Archives of Cardiovascular Disease (2012) **105**, 631—638

Available online at
SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

CLINICAL RESEARCH

Detection of subclinical atrial dysfunction by two-dimensional echocardiography in patients with overt hyperthyroidism

Détection d'une dysfonction auriculaire infra-clinique par échocardiographie bidimensionnelle chez des patients hyperthyroïdiens

Selim Ayhan[a], Serkan Ozturk[a,*], Oğuz Dikbas[b], Alim Erdem[a], Mehmet Fatih Ozlu[a], Davut Baltaci[c], Aytekin Alçelik[d], Mehmet Tosun[e], Mehmet Ozyasar[a], Mehmet Yazici[a]

[a] *Department of Cardiology, Faculty of Medicine, Abant Izzet Baysal University, 14280 Golkoy, Bolu, Turkey*
[b] *Department of Endocrinology, Faculty of Medicine, Abant Izzet Baysal University, Golkoy, Bolu, Turkey*
[c] *Department of Family Medicine, Faculty of Medicine, Duzce Universtity, Duzce, Turkey*
[d] *Department of Internal Medicine, Faculty of Medicine, Abant Izzet Baysal University, Golkoy, Bolu, Turkey*
[e] *Department of Biochemistry, Faculty of Medicine, Abant Izzet Baysal University, Golkoy, Bolu, Turkey*

Received 29 May 2012; received in revised form 5 July 2012; accepted 6 July 2012
Available online 5 October 2012

KEYWORDS
Atrial function;
Atrial conduction time;

Summary
Background. — Hyperthyroidism is an important cardiovascular risk factor in the development of atrial fibrillation and heart failure. Increased atrial electromechanical intervals are used to predict atrial fibrillation, measured by tissue Doppler imaging (TDI).
Aims. — To evaluate atrial electromechanical delay (EMD) and left atrial (LA) mechanical function in patients with overt hyperthyroidism.

Abbreviations: 2D, Two-dimensional; Am, Late diastolic velocity; BMI, Body mass index; BSA, Body surface area; ECG, Electrocardiogram; Em, Early diastolic velocity; EMD, Interatrial electromechanical delay; fT3, Free T3; fT4, Free T4; LA, Left atrial; LV, Left ventricular; PA, Atrial electromechanical coupling; Sm, Peak systolic velocity; TDI, Tissue Doppler imaging; TSH, Thyroid-stimulating hormone; Vmax, LA maximum volume at the end-systolic phase; Vmin, LA minimum volume at the end-diastolic phase; Vp, LA volume before atrial systole.

* Corresponding author. Fax: +90 3742 534 615.
E-mail address: drserkan69@hotmail.com (S. Ozturk).

1875-2136/$ — see front matter
http://dx.doi.org/10.1016/j.acvd.2012.07.003

Interatrial delay;
Hyperthyroidism

Methods. — Thirty-four patients with overt hyperthyroidism and 34 controls were included. A diagnosis of overt hyperthyroidism was reached with decreased serum thyroid-stimulating hormone (TSH) and increased free T4 (fT4) concentrations. Using TDI, atrial electromechanical coupling (PA) was obtained from the lateral mitral annulus (PA lateral), septal mitral annulus (PA septum) and right ventricular tricuspid annulus (PA tricuspid). LA volumes (maximum, minimum and presystolic) were measured by the disks method in apical four-chamber view and indexed to body surface area. LA active and passive emptying volumes and fractions were calculated.
Results. — LA diameter was significantly higher in hyperthyroid patients ($P = 0.001$). LA passive emptying volume and fraction were significantly decreased in hyperthyroid patients ($P = 0.038$ and $P < 0.001$). LA active emptying volume and fraction were significantly increased in hyperthyroid patients ($P < 0.001$ and $P < 0.001$). Left and right intra-atrial (PA lateral—PA septum and PA septum—PA tricuspid) and interatrial (PA lateral—PA tricuspid) EMDs were significantly higher in hyperthyroid patients (29.2 ± 4.4 vs 18.1 ± 2.6, $P < 0.001$; 18.7 ± 4.3 vs 10.6 ± 2.0, $P < 0.001$; and 10.5 ± 2.9 vs 7.1 ± 1.2, $P < 0.001$, respectively). Stepwise linear regression analysis demonstrated that fT4 and TSH concentrations were independent predictors of interatrial EMD ($\beta = 0.436$, $P < 0.001$ and $\beta = -0.310$, $P = 0.005$, respectively).
Conclusion. — This study showed prolonged atrial electromechanical intervals and impaired LA mechanical function in patients with overt hyperthyroidism, which may be an early sign of subclinical cardiac involvement and dysrhythmias in overt hyperthyroidism.

