Assessment of myocardial function in newly diagnosed Egyptian patients with clinical and subclinical thyroid diseases

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Abstract

Introduction: Hyperthyroidism is the term for overactive tissue within the thyroid gland, resulting in overproduction and thus an excess of circulating free thyroid hormones: thyroxine (T4), triiodothyronine (T3), or both. Hypothyroidism is a disease state in humans and in animals caused by insufficient production of thyroid hormone by the thyroid gland. Subclinical form of the disease occurs when there are changes in TSH levels without a change in thyroid hormone levels. The aim of this work is to assess the myocardial systolic and diastolic functions in newly diagnosed Egyptian patients suffering from hypothyroidism, either clinical or subclinical, and hyperthyroidism, either clinical or subclinical also.

Material and methods: One hundred subjects participated in the study including newly diagnosed patients with clinical or subclinical hyperthyroidism, those with clinical or subclinical hypothyroidism, and a control group. For all subjects participating in the study, free thyroxin (FT4), free triiodothyronine (FT3) and thyroid stimulating hormone (TSH) were assessed using solid phase enzyme chemiluminescent immunoassay, echocardiography was done and the correlation between it and the thyroid hormone levels was estimated.

Results: The results of the study revealed that the clinical form of hypothyroidism had negative chronotropic, inotropic and lusitropic effects, whereas the subclinical form had relatively less negative effects. The study also revealed that the clinical form of hyperthyroidism had a positive chronotropic effect, negative lusitropic effect and significant increase in systolic blood pressure with mild left ventricular hypertrophy, whereas the subclinical form had the same effects but in a less significant pattern.

Conclusions: The conclusion of the study is that the clinical forms of thyroid diseases had an effect on the myocardial functions but the subclinical forms of thyroid diseases had less significant effects and so the early treatment of thyroid diseases even in the subclinical cases has a protective effect on the myocardial functions.

Key words: myocardial function, hypothyroidism.

Introduction

Subclinical hypothyroidism is characterized by variably increased serum TSH concentrations with apparently normal serum free T3 and free T4. It occurs in 10-15% of the general population [1].

The clinical presentation of subclinical hypothyroidism is non-specific and the symptoms are usually subtle, as compared with those of overt hypothyroidism, mainly in relation to the intensity and the duration

of thyroid hormone deficiency and the age of the patients [2].

Hypothyroidism, even in the subclinical stage, can cause diastolic dysfunction of the left ventricle. This abnormality in diastolic function can be reversed by thyroxin therapy [3]. The treatment is generally recommended in the presence of serum TSH level of 10 mμ/l or more. When the TSH level is less than 10 mμ/l, the treatment may be indicated in relation to the presence of goitre or anti-thyroid antibodies to prevent the onset of overt hypothyroidism more than for tissue assessment of thyroid hormone deficiency [4].

Overt hyperthyroidism has profound effects on the heart, including arrhythmias, increased systolic function, left ventricular hypertrophy and diastolic dysfunction [5].

The cardiovascular consequences of subclinical hyperthyroidism, defined by suppressed serum TSH levels despite normal free T3 and T4 concentrations, are less well established.

However, the most consistent findings in endogenous subclinical hyperthyroidism include an increased heart rate, supraventricular arrhythmias, increased left ventricular mass with a slightly enhanced systolic function and diastolic dysfunction [6].

Material and methods

Hundred subjects participated in this study. They were classified into 5 groups.

1) group A – consisted of 20 patients with subclinical hypothyroidism, characterized by high serum TSH levels with normal levels of serum free T3 and free T4,
2) group B – consisted of 20 patients with overt hypothyroidism, characterized by high serum levels of TSH and low serum levels of free T3 and free T4,
3) group C – consisted of 20 patients with subclinical hyperthyroidism, characterized by low serum levels of TSH and normal serum levels of free T3 and free T4,
4) group D – consisted of 20 patients with overt hyperthyroidism, characterized by low serum levels of TSH and high serum levels of free T3 and free T4,

(the patients of the above groups were newly diagnosed and did not receive treatment),

5) group E – consisted of 20 healthy subjects matched for age and sex as a control group.

