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ORIGINAL ARTICLE

Role of 2D Speckle Tracking Echocardiography in Detection of Subclinical Cardiac Dysfunction in Ankylosing Spondylitis and Its Correlation to Disease Activity.

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ABSTRACT

Background: Ankylosing spondylitis (AS) is a chronic inflammatory condition that affects the sacroiliac, and peripheral joints. Systolic dysfunction in AS by conventional assessment may not detect early impairment, so we aimed to study the role two-dimensional (2D)-speckle tracking echocardiography (STE) in assessment of the ventricular function and correlate these findings with AS disease activity score (ASDAS).

Methods: This study is a case-control study involving 135 participants; they were classified into three groups, inactive group (I) 57 cases, active group (II) 33 cases, and 45 control group (III) . The ASDAS was calculated for all patients. Laboratory parameters ;c–reactive protein (CRP),lipid profile, conventional echocardiographic assessment of ventricular systolic function and (2D) (STE) on both venticles were done

Results: ASDAS was significantely high in the the active group (II). Right ventricular free wall strain (RVFWS) was more impaired in the same group p-value <0.001. Pulmonary artery systolic pressure (PASP) was also high in the same group p-value <0.001. AS patients were divided into two subgroups according to drug type biological 70 cases versus non-biological 20 cases. RVFWS was more impaired in the biological drug group -18.35%±3.08 versus -20.76±2.21 in the non-biological group, p-value 0.002. The predictor of impaired RVFWS in AS was PASP (p= 0.001), Exp (B) 1.143, 95% C.I: 6.895 to 13.714. RVFWS had a significant negative correlation with ASDAS-CRP, and PASP.

Conclusion: Impaired RVFWS was detected in AS patients and was associated high disease activity score.

Keywords: Ankylosing spondylitis (AS), Speckle tracking echocardiography (STE), Ankylosing spondylitis disease activity score (ASDAS).

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease that first manifests in the second or third decades of life and affects the spine, sacroiliac, and peripheral joints. According to the most recent meta-analysis, Asia has a 16.7 per 10,000 prevalence rate for AS [1**]**. Several extra-articular manifestations have been reported. Cardiovascular disorders (CVDs), which are estimated to affect 10% of patients, have been reported to be more prevalent in AS patients than in the general population [2]. The mortality rate in AS is one and a half folds more than that of the general population and twenty to forty percent of these are due to cardiovascular events [3]. It is well established that the inflammatory mediators produced by AS directly impact cardiovascular risk factors and the atherosclerotic process. Studies have shown that an elevated level of C-reactive protein (CRP), tumor necrosis alpha (TNFα), inflammatory mediators (IL-6), and myocardial collagen deposition cause dysfunction in cardiomyocytes [4]. Two-dimensional speckle-tracking echocardiography (STE) which follows particular speckle paths throughout the cardiac cycle to quantify strain and deformation of the myocardium. STE derived global longitudinal strain (GLS) can assess myocardial function and the subclinical myocardial deterioration earlier before manifesting clinical symptoms and before impairment in left ventricular (LV) ejection fraction (EF), as well as Right ventricular (RV) function assessment by 2 dimensional STE derived RVGLS and RV free wall strain (FWS) to detect subclinical impairment before conventional RV systolic assessment. To our knowledge**,** previous studies used LV STE [5,6] and reported impaired LV-derived GLS in AS and a single study [7] used RV STE and found impaired RV-derived FWS in AS. Our study aimed to take a detailed look at LV and RV systolic function by STE

in comparison to conventional assessments and correlate these parameters to Ankylosing spondylitis disease activity score (ASDAS).

