Original Article

Evaluation of left ventricular myocardial work in patients with hyperthyroidism with different heart rates with noninvasive pressure-strain loop based on two-dimensional speck tracking imaging

Qian Liu[1,2#], Lixin Chen[1,2#], Xiaohua Liu[1,2], Guijuan Peng[1,2], Xiaofang Zhong[1,2], Yuanyuan Sheng[1,2], Shuyu Luo[1,2], Yuxiang Huang[1,2], Jinfeng Xu[1,2], Yingying Liu[1,2]

[1]Shenzhen Medical Ultrasound Engineering Center, Department of Ultrasound, Shenzhen People's Hospital, The Second Clinical Medical College, Jinan University, Shenzhen, China; [2]The First Affiliated Hospital, Southern University of Science and Technology, Shenzhen, China

Contributions: (I) Conception and design: Q Liu, L Chen; (II) Administrative support: J Xu, Y Liu; (III) Provision of study materials or patients: X Liu, G Peng, X Zhong, Y Sheng; (IV) Collection and assembly of data: Q Liu, Y Sheng, S Luo; (V) Data analysis and interpretation: Q Liu, L Chen, G Peng, Y Huang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Jinfeng Xu; Yingying Liu. Shenzhen Medical Ultrasound Engineering Center, Department of Ultrasound, Shenzhen People's Hospital (The Second Clinical Medical College, Jinan University; The First Affiliated Hospital, Southern University of Science and Technology), 1017 Dongmen North Road, Luohu District, Shenzhen 518020, China. Email: jinfengxu@ext.jnu.edu.cn; yingyingliu@ext.jnu.edu.cn.

Background: We investigated the application value of no-invasive myocardial work in evaluating left ventricular (LV) function in patients with hyperthyroidism.

Methods: Sixty-five patients with an initial hyperthyroidism diagnosis were sorted into tachycardia (group TH1, n=31) and without tachycardia (group TH2, n=34) groups. Thirty healthy participants served as the control group (group CON). LV strain parameters and LV myocardial work parameters were evaluated at rest. Each parameter's value in identifying myocardial damage was analyzed using receiver operating characteristic curves. The correlation of myocardial work parameters with global longitudinal strain (GLS), longitudinal peak strain dispersion (normalized by heart rate, PSD_N), and systolic blood pressure (SBP) was analyzed.

Results: There was no difference in classic echocardiographic parameters between the groups. Compared with that in group CON, GLS decreased in groups TH1 and TH2 (TH1 17.99%±2.21% and TH2: 19.00%±2.85% *vs.* 20.27%±1.49%; both P<0.05); there was no significant difference between groups TH1 and TH2. PSD_N increased in groups TH1 and TH2 (TH1 73.13±19.51 ms and TH2 55.06±17.03 *vs.* 44.13±8.65 ms; both P<0.05); it was higher in group TH1 than in group TH2 (P<0.05). Myocardial global work efficiency (GWE) decreased in groups TH1 and TH2 {TH1 95% [interquartile range (IQR), 94–95%] and TH2 96% (IQR, 95–97%) *vs.* 97% (IQR, 96–97%); both P<0.05}; it was lower in group TH1 than in group TH2 (P<0.05). Global constructive work (GCW) decreased in group TH1 (1,865.29±284.13 *vs.* 2,030.33±252.52 mmHg%; P<0.05), but was not different from that in group TH2; there was no difference between groups TH2 and CON. Global wasted work (GWW) increased in groups TH1 and TH2 [TH1 83.00 (IQR, 74.00–97.00) mmHg% and TH2 69.50 (IQR, 51.25–84.25) *vs.* 50.50 (IQR, 40.75–65.25) mmHg%; both P<0.05]; it was higher in group TH1 than in group TH2 (P<0.05). The area under the GWE curve was the largest (area under the curve =0.835), and the optimal cutoff point was 96.5%, with a sensitivity of 0.83 and a specificity of 0.70. GWE and GCW were positively correlated with GLS and negatively correlated with PSD_N. GWW was negatively correlated with GLS and positively correlated with PSD_N. In group

CON, GCW and GWW were positively correlated with SBP; GWE was not correlated with SBP. In groups TH1 and TH2, GCW was positively correlated with SBP, but not with GWW or GWE.

Conclusions: Hyperthyroidism can significantly decrease the GWE and increase GWW of the left ventricle. This change is more pronounced in patients with tachycardia. Myocardial work could be a novel method for the evaluation of LV myocardial function in patients with hyperthyroidism.

Keywords: Hyperthyroidism; tachycardia; left ventricle; pressure-strain loop; myocardial work

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Introduction

In hyperthyroidism, thyroid hormone (TH) synthesis and secretion increase due to thyroid lesions. The hormone enters the blood circulation system and acts on tissues and organs of the whole body, leading to multisystem dysfunction. Hyperthyroidism is a common endocrinological disease, with a global incidence of 0.2–1.3% and an increased incidence with aging (1). The heart is one of the main target organs, and hyperthyroidism may eventually lead to hyperthyroid heart disease, with clinical manifestations including arrhythmia, myocardial ischemia, and heart failure. Some studies (2,3) have shown that increased heart rate, decreased cardiac contractility, and hypertension may worsen heart failure in patients with thyroid dysfunction. For this reason, similarly to atrial fibrillation, European guidelines suggest checking THs as a possible cause of acute heart failure. However, heart function may be impaired before the onset of typical clinical symptoms (4,5). Cardiovascular complications are known to be the main cause of death in patients with hyperthyroidism (6,7), and therefore early diagnosis and management of cardiac dysfunction are important for patients with hyperthyroidism.

