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Running Title: Speckle tracking echocardiography in asthma

ASSESSMENT OF BIVENTRICULAR FUNCTION WITH SPECKLE TRACKING ECHOCARDIOGRAPHY IN NEWLY-DIAGNOSED ADULT-ONSET ASTHMA

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ABSTRACT

Objective: There is limited number of studies on the effect of asthma disease on cardiac functions. The aim of this study was to investigate if there was any association between adult onset asthma and cardiac dysfunction.

Methods: Total of 83 non-smoking adult onset asthma patients aged between 18 and 65, and 83 control subjects with comparable age and sex distribution were included in the study. None of the subjects had any chronic cardiovascular or systemic diseases. Two-dimensional, M-mode and tissue Doppler examinations were performed. STE analysis was obtained using the QLAB software. Complete blood count and high-sensitive C-reactive protein (hsCRP) levels were measured.

Results: There was no difference between two groups in terms of standard echocardiography and Doppler parameters. While tricuspid annular plane systolic excursion (TAPSE) was observed to be lower in asthmatics (24.9 ± 2.0 vs. 25.5 ± 2.1 , $p=0.043$), right ventricular myocardial performance index (RV MPI) was higher (0.36 ± 0.07 vs 0.32 ± 0.06 , $p<0.001$). There was no significant difference between the groups in terms of left ventricular STE parameters. Measurements of right ventricular global longitudinal strain (RVGLS) and right ventricular free wall strain (RVfree) were observed to be lower in the asthma group (-20.3 ± 2.9 vs -21.5 ± 2.9 , $p=0.007$; -24.0 ± 3.0 vs 25.1 ± 2.9 , $p=0.009$, respectively).

Conclusion: -We demonstrated that while adult onset mild-stage asthma patients have normal parameters in standard echocardiography, they have reduced right ventricular functions by STE.

Keywords: adult onset asthma, echocardiography, speckle tracking analysis, heart dysfunction

List of abbreviations:

A late diastolic flow velocity

AUC area under the curve

BMI body mass index

COPD chronic obstructive pulmonary disease

DT deceleration time

E early diastolic flow velocity

ECG electrocardiogram

EDA end-diastolic area

EDD end-diastolic diameter

EF ejection fraction

ESA end-systolic area

ET ejection time

FEV1 forced expiratory volume in 1 second

FVC forced vital capacity

GINA Global Initiative for Asthma Guidelines

hsCRP high-sensitive C-reactive protein

IVCT isovolumic contraction time

IVRT isovolumic relaxation time

IVS interventricular septum

LVGCS left ventricular global circumferential strain

LVGLS left ventricular global longitudinal strain

MPI myocardial performance index

PEF peak expiratory flow

PFT pulmonary function test

ROC receiver operating characteristic curve

ROI region of interest

RV Am tricuspid annular late diastolic velocity

RV Em tricuspid annular early diastolic velocity

RV fac right ventricular fractional area change

RV free right ventricular free wall strain

RVGLS right ventricular global longitudinal strain

sPAP systolic pulmonary arterial pressure

STE speckle tracking echocardiography

TAPSE tricuspid annular plane systolic excursion

TDI tissue Doppler echocardiography

INTRODUCTION

Asthma is a disease caused by chronic inflammation of the airways, characterized with bronchial hyperreactivity and reversible airway obstruction accompanied by the complaints of coughing, wheezing, shortness of breath and chest tightness episodes (1). Estimated to be affecting approximately 300 million people, asthma is one of the most common (5%) chronic diseases in the world (2). Studies have determined that the risk of cardiovascular disease occurrence is increased by 32% and cardiac arrhythmias were more frequently observed in asthma patients (3, 4).

Although symptoms are episodic in asthma, the airway inflammation is persistent. Recurrent hypoxia attacks and release of inflammation mediators and cytokines due to this chronic inflammation causes pulmonary artery stenosis and consequently, pulmonary hypertension(5-7). In the later stages of the disease, this causes increased right ventricular afterload which invokes right ventricular hypertrophy and dilation, leading to systolic and diastolic dysfunction in both ventricles (8, 9).

Echocardiography is an important non-invasive method for the diagnosis and treatment of the cardiovascular complications of asthma. Standard echocardiographic assessments can be insufficient to detect the subclinical cardiovascular disorders caused by asthma(10-12). As a method unaffected by angle in the measurement of regional and global ventricular functions and myocardial deformation, two-dimensional speckle tracking (STE) echocardiography method can provide reliable results for the detection of subclinical cardiovascular disease (13).