MOTS CLÉS
Fonction auriculaire ;
Temps de conduction atrial ;
Délai inter-atrial ;
Hyperthyroïdie

Résumé
Objectif. — L'hyperthyroïdie est un facteur de risque important de développement d'une fibrillation atriale (FA) et d'insuffisance cardiaque. L'augmentation des intervalles électromécaniques atriaux, prédisant la FA sont mesurées en Doppler tissulaire (DTI). L'objectif de cette étude est d'évaluer le délai électromécanique auriculaire (EMD) et la fonction mécanique auriculaire gauche (OG) chez des patients hyperthyroïdiens.
Méthode. — Trentre-quatre patients en hyperthyroïdie et 34 témoins ont été inclus. Le diagnostic d'hyperthyroïdie a été retenu sur une diminution de la concentration en TSH et une augmentation de la T4 libre (fT4). En utilisant le DTI, le couplage électromécanique auriculaire (PA) a été mesuré à l'anneau mitral latéral (PA latéral), à l'anneau mitral septal (PA septum) et à l'anneau tricuspide (PA tricuspide). Les volumes auriculaires gauches (maximum, minimum et présystolique) ont été mesurés par la méthode des disques, en incidence apicale des quatre cavités, et indexés à la surface corporelle. Les volumes de vidange de l'oreillette gauche lors des phases active et passive ainsi que les fractions ont été calculées.
Résultats. — Le diamètre de l'oreillette gauche est significativement plus important chez les patients hyperthyroïdiens ($p = 0{,}001$). Le volume de vidange passif auriculaire gauche et la fraction étaient significativement diminués chez les patients hyperthyroïdiens ($p = 0{,}038$ et $p < 0{,}001$). Le volume de vidange actif auriculaire gauche et la fraction étaient significativement augmentés chez les hyperthyroïdiens ($p < 0{,}001$ et $p < 0{,}001$). Les délais intra-atriaux auriculaire gauche et droit (PA latéral — PA septum et PA septum — PA tricuspide, respectivement) ainsi que les délais inter-atriaux (PA latéral — PA tricuspide). Les délais électromécaniques auriculaires étaient significativement plus élevés chez les hyperthyroïdiens ($29{,}2 \pm 4{,}4$ versus $18{,}0 \pm 2{,}6$, $p < 0{,}001$; $18{,}7 \pm 4{,}3$ versus $10{,}6 \pm 2{,}0$, $p < 0{,}001$; et $10{,}5 \pm 2{,}9$ versus $7{,}1 \pm 1{,}3$, $p < 0{,}001$). L'analyse par régression linéaire a montré que la T4 libre et la concentration en TSH étaient des prédicteurs indépendants du délai électromécanique atrial dans sa composante inter-auriculaire ($\beta = 0{,}388$, $p = 0{,}001$ et $\beta = 0{,}547$, $p < 0{,}001$).
Conclusion. — Cette étude montre que les intervalles électromécaniques auriculaires sont prolongés et que la fonction mécanique auriculaire gauche est altérée chez le patient hyperthyroïdien. L'allongement des intervalles électromécaniques et l'altération de la fonction mécanique auriculaire gauche pourraient être un signe précoce d'une atteinte cardiaque infraclinique et de risque accru d'arythmie chez des patients hyperthyroïdiens.

Background

Thyroid hormone receptors are highly expressed in the myocardium [1]. Consequently, overt hyperthyroidism has profound cardiac effects, including increased heart rate, arrhythmias, LV diastolic dysfunction [2], LV systolic dysfunction [3], decreased systemic vascular resistance [4] and the development of atrial fibrillation and heart failure [5,6].

Hyperthyroidism can lead to decreased diastolic function as a result of impaired myocardial relaxation [1,2]. Moreover, hyperthyroidism is associated with LV diastolic dysfunction due to decreased myocardial relaxation and inhibited rapid ventricular filling, both at rest and with exercise [1,7]; this is frequently related to a changeable impairment of LV systolic function. Thus, hyperthyroidism may result in significant cardiovascular alterations, including atrial fibrillation and heart failure [5,6].

