroid dysfunction and timely and successful conversion therapy. Systolic function however was significantly reduced in hypothyroid patients but subsequently improved after the adequate therapy. Early diagnostic approach in patients with thyroid dysfunctional states is important for avoidance of cardiac complications that accompany these disorders.

KEY WORDS: hypothyroidism, hyperthyroidism, cardiac function, echocardiography

## INTRODUCTION

Thyroid functional disorders, hypothyroidism and hyperthyroidism, are both associated with clinically significant cardiovascular changes. Thyroid hormones have positive chronotropic and inotropic effects on the heart. Increased metabolism and demand for oxygen in peripheral tissues in hyperthyroidism results in increase in cardiac output and heart rate, followed by increased blood flow to the skin, muscles, brain, thyroid gland and kidneys (1). Due to blood volume expands and increased cardiac output, the maximum velocity of fibre shortening myocardial excitability increase, and the pulse pressure widens. Cardiovascular disorders associated with hyperthyroidism include atrial tachyarrhythmias, mitral valve dysfunction, and heart failure (2). Hypothyroidism produces a decrease in myocardial contractility, pericardial effusion, increase in left ventricular mass and prolonged duration of contraction and relaxation. The ejection fraction and cardiac reserve are only slightly diminished (3). Numerous clinical studies have shown that also subclinical form of hypothyroidism or hyperthyroidism is associated with changes in several cardiac parameters (2,4,5). The literature on cardiac involvement in subclinical hypothyroidism consistently shows that patients exhibit resting left ventricular diastolic dysfunction evidenced by delayed relaxation, and impaired systolic function on effort that results in poor exercise capacity (6). Whether subclinical hypothyroidism also affects left ventricular systolic function at rest remains controversial. Several mild cardiac abnormalities, such as impairment of left ventricular diastolic function at rest and of systolic function on effort have been described also in subclinical form of hyperthyroidism. Most of cardiac manifestations are reversible with adequate and timely thyroid therapy. (2) The aim of this study was to assess echocardiography changes in female patients with untreated dysfunctional thyroid states but also to assess the effect of therapy, aimed to normalization of their thyroid dysfunction, on parameters of cardiac function.

## MATERIALS AND METHODS

### *Patients*

All participants included in our study were selected from the subjects who performed control of thyroid hormonal status at the Institute of Nuclear Medicine, University of Sarajevo Clinics Centre, and who had never been treated for any thyroid functional disorders.

We included 104 subjects based on their serum FT<sub>3</sub>, FT<sub>4</sub> and TSH values. Only women were included to exclude intersex variations. After overnight fasting, all the women underwent full medical assessment, laboratory examinations, electrocardiogram and echocardiography. The exclusion criteria were: presence of clinically evident cardiovascular diseases, diabetes mellitus, renal diseases, pituitary/hypothalamic disorders and pregnancy. Based on these criteria a definitive sample was formed which consisted of 90 patients, divided into three, aged matched, groups: 1. Hyperthyroid group, 30 females (mean age 43,6±1 years) with serum TSH level <0,1 mIU/L and increased serum FT<sub>4</sub> level (>23 pmol/L). 2. Hypothyroid group, 30 females (mean age 48,1±2 years), with serum TSH level >10 mIU/L and decreased serum FT<sub>4</sub> level (<10 pmol/L). 3. Euthyroid (control) group, 30 females (mean age 43,68±8 years), with serum FT<sub>3</sub>, FT<sub>4</sub> and TSH levels within the normal reference range. Approval for the study was obtained by the local Ethics Committee. All procedures on human subjects were performed in accordance with the latest version of Helsinki Declaration. All subjects included in the study signed upon informed consent with careful explanation of the study procedures.