Studies on the relationship between asthma and cardiac functions are limited(12, 14, 15). We aimed to assess the cardiovascular functions of adult onset asthma patients without any known chronic cardiovascular or systemic disease, who are not receiving any treatment, using two-dimensional STE method in addition to standard echocardiographic assessments.

METHODS and PROCEDURES

This study was conducted between September 2016 and November 2017 in Mehmet Akif İnan Research and Training Hospital. It was conducted according to ethical principles of the Declaration of Helsinki. It was approved by Harran University Ethics Committee, and all subjects voluntarily signed the informed consent forms after study principles were explained to them.

Ninety-five patients (53 male; mean age: 25.7 ± 4.3 years), who had admitted to our Chest Diseases outpatient clinic between these dates with the complaint of episodic wheezing, chest tightness, shortness of breath and diagnosed with asthma for the first time based on Global Initiative for Asthma Guidelines (GINA) criteria, were included in our study. The control group consisted of 83 healthy volunteers (52 male; mean age: 25.0 ± 4.0 years) with comparable age and sex distribution, who were determined to have no disease after examinations (physical examination, 12-lead electrocardiogram (ECG), blood tests, data obtained by anamnesis and previous medical records). Asthma was diagnosed by a Chest Diseases specialist using pulmonary function test (PFT) and

clinical findings. Later, the patients were referred to our Cardiology outpatient clinic for further evaluation involving electrocardiography, echocardiography and detailed anamnesis obtained by a questionnaire prepared for this study to collect data on history of cardiovascular diseases, chronic systemic diseases, and medication history for each subject. Also, medical records of each patient were checked from our national medical database system (e-nabiz) with their permission. Routine biochemical blood tests, including high-sensitive C-reactive protein (hsCRP) and complete blood count, were performed on the day of polyclinic assessment. Patients with the presence of known atherosclerotic cardiovascular disease (coronary artery disease, cerebrovascular disease, peripheral artery disease), heart failure, high degree heart valve disease, hyperlipidemia, diabetes mellitus, hypertension, asset of active infection, pregnancy, malignancy, chronic renal disease, chronic liver disease, autoimmune diseases, chronic lung disease other than asthma, use of medication and smokers were excluded from the study. Inclusion criteria for all case and control subjects was age $\geq$ 18 years (range for asthma: 19-38 years, for control: 18-36 years). All patients in the study group were diagnosed with mild intermittent asthma and had symptoms for at least 6 months. All of them were in remission and none of them were in the phase of acute disease. Twelve patients were excluded from the study due to insufficient quality of echocardiographic image.

Pulmonary Function Tests

PFT was performed by the same technician using European Respiratory Society Consensus standards with the Vmax 22 SensorMedics (USA) device for all patients. Measurements were taken in a sitting position and the nose was closed with a nasal squeezer. They were asked to make a challenging expiration after the maximum inspiratory. Each person was tested at least 3 times and the most appropriate values were selected. FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), FEV1/FVC and PEF (peak expiratory flow) values were examined. Percentage of the expected value for that age and height was used in the evaluations.

Standard Echocardiography

Echocardiographic examination was performed in left lateral decubitus position using Philips iE33 (Andover, Md., USA) device for all patients in a calm state (heart rates were within normal range). Data collection was performed using 3.5 MHz adult probe at 16-cm depth on parasternal and apical images. All assessments were performed by two cardiologists experienced in echocardiography and blinded to the clinical condition of the patients. Single derivation electrocardiogram was recorded during echocardiographic assessment. Image recordings were acquired to involve three cardiac cycles, and copied to external storage. After that, the images were transferred to a device-specific workstation, and analyzed using QLAB (Philips Medical systems) software. Parasternal long axis, short axis, apical four-chamber and two-chamber images were taken, assessed by M-mode, 2-D, continuous wave Doppler and tissue Doppler (TDI) method and assess according to American Society of Echocardiography criteria (16). Early (E) and late (A) mitral and tricuspid diastolic flow velocities, E/A ratio and deceleration time (DT) were determined. In apical four-chamber imaging, systolic, early diastolic and late diastolic velocities were measured through septal, lateral and tricuspid annulus using TDI. Isovolumic contraction time (IVCT), acceleration time, isovolumic relaxation time (IVRT) and ejection time (ET) were calculated. For the left ventricular TDI values, arithmetic mean of the measurements, obtained from lateral and septal mitral annulus, were used. The values were determined by calculating the mean value of three consecutive beats. Later, right and left ventricular myocardial performance index (MPI) was calculated using $IVCT+IVRT/ET$ formula. Tricuspid annular plane systolic excursion (TAPSE) was checked using M-mode by placing the cursor on the lateral side of the tricuspid annulus and the excursion of the lateral side of the tricuspid valve annulus during right ventricular systole from apical four-chamber to apex was measured in millimeters. Right ventricular fractional area change (RV fac) was calculated by determining the right ventricular end-diastolic area (EDA) and end-systolic area (ESA) and using

EDA-ESA/EDA x 100 ((RV EDA – RV ESA)/RV EDA x 100) formula. Systolic pressure gradient between the right ventricle and right atrium was calculated using “Bernoulli” formula from the maximal velocity of the tricuspid insufficiency flow detected by Doppler. Systolic pulmonary arterial pressure (sPAP) was calculated by adding the mean right atrial pressure to this value (16, 17).