METHODS

This is a case-control study that was conducted in Zagazig university hospital from April 2022 to January 2023 on Ankylosing Spondylitis (AS) who referred from the follow-up clinic unit of the Rheumatology and Rehabilitation Department to our echocardiography unit. The study included AS patients who fulfilled the criteria of modified New York for AS diagnosis [8]. AS patients were classified into active or inactive according to ASDAS who were compared to healthy volunteers as a control. The ASDAS takes into account both patient symptoms and acute-phase reactants [9]. Our cutoff value for categorizing our cases into active and inactive states was 1.3 with a value over that indicating an active state [9]. Excluded participant from our study were diabetics, smokers, hypertensives, dyslipidemics (before the onset of the disease), ischemic heart disease (IHD), had impaired systolic function (EF <50%), significant valvular heart disease (more than mild valvular lesion), atrial fibrillation, poor image quality which impairs good tracking of the endocardial border, patients with right ventricular outflow tract (RVOT) obstruction, any right-sided heart disease and patients on anti-inflammatory drugs as; statins acetylsalicylic acid. Patients with symptoms or signs suggesting other autoimmune diseases were also excluded.

Ethical standards: We gained official permission from the local Institutional Review Board (Zagazig University, Egypt) NO. ZU-IRB # 9467-17-4-2022. Before participants were enrolled in our study, we obtained written informed consent from them and we told them about the study's purpose.

Sample size and technique: calculation based on a previous study Emren et al [10] reported the mean GLS was 20.5±3.3 among AS patients versus 22.3±2.4 control with a confidence interval (CI) of 95%. The minimal required sample was 136

Clinical and laboratory evaluation: All enrolled populations underwent a detailed clinical evaluation. Demographic characteristics, including age, gender, cardiac risk factors, and duration of disease from the start of symptoms. At the time of evaluation, ASDAS was calculated for all patients, medical history including non- steroidal anti-inflammatory drugs(NSAIDs), conventional synthetic DMARD (disease-modified anti Rheumatic drug), and biological DMARD were recorded . Laboratory parameters including CRP and lipid profile were obtained.

Conventional Echocardiographic evaluation: Assessment using a 1.5-3.6 MHz multifrequency phased array probe and a Horton, Norway, Vivid E9 commercial ultrasound scanner with phased-array transducers. The standard evaluation was carried out in accordance with the recommendations of the European Association of Echocardiography and the American Society of Echocardiography [11]. Left ventricular ejection fraction (LVEF) m-mode, Simpson's method, left ventricle tissue doppler velocities, systolic annular velocity (s'), and left ventricular myocardial performance index (MPI) were performed and evaluated by two skilled and independent echo-cardiographers who were blinded to the patient's clinical data regarding the Onset of the disease, duration of symptoms, and medical history. Right ventricular assessment including tricuspid annular plane systolic excursion (TAPSE) Tissue Doppler imaging (TDI). Right ventricular myocardial performance index (MPI) [11]. Pulmonary artery systolic pressure (PASP). In cases of absent tricuspid regurgitant jet, mean pulmonary artery pressure (mPAP) was assessed [12].

Assessment of left ventricle (LV) using speckle tracking echocardiography (STE): Two-dimensional STE images (the same machine used in conventional assessment with soft were included for STE) were obtained from the left ventricular apical three, four, and 2-chamber views. Three successive beats were used to get the views, which were then saved in cine-loop format. Each view's epicardial tracing was created automatically by the software once the endocardial border was defined. The GLS was calculated by the average value of the three apical views considering it abnormal if less negative than -18% [11]. Figure S1, S2, S3 represent LV-STE case demonstration of the control, inactive, and active group respectively**.**

Assessment of right ventricle using (STE): RV global longitudinal strain (RVGLS) and RV free wall strain (RVFWS) were measured in accordance with the American Society of Echocardiography and European Association of Echocardiography guidelines **[11]**. Using the right ventricle-focused view. The right ventricle was divided into six segments (basal, middle, and apical), and six corresponding strain segments were generated for (RVGLS). By averaging the values of the RV free wall's three peak systolic strain segments, the RV free wall longitudinal strain (RVFWS) was determined. For RV-free strain abnormal threshold is defined as less negative than -20%. For RVGLS (Free wall and septal strain) less negative than -21% is considered abnormal [11]. Figure S 4, S 5, S6 represent RV-STE case demonstration of the control, inactive, and active group respectively.