Patients complaining of diabetes mellitus, hypertension, dyslipidaemia or any cardiac diseases either congenital, valvular or ischaemic were excluded from the study. Also patients receiving any treatment affecting thyroid hormone levels such as amiodarone were excluded.

About 5 ml of venous blood samples were taken from each subject participating in the study, left to clot and the serum was separated by centrifugation and stored at –20°C for quantitative determination of the followings: free thyroxin (FT4) [7], free triiodothyronine (FT3) [8] and thyroid stimulating hormone (TSH) [9].

This was done on an Immulite 2000 analyzer (DPC, Cirrus Inc. Los Angeles, CA 90045-5597), using solid phase enzyme chemiluminescent immunoassay. The kits were supplied from DPC (96th Street, Los Angeles, USA).

For all subjects participating in the study, echocardiography was done and the correlation between it and the thyroid hormone levels was estimated. Echo-Doppler study using Sigma 44 Echo-Doppler and 3.5 MM-DS transducer included the following:

1) provisional screening using M-mode, 2D pulsed and continuous wave Doppler, colour flow mapping and colour time motion to exclude the presence of congenital, valvular, ischaemic or other heart diseases that might affect LV function;
2) combined M mode and 2D echo-Doppler study to assess systolic function through:
   – measuring LV dimensions in short axis view from trans-thoracic left lower parasternal approach,
   – calculating fractional shortening through the formula: FS% = LVEDD – LVESD × 100,

Table I. Clinical and biochemical characteristics of all groups participating in the study

Parameters	Group				
	A	B	C	D	E
Age [years]	45.8 ±2.1	47.1 ±5.3	46.2 ±6.1	44.3 ±3.9	46.5 ±5.2
Sex:					
– males	7	9	8	9	10
– females	13	11	12	11	10
Free T3 [pg/ml]	3.6 ±1.0	1.1 ±0.18	2.9 ±0.62	8.2 ±2.3	3.1 ±1.2
Free T4 [ng/dl]	1.2 ±0.2	0.63 ±0.09	1.1 ±0.28	5.9 ±3.2	1.3 ±0.2
TSH [uIU/ml]	10.3 ±2.1	15.3 ±4.4	0.18 ±0.06	0.15 ±0.08	2.5 ±1.3

Group A – patients with subclinical hypothyroidism, group B – patients with clinical hypothyroidism, group C – patients with subclinical hyperthyroidism, group D – patients with clinical hyperthyroidism, group E – control group

Table II. Comparison of the clinical and echocardiographic data between clinical hypothyroidism, subclinical hypothyroidism and control group (mean ± SD)

Data	Group			*P*
	Clinical hypothyroidism	Subclinical hypothyroidism	Control group Group (E)	
Systolic blood pressure	123.6 ±9.54	123.2 ±9.39	124.1 ±9.03	*pa* > 0.05 *pb* > 0.05 *pc* > 0.05
Diastolic blood pressure	81.5 ±7.16	79.5 ±7.39	76.5 ±5.06	*pa* < 0.05 *pb* > 0.05 *pc* > 0.05
Pulse	61.9 ±6.5	73.15 ±5.71	81.7 ±6.09	*pa* < 0.001 *pb* < 0.001 *pc* < 0.001
Septal thickness	0.96 ±0.25	0.964 ±0.09	0.825 ±0.28	*pa* > 0.05 *pb* < 0.05 *pc* > 0.05
Posterior wall thickness	1.033 ±0.08	0.984 ±0.09	0.848 ±0.25	*pa* < 0.05 *pb* < 0.05 *pc* > 0.05
FS%	27.61 ±2.866	33.393 ±4.23	35.148 ±5.5	*pa* < 0.001 *pb* > 0.05 *pc* < 0.001
EF%	55.786 ±2.686	63.836 ±7.065	64.55 ±6.86	*pa* < 0.001 *pb* > 0.05 *pc* < 0.001
E/A ratio	0.69 ±0.147	0.904 ±0.108	1.41 ±0.2	*pa* < 0.001 *pb* < 0.001 *pc* < 0.001

pa – clinical hypothyroidism vs. control, pb – subclinical hypothyroidism vs. control, pc – clinical hypothyroidism vs. subclinical hypothyroidism p < 0.05 – significant, p < 0.001 – highly significant, p > 0.05 – non-significant