Left and Right Ventricular Speckle Tracking Echocardiography Analysis

Biventricular speckle tracking echocardiography analysis was performed using QLAB software (Philips Medical systems). While apical 4-chamber, 3-chamber, 2-chamber and long axis images were used for longitudinal strain analysis, parasternal short axis images (basal, papillary muscle level and apical) were used for circumferential strain analysis. Signs marking the endocardial margin were placed on the end-diastolic phase of the recordings, and then, region of interest (ROI) was automatically formed by the software as secondary concentric circle close to all endocardial segments and epicardium. Caution was exercised to include all of epicardium in the ROI. Left and right ventricular speckle tracking echocardiography data were calculated by automatic analysis of the movements of the speckles on the cardiac cycle (13). Mean strain value was calculated by summing end-diastolic strain values of 6 segments obtained on parasternal short axis, apical long axis, apical 4- and 2-chamber images and dividing this value by 6. Right and left ventricular global longitudinal strain value was determined by taking the mean longitudinal strain values of the apical 4-chamber, 2-chamber and long axis images, and left ventricular global circumferential strain value was determined by taking the mean segmental strain values of the parasternal short axis images. Right ventricular free wall strain (RV free) values were calculated manually by taking the mean of the measurements of 3 segments forming the right ventricular free wall (Figure 1) (18).

Statistical Analysis

Statistical analysis was performed by using SPSS software (ver. 21.0; SPSS Inc., Chicago, IL, USA). Results were expressed as mean $\pm$ standard deviation or frequency and percentage. Normal distribution of continuous variables was assessed with Shapiro-Wilks test. Independent t-test was used to compare the normally distributed continuous variables between different groups. The correlation between STE measurements and clinical, laboratory, PFT and echocardiographic data was analyzed by using Pearson correlation analysis due to normal distribution of the all variables. Multilinear regression analysis was performed to demonstrate the independent relationship between significantly correlated parameters and STE. A p value of <0.05 was considered to be significant.

RESULTS

Our study included a total of 166 patients, 83 being non-smoking adult onset asthma patients, who were not using medication with the mean age of 25.7 ± 4.3 years (53 of them being males), and 83 being control subjects with comparable age and sex distribution. Baseline clinical, laboratory and pulmonary function test data of the patients are shown in Table 1. There was no significant difference between the groups for age, sex, body mass index (BMI), systolic and diastolic blood pressure, heart rate and leukocyte count ($p>0.5$). C-reactive protein (CRP) was higher in the asthma group compared to the control group (0.56 ± 0.41 vs 0.40 ± 0.31 , $p=0.006$).

In the conventional echocardiographic measurements, there was no significant difference between the groups for interventricular septum (IVS), left ventricular end-diastolic diameter (LV EDD), left ventricular ejection fraction (LV EF), left and right atrial diameters, deceleration time (DT), isovolumic relaxation time (IVRT), tricuspid and mitral early diastolic flow (E), late diastolic flow (A) values, and E/A ratio ($p>0.5$). As for tissue Doppler (TDI) measurements, tricuspid annular early diastolic velocity (RV Em) and late diastolic velocity (RV Am) were detected to be lower in the asthma group (11.9 ± 2.0 vs 0.40 ± 0.31 , $p=0.003$; 11.4 ± 1.9 vs 12.2 ± 1.9 , $p=0.007$, respectively),

and tricuspid annular isovolumic relaxation time (RV IVRT) was detected to be higher (47.1 ± 8.6 vs 43.3 ± 5.9 , $p=0.004$). No significant difference was found between the groups for the other TDI values, right ventricular fractional area change (RV fac) and systolic pulmonary arterial pressure (sPAP). While TAPSE was found to be lower in asthmatics (24.9 ± 2.0 vs 25.5 ± 2.1 , $p=0.043$), RV MPI was higher (0.36 ± 0.07 vs 0.32 ± 0.06 , $p<0.001$) (Table 2).