Statistical analysis: The Statistical Package for the Social Sciences (SPSS) version 17.0 was used to

analyze the data. The three groups were compared using the ANOVA (F) test. (P > 0.05) was not statistically significant (p 0.05). For each pair of groups, a post-hoc Least Significant Difference (LSD) test was employed to compare the results. The mean, standard deviation (SD), and median (IQR) were used to convey quantitative data, while absolute frequencies (number) and relative frequencies (%) were used to express qualitative data. The Chi-square test was used to compare categorical variable percentages. To evaluate the link between different study variables, the Pearson correlation coefficient was determined. Significant predictors connected to the dependent variable in the study were present using univariate logistic regression first, followed by multivariate regression.

RESULTS

The study population were classified into three groups, inactive group (I) 57 cases, active group (II) 33 cases, and control group (III) 45 healthy volunteers. There was no statistical significant difference among the studied groups as regards the demographic data (Table 1). CRP was statistically significant higher in the active group (II) compared to the inactive group (I) and the control group (III) (15.4 mg\dl, 4mg\dl, and 5 mg\dl) respectively. ASDAS was also statistically significantly higher in the active group (II) 3.46±0.51versus 1.09±0.07 in the inactive group (I) (Table 1). Conventional LV and LV-STE studies of the studied groups were statistically non-significant (Table 2), while RVFWS was statistically significantly more impaired in the active group (II) as well as the PASP that had statistically significant highest mean value in the active group (II) (Table 3). We assessed clinical, laboratory, and speckle tracking echocardiography parameters in subgroup group analysis according to drug treatment; biological drug group taking tumor necrosis factor alpha inhibitor (TNF-α); Etanerecept , and non-biological drug group taking conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDS) and found that RVFWS was significantly more impaired in the biological drug group -18.35±3.08 versus -20.76±2.21 in the non-biological group (Table 4). Multivariable analysis revealed that the independent predictor of impaired RVFWS in AS patients was PASP (sig t-tailed 0.001), Exp (B) 1.143, 95% C.I: 6.895 to 13.714 (Table 5). We found that: RVFWS had a strong negative correlation with ASDAS (r-0.774, p 0.001 , and a good negative correlation with PASP (r-0.402, p< 0.001) Figure (1), Figure (2) respectively.

Table (1): Demographic characteristics of the studied groups

Variable	**Inactive AS Group (I) (n=57)**		**Active AS Group (II) (n=33)**		**Control Group (III) (n=45)**		**F**	**P value**	**Post -hoc**
Age (years) Mean±SD Range	34.7±5.31 (21-45)		33.79±8.84 (20-60)		36.33±6.43 (20-50)		1.162	0.219	P1=0.572 P2=0.331 P3=0.083
Variable	**No**	**(%)**	**No**	**(%)**	**No**	**(%)**	**X^2**	**P value**	
Sex **Male** **Female**	 21 12	 63.6 36.4	 30 27	 52.6 47.4	 24 21	 52.2 46.7	1.326	0.824	0.618
	Mean±SD Range		**Mean±SD Range**		**Mean±SD Range**				
Duration of disease (years)	5.72±4.71 (1-20)		7.21±5.96 (1-20)		---------		0.858	0.927 ------	-------
LDL(mg\dl)	99.67±9.25 (79-110)		106.99±18.55 (79-162.9)		100.26±19.17 (70-162.9)		2.798	0.065	P1=0.051 P2=0.879 P3=0.048
TG(mg\dl)	95.79±21.98 (60-130)		106.35±12.89 (68-130)		121.5±30.71 (19-170)		13.208	<0.001	P1=0.051 P2=0.879 P3=0.048
Cholesterol (mg\dl)	130.03±12.74 (110-150)		137.6±24.77 (110-219)		115.4±7.63 (100-130)		19.991	<0.001	P1=0.054 P2<0.001 P3<0.001
CRP(mg\dl) Median (IQR)	4 (2.5-4)		15.4 (10.75-27.5)		5 (3.55-5)		5.357	0.006	P1=0.012 P2=0.946 P3=0.05