Cardiovascular symptoms in the early stages of hyperthyroidism are not obvious, and heart function may be impaired before structural changes; however, classical echocardiography is often used to detect abnormalities in heart morphology. In recent years, several studies have reported that the global longitudinal strain (GLS) of the left ventricular (LV) myocardium measured by 2-dimensional speckle tracking imaging (2D-STI) reflects changes in its global longitudinal systolic function, and subclinical LV systolic dysfunction can be assessed early (8-10). Some researchers have found that GLS is an independent predictor of cardiovascular events in some patients (11,12) including those on maintenance hemodialysis and with asymptomatic aortic stenosis. Previous studies (13-15) have shown that most patients with hyperthyroidism have early-stage cardiac function damage and that 2D-STI could be a sensitive tool for detecting subclinical myocardial dysfunction. Furthermore, GLS is recommended by the American Society of Echocardiography and the European Society of Cardiovascular Imaging as a routine tool for the assessment of LV systolic function, with a peak GLS in the range of −20% expected in a healthy person (16). However, 2D-STI has an evident load dependence, which affects the accuracy of its evaluation (17,18) . It has been shown that for any given contractile state of the LV, the pressure-volume area (which is ascertained using invasively obtained LV pressure-volume loops) is linearly correlated to myocardial oxygen consumption (19,20). Russell *et al.* (21,22) demonstrated the validity of noninvasive myocardial work by combining LV strain data with noninvasively estimated LV pressure curves. The LV pressure-strain loop incorporated systolic, diastolic, and isovolumic components which may reflect a more comprehensive assessment of myocardial function (23). In combining 2D-STI with afterload measurements, the use of noninvasive myocardial work measurements can reduce the influence of cardiac afterload on the results of traditional myocardial strain measurement, evaluate LV systolic function more objectively, and detect minor changes in myocardial systolic function at an early stage (24,25). Oberhoffer *et al.* (26) believed that this method may help to identify patients at risk of LV remodeling and LV systolic dysfunction even before abnormalities in GLS are detected. The aim of this study was to evaluate LV function changes in patients with hyperthyroidism using a noninvasive measurement of myocardial work, based on 2D-STI, to provide evidence for early clinical recognition of LV function damage to facilitate timely intervention.

Methods

Study population

This was a single-center prospective study. A total of 65 patients with hyperthyroidism (group TH), who were newly diagnosed at Shenzhen People's Hospital from April 2021 to August 2021 and had not yet started treatment, were selected. The reasons for seeking medical advice included palpitation (18 persons, 27.69%), neck swelling (18 persons, 27.69%) and abnormal TH level accidently found in a routine check-up (29 persons, 44.62%). Time from symptom onset to hospital presentation varied from 3 days to 1 month. There were 31 patients (average age 35.77±12.82 years; 22 women) in the hyperthyroidism group with tachycardia (group TH1), and 34 patients (average age 36.00±14.03 years; 24 women) in the hyperthyroidism group without tachycardia (group TH2). The diagnosis of hyperthyroidism was based on the following criteria: decreased thyrotropin [thyroid-stimulating hormone (TSH) <0.38 mIU/L] and increased free thyrotropin (FT4 >7.64 pmol/L). Tachycardia was diagnosed when the sinus rhythm was over 100 beats per minute at rest on routine electrocardiogram (ECG). The exclusion criteria were the following: cardiac enlargement, heart failure, and other cardiac manifestations of hyperthyroidism heart disease; hypertension, diabetes, coronary heart disease, congenital heart disease, cardiomyopathy, valvular heart disease, arrhythmias except sinus tachycardia, and other diseases that may affect myocardial movement; use of β-blockers, digitalis, and other functional drugs that affect ventricular function; and unable to undergo classical echocardiography examination or poor image quality. The control group (group CON) consisted of 30 healthy volunteers (average age 35.23±11.17 years; 22 women) who underwent physical examination in our hospital from April 2021 to August 2021, with normal TH level and ECG results. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Ethics Board of Shenzhen People's Hospital, and informed consent was obtained from all the patients.

Clinical features

Clinical characteristics included sex, age, height, weight, blood pressure, pulse pressure difference [defined as systolic blood pressure (SBP) – diastolic blood pressure (DBP)], heart rate, body mass index [BMI; defined as weight (kg)/height^2 (m^2)], body surface area {BSA; defined as square root of [height (cm) × weight (kg)/3,600$^{1/2}$]}, FT4, TSH and classic echocardiographic parameters. Due to the detection sensitivity, the TSH level of most patients in hyperthyroidism group (TH1 and TH2) was reported as TSH <0.01 mIU/L or <0.005 mIU/L.

Echocardiographic analysis

A Vivid E95 Color Doppler Ultrasound Machine, M5Sc heart probe (frequency 1.5–4.6 MHz), and Echo PAC v. 2.3 workstation (GE Healthcare) were used for echocardiographic analysis. Before the examination, all participants underwent routine ECG examination, and the left brachial artery blood pressure and heart rate were measured 3 times in the supine position, with the average value being recorded. The participants were placed in the left decubitus position at rest and breathing normally; the ECG was connected, and the data were recorded synchronously. The height and weight of the patients were input. Routine 2-dimensional echocardiography was performed, and the left ventricular ejection fraction (LVEF) was determined using the biplane Simpson method. The left ventricular internal diameter at end-diastole (LVIDd), left ventricular internal diameter at end-systole (LVIDs), interventricular septum diameter at end-diastole (IVSd), and posterior wall thickness at end-diastole (PWTd) were measured using M-mode echocardiography from the parasternal long-axis section. Left ventricular mass (LVM) was calculated according to the Devereux correction formula: $LVM\ (g) = 0.8 \times 1.04 \times [(IVSd + PWTd + LVIDd)^3 - LVIDd^3] + 0.6$ (27,28). The left ventricular mass index (LVMI) was calculated as LVM/BSA (g/m^2). Peaks early (E) and late (A) of the mitral flow velocity were measured using a pulse Doppler. Tissue Doppler imaging was used to measure septal and lateral mitral annular early myocardial relaxation velocities from the apical 4-chamber view, and their average value was recorded as diastolic velocities (E'). Left atrial maximum volume (LAV) was measured using the biplane Simpson method by manually tracing the endocardium of left atrium from the apical 4- and 2-chamber view during the end-systolic phase. Left atrium maximum volume index (LAVI) was calculated as LAV/BSA (mL/m^2). All image acquisition and measurements were performed by an experienced ultrasonologist according to the American Society of Echocardiography guidelines.

LV GLS and myocardial motion synchronization

Gray-scale dynamic images of apical 4-chamber, 3-chamber, and 2-chamber views (50–80 frames/s) of the LV were obtained, and 3 consecutive cardiac cycles with stable heart rates were collected and stored.

