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Evaulation of atrial conduction abnormalities and left atrial mechanical functions in patients with subclinical thyroid disorders

Ocena zaburzeń przewodzenia przedsionkowego i czynności mechanicznej lewego przedsionka u chorych z subklinicznymi zaburzeniami czynności tarczycy

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Abtstract

Introduction: Changes of thyroid hormones levels may lead to effects, not only in ventricular function, but also atrial function. The aim of this study was to investigate left atrial (LA) mechanical functions, atrial electromechanical coupling and P wave dispersion in patients with subclinical thyroid disorders.

Material and methods: Eighty patients with subclinical thyroid disorders and forty controls were included. A diagnosis of subclinical thyroid disorders were reached with increased or decreased serum TSH and normal free T4 (fT4) levels. LA volumes were measured using the biplane area length method and LA active and passive emptying volumes and fraction were calculated. Intra- and interatrial electromechanical delay were measured by tissue Doppler imaging (TDI).

Results: All groups had similar demographic findings. LA mechanical functions significantly impaired in subclinical thyroid disorders than control group. Intra- and Interatrial delay, were measured significantly higher in patients with subclinical thyroid disorders than control group. PA lateral and interatrial delay were positively correlated with TSH ($r = 0.507$, $p = 0.006$ and $r = 0.455$, $p = 0.015$, respectively) in subclinical hypothyroid patients. There was negative correlation between TSH and interatrial delay ($r = –0.492$, $p = 0.006$) in subclinical hyperthyroid patients. Linear multivariate regression analysis demonstrated that, TSH was the only an independent factor of interatrial delay in patients with subclinical thyroid disorders.

Conclusions: This study showed that impaired LA mechanical and electromechanical function in subclinical thyroid disorders. TSH was an independent determinant of interatrial delay. Prolonged atrial electromechanical coupling time and impaired mechanical atrial functions may be related to the increased incidence of arrhythmias. **(Endokrynol Pol 2012; 63 (4): 286–293)**

Key words: *thyroid hormones, atrial function, interatrial delay*

Streszczenie

Wstęp: Zmiany stężeń hormonów tarczycy mogą wpływać nie tylko na czynność komór serca, ale również na czynność przedsionków. Niniejsze badanie przeprowadzono w celu oceny czynności mechanicznej lewego przedsionka (LA), sprzężenia elektromechanicznego i dyspersji załamka P u chorych z subklinicznymi zaburzeniami czynności tarczycy.

Materiał i metody: Do badania włączono 80 chorych z subklinicznymi zaburzeniami czynności tarczycy i 40 osób stanowiących grupę kontrolną. Zaburzenia czynności tarczycy rozpoznawano na podstawie obniżonego lub podwyższonego stężenia TSH w surowicy i prawidłowego stężenia wolnej T4 (fT4). Zmierzono objętości LA, posługując się dwupłaszczyznową metodą *area-lenght* (pole– wymiar podłużny). Obliczono również objętości i frakcje aktywnego i biernego opróżniania LA. Do pomiaru opóźnienia przewodnictwa wewnątrz- i międzyprzedsionkowego zastosowano technikę doplera tkankowego.

Wyniki: Grupy nie różniły się pod względem charakterystyki demograficznej. W grupie z zaburzeniami czynności tarczycy mechaniczna funkcja przedsionków była istotnie upośledzona w porównaniu z osobami z grupy kontrolnej. Opóźnienie przewodnictwa wewnątrz- i międzyprzedsionkowego stwierdzano istotnie częściej u osób z zaburzeniami czynności tarczycy. Stwierdzono dodatnią korelację miedzy opóźnieniem elektromechanicznym (PA *lateral*) i opóźnieniem przewodzenia międzyprzedsionkowego a TSH (odpowiednio $r = 0{,}507$; $p = 0{,}006$ i $r = 0{,}455$; $p = 0{,}015$) u osób z subkliniczną niedoczynnością tarczycy. Z kolei u osób z subkliniczną nadczynnością tarczycy zaobserwowano ujemną korelację między TSH i opóźnieniem przewodzenia międzyprzedsionkowego ($r = –0{,}492$; $p = 0{,}006$). W wieloczynnikowej analizie regresji liniowej wykazano, że stężenie TSH było jedynym parametrem niezależnie związanym z opóźnieniem przewodzenia międzyprzedsionkowego u chorych z subklinicznymi zaburzeniami czynności tarczycy.