Variable	Inactive AS Group (I) (n=57)	Active AS Group (II) (n=33)	Control Group (III) (n=45)	F	P value	Post -hoc
ASDAS	1.09±0.07 (1-1.2)	3.46±0.51 (2.9-4.9)	-------	3.652	<0.001	

LDL:low denisty protein; HDL:high density lipoprotein; TG: triglycerides; ASDAS: Ankylosing spondylities disease activity score; AS;ankylosing spondylitis; P1=active AS vs inactive; P2= active AS vs control; P3=control vs inactive; (IQR): interquartile range

Table (2): Conventional LV and LV speckle tracking study of the studied groups

Variable	Inactive group(I) (n=57)	Active AS group(II) (n=33)	Control Group(III) (n=45)	Tests		Post hoc
				F	*P* value	
	Mean±SD Range	Mean±SD Range	Mean±SD Range			
ESV(ml)	48.88±15 (23-67)	50.11±10.89 (23-67)	43.89±14.26 (23-67)	3.016	0.052	P1=0.670 P2=0.099 P3=0.059
EDV(ml)	77.7±11.21 (58-108)	81.51±19.35 (58-140)	77.17±14.96 (55-140)	1.074	0.345	P1=0.285 P2=0.888 P3=0.180
EF simpson%	63.48±4.96 (53-75)	65.75±5.66 (53-75)	66.76±5.24 (55-79)	3.670	0.281	P1=0.055 P2=0.281 P3=0.345
M-Mode%	64.3±5.56 (55-77)	63.77±6.17 (55-77)	66.58±8.2 (55-79)	2.285	0.106	P1=0.721 P2=0.146 P3=0.050
	Median (IQR)	**Median (IQR)**	**Median (IQR)**			
LV S (Cm\s)wave	12.1 (10.5-13.4)	11.5 (11-12.5)	14 (12.5-15)	0.295	0.745	P1=0.596 P2=0.906 P3=0.471
LV MPI	0.33 (0.32-0.55)	0.33 (0.32-0.49)	0.32 (0.23-0.33)	8.841	0.878	P1=0.395 P2=0.456 P3=0.541
LV (GLS)%	-19.3 (-21.4--16.95)	-18 (-20- -16.95)	-23 (-23- -22)	1.179	0.311	P1=0.506 P2=0.489 P3=0.127

ESV:End systolic volume; EDV:End diastolic volume; EF:Ejection fraction;LV S:Left ventricle systolic wave; LV MPI:Left ventricle myocardial performance index; LV GLS:Left ventricle global longitudinal strain;P1=active AS vs inactive; P2= active AS vs control; P3=control vs inactive; (IQR): interquartile range

Table (3): Conventional RV study and RV speckle tracking of the studied groups

Variable	Inactive AS group(I) (n=57)	Active AS group(II) (n=33)	Control Group (III) (n=45)	Tests		Post hoc
				z/f	*P* value	
RV TAPSE (mm) Mean±SD Range	24.24±4.82 (19-36)	23.6±4.51 (19-36)	23.11±3.9 (18-34)	0.639	0.529	P1=0.503 P2=0.260 P3=0.577
RV (MPI) Median (IQR)	0.32 (0.26-0.42)	0.32 (0.26-0.42)	0.32 (0.23-0.33)	3.717	0.27	P1=0.330 P2=0.233 P3=0.075
RV S wave (cm\s) Mean±SD Range	12.8±1.7 (10-17)	13.2±1.85 (10-17)	14.11±1.4 (11-17)	6.761	0.234	P1=0.271 P2=0.234 P3=0.327