The images were imported into the Echo PAC workstation and entered into the automatic functional imaging (AFI) analysis mode. The apical 3-, 4-, and 2-chamber views of the LV were successively selected. AFI tracked the LV endocardial and epicardial boundaries in the 3 apical dynamic images; manual adjustments were performed if necessary. The GLS and longitudinal peak strain dispersion (PSD) were calculated systematically, and the absolute value of GLS was recorded and normalized by the heart rate as follows: PSD_N = PSD/60 × heart rate. The above operations and data measurements were made according to relevant guidelines (29), by another experienced ultrasonologist, who had no knowledge of the clinical data.

Quantitative analysis of myocardial work done by the left ventricle

The mitral valve closing (MVC) time, aortic valve closing (AVC) time, aortic valve opening (AVO) time, and mitral valve opening (MVO) time were determined in the LV 3-chamber view. The system automatically calculated the LV myocardial work parameters (22), including global work index (GWI), global constructive work (GCW), global wasted work (GWW), and global work efficiency (GWE) after inputting the participant's blood pressure. GWI (mmHg%) is the total work done during LV systole from mitral valve closure to mitral valve opening. The GCW (mmHg%) is the work that contributes to ventricular ejection, including systolic myocardial shortening and isovolumic diastolic myocardial elongation. GWW (mmHg%) is the work that is not conducive to ejection, including systolic myocardial elongation and isovolumic diastolic period shortening. GWE (%) is defined as follows: GCW/(GCW + GWW) ×100%.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median (interquartile range). The Shapiro-Wilk test was used to check the normal distribution of date. When the variance followed a normal distribution, comparisons among groups and pairwise comparisons between groups were performed with analysis of variance (ANOVA). The Kruskal-Wallis test was used for comparison among groups of variables that were not normally distributed. Pearson correlation coefficients were used to evaluate the correlations between different variables with a normal distribution, while Spearman test was used for abnormally distributed data. The area under the receiver operating characteristic (ROC) curve was used to compare the accuracy of the GLS and myocardial work parameters in identifying myocardial injury. Interobserver consistency was assessed in 15 randomly selected participants by 2 independent observers. Intraobserver consistency was assessed by performing 2 analyses of 15 participants by the same observer. Intraclass correlation coefficients (ICCs) and the Bland-Altman method were used to assess the consistency of myocardial work parameters between and within observers. SPSS Statistical software (version 23.0, IBM Corp.) was used to analyze the data, and P<0.05 was considered to be statistically significant.

Results

Clinical parameters and echocardiographic parameters

There was no significant difference in age, sex, or BMI between the groups (P>0.05). The SBP of group TH1 was higher than that of groups CON and TH2 (P<0.05); there was no significant difference in DBP between the groups. The pulse pressure difference in groups TH1 and TH2 were both higher than that in group CON (P<0.05). The heart rate in groups TH1 and TH2 were both higher than that in group CON (P<0.05) and higher in group TH1 than in group TH2 (P<0.05). The FT4 level was higher in groups TH1 and TH2 than in group CON (P<0.05) and higher in group TH1 than in group TH2 (P<0.05). Classical echocardiography parameters, including LVIDd, LVEF, LVMI, E/A, E', E/E' and LAVI, showed no significant differences between all groups (P>0.05; *Table 1*).

LV strain parameters and myocardial work parameters

Compared with group CON, groups TH1 and TH2 had decreased GLS (P<0.05), although there was no significant difference between groups TH1 and TH2. Compared with group CON, the PSD_N in groups TH1 and TH2 increased

Table 1 Clinical parameters and echocardiographic parameters of the study population

Parameters	TH1 (n=31)	TH2 (n=34)	CON (n=30)	P		
				TH1 *vs.* CON	TH2 *vs.* CON	TH1 *vs.* TH2
Female	22 (70.97)	24 (70.59)	22 (73.33)	0.841	0.811	0.973
Age (years)	35.77±12.82	36.00±14.03	35.23±11.17	0.869	0.811	0.943
BMI (kg/m^2)	20.96±2.93	21.17±3.10	21.72±3.19	0.334	0.475	0.782
SBP (mmHg)	123.41±10.10	117.68±9.91	113.30±10.11	<0.001	0.085	0.023
DBP (mmHg)	75.55±7.56	72.82±8.14	72.87±6.50	0.164	0.982	0.145
Pulse pressure (mmHg)	47.87±8.66	44.85±6.57	40.43±7.29	<0.001	0.021	0.110
Heart rate (bpm)	110.13±9.85	82.38±10.54	75.40±10.31	<0.001	0.008	<0.001
FT4 (pmol/L)	50.62±20.07	37.20±16.26	10.80±1.14	<0.001	<0.001	0.001
LVIDd (mm)	44.77±4.21	44.71±4.33	44.07±3.99	0.511	0.544	0.948
LVEF (%)	68.77±5.04	68.26±4.58	67.60±5.56	0.367	0.601	0.686
LVMI (g/m^2)	73.61±17.15	73.22±16.36	67.71±13.58	0.148	0.167	0.921
E/A	1.26±0.23	1.28±0.27	1.36±0.30	0.147	0.249	0.736
E' (cm/s)	12.87±2.00	12.71±2.24	13.13±2.19	0.635	0.429	0.758
E/E'	7.43±1.38	7.01±1.53	6.77±1.17	0.062	0.364	0.306
LAVI (mL/m^2)	24.43±5.97	24.40±5.03	21.98±3.63	0.058	0.056	0.980

P<0.05 was considered statistically significant. Data are presented as mean ± SD or n (%). TH1: the hyperthyroidism group with tachycardia; TH2: the hyperthyroidism group without tachycardia; CON: the control group. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; bpm, beats per minute; FT4, free thyrotropin; LVIDd, left ventricular internal diameter at end-diastole; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LAVI, left atrium maximum volume index; SD, standard deviation.