Left and right ventricular global longitudinal strain (LVGLS, RVGLS), left ventricular global circumferential strain (LVGCS) and right ventricular free wall longitudinal strain (RV free) measurements are shown in Table 2. No significant difference was found between the groups for LVGLS, LVGCS measurements. RVGLS and RV free measurements were lower in the asthma group (-20.3 ± 2.9 vs -21.5 ± 2.9 , $p=0.007$; -24.0 ± 3.0 vs -25.1 ± 2.9 , $p=0.009$, respectively).

In the Pearson correlation analysis, a positive correlation was detected between RVfree with RVGLS ($r=0.988$, $p<0.001$) and TAPSE ($r=0.803$, $p<0.001$), and a negative correlation between hsCRP ($r=-0.191$, $p=0.014$), sPAP ($r=-0.724$, $p<0.001$) and RV MPI ($r=-0.446$, $p<0.001$). A positive correlation was detected between RVGLS with RVfree ($r=0.988$, $p<0.001$) and TAPSE ($r=0.806$, $p<0.001$), and a negative correlation between hsCRP ($r=-0.190$, $p=0.014$), sPAP ($r=-0.705$, $p<0.001$) and RV MPI ($r=-0.428$, $p<0.001$). When all variables demonstrating association with RVfree and RVGLS are subjected to multilinear regression analysis, the association between RVfree with RVGLS ($\beta=0.939$, $p<0.001$) and sPAP ($\beta=-0.053$, $p=0.001$); and RVGLS with RVfree ($\beta=0.964$, $p<0.001$) and sPAP ($\beta=-0.048$, $p=0.008$) was found to be persistent.

In the ROC analysis performed to determine the subclinical cardiovascular right ventricular dysfunction in asthma patients, area under the curve (AUC) for RVfree was 0.623 (95% CI: 0.537-0.710, $p=0.006$) with a cut-off value below -24.65, and sensitivity was found to be 0.663 and specificity was 0.624. Area under the curve (AUC) for RVGLS 0.629 (95% CI: 0.543-0.715, $p=0.004$) with a cut-off value below -20.85, and sensitivity was found to be 0.687 and specificity was 0.620 (Figure 3).

DISCUSSION

Results of this study proves subclinical right ventricular impairment evaluated by STE method in adult onset mild stage asthma without smoking and use of medication history. This is also supported by other echocardiographic indices such as increased RV MPI, RV IVRT and decreased TAPSE, RV Em and RV Am compared to healthy controls.

While there are many studies showing the relationship between COPD and cardiovascular diseases (19-21), there are limited number of studies exploring the relationship between asthma and cardiovascular diseases (20, 22-25). In their study, Lee et al. reported that the risk of developing cardiovascular diseases is higher in adult asthma population than the healthy population (22). However, a study conducted in a biracial cohort of 45-64 year 13501 old adults by Schanen JG et al, the incidence of stroke in adult asthma patients was found to be increased, yet no such result was obtained for cardiovascular diseases (23). Onufrak et al. detected an association between asthma and cardiovascular disease incidence only in women (24). Iribarren C et al. noted that the risk of cardiac failure is higher in asthma patients (25). Based on these aforementioned studies, however contradictory they might be, it can be said that, asthma has a negative impact on cardiac function.

Although the exact mechanism by which asthma affects cardiac functions is not known, several pathophysiological mechanisms were considered. The cumulative effect of hypoxemia due to recurrent episodes in asthma causes pulmonary vasoconstriction and remodeling in the pulmonary vascular wall, consequently leading to pulmonary hypertension. As a result right ventricular hypertrophy and dilation occurs which eventually causes biventricular systolic and diastolic

dysfunction in the later stages of the disease (8, 9). Increased right ventricular afterload, together with the increased intrathoracic pressure due to forced respiration effort, also contributes to this process. Chronic airway inflammation and endothelial dysfunction are the other mechanisms which are considered to have a role in this process (26-28).

Advanced stage asthma may even result in cor pulmonale by causing cardiac dysfunction (29). Subclinical asthma's effect on the heart during earlier stages is difficult to detect but it is important for planning the treatment schedule and preventing the cardiac complications. In this regard, there is an apparent need for a non-invasive test can help us. Two-dimensional echocardiography is the most common non-invasive imaging method used for the assessment of cardiac functions. In the conventional echocardiography methods, regional myocardial functions are assessed qualitatively by combining wall excursions and wall thickness measurements with visual analyses, and there is a high inter-observer variability. Assessing the myocardial functions using tissue Doppler (TDI) echocardiography has disadvantages such as angle dependence, limited spatial resolution and single-dimensional deformation analysis. Two-dimensional STE overcomes these limitations; intra-myocardial movements can be assessed three dimensionally (longitudinal, radial, circumferential), and its inter- and intra-observer variability is decreased. For these characteristics, STE stands out as an echocardiographic parameter that can predict left ventricular myocardial injury and possible future cardiac events (13, 18). Even though this method was developed to assess left ventricular functions, as with our study, it was also used to assess right ventricular functions in several studies (14, 30, 31).