Variable	Inactive AS group(I) (n=57)	Active AS group(II) (n=33)	Control Group (III) (n=45)	Tests		Post hoc
				z/f	*P* value	
PASP (mmgHg) Mean±SD Range	36.63±7.74 (25-40)	51.596±7.2 (22-55)	19.41±3.5 (11-25)	7.879	<0.001	P1=0.001 P2=0.001 P3=0.001
RVFWS% Median (IQR)	-19 (-20.8- -17)	-15.3 (-21- -15)	-23 (-23- -20)	31.479	<0.001	P1=0.0495 P2<0.001 P3<0.001
RV GLS% Median (IQR)	-19.2 (-20- -17.1)	-19.7 (-21- -17.3)	-21 (-25- -21.5)	16.801	0.564	P1=0.728 P2=324 P3=0.768

RV TAPSE: Right ventricle tricuspied annular plane systolic excursion; RV(MPI):Right ventricle myocardial performance index; RV S :Right ventricle systolic wave; PASP:Pulmonary artery systolic pressure ; RV FWS: Right ventricle free wall strain; RV GLS: Right ventricle global longitudinal strain; P1=active AS vs inactive; P2= active AS vs control; P3=control vs inactive

Table (4): Clinical, laboratory and speckle tracking echocardiography parameters assessment in subgroup analysis according to drug type

Variable	Biological drug group* (n=70)	Non-biological drug group** (n=20)	*P* value
ASDAS	3 (1.1-3.5)	2.95 (1.1-3.45)	0. 4788
LV GLS %	-17.28±3.69	-18.52±3.27	0.150
RVGLS %	-17.12±4.1	-18.82±2.88	0.104
RV FWS%	-18.35±3.08	-20.76±2.21	0.002
	Mean ±SD	**Mean ±SD**	
CRP(mg\dl)	10.56±7.7	9.5±6.1	0.5
LDL(mg\dl)	103.6±17.7	106.5±8.1	0.49
HDL(mg\dl)	55.3±6.6	53.2±4.1	0.19
TG(mg\dl)	99.6±18.03	112.5±10.4	0.003
Cholesterol(mg\dl)	123.5±15.3	138.05±21.8	0.007

* (TNFα) Tumor necrosis factor alpha inhibitor (Etanercept),** Conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDS); ASDAS: Ankylosing spondylities disease activity score; LVGLS: Left ventricle global longitudinal strain; RVGLS: Right ventricle global longitudinal strain; RVFWS: Right ventricle free wall strain; LDL: Low density lipoprotein; HDL: High density lipoprotein; TG: Triglycerides; CRP:C-reactive protein; SD: standard deviation.

Table (5): Multivariate logistic regression for predictors of impaired RVFWS (less than -20%) the studied groups

Variables	Sig. 2-tailed	Exp(B)	95% C.I.for EXP(B)	
			Lower	Upper
ASDAS	0.472	-1.009	0.679	1.500
Duration Of disease (years)	0.623	1.038	0.940	1.145
Drug type (biological and non biological)	0.871	1.110	0.307	4.015
PASP(mmHg)	**0.001**	-1.143	6.895	13.714
Constant	0.007	88564.722		

ASDAS: Ankylosing spondylitis disease activity score; PASP: pulmonary artery systolic pressure.