In a study, the atrial systolic time interval, atrial ejection time and atrial pre-ejection period were used to evaluate atrial function. In addition, the relationship between hyperthyroidism and atrial function was examined [8]. LA volume and mechanical function has recently been identified as a potential indicator of cardiac disease and arrhythmias [9—11]. Inter- and intra-atrial conduction disorders are well-known electrophysiological distinctions of atria prone to fibrillation [12]. Unlike LA size, atrial conduction time reflects the levels of both electrical and structural remodelling of the atria. All of these variables are similar and result in impaired atrial function [12—14].

Alterations in thyroid status may lead to changes in both ventricular and atrial function. However, LA mechanical function and atrial conduction abnormalities have not been investigated in overt hyperthyroidism. The aim of the present study was to evaluate atrial electromechanical delay and LA mechanical function in patients with overt hyperthyroidism.

Methods

Study population

We studied 34 newly treated or untreated patients, previously diagnosed with overt hyperthyroidism (25 women and nine men; mean age 45.2 ± 9.3 years). The control group consisted of 34 sex- and age-matched healthy subjects (24 women and ten men; mean age of 43.6 ± 8.0 years) who were free of endocrinological, inflammatory, connective tissue, cardiovascular, pulmonary and other known systemic disease, and were admitted to hospital for a check-up. All subjects in the study population had normal sinus rhythm on ECG. The study was designed as cross-sectional.

A diagnosis of overt hyperthyroidism was reached with decreased serum TSH concentrations, increased fT4 concentrations and/or increased fT3 concentrations in fasting blood samples (normal values in our laboratory were: 0.4—4.0 mIU/mL for TSH; 0.89—1.76 ng/dL for fT4; and 1.80—5.00 pg/mL for fT3). Demographic characteristics, biochemical variables, lipid values and ECGs were obtained for the entire study population. Exclusion criteria were as follows: subclinical hyperthyroidism, acute coronary syndrome, prior myocardial infarction and coronary artery disease, congestive heart failure, LV hypertrophy, prolonged QRS duration (≥ 120 ms), reduced LV ejection fraction (< 55%), atrial flutter or fibrillation, significant valvular heart disease, pacemaker implantation, frequent ventricular preexcitation and atrioventricular conduction abnormalities, diabetes mellitus, arterial hypertension (resting blood pressure ≥ 140/90 mmHg), medications known to alter cardiac conduction, peripheral vascular disease, congenital heart disease, pulmonary or neurological disease, pericarditis, peripheral neuropathy, alcohol abuse, renal or hepatic disease and poor echocardiographic imaging. Approval for the study was obtained from the local ethics committee and all subjects gave informed consent.

Standard echocardiography

At study entry, all patients were evaluated by transthoracic, M-mode, 2D, pulsed-wave, continuous-wave, colour-flow and TDI. Echocardiographic examinations were performed with the GE Vivid-7 system (GE Vingmed, Horten, Norway) with a 2—4 MHz transducer at a dept 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 [15]. LV diameters and wall thickness were measured by M-mode echocardiography. LV ejection fraction was calculated using the apical two-and four-chamber views by Simpson's method, according to American Society of Echocardiography guidelines [15]. The mitral valve inflow pattern (E-wave, A-wave, E-wave deceleration time, E/A ratio and isovolumic relaxation time) were measured using pulsed-wave Doppler. LV mass index was calculated using the Devereux equation [16]. LA volumes were obtained echocardiographically from the apical four-chamber views by the disks method [17,18]. LA Vmax at the end-systolic phase (onset of the mitral opening), LA Vmin at the end-diastolic phase (onset of the mitral closure) and Vp were measured at the beginning of atrial systole (onset of P wave on ECG) and indexed to BSA. LA function variables 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% [12].

Atrial electromechanical interval

TDI was performed using 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 (Sm, Em and Am velocities) were measured via spectral pulsed Doppler of the LV free wall from the apical four-chamber view [15]. The ultrasound beam was positioned as parallel as possible to the myocardial segment to acquire the optimal angle of imaging. The monitor sweep speed was set at 50 to 100 mm/s to optimize the spectral display of myocardial velocities. The time interval from the P wave onset on the surface ECG to the beginning of the Am is defined as PA; it was obtained from the lateral mitral annulus, the septal mitral annulus and the right ventricular tricuspid annulus, and named PA lateral (Fig. 1), PA septum, and PA tricuspid, respectively. The difference between PA lateral and PA tricuspid was defined as the EMD, the difference between PA lateral and PA septum was defined as the left intra-atrial EMD and the difference between PA septum and PA tricuspid was defined as the right intra-atrial EMD [12—15]. All measurements were repeated three times and average values were obtained for each of the atrial conduction delay times. All measurements