Assessment of right ventricular functions is difficult due to its location posterior to the sternum, irregular endocardial boundaries and its complex geometric structure. Moreover, its intrinsically higher sensitivity for preload, afterload and heart rate in comparison to the left ventricle, also increases the assessment difficulty (17, 18). In our work, no pulmonary hypertension or cor pulmonale was present in any of our patients and group differences were not identified in conventional echocardiographic and flow Doppler assessments. Findings of the study conducted by Abdalla et al. was in agreement with our study results (32) in adult asthma patients. These results were corresponding to two other studies performed in pediatric population, especially in mild asthma patients similar to the patients in our study (10, 11). In tissue Doppler examination, we detected lower RV Em, RV Am, and higher RV IVRT values in the asthma patients compared to the control group. TAPSE was detected to be lower in the asthma group. While Özdemir et al. (10) obtained comparable results with our study, Zeybek et al. did not detect a considerable difference between mild asthma patients and the control group. Abdalla et al. (32) found no significant difference between the asthma and the control groups for right ventricular functions. In our study, RV MPI values were considerably higher in the asthma group. Shedeed et al. (33) also obtained a similar result. However, Abdalla et al. (32) found an exact opposite result. Recently, in their study, Tuleta et al. (14) did not detect a significant difference between the asthma patients and the control group for the assessment of right and left ventricular functions using conventional and tissue Doppler.

In our STE analysis, right ventricle parameters (RV free and RVGLS) were significantly lower in the asthma group; which were corresponding to the study conducted by Tuleta et al. (14) . However, contrary to that study, left ventricular STE parameters in our study did not differ between case and control groups. While our study only included adult onset mild asthma patients, the other study (14) included asthma patients of all stages. This may explain the difference in the results. Tuleta et al. (14) detected an independent association between RVGLS and body mass index (BMI). In our study, we detected an independent association between right ventricular strain parameters and SPAP in the multilinear regression analysis. While an association between PFT and echocardiographic assessments was detected in the previous studies (10, 11, 33), we did not detect such an association in our study. This may be caused by the fact that our study only included mild asthma patients.

Chronic systemic inflammation is one of the mechanisms implicated for the cardiovascular complications of asthma. It is known that mediators released during inflammation process suppress the cardiac functions. Previous studies have found elevated CRP levels in asthma patients (27, 28). In support of this, we found elevated hsCRP levels in the patient group in our study.

Limitations

One of the limitations of our study is the relatively small size of our study population and the cross-sectional design of the study. Our study population consisted of newly diagnosed, mild stage asthmatics with no medication which was very different from other studies conducted in chronic asthmatics thus comparability of data is very limited. Software used for the assessment of right ventricle functions by STE was actually developed for left ventricle, but was also used to assess right ventricle in other studies (14, 30, 31). Right ventricular echocardiography results could not be confirmed using gold standard methods, such as cardiac MR or radionuclide ventriculography. Also, as right cardiac catheterization was not performed, we were unable to obtain a more precise assessment of sPAP and right ventricular functions. As software could not analyze how much of the septal wall is comprised of right ventricle and how much left ventricle in the RVGLS analysis, and as it was not a RV free study, it is unclear how subclinical cardiac impairment affects the prognosis.

CONCLUSION

In our study, right ventricular global longitudinal (RVGLS) and right ventricular free wall strain (RV free) values were found to be lower in adult onset mild asthma patients, who were not using medication, than the control group. However, left ventricular global longitudinal and circumferential strain values were comparable in both groups. No significant association was found between right and left ventricular strain values and pulmonary function testing parameters.

Based on these results, we can conclude that speckle tracking echocardiography method (STE) is an effective and reliable method for detecting subclinical cardiovascular impairment in the earlier stages of asthma disease which could help clinicians in planning therapy strategy.

