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ORIGINAL ARTICLE

Prospective echocardiographic evaluation of patients with endogenous subclinical hyperthyroidism and after restoring euthyroidism

Grzegorz Kaminski*, Dariusz Michalkiewicz†, Karol Makowski†, Zbigniew Podgajny*, Norbert Szalus‡, Marek Ruchala§, Ewelina Szczepanek§ and Grzegorz Gielerak†

*Departments of Endocrinology and Isotope Therapy, †Internal Medicine and Cardiology, ‡Nuclear Medicine, Military Institute of Medicine, Warsaw and §Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznan, Poland

Summary

Objectives Clinical significance of, and the need for, treatment in subclinical hyperthyroidism (sHT) is still a matter of debate. The aim of the study was to assess the impact of sHT on echocardiographic parameters.

Design Patients with endogenous sHT of nonautoimmune origin underwent full echocardiographic assessment at diagnosis and after restoring euthyroidism with radioiodine treatment.

Patients Studied group consisted of 44 patients (37 women, 7 men), aged 22–65 years (mean 45·9 ± 11·0).

Measurements Full echocardiographic assessment included estimation of cardiac chamber diameters and volume as well as cardiac contractility, according to the guidelines of the American Society of Echocardiography. Left ventricular mass was calculated according to Penn's convention. For estimation of left ventricle diastolic function, the following echocardiographic parameters were obtained: maximal early filling wave velocity (E), maximal late filling wave velocity (A), E/A ratio, isovolumetric relaxation time and early filling wave deceleration time.

Results In the studied group, phase of sHT was associated with increased volume of heart chambers, increased diameter of ascending aorta, increased left ventricle mass and disturbed left ventricle relaxation ($P < 0{\cdot}05$). The systolic function of the left ventricle was unaffected; however, the ejection time was shortened. The changes were reversible with restoring biochemical euthyroidism ($P < 0{\cdot}05$). Moreover, a significant correlation between some of the parameters and thyroid hormones concentration was demonstrated.

Conclusions sHT was associated with significant changes in echocardiographic parameters, which may contribute to increased cardiovascular risk in these patients. The alterations were reversible with restoring biochemical euthyroidism, what supports the necessity of treatment introduction in sHT.

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Correspondence: Grzegorz Kaminski, MD, PhD, Associate Professor, Department of Endocrinology and Isotope Therapy, Military Institute of Medicine, Szaserów St 128, 04-141 Warsaw, Poland. Tel.: +48 22 6816110; Fax: +48 22 6816110; E-mail: gkam@wim.mil.pl

Introduction

Subclinical hyperthyroidism (sHT) is a condition, which affects 0·6–16% of the population and is characterized by a decreased or undetectable TSH level and normal concentration of free thyroid hormones.[1] There is more and more compelling evidence that patients with sHT experience deleterious effects of thyroid hormone excess.[2,3] It was observed that even subclinical thyroid hyperfunction manifests in significant anatomical and functional changes in the heart. Patients with sHT have significantly accelerated heart rates compared to euthyroid subjects.[4,5] sHT was also shown to be associated with an increased incidence of supraventricular arrhythmias, including atrial fibrillation, which is an independent risk factor of cerebral stroke, exacerbation of ischaemic heart disease, heart failure and death.[6,7] It has also been observed that sHT exerts important influence on heart haemodynamics, of which left ventricular diastolic function is particularly affected.[8] Moreover, sHT is supposed to induce prolonged haemodynamic overload and, therefore, left ventricular hypertrophy, itself associated with increased risk of cardiovascular morbidity and mortality.[4,5,9,10]

Although the deleterious effect of overt hyperthyroidism on the cardiovascular system is unquestionable, the clinical consequences of sHT are yet unclear. The functional implications of sHT have to date been studied predominantly in subjects on L-thyroxine therapy: an iatrogenic form of sHT. Because of paucity of prospective studies in large groups of patients, it is unclear whether endogenous sHT exerts the same impact on the heart and whether these changes are reversible with restoration of euthyroidism. The diagnosis of sHT is often underestimated and the need for treatment of

sHT, especially in the young and middle-aged patients, is still discussed, while recent guidelines provide conflicting recommendations.[3,11–13]

The aim of the study was to assess the impact of sHT on the heart by providing full prospective echocardiographic evaluation of patients with endogenous sHT at the time of diagnosis and after restoring biochemical euthyroidism with radioiodine treatment.