Wnioski: W niniejszym badaniu wykazano upośledzoną czynność mechaniczną i elektromechaniczną LA u chorych z subklinicznymi zaburzeniami czynności tarczycy. Stężenie TSH było niezależnym czynnikiem determinującym opóźnienie przewodzenia międzyprzedsionkowego. Wydłużenie czasu sprzężenia elektromechanicznego i upośledzenie mechanicznej czynności przedsionków mogą się wiązać ze zwiększoną zapadalnością na zaburzenia rytmu. **(Endokrynol Pol 2012; 63 (4): 286–293)**

Słowa kluczowe: *hormony tarczycy, czynność przedsionków, opóźnienie przewodzenia międzyprzedsionkowego*

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Introduction

Thyroid hormone receptors are abundant in the myocardium, so the heart is extremely sensitive to thyroid hormones [1]. There are many regulatory effects of thyroid hormones, such as cardiac protein transcription, gene expression [2], impaired myocardial contractility, decreased cardiac output, variability of heart rate, increased systemic vascular resistance [3], cardiomyocyte atrophy, endothelial dysfunctions [4, 5], higher prevalence of atherosclerosis and development of heart failure [6, 7]. Some clinical studies have shown that even subclinical hyperthyroidism and subclinical hypothyroidism were associated with changes in various cardiac parameters [8, 9]. Subclinical hyperthyroidism is related to a few elevated systolic functions and decreased diastolic functions due to slowed myocardial relaxation [1, 8, 10]. Moreover, subclinical hypothyroidism is associated with LV diastolic dysfunction qualified by slowed myocardial relaxation and disabled rapid ventricular filling, both at rest and after exercise. Frequently this is related to a changeable impairment in LV systolic function even at the very early stage [11, 12]. Therefore, subclinical thyroid disorders could result in significant changes in the cardiovascular system.

Alterations in thyroid status may lead to changes not only in ventricular function, but also in atrial function. In a study, atrial systolic time interval, atrial ejection time and atrial preejection period were used to evaluate atrial function and examine the relationship between hyperthyroidism and atrial function [13]. Currently, measurement of the left atrial (LA) size is the most commonly used method to estimate the amount of atrial remodelling. Left atrial (LA) volumes and LA mechanical functions have recently been identified as a potential indicator of cardiac disease and arrhythmias [14–16]. Intra- and interatrial conduction delay are well known electrophysiological phenomena distinguishing the atria prone to fibrillation [17]. Unlike LA size, atrial conduction times reflect the amount of both electrical and structural remodelling of the atria. Some authors have used left atrial sizes and atrial conduction time to show atrial function. All of these parameters have shown similar and correlated results for impaired atrial function [17–19]. However, LA mechanical functions and atrial conduction abnormalities have not been investigated in subclinical thyroid disorders. Therefore, the aim of the present study was to evaluate atrial conduction abnormalities and left atrial mechanical function in patients with subclinical thyroid disorders.