(P<0.05), and it was higher in group TH1 than in group TH2 (P<0.05). Compared with group CON, the GWE of groups TH1 and TH2 decreased (P<0.05) and was lower in group TH1 than in group TH2 (P<0.05). The GCW of the TH1 group decreased (P<0.05), but it was not significantly different to that of the TH2 group, and there was no significant difference between the TH2 and CON groups. The GWW of groups TH1 and TH2 increased (P<0.05) and was higher in group TH1 than in group TH2 (P<0.05). There was no significant difference in GWI between the 3 groups (P>0.05; *Table 2*, *Figure 1*).

Accuracy of identification of myocardial injury between patients with hyperthyroidism and the controls

ROC curve analysis showed that the maximum area under the GWE curve was 0.835 (P<0.01), the optimal cutoff value was 96.5%, and the sensitivity and specificity were 0.83 and 0.70, respectively (*Figure 2*).

Correlations between different variables

In all participants, GWE and GCW were positively correlated with GLS with correlation coefficients of 0.698 and 0.648, respectively, and negatively correlated with PSD_N, with correlation coefficients of –0.640 and –0.347, respectively. GWW was negatively correlated with GLS, with a correlation coefficient of –0.549 and positively correlated with PSD_N, with a correlation coefficient of 0.489. GCW and GWW were positively correlated with SBP in group CON, with correlation coefficients of 0.722 and 0.403, respectively, while GWE was not correlated with SBP (P=0.12). GCW was positively correlated with SBP in groups TH1 and TH2, with correlation coefficients of 0.427 and 0.389, respectively. GWW and GWE were not correlated with SBP (TH1: P=0.36 and 0.90; TH2: P=0.16 and P=0.89; *Figure 3*).

In all participants, FT4 was positively correlated with heart rate, with correlation coefficients of 0.574. FT4 showed no correlation with any myocardial work parameters.

Table 2 Left ventricular strain parameters and myocardial work parameters of the study population

Parameters	TH1 (n=31)	TH2 (n=34)	CON (n=30)	P		
				TH1 *vs.* CON	TH2 *vs.* CON	TH1 *vs.* TH2
GLS (%)	17.99±2.21	19.00±2.85	20.27±1.49	<0.001	0.029	0.079
PSD_N (ms)	73.13±19.51	55.06±17.03	44.13±8.65	<0.001	0.007	<0.001
GWE (%)	95 [94, 95]	96 [95, 97]	97 [96, 97]	<0.001	0.003	0.006
GWI (mmHg%)	1,669.32±251.86	1,760.03±290.73	1,774.37±227.14	0.117	0.826	0.162
GCW (mmHg%)	1,865.29±284.13	1,945.35±296.46	2,030.33±252.52	0.023	0.227	0.251
GWW (mmHg%)	83.00 [74.00, 97.00]	69.50 [51.25, 84.25]	50.50 [40.75, 65.25]	<0.001	0.029	0.011

P<0.05 was considered statistically significant. Data are presented as mean ± SD, or median [interquartile range]. TH1: the hyperthyroidism group with tachycardia; TH2: the hyperthyroidism group without tachycardia; CON: the control group. GLS, global longitudinal strain; PSD_N, longitudinal peak strain dispersion normalized by heart rate; GWE, global work efficiency; GWI, global work index; GCW, global constructive work; GWW, global waste work.

Repeatability of the parameters of myocardial work

The correlation coefficients of the myocardial work parameters, including GWI, GCW, GWW, and GWE, measured by the same observer and between observers were all greater than 0.8 (P<0.01), showing very good consistency (*Table 3*). Bland-Altman analysis showed good interobserver and intraobserver repeatability and consistency in the analysis of myocardial work parameters (*Figure 4*).

Discussion

In this study, the global LV myocardial function in patients with hyperthyroidism was impaired, especially in patients with tachycardia. GWE can detect subtle myocardial function differences between patients with tachycardia and patients with hyperthyroidism only, while GLS cannot. These differences may result from the increase in GWW, which reflects the dyssynchrony of LV myocardial contraction. The correlation analysis of myocardial work and afterload indicated that GWE was an afterload-independent parameter. The ROC curve also found that GWE could detect subclinical myocardial injury in patients with early-stage hyperthyroidism with high sensitivity. These results indicate that myocardial work can be used as an additional measure to diagnose subclinical myocardial injury in patients with hyperthyroidism.

Analysis of clinical parameters and classical echocardiographic parameters

The clinical manifestations of hyperthyroidism include symptoms and signs related to hypermetabolism, such as emaciation and hunger (4,5). The cardiovascular system is sensitive to changes in circulating TH levels. When hyperthyroidism is caused by excessive TH in the body, the sensitivity of the vagus nerve is reduced, the sensitivity of the heart to catecholamines is enhanced, and the excitability of the sympathetic nerves is increased. Excessive TH can also act on the ion channels of the myocardial cell membranes and affect the systolic function of myocardial cells, increasing the excitability and instability of myocardial cells. In turn, this can enhance cardiac contractility, increase cardiac output, increase cardiac frequency, and cause an abnormal rhythm. Simultaneously, peripheral vascular dilation and resistance decrease, causing increased arterial systolic pressure, normal or slightly decreased diastolic pressure, and increased pulse pressure difference (5,30,31).

In this study, the pulse pressure difference in groups TH1 and TH2 were both higher than that in group CON; furthermore, the SBP in group TH1 was higher than that in groups TH2 and CON, which is consistent with the clinical manifestations of hyperthyroidism. Although the BMI of group CON was higher than that of groups TH1 and TH2, there was no statistically significant difference, possibly due to the short disease course in this cohort of newly diagnosed patients.

In this study, there were no statistically significant differences between groups in classical echocardiographic parameters, including LVIDd, LVEF, LVMI, E/A, E', E/E', and LAVI. This showed that classical echocardiography could not detect early changes in the LV myocardium in this population of newly diagnosed patients with hyperthyroidism.

