Evaluation of right and left ventricular function using pulsed-wave tissue Doppler echocardiography in patients with subclinical hypothyroidism

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ABSTRACT. Previous studies showed that subclinical hypothyroidism (SH) was associated with cardiovascular disorders, such as endothelial dysfunction, atherosclerosis and myocardial dysfunction. Only one study investigated left ventricular (LV) function using pulsed tissue Doppler echocardiography (TDE) in patients with SH. However, no study has used this technique in the identification of right ventricular (RV) function in these patients. We aimed to investigate the effect of SH on RV and LV function using TDE technique. The present study included 36 newly diagnosed SH patients and 28 healthy controls. For each subject, serum free T₃ (FT₃), free T₄ (FT₄), total T₃ (TT₃), total T₄ (TT₄), TSH, peroxidase antibody (TPOab) and thyroglobulin antibody (TGab) levels were measured, and standard echocardiography and TDE were performed. In patients with SH, TSH levels were significantly higher, and TPOab and TGab levels were significantly higher when compared to healthy controls. TDE showed that the patients had significantly lower early diastolic mitral and tricuspid annular velocity (Ea) and early/late (Ea/Aa) diastolic mitral and tricuspid annular velocity ratio (p<0.05, p<0.05 and p<0.001, p<0.001, respectively), and significantly longer isovolumetric relaxation time (IRT) of left and right ventricles (p<0.001 and p<0.001, respectively). However, Aa, Sa, and isovolumetric contraction time (ICT) and ET (ejection time) of left and right ventricle did not significantly differ (p=ns for all). In addition, a negative correlation between TSH and TD-derived tricuspid Ea velocity and Ea/Aa ratio, and a positive correlation between TSH and IRT of right ventricle were observed. Our findings demonstrated that SH is associated with impaired RV diastolic function in addition to impaired LV diastolic function.


INTRODUCTION
Thyroid hormones have an important role in the heart and cardiovascular system (1-4). Subclinical hypothyroidism (SH) is defined as isolated elevated serum TSH level in the setting of normal serum thyroid hormone levels. SH usually occurs due to Hashimoto’s disease, Graves’ disease after surgery and radioactive iodine treatment. Current data supports the hypothesis that SH is a mild form of thyroid failure rather than a compensated state. It has been demonstrated that SH may lead to various cardiovascular abnormalities such as cardiac problems (5), endothelial dysfunction (6, 7), atherosclerosis (8, 9), and left ventricular (LV) dysfunction (10, 11).

Standard Doppler echocardiographic technique (12) has been used for the evaluation of LV and right ventricular (RV) function, and this technique provides information about LV and RV global chamber function. Tissue Doppler echocardiography (TDE) is a promising ultrasonographic technique that quantitatively measures the velocity of the myocardium in systole and diastole (13, 14). TDE technique provides reliable measurements of LV and RV systolic and diastolic function, even in difficult-to-image patients and subclinical ventricular dysfunction in several diseases. Several studies have utilized this technique in the assessment of LV and RV function in various clinical conditions (15-20). Few studies have examined the effect of clinical hypothyroidism or subclinical hypothyroidism on LV function (21-24).
However, RV function in patients with SH has not been studied using TDE yet. Accordingly, we aimed to examine the effect of subclinical hypothyroidism on RV and LV function using pulsed tissue Doppler technique.