Material and methods

Study population

We studied 40 patients (32 female and eight male with a mean age of 42.4 ± 11.0 years) with subclinical hyperthyroidism and 40 patients (33 female and seven male with a mean age of 38.6 ± 11.5 years) with subclinical hypothyroidism who were newly diagnosed and untreated, or previously diagnosed patients. The study patients had normal sinus rhythm and narrow QRS complex on electrocardiography (ECG). In addition, 40 healthy control subjects (32 female and eight male with a mean age of 42.0 ± 5.1 years) were included. The diagnosis of subclinical hyperthyroidism was reached with decreased serum TSH (< 0.1 uIU/mL) and normal free T4 (fT4) levels in fasting blood samples (normal values in our laboratory were 0.4–4.0 mU/L for TSH and 0.9–1.9 ng/mL for fT4). The diagnosis of subclinical hypothyroidism was reached with increased serum TSH (> 4.0mU/L) and normal free T4 (fT4) levels in fasting blood samples (normal values in our laboratory were 0.4–4.0 mU/L for TSH and 0.9–1.9 ng/mL for fT4). The entire study population's demographic characteristics, biochemical parameters, lipid values and ECGs were obtained. Exclusion criteria were as follows: overt hypothyroidism or hyperthyroidism, acute coronary syndrome, prior myocardial infarction and coronary artery disease, congestive heart failure, left ventricular (LV) hypertrophy, prolonged QRS duration (≥ 120 msn), reduced LV ejection fraction (< 55%), chronic obstructive pulmonary disease, significant valvular heart disease, pacemaker implantation, atrial flutter or fibrillation, frequent ventricular pre-excitation and atrio-ventricular conduction abnormalities, hypertension (resting blood pressure ≥ 140/90 mm Hg), diabetes mellitus, medications known to alter cardiac conduction, peripheral vascular diseases, pulmonary or neurological disease, pericarditis, congenital heart disease, alcohol abuse, renal or hepatic disease and poor echocardiographic imaging. Approval for the study was obtained from the local ethics committee. All subjects included in the study signed informed consent after careful explanation of the study procedures.

Electrocardiography

At study entry, all subjects underwent standard 12-lead ECG, acquired using the MAC 5500 electrocardiograph (GE Healthcare, Milan, Italy) at a paper speed of 50 mm/s and 20 mm/mV. All recordings were performed in the same quiet room through spontaneous breathing, with a subsequent 20 minutes of adjustment in the supine position. P wave duration measurements were performed manually by two of the observers using calipers and a magnifying lens for the exact definition of the ECG deflection, as defined in a previous study [20]. The beginning of the P wave was defined as the point where the initial deflection of the P wave crossed the iso-electric line, and the end of the P wave was defined as the point where the final deflection of the

P wave crossed the iso-electric line. ECG recordings with measurable P waves in fewer than ten leads were excluded from the analysis. The difference between P wave maximum and P wave minimum durations was defined as P wave dispersion [20, 21]. Intra-observer and inter-observer mean percent mistake (absolute difference between two observations divided by the mean and expressed in percent) for maximum and minimum P wave duration measurements were determined in 50 randomly selected study applicants (30 patients/20 controls) and were < 5% for p maximum and < 6% for p minimum.

Standard echocardiography

All patients were evaluated by transthoracic M mode, two dimensional (2D), pulsed-wave (PW), continuous wave (CW), colour flow and tissue Doppler imaging (TDI). All examinations were performed with the GE Vivid-7 system (GE Vingmed, Horten, Norway) with a 2–4 MHz transducer at a depth of 16 cm. During echocardiography, a continuous single-lead ECG recording was obtained. All patients were imaged in the left lateral decubitus position. 2D and conventional Doppler examinations were obtained in the parasternal and apical views, according to the guidelines of the American Society of Echocardiography [21]. LV diameters and wall thickness were measured by M-mode echocardiography. LV ejection fraction was calculated using apical two-and four-chamber views by Simpson's method, according to the American Society of Echocardiography guidelines [21]. The mitral valve inflow pattern (E-wave, A-wave, E-wave deceleration time [Dt], E/A ratio and isovolumic relaxation time [IVRT]) was measured using pulsed wave Doppler. LV mass index was calculated using the formula with the Deveraux equation [22]. LA volumes were obtained via apical four-chamber views by a disc method [21, 23]. LA maximum volume (Vmax) at the end-systolic phase, LA minimum volume (Vmin) at the end-diastolic phase, and LA volume before atrial systole (Vp) were measured and calculated indexed to body surface area. The LA function parameters were calculated as follows:

— LA passive emptying volume = Vmax – Vp;
— LA passive emptying fraction = [(Vmax – Vp)/ /Vmax] × 100%;
— LA active emptying volume = Vp – Vmin;
— LA active emptying fraction = [(Vp – Vmin)/ /Vp] × 100% [17].