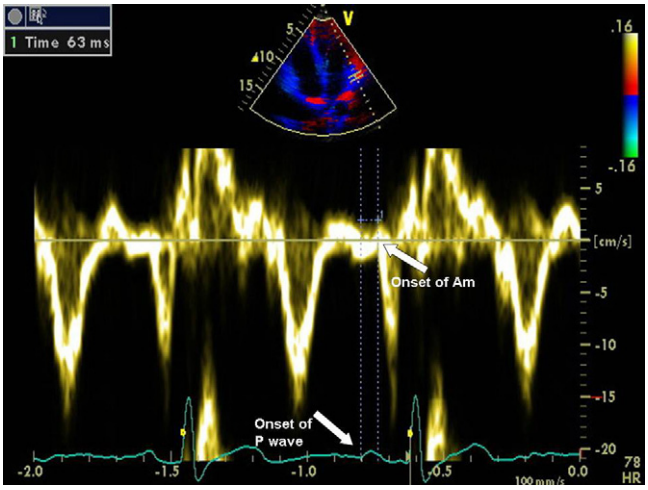

Figure 1. The time interval from the P wave onset on the surface electrocardiogram to the beginning of the late diastolic wave (Am), which is defined as atrial electromechanical delay.

were performed by two experienced investigators who were unaware of the subject's clinical status.

Reproducibility

Intraobserver variability was evaluated in 20 subjects selected randomly from the study population by repeating the measurements under the same basal conditions. To test inter-observer variability, the measurements were performed offline from video recordings by a second observer. Reproducibility of atrial electromechanical coupling and LA volumes obtained by 2D echocardiography were evaluated by the coefficient of variation between measurements.

Intraobserver variability was 4.1% for PA lateral, 4.5% for PA septum, 4.8% for PA tricuspid, 4.7% for Vmax, 4.3% for Vp and 4.7% for Vmin. Inter-observer variability was 4.0% for PA lateral, 4.3% for PA septum, 4.5% for PA tricuspid, 4.9% for Vmax, 4.6% for Vp and 4.5% for Vmin.

Statistical analysis

All analyses were performed using the SPSS (SPSS for Windows 15.0) software package. Continuous variables are presented as means ± standard deviations. Categorical variables are presented as percentages. The chi-square test was used for categorical variables and the unpaired *t* test was used for continuous variables. Pearson's correlation coefficient was used for correlation analysis. A stepwise multiple regression analysis was used to recognize the significant determinants of interatrial EMD, which incorporated variables that correlated with a value of $P < 0.1$ in the correlation analysis. A value of $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

The clinical and laboratory characteristics and echocardiographic findings for the two groups are shown in Table 1. Age, sex, smoking, systolic and diastolic blood pressure, LV end-diastolic and end-systolic diameters, LV mass index and LV ejection fraction were similar in the two groups ($P > 0.05$). BMI and BSA were significantly lower in hyperthyroid patients ($P = 0.023$ and $P = 0.001$, respectively). So, as expected, hyperthyroid patients had significantly lower TSH and higher fT4 and fT3 concentrations compared with controls. Heart rate and LA diameter were significantly higher in hyperthyroid patients than in controls ($P = 0.001$ and $P = 0.001$, respectively). Also, Am velocity, Em/Am and E/E' ratio were significantly lower in hyperthyroid patients ($P = 0.035$, $P = 0.004$ and $P = 0.002$, respectively).

Left atrial mechanical function

Measurements of LA volume and mechanical function are presented in Table 2. Both groups were similar in terms of Vmax and Vmin ($P = 0.212$ and $P = 0.203$, respectively) but Vp was significantly higher in hyperthyroid patients than in controls ($P = 0.001$). Also, LA passive emptying volume and fraction were significantly decreased in hyperthyroid patients ($P = 0.038$ and $P < 0.001$, respectively). Additionally, LA active emptying volume and fraction were significantly increased in hyperthyroid patients compared with in controls ($P < 0.001$ and $P < 0.001$, respectively).