### *Measurements*

After the selection and inclusion of the patients in the study groups, blood samples were taken from all patients to determine the serum FT<sub>3</sub>, FT<sub>4</sub>, TSH concentration. Hyperthyroid patients have been treated with adequate therapy (tiamazol, propiltiouracil, radioiodine I-131) to achieve euthyroid state, defined as decrease in FT<sub>3</sub> and FT<sub>4</sub> concentrations to the reference values. The average duration of therapeutic treatment was 5,3±1 months. Hypothyroid patients have been treated with L-thyroxin therapy aiming to normalise FT<sub>3</sub>, FT<sub>4</sub> and TSH levels. The average duration of therapeutic treatment to achieve euthyroid state was 6,1±1 months. Control of hormonal status was done periodically.

### *FT<sub>3</sub>, FT<sub>4</sub> and TSH measurements*

Blood samples were collected in the fasting state, immediately put on ice and processed within 30 minutes. Thereafter, the obtained serum samples were kept frozen at - 70 ° C. FT<sub>3</sub>, FT<sub>4</sub> and TSH plasma levels were determined using electrochemiluminescence immunoassay "ECLIA" on Elecsys 2010 (Roche Diagnostic). All measurements were performed at the Institute of Nuclear Medicine, University of Sarajevo Clinics Centre.

*Echocardiography*

Echocardiography measurements were performed on commercially available Toshiba, SSH 140, echo machine using 2,5 MHz transducer. Measurements were taken according to the recommendations of the American Society for Echocardiography (7). As a parameter of systolic function we measured LVEF (left ventricular ejection fraction). A LVEF <50% was indicative of LV systolic dysfunction. In addition, the peak early (E; meters per second) and late (A; meters per second) mitral inflow velocities were measured. With these values, E/A ratios were determined, and diastolic dysfunction was defined as an E/A ratio <1,0.

*Statistical analysis*

Data are presented as mean ± standard deviation (SD). Analysis was performed using SPSS package 16.0 (SPSS Inc., Chicago, Illinois, USA). Changes in parameters before and after the treatment were compared using the paired t-tests. Differences in mean values between groups were assessed using the Student t test. Pearson correlation analysis was used to assess the correlation between variables. A two-tailed p value < 0,05 was considered significant.

**RESULTS**

Mean serum FT<sub>3</sub>, FT<sub>4</sub> and TSH values significantly changed in hypothyroid and hyperthyroid group before and after therapy are presented in table 1. After the therapy there was no significant difference in mean FT<sub>3</sub> and FT<sub>4</sub> concentration between hypothy-

roid or hyperthyroid and control group. TSH values after the therapy remained significantly lower in hyperthyroid group compared to control group (p <0,05). Before the therapy no statistically significant differences in diastolic function between the study groups was observed. The average E/A value, as parameter of diastolic function, in hypothyroid group was lower (1,06±0,07) compared to hyperthyroid (1,12±0,07) and euthyroid group (1,15±0,04) but the difference was not statistically significant. In hypothyroid group a significant elevation in E/A values was observed after the therapy (1,06±0,07 vs. 1,17±0,08 ; p=0,006). There were no statistically significant differences in average LVEF values between control and hyperthyroid group before as well as after therapy. In hypothyroid group mean LVEF values were significantly lower before therapy (58,30±1,05) compared to control (64,96±0,71) and hyperthyroid group (64,69±1,31) (p<0,001) (Table 2). After the normalization of thyroid hormone status we found significant improvement of systolic function in hypothyroid group (p=0,0002), and there were no differences in values between control and hypothyroid group. We didn't find any significant differences in average values of other measured echocardiographic parameters between groups before and after therapy (Table 2).

**DISCUSSION**

The cardiac complications of long standing hyperthyroidism and hypothyroidism are serious if are not diagnosed properly earlier. As an non-invasive method, echocardiography can play important role in recogniz-

	Hypothyroid group (N=30)			Hyperthyroid group (N=30)		
	Before therapy	After therapy	p-value	Before therapy	After therapy	p-value
FT3 nmol/L)	3,27±0,19	4,57±0,16	p<0,01	13,45±1,29	4,91±0,13	p<0,01
FT4 nmol/L)	8,39±1,66	13,3±1,27	p<0,01	27,46±2,81	14,67±0,43	p<0,01
TSH (mU/L)	14,35±2,1	3,24±0,24	p<0,01	0,03±0,07	0,5±0,11	p<0,01

TABLE 1. Serum FT<sub>3</sub>, FT<sub>4</sub> and TSH concentration in hypo-and hyperthyroid group before and after the therapy.