Tissue Doppler echocardiography

TDI was performed by transducer frequencies of 3.5 to 4.0 MHz, adjusting the spectral pulsed Doppler signal filters to acquire the Nyquist limit of 15 to 20 cm/s and using the minimal optimal gain. Myocardial TDI velocities (peak systolic [Sm], early diastolic [Em] and late diastolic velocities [Am]) were measured via spectral pulsed Doppler as of the LV-free wall from the apical four-chamber view [21]. The ultrasound beam was positioned as parallel as possible with the myocardial segment to acquire the optimal angle of imaging. The time interval from the P wave onset on the surface ECG to the beginning of the late diastolic wave (Am), which is defined as atrial electromechanical coupling (PA), was obtained from lateral mitral annulus, septal mitral annulus, and right ventricular tricuspid annulus and named as PA lateral, PA septum, and PA tricuspid, respectively. The difference between PA lateral and PA tricuspid was defined as inter-atrial electromechanical delay (EMD), and the difference between PA lateral and septum was defined as intra-atrial EMD [20, 21]. All measurements were repeated three times, and average values were received for each of the atrial conduction delay times. All measurements were performed by two experienced investigators unaware of the subject's clinical status. If a difference of > 5% in any of the variables measured by both investigators was found, the patient was not included, whereas if the difference was < 5%, the measurements were averaged.

Statistical analysis

All analyses were performed using the SPSS (SPSS for Windows 15.0) software package. Continuous variables were presented as mean ± standard deviation. Categorical variables were presented as the percentage. All the numerical variables of the study groups presented a normal distribution, and the variances between the groups were equal. Thus, one-way analyses of variance (ANOVA) for mean and post hoc Tukey test were used for individual group differences for the comparison of groups. The relationships between variables were examined with Pearson and Spearman correlation coefficients. Linear multivariate regression analysis was used to recognise the significant determinants of interatrial delay, which incorporated variables that correlated with a P value of less than 0.1 in the correlation analysis. A value of $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

The baseline demographic and biochemical parameters of the three groups are set out in Table I. All groups had similar demographic findings such as age, sex, body mass index (BMI), body surface area (BSA), smoking, heart rate, systolic and diastolic blood pressure and lipid levels ($p > 0.05$). Unsurprisingly, patients with subclinical hypothyroidism had significantly higher TSH and significantly lower fT4 ($p < 0.001$ and $p < 0.001$ respec-

Table I. *Baseline demographic and biochemical characteristics of the groups*
Tabela I. *Wyjściowa charakterystyka demograficzna i biochemiczna badanych grup*

Parameter	Subclinical hypothyroid n = 40	Subclinical hyperthyroid n = 40	Control n = 40	p value
Age	38.6 ± 11.5	42.4 ± 11.0	42.0 ± 10.1	0.226
Gender (female, %)	32 (80.0%)	33 (82.5%)	32 (80.0%)	0.701
Smoking	9 (22.5%)	8 (20.0%)	10 (25.0%)	0.386
BMI [kg/m^2]	27.4 ± 4.6	27.3 ± 4.5	28.3 ± 5.1	0.517
BSA	1.80 ± 0.16	1.77 ± 0.19	1.86 ± 0.17	0.111
Heart rate [beats/min]	74.6 ± 10.6	75.2 ± 9.8	74.6 ± 9.0	0.869
SBP [mm Hg]	117.8 ± 18.3	117.3 ± 17.4	119.1 ± 19.3	0.436
DBP [mm Hg]	77.8 ± 7.0	76.8 ± 9.0	78.1 ± 8.3	0.572
Total cholesterol [mg/dL]	186.0 ± 26.7	185.6 ± 27.6	186 ± 28.3	0.805
LDL [mg/dL]	114.7 ± 16.4	111.5 ± 17.7	111.0 ± 18.3	0.588
HDL [mg/dL]	42.3 ± 7.1	43.9 ± 7.7	42.5 ± 5.8	0.701
Triglycerides [mg/dL]	151 ± 28.2	154 ± 29.0	152 ± 29.1	0.964
Glucose	95.6 ± 7.1	95.5 ± 12.2	97.9 ± 14.2	0.547
Haemoglobin [g/dL]	13.4 ± 3.2	13.5 ± 2.7	13.1 ± 2.8	0.692
Creatinine [mg/dL]	0.79 ± 0.18	0.81 ± 0.14	0.77 ± 0.16	0.217
TSH [uIU/mL]	**8.6 ± 4.9**	**0.06 ± 0.09**	**2.0 ± 0.8**	**< 0.001**
Free T3 [pg/mL]	2.9 ± .71	4.01 ± 0.87	3.4 ± 0.83	0.492
Free T4 [ng/dL]	**0.97 ± 0.12**	**1.46 ± 0.23**	**1.25 ± 0.20**	**< 0.001**