MATERIALS AND METHODS

Study population
The present study included 36 newly diagnosed, untreated and asymptomatic patients with subclinical hypothyroidism (32 females and 4 males, mean age 38±6 yr), and 28 healthy subjects (25 females and 3 males, mean age 37±10 yr) as a control group. All patients had elevated serum concentration of TSH, with levels of free T4 (FT4) and T3 (FT3) within reference range. Patients who had valvar heart disease, LV hypertrophy, left and right bundle-branch block, atrial fibrillation, pericardial disease, anemia, and other systemic disease were excluded from the study. Since high pulmonary artery pressure may influence RV function, patients with mean systolic pulmonary artery pressure >30 mmHg at rest were excluded from the study. All patients were examined in detail by a pulmonologist to exclude the pulmonary disorders which might influence the RV function. The patients with pulmonary disorders were not enrolled. No history or clinical signs of coronary artery disease were confirmed in any study participant. All patients had a normal chest radiogram and were in sinus rhythm on electrocardiogram (ECG). No patient was on medication, or had mitral and/or tricuspid regurgitation >1, as assessed by Doppler echocardiography. Routine electrolytes, blood urea nitrogen, creatinine, hematocrit, liver function test, and serum proteins were obtained from all subjects. All patients’ thyroid hormones, TSH and thyroid auto-antibodies were measured using chemiluminescent sequential immuno-metric assay (IMMULITE-2000 analyzer). Reference values for TSH, peroxidase antibody (TPOab) and thyroglobulin antibody (TGab) were 0.4-4.3, 0-35 and 0-40 IU/ml, respectively. Minimal analytical sensitivities for TPOab and TGab were 5.0 and 2.2 IU/ml, respectively. Subclinical hypothyroidism was defined as a serum TSH concentration above the statistically defined upper limit of the reference range (TSH>4.4 mU/l), while serum T3 concentration was within its reference range. Study protocol was approved by the local Ethics Committee, and informed consent was obtained from all patients and controls. The control group comprised 28 healthy subjects with no history of hypertension, clinical or laboratory evidence of coronary artery disease or other cardiovascular disease, diabetes or other systemic disease. All control subjects had entirely normal physical examination, laboratory evaluation, ECG, chest radiogram, M-mode, two-dimensional and Doppler echocardiography. They also underwent pulsed TDE.

Laboratory determinations
For each subject, blood samples for circulating serum FT3, FT4, total T3 (TT3), total T4 (TT4), and TSH were collected from antecubital vein after an overnight fast. Evaluation of TSH levels was performed by a chemiluminescent microparticle immunoassay assay (IMMULITE-2000 analyzer). Serum FT3, FT4, TT3, and TT4 levels were measured using a chemiluminescent immunoassay (BioDPC, Los Angeles, U.S.A).

Echocardiographic examination
Standard two-dimensional, M-mode, and Doppler echocardiographic studies were performed for all subjects in partial left decubitus using ATL system (HD1 5000) equipped with harmonic and tissue Doppler imaging capabilities. All subjects rested for 10 min in the supine position before imaging. A variable frequency phased array transducer (2.5-3.5 MHz) was used for echo-Doppler and TDE. Standard echocardiography measurements were obtained according to the recommendations of the American Society of Echocardiography (12). The following parameters were calculated: interventricular septum thickness, LV posterior wall thickness, LV end diastolic diameter, LV end systolic diameter, RV free wall thickness, right, left atrium diameter and LV ejection fraction. Right atrial diameter and right ventricular end diastolic diameter were calculated from the apical four-chamber view. Besides, RV global systolic function was assessed as tricuspid annular plane systolic excursion (TAPSE), by two-dimensional difference of end-diastolic and end-systolic lines (in mm) traced between the centre of the ultrasound fan origin and the junction of RV lateral tricuspid annulus, in apical four-chamber view. In the presence of tricuspid regurgitation, the pulmonary artery systolic pressure was calculated from the sum of the estimated mean right atrial pressure, and the maximum pressure difference between the right ventricle and right atrium, as determined by continuous wave Doppler echocardiography. Tricuspid inflow velocities were obtained by pulsed Doppler recording in the apical 4-chamber view with the sample volume placed at the tips of the tricuspid valve leaflets. The peak early and late diastolic tricuspid inflow velocities and deceleration time were measured and averaged over 5 consecutive beats during normal respiration.

Tissue Doppler analyses
Pulsed tissue Doppler images were acquired by activating the tissue Doppler imaging (TDI) function of the cardiac ultrasonographic unit. When measuring the annular velocity by TDI, the sample

![](https://example.com/tissue_doppler.png)

Fig. 1 - Tissue Doppler of right ventricular (RV) lateral tricuspid annulus in healthy controls and measurement methodology. Diastolic indexes include the peak early diastolic annular velocity (Ea) and the peak diastolic annular velocity with atrial contraction (Aa). Systolic indexes include the peak systolic annular velocity (Sa). Time intervals that can be calculated include the ejection time (ET), isovolumic relaxation (IRT) and isovolumic contraction (ICT) time intervals. Small, very low velocity waveforms can be seen during isovolumic contraction and relaxation.