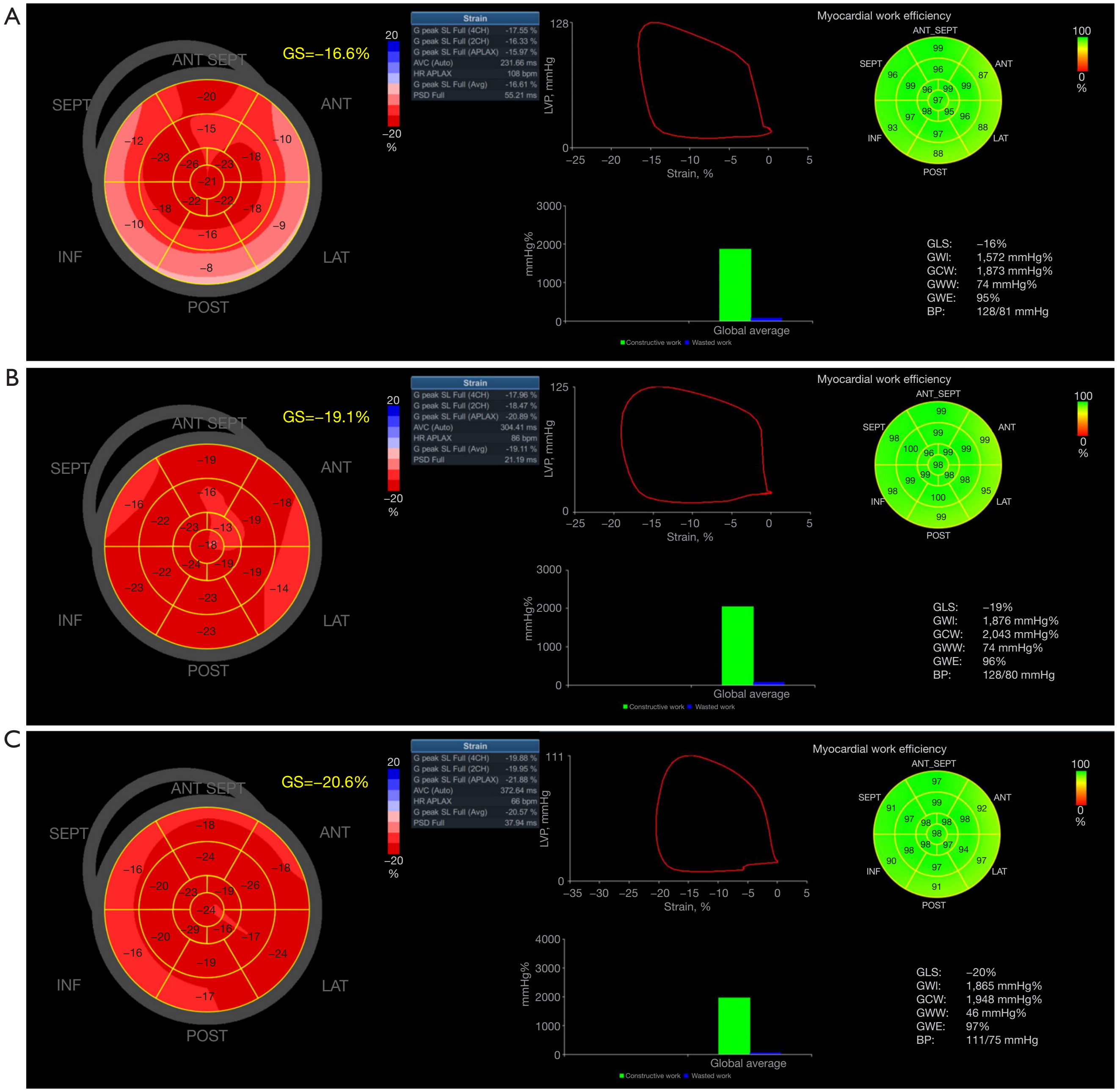

Figure 1 Longitudinal peak strain bull's-eye diagram and pressure-train loop and myocardial work parameters. (A) A patient with hyperthyroidism and tachycardia: HR =108 bpm, BP =128/81 mmHg, PSD =55.21 ms, GLS =–16%, GWI =1,572 mmHg%, GCW =1,873 mmHg%, GWW =74 mmHg%, GWE =95%. (B) A patient with hyperthyroidism but no tachycardia: HR =86 bpm, BP =125/80 mmHg, PSD =21.19 ms, GLS =–19%, GWI =1,876 mmHg%, GCW =2,043 mmHg%, GWW =74 mmHg%, GWE =96%. (C) Healthy volunteer: HR =66 bpm, BP =111/75 mmHg, PSD =37.94 ms, GLS =–20%, GWI =1,865 mmHg%, GCW =1,948 mmHg%, GWW =46 mmHg%, GWE =97%. HR, heart rate; bpm, beats per minute; BP, blood pressure; PSD, longitudinal peak strain dispersion; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; GS, global strain; ANT, anterior segment; INF, inferior segment; LAT, lateral segment; POST, posterior segment; SEPT, septal segment; G peak SL Full, global peak strain longitudinal full; AVC, aortic valve closure; HR APLAX, heart rate; LVP, left ventricular pressure.