BMI — body mass index; BSA — body surface area; SBP — systolic blood pressure; DBP — diastolic blood pressure; LDL — low-density lipoprotein; HDL — high-density lipoprotein; TSH — thyroid-stimulating hormone

tively). The patients with subclinical hyperthyroidism had significantly lower TSH and significantly higher fT4 ($p < 0.001$ and $p < 0.001$ respectively). All groups were similar in terms of conventional and Doppler echocardiographic parameters. Only peak systolic velocity (Sm) and early diastolic velocity (Em) were significantly lower in patients with subclinical hypothyroidism, and subclinical hyperthyroid patients on TDI compared to controls ($p = 0.027$ and $p = 0.001$ respectively, Table II).

Atrial conduction parameters

Atrial electromechanical time intervals and P wave analysis are set out in Table III. The PA lateral and septal durations were significantly higher in patients with subclinical thyroid disorders than the control group, but there was no difference in PA tricuspid duration between the groups. Intra- and interatrial EMD were significantly higher in patients with subclinical thyroid disorders than the control group. P wave dispersion (PWD) was significantly higher in patients with subclinical thyroid disorders than the control group. There was no correlation between PWD and TSH. PA lateral and interatrial delay were positively correlated with TSH ($r = 0.507$, $p = 0.006$ and $r = 0.455$, $p = 0.015$, respectively, Figure I) in subclinical hypothyroid patients. There was a negative correlation between TSH and interatrial delay ($r = –0.492$, $p = 0.006$, Figure II) in subclinical hyperthyroid patients.

Left atrial mechanical function

LA volume measurements and mechanical functions are set out in Table IV. Both groups were similar in terms of Vmax, Vmin and Vp ($p = 0.292$, $p = 0.257$ and $p = 0.242$ respectively). However, LA passive emptying volume and LA passive emptying fraction were significantly decreased in patients with subclinical thyroid disorders. Moreover, LA active emptying volume and LA active emptying fraction were significantly increased in patients with subclinical thyroid disorders. There was positive correlation only between LA active emptying volume and TSH levels ($r = 0.586$, $p = 0.001$) in patients with subclinical thyroid disorders.

Linear multivariate regression analysis demonstrated that TSH was the only independent factor of interatrial delay in patients with subclinical hypothyroidism and subclinical hyperthyroidism ($R^2 = 0.207$, $\beta = 0.455$, $p = 0.015$ and $R^2 = 0.242$, $\beta = –0.492$, $p = 0.006$, respectively).

Table II. *Echocardiographic charactheristics of groups*
Tabela II. *Charakterystyka echokardiograficzna badanych grup*