Methods

The studied group consisted of 44 patients (37 women and 7 men), aged 22–65 years (mean 45·9 ± 11·0), diagnosed with sHT. The patients were enrolled in the study from a group of 1080 subjects referred to the department of endocrinology and endocrine outpatient clinic for treatment of hyperthyroidism from April 2002 to December 2004. Patients were included on the basis of the following laboratory criteria:

- TSH concentration below the assay normal range (<0·36 μIU/ml) on at least two measurements, performed at an interval of 6 weeks to exclude subjects with temporary TSH suppression.
- free thyroid hormones within the assay normal range: free triiodothyronine – FT_3 (3·5–7·9 pmol/l) and free thyroxine – FT_4 (7·64–19·7 pmol/l) on at least two measurements performed at the interval of 6 weeks.
- negative anti-thyroid peroxidase, anti-thyroglobulin and anti-TSH receptor autoantibodies to exclude patients with autoimmune thyroid disease and ensure homogeneity of the studied group.

Therefore, a studied group of patients was selected, in whom sHT was caused by one of the following conditions: toxic multinodular goitre and diffuse thyroid autonomy or autonomous nodule. Other possible causes of sHT or TSH suppression, i.e. Graves' disease, thyroiditis, pregnancy, psychiatric disorders, secondary hypothyroidism, sick euthyroid syndrome in the course of neoplastic disease, fever, liver failure or starvation, were excluded. The patients had also negative history of other diseases and were taking no medications.

Following the diagnosis of sHT, the patients were subjected to radioiodine treatment. The dose of radioisotope was calculated with the use of the following formula:[14]

$$A = \frac{(100 \div 150\,\mu Ci) \cdot m}{\mathrm{RAIU}_{24}}$$

where: A – activity [mCi].

m – mass of hyperthyroid tissue [g].

$RAIU_{24}$ – iodine uptake after 24 h expressed as decimal.

The protocol of the study is in accordance with the Declaration of Helsinki and was approved by the local ethical committee, and all patients gave informed consent to participate.

In all subjects, concentrations of TSH and free thyroid hormones were assessed on admission and during follow-up visits every 3 months following radioiodine therapy, with the use of commercially available AutoDELFIA kits (Perkin Elmer Life and Analytical Sciences, Turku, Finland). Each patient, in addition, underwent thyroid Tc-99m scintiscan and $RAIU_{24}$ assessment as well as thyroid ultrasound examination, performed by the same experienced sonographist with a 7·5 MHz linear probe using the Vingmed System Five. Thyroid volume was measured by the mean of elliptical shape volume formula ($\pi/6 \times$ length $\times$ width $\times$ depth).

In all patients, noninvasive 24-h ambulatory blood pressure and heart rate measurement (24-h ABPM) was performed. The examination was carried out by the means of oscillometric method, with the use of automatic device by Spacelabs 90217 (SpaceLabs Medical, Inc., Redmond, WA, USA). The following upper blood pressure limits were assumed as normative values: <135/85 mmHg during the day, <120/75 mmHg at night and <130/80 mmHg for 24 h.[15] The patients, in whom blood pressure exceeded the given reference range, were excluded from further evaluation.

Moreover, patients underwent full echocardiographic evaluation, with estimation of cardiac chambers' diameters and volume as well as heart muscle contractility, according to the guidelines of the American Society of Echocardiography.[16] Left ventricular mass was calculated according to Penn's convention.[17] For estimation of left ventricular diastolic function, the following standard echocardiographic parameters were used:[18]

- isovolumetric relaxation time (IVRT) [ms].
- maximal early filling wave velocity (E) [m/s].
- maximal late filling wave velocity (A) [m/s].
- E/A ratio.
- early filling wave deceleration time (DT) [ms].