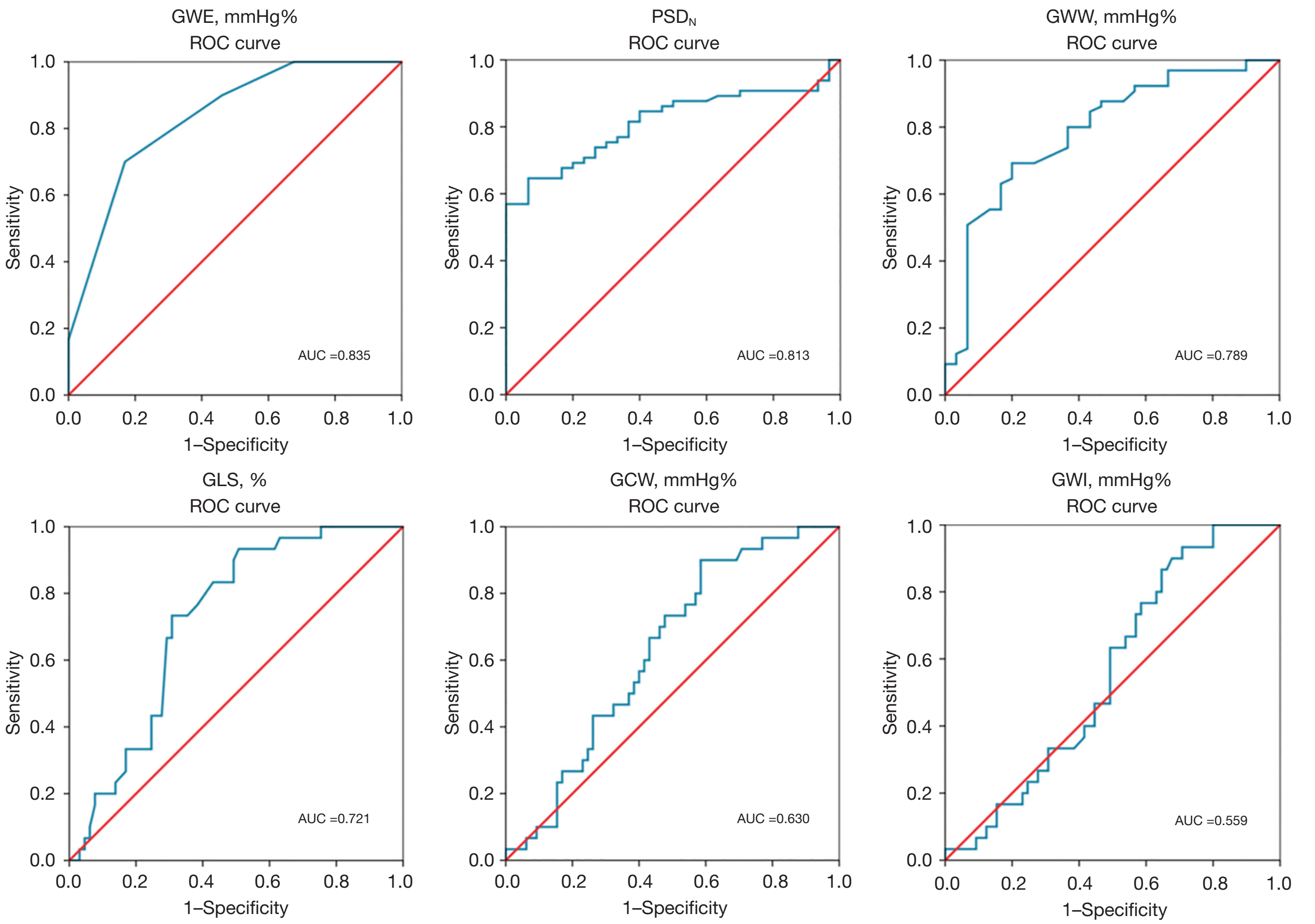

Figure 2 ROC curve analyses for the accuracy of GWI, GCW, GWW, GWE, GLS, and PSD_N parameters to identify patients with hyperthyroidism with myocardial injury. The analyses include all study participants (N=95). AUC, area under the curve; ROC, receiver operating characteristic; GLS, global longitudinal strain; PSD_N, longitudinal peak strain dispersion normalized by heart rate; GWE, global work efficiency; GCW, global constructive work; GWW, global waste work.

Analysis of LV strain parameters

GLS in groups TH1 and TH2 was significantly decreased compared with that in the CON group, but the difference between the TH1 and TH2 groups was not statistically significant. This result indicates that LV longitudinal strain was damaged in group TH; however, GLS was not able to detect the difference of LV myocardial function between hyperthyroidism patients with and without tachycardia. PSD is a parameter that can accurately reflect dyssynchrony and has been used to evaluate early LV systolic dysfunction in several diseases, including diabetes, hypertension, and hypertrophic cardiomyopathy (32). The PSD_N of groups TH1 and TH2 were both raised, and was higher in group TH1 than in group TH2. This result indicates that the synchronization of LV contraction was impaired in patients with hyperthyroidism compared with healthy participants and that the synchronization of LV contraction was further impaired in patients with hyperthyroidism with tachycardia compared to those without tachycardia. Studies have shown that patients with hyperthyroidism are at increased risk of developing a ventricular late potential response in one or more small myocardium, as well as conduction disorders and delayed depolarization (33); this is consistent with the results of this study. This may be due to the infiltration of lymphocytes into the myocardium of patients with hyperthyroidism, causing myocardial cell necrosis and fibrosis, and ultimately affecting cardiac conduction system function. As a result of increased sympathetic nerve excitability, the heart rate increases rapidly, oxygen