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Table 1 Clinical, laboratory and pulmonary function testing data of the study population

	Patients (n=83)	Controls (n=83)	P Value
Age (years)	25.7 ± 4.3	25.0 ± 4.0	0.263
Male (n)	53	52	0.931
BMI (kg/m²)	25.2 ± 1.9	24.9 ± 2.1	0.272
SBP (mmHg)	121.6 ± 6.9	120.5 ± 7.1	0.412
DBP (mmHg)	77.7 ± 6.1	76.5 ± 8.1	0.489
Heart rate (beats/minute)	77 ± 11	75 ± 8	0.178
HsCRP (mg/dl)	0.56 ± 0.41	0.40 ± 0.31	0.006
Leukocytes (G/I)	7.18 ± 0.44	6.82 ± 0.38	0.376
PEF	82.9 ± 11.0	85.2 ± 6.2	0.103
FEV₁	92.4 ± 12.9	96.5 ± 8.7	0.016
FVC	87.2 ± 8.7	90.1 ± 8.0	0.019
FEV₁/ FVC	98.4 ± 11.2	101.6 ± 9.5	0.125

BMI: body mass index, DBP: diastolic blood pressure, FEV₁: forced expiratory volume in 1 second, FVC: forced vital capacity, hsCRP: high sensitive C- reactive protein PEF: peak expiratory flow, SBP: systolic blood pressure

Bolded data indicate significance

Table 2 2-dimensional, Doppler and tissue Doppler echocardiography data of the study population

	Patients (n=83)	Controls (n=83)	P Value
LV EDD (mm)	45.5 ± 3.7	44.9 ± 3.6	0.339
IVS thickness (mm)	9.7 ± 0.4	9.4 ± 0.7	0.548
LV EF (%)	65.6 ± 3.5	66.2 ± 3.4	0.179
LA diameter (mm)	35.2 ± 2.1	35.0 ± 2.8	0.517
RA diameter (mm)	31.9 ± 2.5	31.5 ± 2.3	0.521
Mitral E (cm/s)	85.8 ± 8.3	83.7 ± 8.8	0.412
Mitral A (cm/s)	67.9 ± 8.8	65.1 ± 8.0	0.392
Mitral E/A	1.26 ± 0.23	1.28 ± 0.21	0.442
DT (ms)	216.7 ± 15.3	211.8 ± 15.7	0.279
IVRT (ms)	88.5 ± 8.0	86.4 ± 7.2	0.179
Tr. E (cm/s)	68.3 ± 9.5	68.7 ± 7.2	0.745
Tr. A (cm/s)	53.0 ± 8.8	52.1 ± 7.1	0.411
Tr. E/A	1.31 ± 0.20	1.34 ± 0.20	0.431
LV Sm (cm/s)	9.7 ± 2.8	9.9 ± 2.4	0.566
LV Em (cm/s)	12.3 ± 2.1	12.1 ± 1.7	0.345
LV Am (cm/s)	10.9 ± 2.7	11.0 ± 2.4	0.802
LV IVRT (ms)	84.1 ± 9.3	81.7 ± 10.9	0.513
LV MPI	0.33 ± 0.05	0.32 ± 0.05	0.272
RV Sm (cm/s)	13.1 ± 3.1	13.5 ± 2.2	0.427
RV Em (cm/s)	11.9 ± 2.0	13.0 ± 2.3	0.003
RV Am (cm/s)	11.4 ± 1.9	12.2 ± 1.9	0.007
RV IVRT (ms)	47.1 ± 8.6	43.3 ± 5.9	0.004
RV fac (%)	47.35 ± 2.3	47.88 ± 2.4	0.262
RV MPI	0.36 ± 0.07	0.32 ± 0.06	<0.001
TAPSE (mm)	24.9 ± 2.0	25.5 ± 2.1	0.043
sPAP (mmHg)	23.9 ± 4.1	23.1 ± 3.6	0.238

Am: late myocardial diastolic velocity, DT: deceleration time, EF: ejection fraction, Em: early myocardial diastolic velocity IVRT: isovolumic relaxation time, IVS: interventricular septum, LA: left atrium, LV: left ventricle, LV EDD: LV end-diastolic dimension, MPI: myocardial performance index, P_{acct}: pulmonary artery acceleration time, RA: right atrium, RV: right ventricle, RV fac: right ventricle fractional area change, TAPSE: tricuspid annular plane systolic excursion, Tr.: Tricuspid, Sm: systolic myocardial velocity, sPAP: systolic pulmonary artery pressure