All echocardiographic parameters were averaged from three independent measurements. To eliminate the influence of pericardium pathologies on left ventricle relaxation, patients in whom pericardial effusion or any other pericardium pathology was detected were excluded from further evaluation. Additionally, detection in a patient of any morphological or functional pathology of the valves resulted in exclusion from the study.

Echocardiographic assessment of patients was performed twice – at the time of diagnosis of sHT and 6 months after restoring euthyroidism, confirmed by complete TSH normalisation.

The mean values of hormone concentrations and echocardiographic parameters evaluated before and after radioiodine treatment were compared with the use of Student's t-test for dependent variables. Additionally, the correlation between the echocardiographic parameters and hormone concentration, reflecting the severity of hyperthyroidism, was assessed with the use of Pearson's correlation test. All calculations were performed with STATISTICA version 8.0 (StatSoft Polska, Krakow, Poland). Assumed significance level was equal to 0·05.

Results

Thirty-eight of 44 patients enrolled to the study had toxic multinodular goitre. Less frequently, the diagnosis of diffused thyroid autonomy (in four patients) and autonomous nodule (in two patients) was established. According to Gharib *et al.*, 30 patients at diagnosis of sHT had partial TSH suppression (0·1–0·36 μIU/ml), while 14 subjects demonstrated complete TSH suppression $(<0{\cdot}1\ \mu IU/ml)^2$. The mean TSH, FT_3 and FT_4 values differed significantly between the phase of sHT and euthyroidism. The detailed hormonal profile of studied patients before and after radioiodine treatment is presented in the Table 1. The median time from

Table 1. The comparison of hormonal profile of the studied patients in the phase of subclinical hyperthyroidism (sHT) and after restoring normal thyroid function with radioiodine treatment

	Mean ± SD		
Parameter	sHT	Euthyroidism	*P*-value
TSH [mIU/l]	0·164 ± 0·10	1·322 ± 0·75	<0·005
FT_4 [pmol/l]	14·16 ± 2·37	13·05 ± 1·85	<0·005
FT_3 [pmol/l]	6·48 ± 0·69	5·77 ± 0·57	<0·005

SD, standard deviation; FT_4, free thyroxine; FT_3, free triiodothyronine.

establishing the diagnosis of sHT to radioiodine treatment was 12·7 months, while the median time period from the radioisotope administration to restoration of biochemical euthyroidism – 6·9 months. Repeated TSH measurements during the follow-up allowed to precise detection of the moment of transition from sHT to normal thyroid function and to confirm that all patients during second echocardiographic evaluation were euthyroid for at least 6 months.

The mean thyroid volume was 33·4 ± 18·8 ml before treatment and 22·4 ± 14·6 ml after radioiodine therapy ($P < 0·001$). The $RAIU_{24}$ ranged from 19% to 81%, with a median value of 30%. The radioiodine doses given were with a range of 185 MBq to 1125 MBq, while median dose given was 448 MBq.

As a result of radioiodine treatment, all patients eventually achieved euthyroidism in a 36-month follow-up. Three patients experienced transient exacerbation of hyperthyroidism 3 months after radioiodine administration, requiring a short period of methimazole treatment. After cessation of the drug, two patients remained constantly euthyroid, while one patient developed subclinical hypothyroidism, requiring L-thyroxine substitution. Another two patients developed hypothyroidism 21 months following radioiodine administration. In all hypothyroid patients, introduction of L-thyroxine substitution restored euthyroidism.

Only subjects with normal blood pressure in 24-h ABPM were included to the study. The results of blood pressure and heart rate assessment are presented in the Table 2.