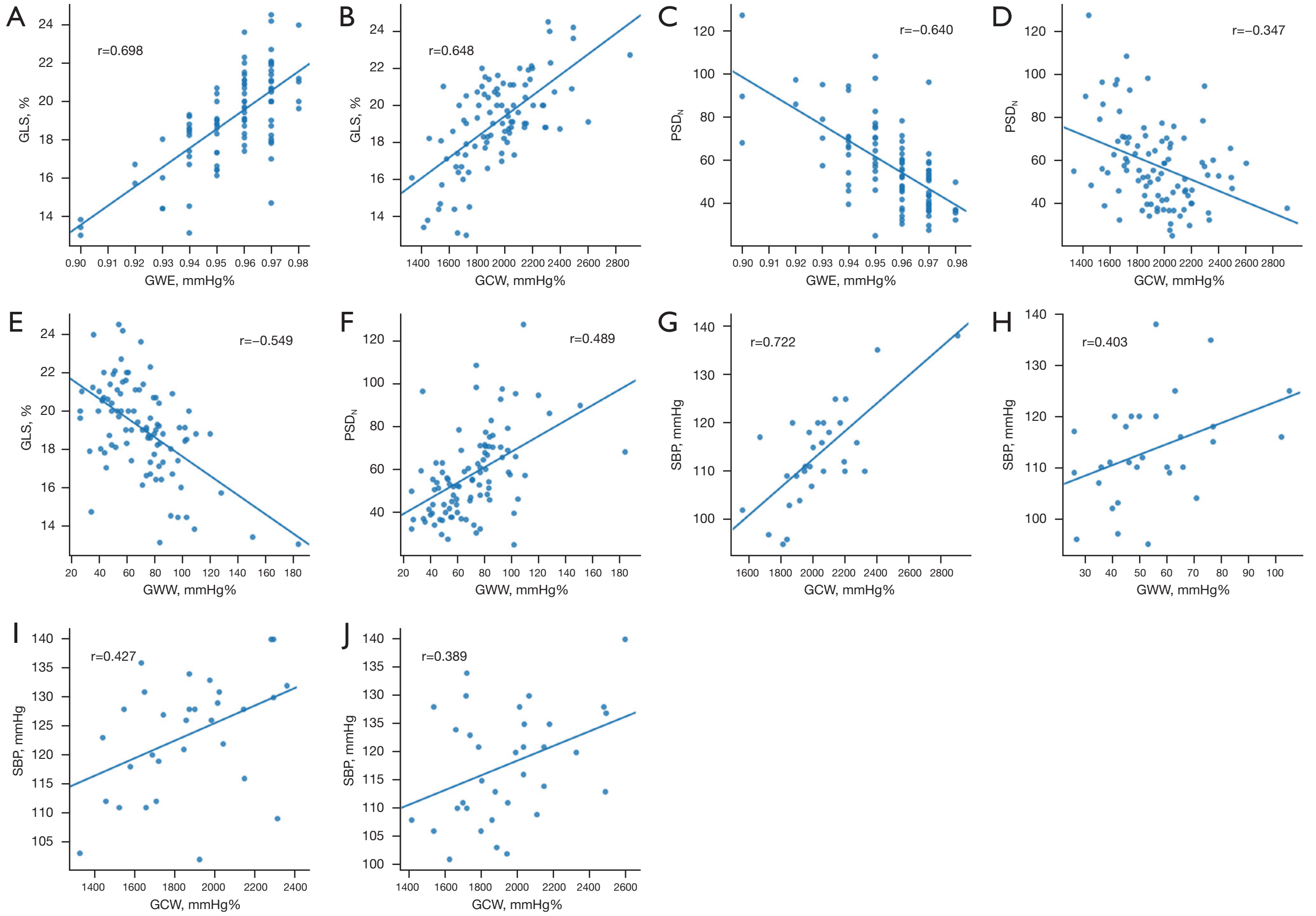

Figure 3 Correlation coefficients plots of parameters. Correlation of all participants between GWE and GLS (A), GCW and GLS (B), GWE and PSD_N (C), GCW and PSD_N (D), GWW and GLS (E), and GWW and PSD_N (F). Correlation between GCW and SBP (G) and between GWW and SBP (H) in group CON. Correlation between GCW and SBP of group TH1 (I) and group TH2 (J). GWE, global work efficiency; GLS, global longitudinal strain; GCW, global constructive work; PSD_N, longitudinal peak strain dispersion normalized by heart rate; GWW, global waste work; SBP, systolic blood pressure.

Table 3 Intraobserver and interobserver intraclass correlation coefficients

Variables	Intraobserver (95% CI)	Interobserver (95% CI)
GWI	0.98 (0.95–0.99)	0.97 (0.91–0.99)
GCW	0.99 (0.97–0.99)	0.95 (0.88–0.93)
GWW	0.93 (0.81–0.97)	0.82 (0.55–0.93)
GWE	0.90 (0.74–0.96)	0.87 (0.65–0.95)

GWE, global work efficiency; GWI, global work index; GCW, global constructive work; GWW, global waste work; CI, confidence interval.

consumption of the myocardium increases further with tachycardia, and subsequently, myocardial strain, cardiac hypertrophy, or coronary artery spasm occurs. These factors can lead to myocardial movement maladjustment and LV local systolic function change (5,31,34).

Analysis of myocardial work parameters

GWW of the TH1 and TH2 groups was increased compared with that in group CON, and was higher in group