Atrial electromechanical intervals

Atrial electromechanical coupling intervals are presented in Table 3. PA lateral, PA septum, PA tricuspid and intra- and interatrial EMDs were significantly prolonged in hyperthyroid patients compared with in healthy controls ($P < 0.001$, $P < 0.001$, $P = 0.001$, $P < 0.001$ and $P < 0.001$, respectively). Interatrial EMD and left intra-atrial EMD were positively correlated with fT4 concentration ($r = 0.628$, $P < 0.001$ and $r = 0.772$, $P < 0.001$, respectively) and were negatively correlated with TSH concentration ($r = -0.379$, $P = 0.035$ and $r = -0.726$, $P < 0.001$, respectively; Fig. 2). Additionally, left intra-atrial EMD was correlated with Em/Am and E/E' ratio ($r = -0.282$, $P = 0.029$ and $r = 0.324$, $P = 0.011$, respectively). Also, there was a slight positive correlation between right intra-atrial EMD and fT4 concentration ($r = 0.365$, $P = 0.043$) but right intra-atrial EMD was not correlated with TSH concentration ($r = -0.260$, $P = 0.158$).

Stepwise linear regression analysis demonstrated that LA passive and active emptying fractions and fT4 and TSH concentrations were significantly related to interatrial EMD ($\beta = -0.155$, $P = 0.032$; $\beta = 0.189$, $P = 0.007$; $\beta = 0.436$, $P < 0.001$ and $\beta = -0.310$, $P = 0.005$, respectively). However, there was no relationship between age, BMI, BSA, heart rate, LA passive and active emptying volumes, LA diameter, fT3 or Em/Am ratio and interatrial EMD (Table 4).

Discussion

The present study demonstrates that patients with overt hyperthyroidism display lengthened intra- and interatrial EMD as measured by TDI and impaired LA mechanical function. Furthermore, we have shown that intra- and interatrial EMDs correlate with fT4 concentration. Additionally, we found that fT4 and TSH concentrations are independent

Table 1 Patient demographics, laboratory characteristics and echocardiographic findings.

	Hyperthyroid ($n = 34$)	Control ($n = 34$)	P
Age	45.2 ± 9.3	43.6 ± 8.0	0.328
Women	25 (73.5)	24 (70.5)	0.749
Smoker	10 (26.3)	7 (23.3)	0.620
BMI (kg/m^2)	26.8 ± 2.0	28.1 ± 2.4	0.023
BSA	1.71 ± 0.13	1.88 ± 0.15	0.001
Heart rate (beats/minute)	83.5 ± 8.9	74.3 ± 6.5	0.001
Systolic blood pressure (mmHg)	119.8 ± 8.7	118.3 ± 7.9	0.301
Diastolic blood pressure (mmHg)	77.8 ± 7.4	78.1 ± 8.0	0.359
Glucose	95.6 ± 8.1	97.7 ± 11.8	0.417
Haemoglobin (g/dL)	12.9 ± 1.2	13.4 ± 1.2	0.531
Creatinine (mg/dL)	0.80 ± 0.17	0.81 ± 0.16	0.412
TSH (μIU/mL)	0.02 ± 0.04	2.04 ± 0.43	< 0.001
Free T3 (pg/dL)	5.48 ± 1.75	2.63 ± 0.41	< 0.001
Free T4 (ng/dL)	2.08 ± 0.42	1.06 ± 0.16	< 0.001
LVEDD (mm)	49.0 ± 3.5	48.7 ± 2.9	0.435
LVESD (mm)	30.8 ± 3.9	30.2 ± 2.8	0.513
Ejection fraction (%)	63.9 ± 6.7	64.2 ± 5.1	0.679
LV mass index (g/m^2)	82.5 ± 21.8	78.9 ± 14.5	0.342
Septum thickness (mm)	9.9 ± 1.1	9.7 ± 0.8	0.401
Posterior wall thickness (mm)	8.9 ± 0.9	8.7 ± 1.0	0.389
Deceleration time (ms)	180 ± 35	186 ± 45	0.821
Em/Am ratio	0.91 ± 0.26	1.14 ± 0.32	0.004
E/E' ratio	7.2 ± 0.9	9.2 ± 1.0	0.002
LA diameter (mm)	35.5 ± 2.5	33.5 ± 1.8	0.001

Data are number (%) or mean ± standard deviation. BMI: body mass index; BSA: body surface area; LA: left atrium; LVEDD: left ventricle end-diastolic diameter; LVESD: left ventricle end-systolic diameter; TSH: thyroid-stimulating hormone.

Table 2 Measurements of left atrial mechanical function.