All measured echocardiographic parameters were within the reference ranges in all studied patients in both sHT and euthyroid phase. However, a significant difference of all evaluated echocardiographic parameters, except ejection fraction (EF) and left ventricle end-systolic diameter (LVSD), measured in the phase of sHT and after restoring euthyroidism, was observed (Table 3). Moreover, a statistically significant correlation between some of the measured parameters and hormone concentrations before treatment was demonstrated. A statistically significant positive correlation between FT_3 level and the following echocardiographic parameters were observed: left ventricle posterior wall diameter in diastole (LVPWD, $r = 0·321$, $P = 0·038$), interventricular septum diameter in diastole (IVSD, $r = 0·311$, $P = 0·045$) and systole (IVSS, $r = 0·314$, $P = 0·043$) as well as left atrium diameter (LA, $r = 0·393$, $P = 0·008$).

Table 2. The results of 24-h blood pressure and heart rate measurement in patients included in the study in the phase of subclinical hyperthyroidism (sHT) and after restoring normal thyroid function with radioiodine treatment

			sHT	Euthyroidism	*P*-value
24 h	SBP	Mean value [mmHg]	115·8	114·9	>0·05
		SD [mmHg]	9·0	8·3	NS
	DBP	Mean value [mmHg]	72·7	71·7	>0·05
		SD [mmHg]	7·0	5·9	NS
	HR	Mean value [beats/min]	78·4	75·5	<0·005
		SD [beats/min]	6·8	8·0	

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

An additional analysis was performed for a subgroup of 14 subjects with TSH<0·1 μIU/ml (mean ± SD: 0·035 ± 0·03 μIU/ml). The comparison of studied echocardiographic parameters assessed in sHT state and after restoring euthyroidism in this subgroup is presented in the Table 4.

Discussion

Echocardiography enables detection of cardiac dysfunction in patients without clinical evidence of heart disease. Impaired heart relaxation identified by the means of echocardiography precedes deteriorated contractility.[19] Thus, noninvasive assessment of heart relaxation appears as an attractive method to evaluate the effect that sHT has on the heart.

The vast majority of previous studies concerned the influence of iatrogenic sHT on cardiovascular system.[4,20,21] However, because of the dissimilar degree of TSH suppression as well as differences in duration, it seems unwarranted to derive conclusions on the significance of endogenous sHT from those studies. Moreover, apart from patients after thyreoidectomy caused by differentiated thyroid cancer, proper correction of L-thyroxine dose terminates sHT and reverses its clinical consequences. An extensive literature search found only a few papers in which an influence of endogenous sHT on selected echocardiographic parameters was studied.[5,9,22]

In the first of these, Biondi *et al.*[9] compared the results of echocardiographic assessment performed in 23 patients with endogenous sHT and the same number of healthy controls. The mean TSH value and age of studied patients were similar to ours. In subjects with sHT, Biondi *et al.* detected a significantly increased left ventricular mass, fractional shortening, left ventricle systolic diameter, interventricular septum end-diastolic diameter and left ventricle posterior wall thickness. These results are similar to our findings. In their study, however, the diameter of right ventricle, left atrium, left ventricle volume index in systole or diastole, stroke volume index, cardiac index, relative wall thickness and left ventricle mass index were not assessed. Moreover, in contrast to ours, theirs was a case–control study aimed to prospectively evaluate the same group of subjects in two different thyroid functional states. Additionally, their assessment of diastolic function in this group revealed significantly disturbed left ventricle relaxation documented by prolonged IVRT and reduced E/A ratio, consistent with our study.[9]

In another paper, Sgarbi *et al.*[5] report the results of echocardiographic evaluation in ten patients with sHT, but with TSH

Table 3. The comparison of echocardiographic parameters assessed in all 44 patients with initial TSH < 0·36 μIU/ml in the phase of subclinical hyperthyroidism (sHT) and after restoring normal thyroid function with radioiodine treatment