Bolded data indicate significance

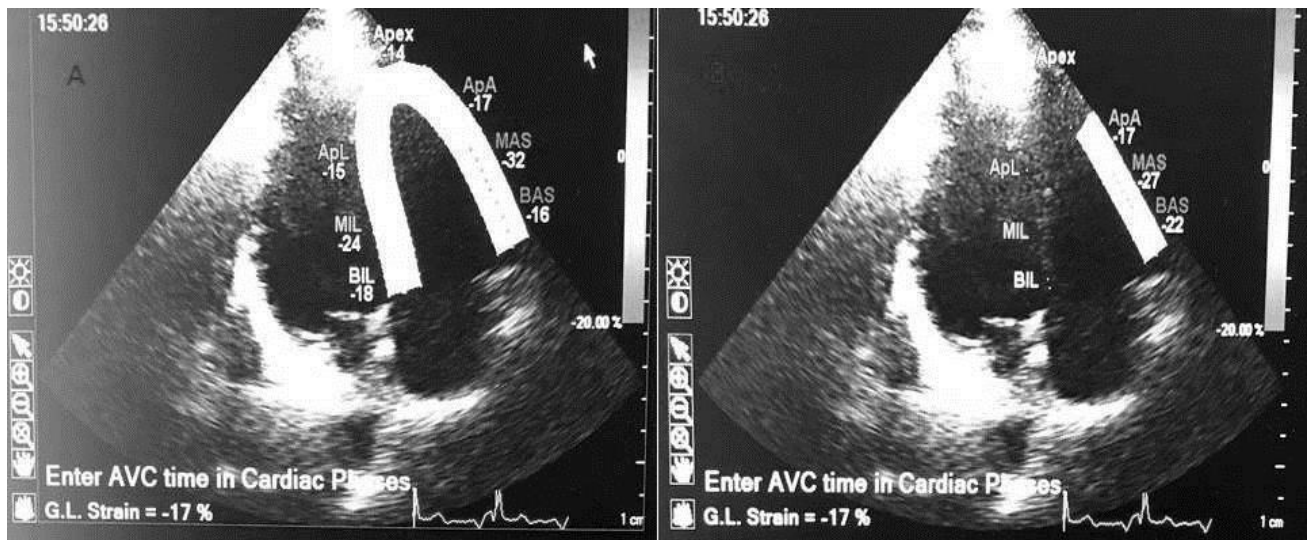


Figure 1 A- Right ventricular global longitudinal strain analysis (RVGLS), B- Right ventricular free wall strain analysis (RVfree)