	Hyperthyroid ($n = 34$)	Control ($n = 34$)	P
Vmax (mL/m^2)	30.3 ± 8.4	27.7 ± 7.5	0.212
Vmin (mL/m^2)	9.6 ± 4.4	8.3 ± 3.2	0.203
Vp (mL/m^2)	19.0 ± 6.1	14.1 ± 5.0	0.001
LA passive emptying volume (mL/m^2)	11.4 ± 3.5	13.4 ± 3.6	0.038
LA passive emptying fraction (%)	37.5 ± 8.5	47.4 ± 8.0	< 0.001
LA active emptying volume (mL/m^2)	9.4 ± 3.2	5.7 ± 2.4	< 0.001
LA active emptying fraction (%)	49.6 ± 11.5	39.8 ± 5.9	< 0.001

Data are mean ± standard deviation. LA: left atrium; Vmax: LA maximum volume; Vmin: LA minimum volume; Vp: LA volume before P wave.

predictors of interatrial EMD in patients with overt hyperthyroidism.

The myocardium is well understood in tissues that include thyroid hormone receptors [4]. The cardiac effects of hyperthyroidism are caused by increased metabolic demands and the direct chronotropic and inotropic effects of excess thyroid hormones on the myocardium. Thyroid hormones change the action potential period and repolarization speed of atrial and ventricular myocytes [19,20]. An increased heart rate and supraventricular ectopic activity are observed in patients with overt hyperthyroidism [21]. Similarly, we report that patients with overt hyperthyroidism have increased heart rates. Komiya et al. [22] showed differences in the atrial effective refractory period and atrial conduction delay in patients with hyperthyroidism. Similarly, we observed prolonged intra- and interatrial EMDs in patients with overt hyperthyroidism in this study. Additionally, our results suggest that impaired LA mechanical function occurs in overt hyperthyroid patients. Previous studies reported lengthening of the atrial electromechanical coupling interval and impaired atrial function in the development of supraventricular arrhythmias [13,14]. As a

Table 3 Atrial electromechanical interval findings measured by tissue Doppler imaging.

	Hyperthyroid ($n = 34$)	Control ($n = 34$)	*P*
PA lateral (ms)	70.4 ± 8.6	55.3 ± 3.9	< 0.001
PA septum (ms)	51.7 ± 5.8	44.4 ± 2.7	< 0.001
PA tricuspid (ms)	40.2 ± 4.7	37.2 ± 2.2	0.001
PA lateral—PA tricuspid (ms)[a]	29.2 ± 4.4	18.1 ± 2.6	< 0.001
PA lateral—PA septum (ms)[b]	18.7 ± 4.3	10.6 ± 2.0	< 0.001
PA septum—PA tricuspid (ms)[c]	10.5 ± 2.9	7.0 ± 1.2	< 0.001

Data are mean ± standard deviation. PA: the interval measured by tissue Doppler imaging from the onset of the P wave on the surface electrocardiogram to beginning of the late diastolic (Am) wave.
[a] Interatrial electromechanical delay.
[b] Left intra-atrial electromechanical delay.
[c] Right intra-atrial electromechanical delay.