		Mean ± SD		
Parameter	Normal range	sHT	Euthyroidism	*P*-value
LVVDI [ml/m^2]	35–75	50·17 ± 10·0	46·23 ± 9·5	<0·005
LVVSI [ml/m^2]	12–30	17·31 ± 4·8	15·91 ± 4·1	0·015
SVI [ml/m^2]	33–47	32·85 ± 6·9	30·32 ± 6·9	<0·005
EF [%]	>55	65·52 ± 5·9	65·32 ± 4·9	0·817
LVDD [cm]	3·9–5·3 (F), 4·2–5·9 (M)	4·83 ± 0·5	4·75 ± 0·5	0·011
LVPWD [cm]	0·6–1·1	0·95 ± 0·1	0·89 ± 0·1	<0·005
LVDS [cm]	2·2–4·0	2·90 ± 0·4	2·95 ± 0·4	0·124
LVPWS [cm]	N/A	1·58 ± 0·3	1·47 ± 0·3	0·020
IVSD [cm]	0·6–1·1	0·91 ± 0·1	0·85 ± 0·1	<0·005
IVSS [cm]	N/A	1·51 ± 0·3	1·43 ± 0·3	<0·005
RWT	0·3–0·4	0·39 ± 0·1	0·37 ± 0·0	<0·005
LVMI [g/m^2]	44–88 (F), 50–102 (M)	101·41 ± 11·5	92·25 ± 11·4	<0·005
SF [%]	18–42	39·75 ± 7·0	37·73 ± 7·0	<0·005
LA [cm]	2·7–3·8 (F), 3·0–4·0 (M)	3·23 ± 0·4	3·12 ± 0·4	<0·005
RV [cm]	2·0–2·8	2·47 ± 0·2	2·41 ± 0·2	0·010
Ao [cm]	2·1–3·4	2·53 ± 0·3	2·45 ± 0·3	0·006
ET [s]	0·304–0·340	0·31 ± 0·0	0·34 ± 0·0	<0·005
CI [l/min/m^2]	2·5–4·0	3·87 ± 0·8	3·18 ± 0·7	<0·005
E [m/s]	N/A	0·72 ± 0·2	0·79 ± 0·2	<0·005
A [m/s]	N/A	0·69 ± 0·2	0·62 ± 0·1	<0·005
E/A	1–2	1·08 ± 0·3	1·32 ± 0·3	<0·005
DT [ms]	150–240	227·33 ± 33·3	205·98 ± 32·3	<0·005
IVRT [ms]	70–100	85·86 ± 7·8	79·34 ± 7·2	<0·005

LVVDI, left ventricle volume index in diastole; LVVSI, left ventricle volume index in systole; SVI, stroke volume index; EF, ejection fraction; LVDD, left ventricle diastolic diameter; LVPWD, left ventricle posterior wall diameter in diastole; LVDS, left ventricle diameter in systole; LVPWS, left ventricle posterior wall diameter in systole; IVSD, interventricular septum diameter in diastole; IVSS, interventricular septum diameter in systole; RWT, relative wall thickness; LVMI, left ventricular mass index; SF, shortening fraction; LA, left atrium diameter; RV, right ventricle volume; Ao, diameter of aorta; ET, ejection time; CI, cardiac index; E, maximal early filling wave velocity; A, maximal late filling wave velocity; E/A, maximal early/late filling wave velocity ratio; DT, early filling wave deceleration time; IVRT, isovolumetric relaxation time; N/A, no well-documented normal values for these parameters; F, female, M, male.

suppression different to our study and that of Biondi *et al.*[9] The authors compared the initial results with those attained 6 months after TSH normalization on methimazole treatment. Moreover, a control group of 10 healthy subjects, matched for age, gender and body mass index, were examined. The authors concluded that sHT was associated with an increased interventricular septum and left ventricle posterior wall thickness as well as left ventricle mass index when compared to euthyroid controls. Similar differences in the measured parameters were found if the results of examination in patients with sHT were compared to those obtained 6 months after restoring euthyroidism in the same group. However, no difference was noticed in regard to diameters of cardiac chambers and indexes of systolic and diastolic function.