– ejection fraction is calculated through the formula: EF = LVEDD – LVESV/LVEDV;

3) combined 2D and pulsed wave Doppler examination of LV inflow at mitral valve level from apical 4 chamber trans-thoracic approach was used to assess LV diastolic function through:
   – measurement of E-wave (peak velocity at early diastole),
   – measurement of A-wave (peak velocity following atrial systole),
   – calculation of E/A ratio.

Statistical analysis

Results were expressed as mean ± SD. Data were statistically analyzed using SPSS package for Windows, version 7.5. One-way analysis of variance was used for comparing between more than two means of the studied variables. The correlation matrix test was used for studying the relation between two continuous variables. Student's *t*-test was done for comparing two means and the χ^2 test was performed to compare the frequency between two categorical variables.

Results

Compared to normal controls, patients with clinical hypothyroidism showed a highly significant decrease in heart rate, non-significant decrease in systolic blood pressure, significant increase in diastolic blood pressure, highly significant decrease in fractional shortening and ejection fraction and highly significant decrease in E/A ratio (Tables I, II).

Compared to normal controls, patients with subclinical hypothyroidism showed a highly significant decrease in heart rate, non-significant decrease in systolic blood pressure, non-significant increase in diastolic blood pressure, highly significant decrease in E/A ratio, non-significant decrease in fractional shortening and ejection fraction and significant increase in posterior and septal wall thickness (Table II).

Compared with subclinical hypothyroidism, patients with clinical hypothyroidism showed a highly significant decrease in heart rate, non-significant difference in systolic blood pressure, non-significant increase in diastolic blood pressure,

Table III. Comparison of the clinical and echocardiographic data between clinical hyperthyroidism, subclinical hyperthyroidism and control group (mean ± SD)

Data	Group			*P*
	Clinical hypothyroidism	Subclinical hypothyroidism	Control group Group (E)	
Systolic blood pressure	131.55 ±7.2	128.8 ±5.89	124.1 ±9.03	*pa* < 0.05 *pb* < 0.05 *pc* > 0.05
Diastolic blood pressure	75.7 ±5.55	77.9 ±6.85	76.5 ±5.06	*pa* > 0.05 *pb* > 0.05 *pc* > 0.05
Pulse	95.2 ±8.47	83.8 ±6.25	81.7 ±6.09	*pa* < 0.001 *pb* > 0.05 *pc* < 0.001
Septal thickness	1.132 ±0.13	1.18 ±0.01	0.825 ±0.28	*pa* < 0.001 *pb* < 0.001 *pc* > 0.05
Posterior wall thickness	1.117 ±0.09	1.178 ±0.09	0.848 ±0.25	*pa* < 0.001 *pb* < 0.001 *pc* < 0.05
FS%	33.25 ±4.33	28.906 ±2.38	35.148 ±5.53	*pa* > 0.05 *pb* < 0.001 *pc* < 0.001
EF%	63.18 ±7.11	55.779 ±2.73	64.557 ±6.86	*pa* > 0.05 *pb* < 0.001 *pc* < 0.001
E/A ratio	0.745 ±0.16	1.448 ±0.19	1.41 ±0.2	*pa* < 0.001 *pb* > 0.05 *pc* < 0.001

pa – clinical hyperthyroidism vs. control, pb – subclinical hyperthyroidism vs. control, pc – clinical hyperthyroidism vs. subclinical hyperthyroidism
p < 0.05 – significant, p < 0.001 – highly significant, p > 0.05 – non-significant

and highly significant decrease in fractional shortening, ejection fraction and E/A ratio (Table II).

Compared to normal controls, patients with clinical hyperthyroidism showed a highly significant increase in heart rate, significant increase in systolic blood pressure, highly significant increase in posterior and septal wall thickness, non-significant increase in fractional shortening, ejection fraction and diastolic blood pressure, and highly significant decrease in E/A ratio (Table III).