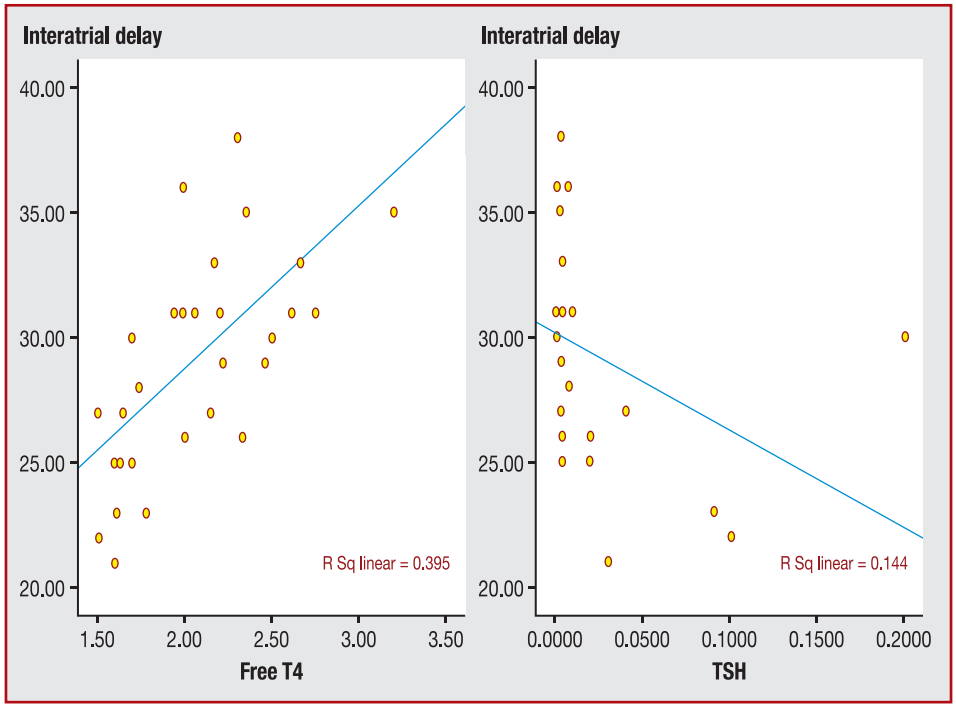

Figure 2. A positive correlation between interatrial delay and free T4, and a negative correlation between interatrial delay and thyroid-stimulating hormone (TSH).

consequence, lengthened intra- and interatrial EMDs may be related to an increased risk of arrhythmias in patients with overt hyperthyroidism.

The majority of previous studies focused on the relationship between ventricular function and thyroid hormones. Alterations in thyroid status may lead to changes not only in ventricular function but also in atrial function. Guntekin et al. [23] observed prolonged P wave duration and dispersion in patients with hyperthyroidism. Shenoy et al. [24] demonstrated the effects of thyroid hormones on sarcoplasmic reticulum calcium transporters in rat atria. Nevertheless, LA mechanical function has not been evaluated in patients with overt hyperthyroidism. When atrial mechanical function was investigated in the present study, we found that LA mechanical function was significantly impaired in patients with overt hyperthyroidism. LA passive emptying volume and fraction significantly decreased, while LA active emptying volume fraction significantly increased in hyperthyroid patients. Also, we found that the LV Em/Am and E/E' ratio were significantly lower in hyperthyroid patients than in controls. Therefore, impaired LA mechanical function is related to increased wall tension as a result of increased LV filling pressure in hyperthyroid patients. LA mechanical functions include passive emptying, active emptying and reservoir functions at different stages of the cardiac cycle. Reservoir functions arise during ventricular systole, passive emptying functions occur during early diastole and active emptying functions take place during ventricular diastole in the presence of sinus rhythm. When left ventricular diastolic dysfunction develops, the left

Table 4 Stepwise linear regression analyses of variables associated with interatrial electromechanical delay.

	β	t	*P*
Age	0.098	1.651	0.104
BMI	0.001	0.010	0.992
BSA	0.019	0.269	0.732
Heart rate	0.053	0.747	0.458
LA size (mm)	0.076	1.091	0.280
Em/Am ratio	−0.075	−1.253	0.223
LA passive emptying volume (mL)	−0.016	0.244	0.802
LA passive emptying fraction (%)	−0.155	−2.243	0.032
LA active emptying volume (mL)	0.018	0.201	0.841
LA active emptying fraction (%)	0.189	2.797	0.007
Free T3	0.078	0.694	0.490
Free T4	0.436	4.055	< 0.001
TSH	−0.310	−2.950	0.005

Am: late diastolic velocity; BMI: body mass index; BSA: body surface area; Em: early diastolic velocity; LA: left atrium; TSH: thyroid-stimulating hormone.

atrium may preserve an adequate cardiac output through the regulation of the reservoir and booster pump functions [11,25]. Conversely, atrial function intensely affects heart function. This effect is more prominent in patients with reduced LV function [11,25]. Therefore, impaired LA function may result in the development of heart failure in patients with overt hyperthyroidism.

Study limitations

The major limitation of this study was the size of the study population, which was relatively small. Patients could not be followed up for arrhythmic episodes. Therefore, we do not know whether prolongation of intra- and interatrial EMD and impaired LA mechanical function occurs in patients with overt hyperthyroidism and whether these factors can be used for the prediction of arrhythmias and heart failure. For these reasons, long-term follow-up and large-scale prospective studies with clinical events and the use of new deformation tools are needed to change our clinical behaviour.