Petretta *et al.*[22] compared the results of echocardiographic assessment performed in 30 patients with endogenous sHT with those obtained from 20 healthy controls and concluded that IVRT was significantly shortened in sHT, in contrast to our results and those obtained by Biondi *et al.*[9] This could be explained with the fact that exposure to excess of thyroid hormone was not long enough to induce significant changes in the heart muscle in the studied group. Nevertheless, it was observed that sHT is associated with increased left ventricle volume in systole and diastole, shortening of ejection time and decreased E/A ratio, although the differences were not statistically significant.[22]

Biondi *et al.*[9] did not find significant correlation between hormonal status and left ventricular mass. In our study, however, where a larger group was studied in comparison with previously reported,[5,9,22] and with a minimal disease duration of 1 year, a significant positive correlation was found between FT_3 concentration and the following echocardiographic parameters: left ventricle posterior wall diameter in diastole, interventricular septum diameter in diastole and systole as well as left atrium diameter.

What is particularly important is that the results of our study and those obtained by Biondi *et al.*[9] additionally suggest that in patients with sHT, increased heart wall thickness, which might be related to chronic haemodynamic overload, is accompanied by impaired left ventricle relaxation. A significant increase in left ventricle mass caused by endogenous sHT was also observed by Sgarbi *et al.*[5]

In our study, sHT was associated with worse left ventricle diastolic function compared to the euthyroid state, manifesting by reduced early to late filling wave velocity (E/A) ratio as well as prolonged DT and IVRT. This could be related to increased left ventricle wall thickness and reflect disturbance of active phase of diastole.

Table 4. The comparison of echocardiographic parameters assessed in a subgroup of 14 patients with initial TSH < 0·1 μIU/ml in the phase of subclinical hyperthyroidism (sHT) and after restoring normal thyroid function with radioiodine treatment

		Mean ± SD		
Parameter	Normal Range	sHT	Euthyroidism	*P*-value
LVVDI [ml/m^2]	35–75	48·17 ± 8·7	42·26 ± 8·1	0·073
LVVSI [ml/m^2]	12–30	16·72 ± 4·6	15·15 ± 3·9	0·337
SVI [ml/m^2]	33–47	31·45 ± 5·6	27·10 ± 5·6	0·051
EF [%]	>55	65·21 ± 6·7	64·21 ± 4·7	0·652
LVDD [cm]	3·9–5·3 (F), 4·2–5·9 (M)	4·70 ± 0·4	4·57 ± 0·4	0·412
LVPWD [cm]	0·6–1·1	0·93 ± 0·1	0·88 ± 0·1	0·194
LVDS [cm]	2·2–4·0	2·83 ± 0·4	2·87 ± 0·5	0·815
LVPWS [cm]	N/A	1·54 ± 0·3	1·42 ± 0·3	0·259
IVSD [cm]	0·6–1·1	0·89 ± 0·1	0·83 ± 0·1	0·074
IVSS [cm]	N/A	1·48 ± 0·3	1·41 ± 0·2	0·467
RWT	0·3–0·4	0·40 ± 0·1	0·37 ± 0·0	0·047
LVMI [g/m^2]	44–88 (F), 50 – 102 (M)	96·49 ± 14·0	88·75 ± 10·1	0·105
SF [%]	18–42	39·90 ± 7·1	37·95 ± 6·7	0·460
LA [cm]	2·7–3·8 (F), 3·0–4·0 (M)	3·20 ± 0·3	3·06 ± 0·3	0·231
RV [cm]	2·0–2·8	2·52 ± 0·2	2·42 ± 0·2	0·253
Ao [cm]	2·1–3·4	2·51 ± 0·3	2·45 ± 0·3	0·637
ET [s]	0·304–0·340	0·31 ± 0·0	0·33 ± 0·0	0·367
CI [l/min/m^2]	2·5–4·0	4·13 ± 0·9	3·23 ± 0·6	0·006
E [m/s]	N/A	0·71 ± 0·1	0·78 ± 0·2	0·185
A [m/s]	N/A	0·69 ± 0·1	0·63 ± 0·1	0·230
E/A	1–2	1·06 ± 0·3	1·26 ± 0·3	0·068
DT [ms]	150–240	242·01 ± 40·5	211·14 ± 38·8	0·050
IVRT [ms]	70–100	86·32 ± 5·5	79·28 ± 5·4	0·002