Echocardiographic parameters	Control (euthyroid) group (n=30)	Hyperthyroid group (n=30)		Hypothyroid group (n=30)	
		Before therapy	After therapy	Before therapy	After therapy
LVIDD (cm)	4,35±0,09	4,45±0,12	4,44±0,12	4,55±0,09	4,54±0,08
LAD (cm)	3,27±0,07	3,20±0,10	3,16±0,11	3,29±0,10	3,30±0,10
AoD (cm)	2,53±0,05	2,60±0,07	2,60±0,06	2,65±0,06	2,69±0,06
IVSd (cm)	0,92±0,02	0,99±0,03	0,99±0,03	0,98±0,02	0,99±0,03
LVPWd (cm)	0,87±0,01	0,92±0,03	0,92±0,03	0,93±0,02	0,93±0,02
LVEF (%)	64,96±0,71	64,69±1,31	66±1,44	<b>58,30±1,05***</b>	<b>64,95±0,86***</b>
E/A	1,15±0,04	1,12±0,07	1,13±0,06	1,06±0,07	<b>1,17±0,08***</b>

Results are presented as mean ±SEM \*\*\*p<0,001 \* in comparison with control group values

\*\* in comparison with hyperthyroid group values before therapy

\*\*\* in comparison with values in the same group before and after the therapy

TABLE 2. Echocardiographic parameters in euthyroid, hyperthyroid and hypothyroid patients before and after therapy

ing the cardiac pathology as well as to follow up effect of the therapy (8). In the present study we carried out an investigation of cardiac function in patients with untreated thyroid functional disorders. Previous studies showed the presence of a diastolic as well as systolic dysfunction in patients with diagnosed hypothyroidism (9), even in patients with subclinical form of hypothyroidism (4,6). Zoncu et al. (10) found impairment in both systolic and diastolic function in subclinical hypothyroidism, also detected in patients with autoimmune thyroiditis, even though TSH level was within the normal range. Our results showed no statistically significant differences in systolic and diastolic function before therapy between patients with thyroid dysfunctional states and euthyroid (control) group. Discordance that we found in comparison with previous results could be explained with the fact that the duration period of dysfunctional state of patients included in our study was unknown. So we suppose that this period was too short for the development of cardiac functional changes. But we have to stress that average values of E/A, as parameter of diastolic function was lower in hypothyroid group in comparison with hyperthyroid (1.12) and euthyroid group (1.15). When we analyzed systolic function we also

found significantly lower mean LVEF values in hypothyroid group before therapy compared to the control and hyperthyroid group. In addition, after adequate therapy we found a significant improvement in diastolic as well as in systolic function in hypothyroid group of patients. So, despite the fact that we have not found cardiac functional changes, our results confirm the tendency for development of diastolic and systolic functional cardiac changes in hypothyroidism. Our results also confirmed, as previously reported, the beneficial effect of substitutional therapy on cardiac function in hypothyroidism. It has been reported that hyperthyroidism has profound effects on cardiac diastolic function that are at least in part reversible after restoration of euthyroidism (11). Our results showed no differences in echocardiographic parameters of systolic as well as of diastolic function between hyperthyroid and control group. We could explain this with the specific selection criteria and we suppose that the duration of thyroid dysfunctional state in our patients did not last long enough for the development of cardiac impairment. This additionally confirms the importance of early diagnosis to prevent cardiac impairment associated with even subclinical form of thyroid functional disorders.

## CONCLUSION

Results of our study showed importance of early diagnostic approach in patients with thyroid dysfunctional states that will surely diminish the extent of cardiac complication that accompany these disorders.

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