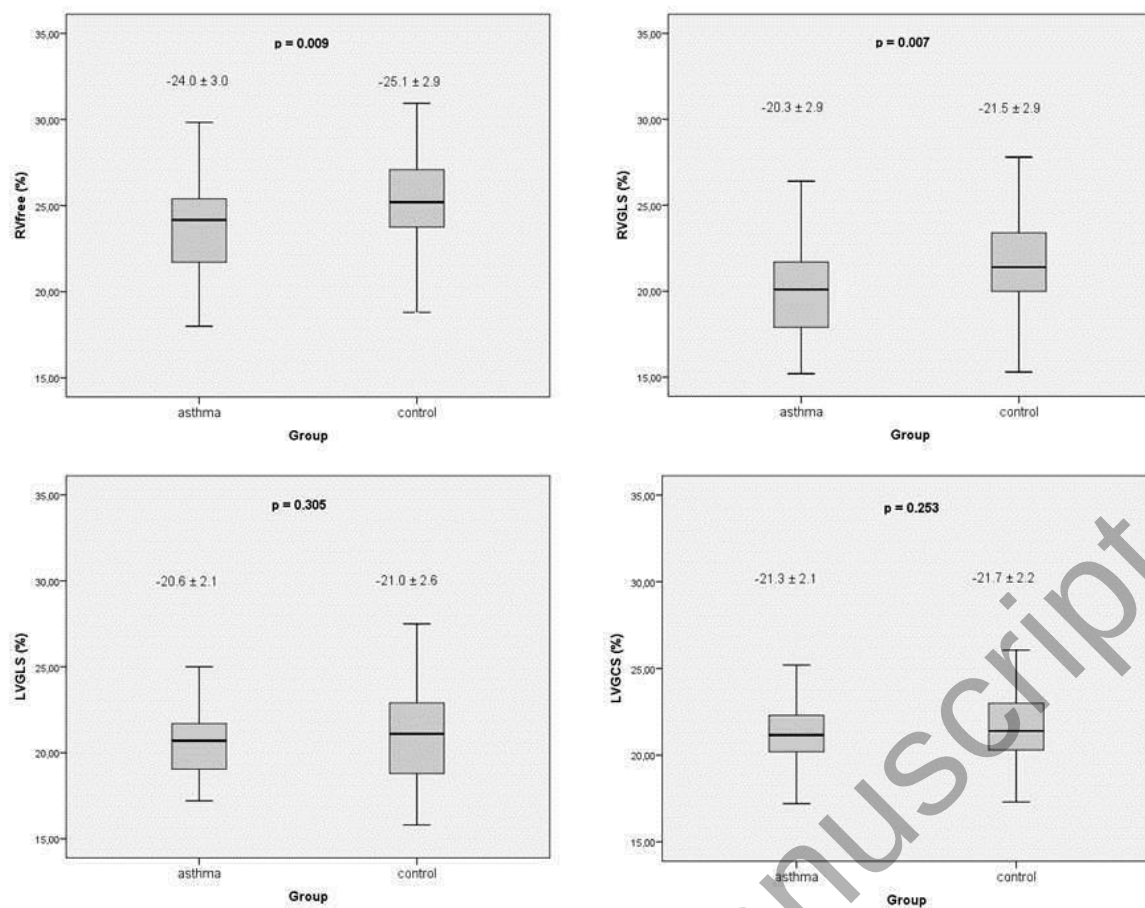


Figure 2 Box plots of the left and right ventricular global longitudinal strain (LVGLS, RVGLS), left ventricular global circumferential strain (LVGCS) and right ventricular free wall longitudinal strain (RVfree) measurements

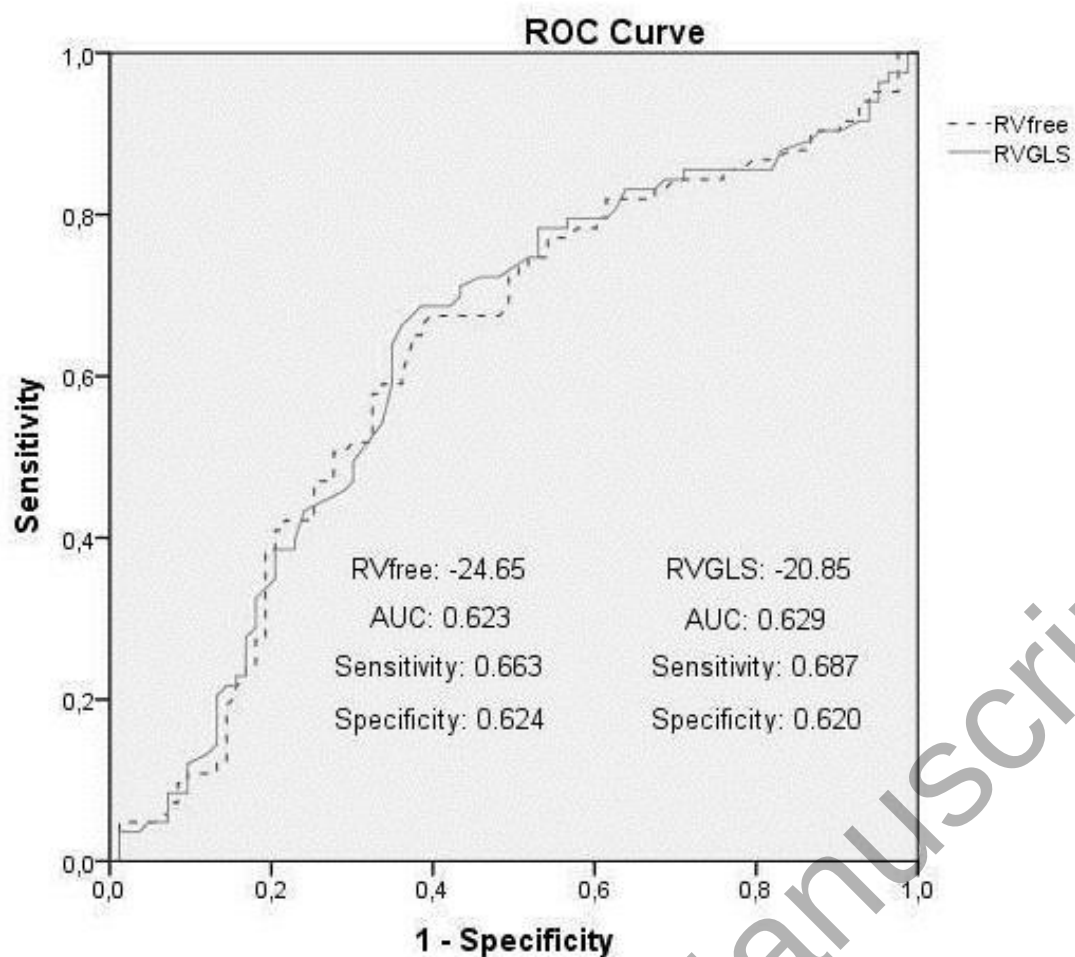


Figure 3 Receiver Operating Characteristics (ROC) curve analysis performed to detect the function of right ventricular global longitudinal strain (RVGLS) and right ventricular free wall longitudinal strain (RVfree) in determining the subclinical cardiac function