Parameter	Subclinical hypothyroid n = 40	Subclinical hyperthyroid n = 40	Control n = 40	p value
LVESD [mm]	30.0 ± 3.5	29.9 ± 3.1	30.1 ± 4.1	0.930
LVEDD [mm]	48.2 ± 5.5	47.0 ± 5.1	47.2 ± 4.2	0.341
LVESV [mL]	27.7 ± 8.0	28.1 ± 8.7	27.1 ± 5.3	0.868
LVEDV [mL]	82.7 ± 16.2	90.4 ± 18.4	85.4 ± 18.0	0.177
IVS [mm]	10.1 ± 1.7	9.8 ± 19	9.5 ± 1.5	0.216
PW [mm]	9.5 ± 1.2	9.5 ± 1.4	9.2 ± 1.0	0.709
LA [mm]	35.0 ± 8.7	35.3 ± 7.1	32.3 ± 6.1	0.180
E [cm/s]	77.8 ± 27.0	76.8 ± 19.0	78.1 ± 18.3	0.572
A [cm/s]	66.0 ± 26.7	65.6 ± 27.6	59.6 ± 22.3	0.305
DT [ms]	216.7 ± 36.4	215.5 ± 37.7	211.0 ± 38.3	0.788
IVRT [ms]	90.3 ± 27.1	88.9 ± 27.7	87.5 ± 25.8	0.701
LV mass index	84.4 ± 18.2	83.9 ± 19.0	83.2 ± 19.1	0.461
LVEF [%]	64.0 ± 18.2	64.2 ± 19.0	64.4 ± 19.1	0.811
Sm [cm/s]	**10.8 ± 2.2**	**11.3 ± 1.8**	**12.3 ± 2.2**	**0.027**
Em [cm/s]	**11.4 ± 2.2**	**11.5 ± 2.5**	**13.4 ± 1.9**	**0.001**
Am [cm/s]	13.6 ± 3.1	13.1 ± 2.7	12.8 ± 2.4	0.653

LVESD — left ventricular end-systolic diameter; LVEDD — left ventricular end diastolic diameter; LVESV — left ventricular end systolic volume; LVEDV — left ventricular end diastolic volume; IVS — interventricular septum; PW — posterior wall; LA — left atrium; E — early diastolic mitral inflow velocity; A — late diastolic mitral inflow velocity; DT — deceleration time; IVRT — isovolumetric relaxation time; LVEF — left ventricular ejection fraction; Sm — peak systolic mitral annular velocity; Em — early diastolic mitral annular velocity; Am — late diastolic mitral annular velocity

Table III. *Comparison of parameters of atrial conduction times and P wave dispersion between the groups*
Tabela III. *Porównanie parametrów czasu przewodzenia przedsionkowego i dyspersji załamka P między grupami*

	Subclinical hypothyroid	Subclinical hyperthyroid	Control	p value
PA lateral [ms]	67.3 ± 18.9	66.9 ± 15.1	55.8 ± 12.4	< 0.001
PA septum [ms]	49.9 ± 13.2	50.2 ± 13.1	44.2 ± 7.2	< 0.001
PA tricuspid [ms]	39.1 ± 5.4	39.3 ± 4.7	37.7 ± 5.3	0.112
PA lateral-PA tricuspid [ms]*	26.5 ± 5.4	26.0 ± 9.9	18.4 ± 8.0	< 0.001
PA septum-PA tricuspid [ms]#	8.9 ± 4.0	9.5 ± 4.7	6.7 ± 3.3	0.001
Max P-wave duration [ms]	102.7 ± 25.3	98.5 ± 24.5	95.3 ± 18.9	0.090
Min P-wave duration [ms]	56.7 ± 11.0	55.0 ± 9.9	55.3 ± 9.7	0.383
P-wave dispersion [ms]	46.0 ± 6.9	43.5 ± 8.3	40.0 ± 8.7	0.026

PA — interval with tissue Doppler imaging from the onset of p wave on the surface electrocardiogram to beginning of the late diastolic wave (Am wave); *inter-atrial electromechanical delay; #intra-atrial electromechanical delay

Discussion

The objective of this study was to analyse the changes of atrial functions in patients with subclinical thyroid disorders. We demonstrated significantly impaired left atrial functions in patients with subclinical thyroid disorders. Furthermore, atrial conduction parameters were significantly prolonged in patients with subclinical thyroid disorders compared to the control group. Additionally, we found that TSH level was the only independent factor of interatrial delay in patients with subclinical thyroid disorders.