LVVDI, left ventricle volume index in diastole; LVVSI, left ventricle volume index in systole; SVI, stroke volume index; EF, ejection fraction; LVDD, left ventricle diastolic diameter; LVPWD, left ventricle posterior wall diameter in diastole; LVDS, left ventricle diameter in systole; LVPWS, left ventricle posterior wall diameter in systole; IVSD, interventricular septum diameter in diastole; IVSS, interventricular septum diameter in systole; RWT, relative wall thickness; LVMI, left ventricular mass index; SF, shortening fraction; LA, left atrium diameter; RV, right ventricle volume; Ao, diameter of aorta; ET, ejection time; CI, cardiac index; E, maximal early filling wave velocity; A, maximal late filling wave velocity; E/A, maximal early/late filling wave velocity ratio; DT, early filling wave deceleration time; IVRT, isovolumetric relaxation time; N/A, no well-documented normal values for these parameters; F, female; M, male.

The observation is consistent with the results obtained in iatrogenic sHT, the same as improvement of these parameters with restoring euthyroidism.[23,24] Some of the authors did not demonstrate impaired left ventricle relaxation in hyperthyroidism, however, this might be explained with dissimilar duration of the disease.[25,26]

The definition of sHT varies between papers. In our study, all patients with a TSH below the lower normal range (<0·36 μIU/ml in our laboratory) and normal concentration of free thyroid hormones were included. Moreover, a separate analysis was performed for a subgroup of 14 patients with complete TSH suppression (<0·1 μIU/ml). It appeared that while not as significant because of a lower number of subjects, consistent findings apply for both groups of subjects with partial and complete TSH suppression.

Large cohort studies revealed that patients with sHT are at higher risk of cardiac and total mortality, especially in the presence of comorbid conditions.[27,28] It is possible that observed echocardiographic changes might, at least partially, contribute to that fact. According to the literature, increase in left atrium and left ventricle diameter is associated with significant elevation of cardiovascular risk.[29,30] Moreover, even subclinical diastolic dysfunction was found to be associated with increased cardiovascular morbidity and mortality, therefore subtle changes observed in sHT might be of clinical relevance.[31,32] On the other hand, in the community-based study of subjects with different cardiac conditions, DT was weakly associated with heart failure and mortality, while IVRT and E/A ratio were not.[33] Therefore, the long-term clinical significance of changes in echocardiographic parameters observed in sHT is still to be evaluated in large prospective studies.

In conclusion, the main strength of our study is that it was designed to compare prospectively the results of echocardiographic evaluation in a relatively large group of patients with endogenous sHT, which served as self-control group. To maintain homogeneity of the group and to eliminate the variable character of thyroid function in autoimmune thyroid disease, patients presenting hyperthyroidism of autoimmune origin were excluded. However, selection bias because of inclusion of patients with entirely nonautoimmune hyperthyroidism as well as the nonrandomized and noncontrolled character of the research sets limits in its interpretation.

In spite of the limitations, our study suggests that even slight excess of thyroid hormones in subclinical hyperthyroidism (sHT) might exert significant impact on the structure and function of the heart muscle. sHT in the studied group was characterized by increased volume of heart chambers and the diameter of the

ascending aorta, increased left ventricle mass and its disturbed relaxation, which may contribute to increased cardiovascular risk in these patients. The study demonstrated reversibility of these alterations with restoration of euthyroidism. Our results support the argument for early introduction of treatment, even in patients with subclinical thyroid hyperfunction.

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