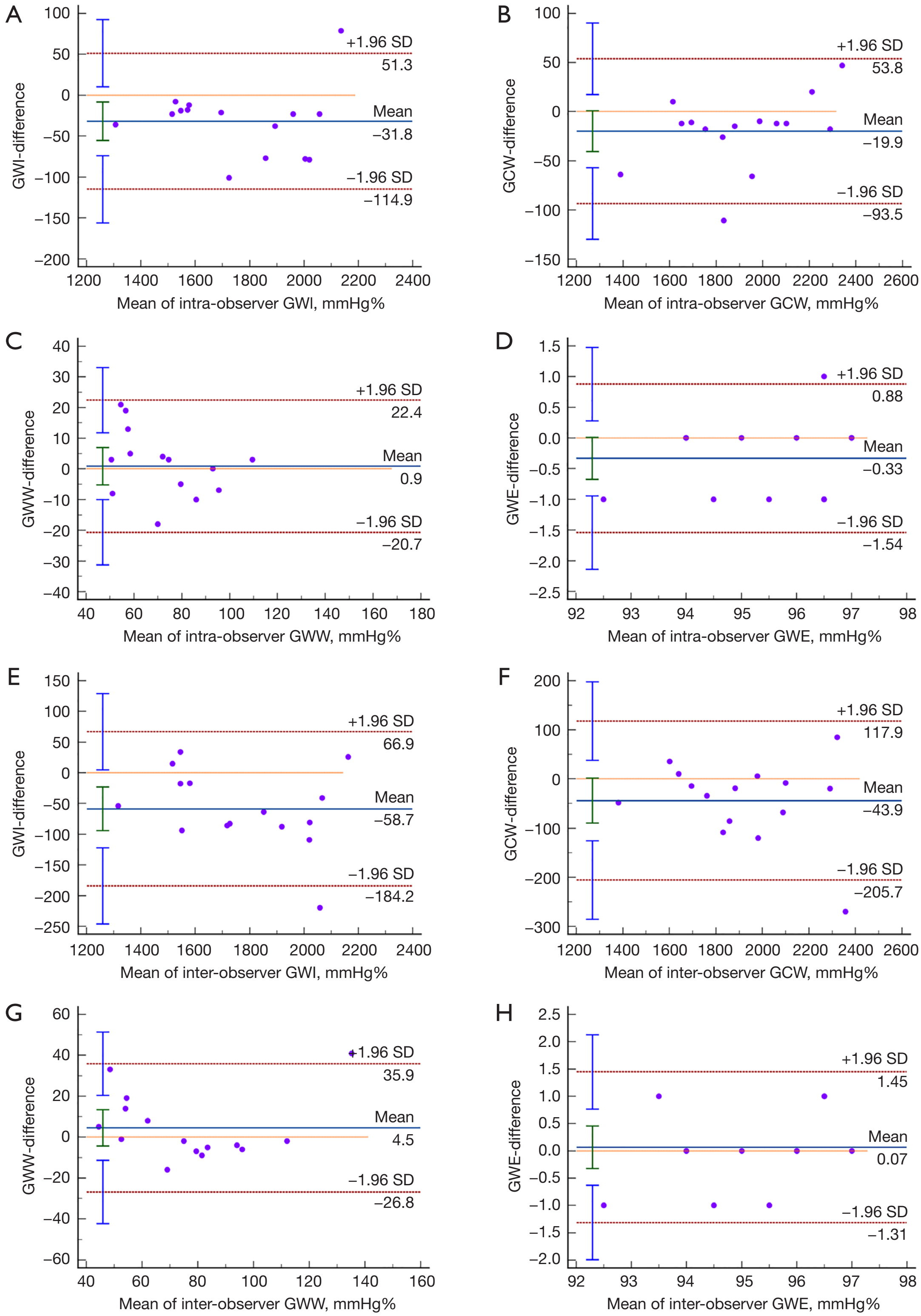

Figure 4 Bland-Altman plots of the intraobserver agreement for GWI (A), GCW (B), GWW (C), and GWE (D). Bland-Altman plots of the inter-observer agreement for GWI (E), GCW (F), GWW (G), and GWE (H). GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; SD, standard deviation.

TH1 than in group TH2. GWW reflects the dyssynchrony of LV contraction, which is the work that makes no conducive to cardiac ejection, including systolic myocardial elongation and isovolumic diastolic period shortening. Previous literature has shown that the GWW of patients with left bundle branch block improves after cardiac resynchronization therapy (35). The results of GWW were consistent with those of PSD_N in groups TH1, TH2, and CON, suggesting that the dyssynchrony of LV contraction may be one of the important early manifestations of myocardial damage in patients with hyperthyroidism, especially those with tachycardia, which further exacerbates this dyssynchrony.

Compared with group CON, the GWE of groups TH1 and TH2 was decreased and was lower in group TH1 than in group TH2. As previously mentioned, the GWW of group TH1 was higher than that of group TH2; however, there was no difference in GCW between the 2 groups, indicating that this change was caused by the increase of wasted work in the patients in group TH1. Some studies (23,36) have suggested that an increase in SBP leads to an increase in GCW and GWW to preserve GWE. In this study, the SBP of group TH1 was higher than that in group TH2, and the increased SBP in group TH1 was accompanied by an increase in GWW and a decrease in GWE; however, the GCW in group TH1, which refers to the ventricular ejection work, did not increase as expected, indicating that the myocardial damage in group TH1 was more serious. This may be because, in addition to the increased oxygen consumption and myocardial tension, the duration of cardiac cycle is shortened in patients with tachycardia, especially during diastole. However, myocardial blood supply mainly occurs in the diastolic period. Shortening of the diastolic phase result in a decrease in myocardial blood supply (mainly subendothelial), which may aggravate the myocardial injuries. Another study (37) suggested that subclinical hyperthyroidism may increase the risk of acute heart failure, possibly due to increased heart rate.

Analysis of correlations between different variables

The GWE, GCW, and GWW of all participants had moderate correlations with GLS and PSD_N. GCW and GWW had a moderate positive correlation with SBP in group CON, while GWE did not correlate with SBP, which was consistent with previous studies (23,36). This indicated that both GCW and GWW increased to preserve GWE when SBP increased. It should be noted that GWE is a parameter independent of afterload. GCW had a moderate positive correlation with SBP in groups TH1 and TH2, but GWW and GWE were not correlated with SBP. No correlation was between GWW and SBP like in previous studies. This might have been due to the elevated GWW in the patients with hyperthyroidism caused by the impaired myocardial function, secondary to disease progression and tachycardia. FT4 had a moderate positive correlation with heart rate but not with myocardial work parameters, which was consistent with previous studies (15).

Analysis of ROC curve for myocardial injury identification

Compared with GLS and PSD_N, GWE had the largest area under the ROC curve (0.835; P<0.01); the optimal cutoff value was 96.5%, and the sensitivity and specificity were 0.83 and 0.70, respectively. These results indicate that GWE can diagnose LV myocardial damage more accurately than can GLS or PSD_N in patients with hyperthyroidism.

Analysis of repeatability

Reproducibility of myocardial work parameters was analyzed using intraobserver and interobserver variability analysis. The robustness and high reproducibility have also been validated in several studies (38-40), which found that these parameters could offer incremental predictive value in resting function assessment among unselected patients undergoing echocardiography.

Study limitations

This study had a small sample size and did not provide prospective long-term follow-up data to determine whether patients with poor noninvasive myocardial work had worse clinical outcomes or if cardiac damage was reversible after intervention. Except for that in patients with hypertension, the influence of blood pressure on the parameters of myocardial work may not be accurately and require further analysis. Although patients with newly diagnosed hyperthyroidism were selected for this study, the duration of the disease was not strictly limited, and these differences might have affected the results. Although all participants had undergone routine ECG examination and the echocardiography was performed with ECG monitoring, it is possible that these results could have been affected by unexpected paroxysmal arrhythmia. Subsequently, we expanded the sample size and prolonged the study period to further investigate the influence of hyperthyroidism on other cardiac function indicators in patients. Finally, myocardial work is based on 2-dimensional speckle tracking technology. As this requires high image quality, poor image quality could have affected some data collection (41,42).

Conclusions

Hyperthyroidism can lead to a decrease in global myocardial work efficiency and an increase in GWW of the left ventricle; this is more pronounced in patients with tachycardia. LV myocardial work is a sensitive and specific method with high reproducibility in detecting myocardial injury. This measure could serve as a novel method for the detection of subclinical myocardial injury in patients with hyperthyroidism.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-534/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Ethics Board of the Shenzhen People's Hospital, and informed consent was obtained from all the patients.

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