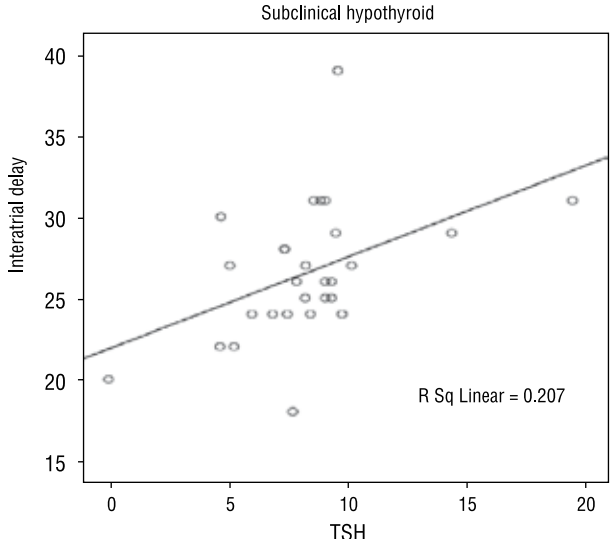

Figure 1. *Positive correlation between TSH levels and interatrial delay in patients with subclinical hypothyroidism*

Rycina 1. *Dodatnie korelacje między stężeniami TSH i opóźnieniem przewodzenia międzyprzedsionkowego u chorych z subkliniczną niedoczynnością tarczycy*

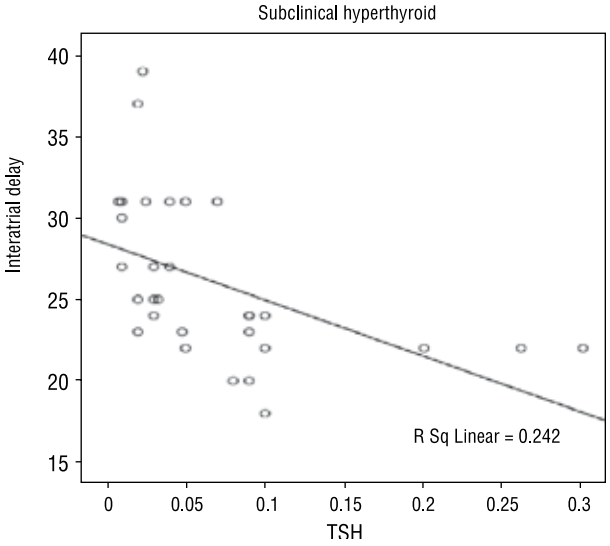

Figure 2. *Negative correlation between TSH levels and interatrial delay in patients with subclinical hyperthyroidism*

Rycina 2. *Ujemne korelacje między stężeniami TSH i opóźnieniem przewodzenia międzyprzedsionkowego u chorych z subkliniczną nadczynnością tarczycy*

Table IV. *Measurements of left atrial mechanical functions*

Tabela IV. *Pomiary czynności mechanicznej lewego przedsionka*

Parameter	Subclinical hypothyroid	Subclinical hyperthyroid	Control group	p value
Vmax [mL/m²]	28.7 ± 8.0	28.2 ± 7.8	27.4 ± 8.8	0.292
Vmin [mL/m²]	8.4 ± 3.2	9.9 ± 4.2	7.8 ± 3.7	0.257
Vp [mL/m²]	15.9 ± 5.5	17.3 ± 6.1	15.1 ± 5.9	0.242
LA passive emptying volume [mL/m²]	10.3 ± 3.7	10.7 ± 4.6	14.1 ± 3.9	0.001
LA passive emptying fraction [%]	38.7 ± 9.9	37.2 ± 9.2	49.3 ± 12.9	<0.001
LA active emptying volume [mL/m²]	7.9 ± 3.5	8.1 ± 2.7	6.3 ± 2.5	0.006
LA active emptying fraction [%]	48.7 ± 9.9	46.3 ± 8.4	40.5 ± 9.7	0.001

LA — left atrium; Vmax — LA maximum volume; Vmin — LA minimum volume; Vp — LA volume before P wave