Conclusion

The current study showed prolongation of intra- and interatrial electromechanical intervals and impairment of LA mechanical function in patients with overt hyperthyroidism. The study also showed that lengthened intra- and interatrial delays were related to TSH and fT4 concentrations. Prolonged atrial electromechanical intervals and impaired LA mechanical function may be early signs of subclinical cardiac involvement and dysrhythmias in overt hyperthyroidism.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

[1] Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med 2001;344:501—9.
[2] Klein I. Endocrine disorders and cardiovascular disease. In: Zipes DP, Libby P, Bonow RO, et al., editors. Braunwald's heart disease: a textbook of cardiovascular medicine. 7th ed. Philadelphia: Elsevier Saunders; 2005. p. 2056—63.
[3] Forfar JC, Muir AL, Sawers SA, et al. Abnormal left ventricular function in hyperthyroidism: evidence for a possible reversible cardiomyopathy. N Engl J Med 1982;307:1165—70.
[4] Klein I, Ojamaa K. Thyrotoxicosis and the heart. Endocrinol Metab Clin North Am 1998;27:51—62.
[5] Siu CW, Pong V, Zhang X, et al. Risk of ischemic stroke after new-onset atrial fibrillation in patients with hyperthyroidism. Heart Rhythm 2009;6:169—73.
[6] Siu CW, Yeung CY, Lau CP, et al. Incidence, clinical characteristics and outcome of congestive heart failure as the initial presentation in patients with primary hyperthyroidism. Heart 2007;93:483—7.
[7] Yue WS, Chong BH, Zhang XH, et al. Hyperthyroidism-induced left ventricular diastolic dysfunction: implication in hyperthyroidism-related heart failure. Clin Endocrinol (Oxf) 2011;74:636—43.
[8] Dazai Y. Left atrial systolic time interval in hyperthyroidism. Angiology 1999;50:591—8.
[9] Abecasis J, Dourado R, Ferreira A, et al. Left atrial volume calculated by multi-detector computed tomography may predict successful pulmonary vein isolation in catheter ablation of atrial fibrillation. Europace 2009;11:1289—94.
[10] Hof I, Chilukuri K, Arbab-Zadeh A, et al. Does left atrial volume and pulmonary venous anatomy predict the outcome of catheter ablation of atrial fibrillation? J Cardiovasc Electrophysiol 2009;20:1005—10.
[11] Prioli A, Marino P, Lanzoni L, et al. Increasing degrees of left ventricular filling impairment modulate left atrial function in humans. Am J Cardiol 1998;82:756—61.
[12] Acar G, Akcay A, Sokmen A, et al. Assessment of atrial electromechanical delay, diastolic functions, and left atrial mechanical functions in patients with type 1 diabetes mellitus. J Am Soc Echocardiogr 2009;22:732—8.
[13] Cui QQ, Zhang W, Wang H, et al. Assessment of atrial electromechanical coupling and influential factors in non-rheumatic paroxysmal atrial fibrillation. Clin Cardiol 2008;31:74—8.
[14] Dogdu O, Yarlioglues M, Kaya MG, et al. Assessment of atrial conduction time in patients with systemic lupus erythematosus. J Investig Med 2011;59:281—6.
[15] Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440—63.
[16] Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. Circulation 1977;55:613—8.

[17] Quinones MA, Otto CM, Stoddard M, et al. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. J Am Soc Echocardiogr 2002;15:167—84.
[18] Tiryakioglu SK, Tiryakioglu O, Ari H, et al. Left ventricular longitudinal myocardial function in overt hypothyroidism: a tissue Doppler echocardiographic study. Echocardiography 2010;27:505—11.
[19] Johnson PN, Freedberg AS, Marshall JM. Action of thyroid hormone on the transmembrane potentials from sinoatrial node cells and atrial muscle cells in isolated atria of rabbits. Cardiology 1973;58:273—89.
[20] Sun ZQ, Ojamaa K, Coetzee WA, et al. Effects of thyroid hormone on action potential and repolarizing currents in rat ventricular myocytes. Am J Physiol Endocrinol Metab 2000;278:E302—7.
[21] Wustmann K, Kucera JP, Zanchi A, et al. Activation of electrical triggers of atrial fibrillation in hyperthyroidism. J Clin Endocrinol Metab 2008;93:2104—8.
[22] Komiya N, Isomoto S, Nakao K, et al. Electrophysiological abnormalities of the atrial muscle in patients with paroxysmal atrial fibrillation associated with hyperthyroidism. Clin Endocrinol (Oxf) 2002;56:39—44.
[23] Guntekin U, Gunes Y, Simsek H, et al. P wave duration and dispersion in patients with hyperthyroidism and the short-term effects of antithyroid treatment. Indian Pacing Electrophysiol J 2009;9:251—9.
[24] Shenoy R, Klein I, Ojamaa K. Differential regulation of SR calcium transporters by thyroid hormone in rat atria and ventricles. Am J Physiol Heart Circ Physiol 2001;281:H1690—6.
[25] Matsuda Y, Toma Y, Ogawa H, et al. Importance of left atrial function in patients with myocardial infarction. Circulation 1983;67:566—71.