Compared to normal controls, patients with subclinical hyperthyroidism showed a non-significant increase in heart rate and diastolic blood pressure, significant increase in systolic blood pressure, and highly significant increase in posterior and septal wall thickness, fractional shortening and ejection fraction (Table III).

Compared to subclinical hyperthyroidism, clinical hyperthyroidism patients showed a highly significant increase in heart rate, non-significant increase in systolic and diastolic blood pressure, highly significant increase in fractional shortening and ejection fraction, highly significant decrease in E/A ratio and highly significant increase in posterior wall thickness (Table III).

Discussion

Clinical hypothyroidism is often associated with cardiovascular disturbances, such as endothelial and myocardial dysfunction [10]. Hypothyroidism, even in subclinical form, can cause diastolic dysfunction of the left ventricle. This abnormality in diastolic function can be reversed by thyroxin therapy [11].

In this study, we assess the cardiac function of 20 patients with subclinical hypothyroidism and 20 patients with clinical hypothyroidism. All patients were newly diagnosed and did not receive any previous treatment for their thyroid disease.

The study revealed that clinical forms of hypothyroidism had a negative chronotropic effect, negative inotropic effect and negative lusitropic effect, whereas subclinical forms of hypothyroidism showed relatively less negative chronotropic effect, inotropic effect and lusitropic effect.

Biondi *et al.* 1999 [11] demonstrated that LV diastolic filling (suggestive of impaired LV relaxation) is a common finding in patients with subclinical hypothyroidism and that this abnormality may be reversed by short-term

substitutive T4 therapy. Biondi *et al*. also stated that the impaired diastolic function in patients with subclinical hypothyroidism is a condition of minimal tissue hypothyroidism rather than a compensated state. In contrast to Biondi *et al*., Arem *et al*. 1969 [12], using Doppler echocardiography at rest and during exercise in patients with subclinical hypothyroidism, found normal cardiac structure and function.

Subclinical hypothyroidism may directly impair diastolic function by reducing sarcoplasmic calcium ATPase activity, with the consequence of impairment of ventricular diastolic function [13].

We also assess in our study the cardiac function of 20 newly diagnosed patients with subclinical hyperthyroidism and 20 patients with clinical hyperthyroidism who did not receive any previous treatment for their thyroid disease.

The study showed that clinical hyperthyroidism had a positive chronotropic effect, and negative lusitropic effect, with significant increase in systolic blood pressure associated with mild left ventricular hypertrophy, whereas subclinical forms of hyperthyroidism showed a relatively less significant chronotropic effect and lusitropic effect and relatively less significant change in blood pressure, left ventricular posterior wall and septal wall thickness.

It has been suggested that the diastolic dysfunction in subclinical hyperthyroidism results from the increased left ventricular mass and that this effect counteracts the favourable effects of thyroid hormone on diastolic function [14]. Fazios *el al*. 1995 revealed left ventricular hypertrophy in patients with subclinical hyperthyroidism which was reversed by β-blocking agents [15].

Smith (2005) stated that prolonged subclinical hyperthyroidism only is accompanied by marked diastolic dysfunction that is at least partly reversible [16]. Harun (2007) [17] concluded that there was no correlation between free thyroxin level and left ventricular mass in Graves' disease.

Our study has proved that disturbed thyroid function is associated with disturbances in cardiac systolic and diastolic function.

The disturbance in systolic function was more prevalent in the clinical form, which proves a direct relation with thyroxin and TSH levels. The mild left ventricular hypertrophy observed with cases of hyperthyroidism might be explained by a relative increase in blood pressure.

Disturbed diastolic function was observed in all forms of thyroid dysfunction, so thyroxin level and TSH level are not the only causes of the negative lusitropic effect.

In conclusion, hypothyroidism, either clinical or subclinical, and hyperthyroidism, either clinical or subclinical, had an effect on myocardial function, but the subclinical forms of thyroid diseases had less significant effects and so the early treatment of thyroid diseases, even in subclinical cases, has a protective effect on myocardial function.

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