The myocardium is well-known among tissues that include thyroid hormone receptors [10]. Thyroid hormone deficiency can alter cardiac muscle function by decreasing the activity of several enzymes involved in the regulation of myocyte calcium fluxes [10] and the expression of several contractile proteins [24]. In addition, thyroid hormone has been shown to affect calcium uptake by the sarcoplasmic reticulum, to stimulate plasma membrane Ca-ATPase activity. and to increase voltage-dependent channels in animal ventricular cells [10, 24, 25]. Subclinical thyroid disorders are defined as an asymptomatic state characterised by normal serum concentration of fT4 and increased or decreased serum concentrations of TSH. Thus, it may seem surprising to find cardiac alterations similar to those observed in overt thyroid disorders. However, minute decrements in hormone synthesis may over time lead to biochemical and functional signs that are qualitatively similar to those of thyroid disorders. The most consistent cardiac abnormalities recognised in subclinical hyperthyroid patients are increased heart rate and enhanced LV mass [12, 26]. However, in our study, LV mass index was similar in all groups because the study population consisted of young patients. Di Bello et al. [27] inves-

tigated and reported early systolic hyperdeformability and hypercontractility together with impaired diastolic function by strain echocardiography in patients with subclinical hyperthyroidism. They speculated that the direct effect of thyroid hormones on the heart may cause these results. Galetta et al. [28] demonstrated increased sympathetic activity and increased inhomogeneity of ventricular recovery times in subclinical hyperthyroid patients. Another study demonstrated a significant increase in serum levels of NT-pro-BNP in patients with overt and subclinical hyperthyroidism [29]. Additionally, our results suggested prolonged atrial conduction times and impaired left atrial mechanical functions in subclinical hyperthyroid patients. Subclinical hyperthyroidism could cause many significant effects on the cardiovascular system. It has been related to higher heart rate and higher risk of supraventricular arrhythmias [28–31]. Previous studies also showed the effect of prolonged atrial electromechanical coupling interval and impaired atrial functions on the development of supraventricular arrhythmias [19, 20]. We thought that our results may explain an increased risk for development of arrhythmias in subclinical hyperthyroid patients.

On the other hand, thyroid hormones also affect the transcription of structural and regulatory proteins on the cardiovascular system [2]. Also, mild changes in blood levels of thyroid hormones have many adverse effects on both the function and structure of the heart. These effects are decreased cardiac contractility and cardiac output, cardiomyocyte atrophy [1–4], myocardial fibrosis and the development of heart failure [32, 33]. Aghini-Lombardi et al. [34] demonstrated early functional and textural alterations in subclinical hypothyroid patients using intra-myocardial ultrasonic video-densitometry analysis. Additionally, our study suggests prolonged atrial electromechanical coupling interval and impaired left atrial functions in subclinical hypothyroid patients. The increased myocardial fibrosis and cardiomyocyte atrophy could be considered as causes of impaired atrial functions in subclinical hypothyroid patients.

Study limitations

The major limitation of our study is its cross-sectional design and lack of follow-up of the patients. Another limitation is the relatively small study population. Patients could not be followed-up prospectively for arrhythmic episodes. Therefore, we do not know whether prolongation of intra- and interatrial EMD and impaired LA mechanical functions predict arrhythmias and heart failure in subclinical thyroid disorders. For these reasons, long-term follow-up and large-scale prospective studies are needed to determine the predictive value of prolonged intra- and interatrial EMD and LA mechanical functions in this population.

Conclusions

The current study is the first to report impaired LA mechanical and electromechanical function in patients with subclinical thyroid disorders. Secondly, impaired atrial mechanical function and atrial electromechanical coupling interval were related to TSH levels. Finally, interatrial electromechanical delay was increased in subclinical thyroid disorders, and TSH is an independent determinant of interatrial electromechanical delay. Prolonged atrial electromechanical coupling time and impaired mechanical atrial functions may be related to the increased incidence of arrhythmias and heart failure in subclinical thyroid disorders. In the light of these results, we emphasise that subclinical thyroid disorders should be carefully followed up and treated with the same thoroughness as clinical thyroid disorders.

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