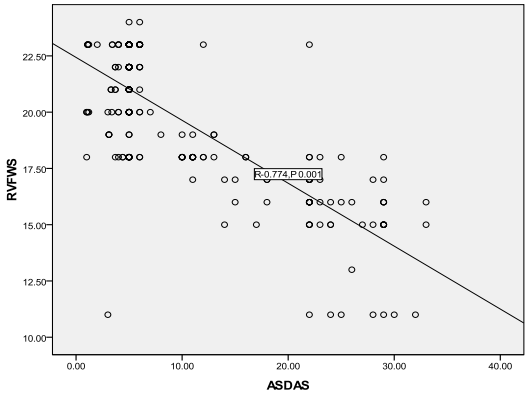

Figure (1): Correlation between RVFWS and ASDAS
RVFWS: right ventricle free wall strain; ASDAS: Ankylosing spondylitis disease activity score

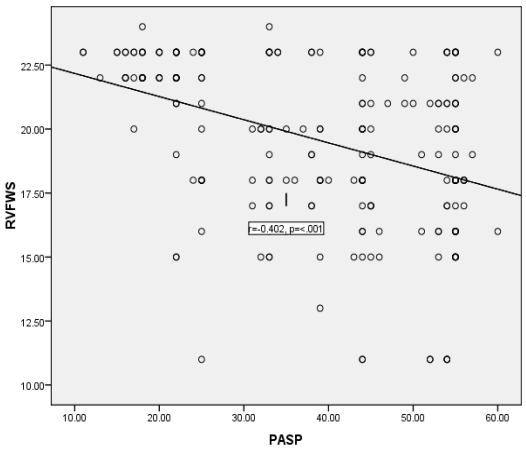

Figure (2): Correlation between RVFWS and PASP
PASP: pulmonary artery systolic pressure; RVFWS: right ventricle free wall strain.

SUPPLEMENTRY FIGURES

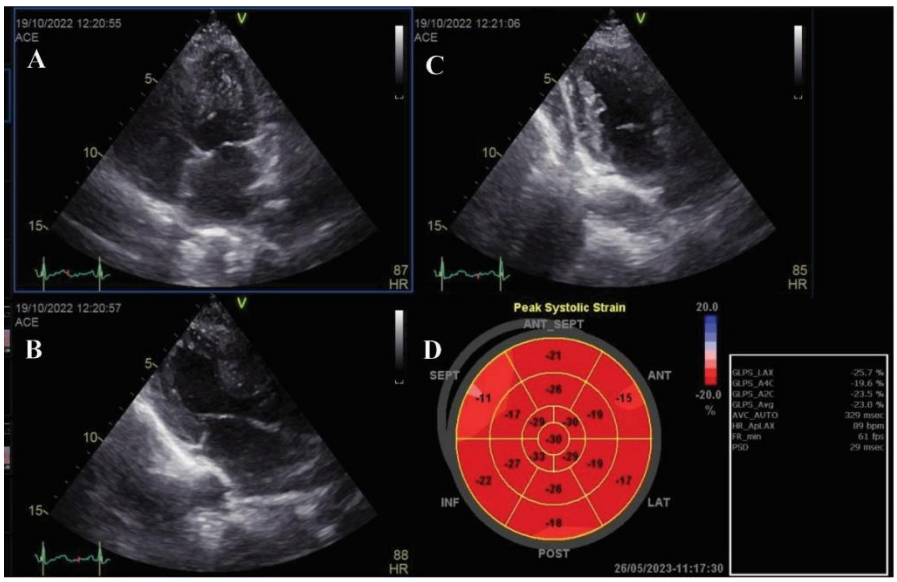

Figure S 1: LV STE case demonstration of the control group; **A** image: shows apical 4 chamber, **B** shows apical 3 chamber ,**C** images shows apical 2 chamber view and the **D** image shows Bull's Eye Map of average global longitudinal strain = -23%.GLPS-LAX: global longitudinal peak strain –long axis;GLPS-A4C: global longitudinal peak strain-apical 4 chamber;GLPS-A2C: global longitudinal peak strain-apical 2 chamber; GLPS-Avg: global longitudinal peak strain-average; AVC: aortic valve closure; ANT: anterior; POST: posterior; SEPT: septal; LAT: lateral; INF: inferior; ANT-SEPT: antroseptal.

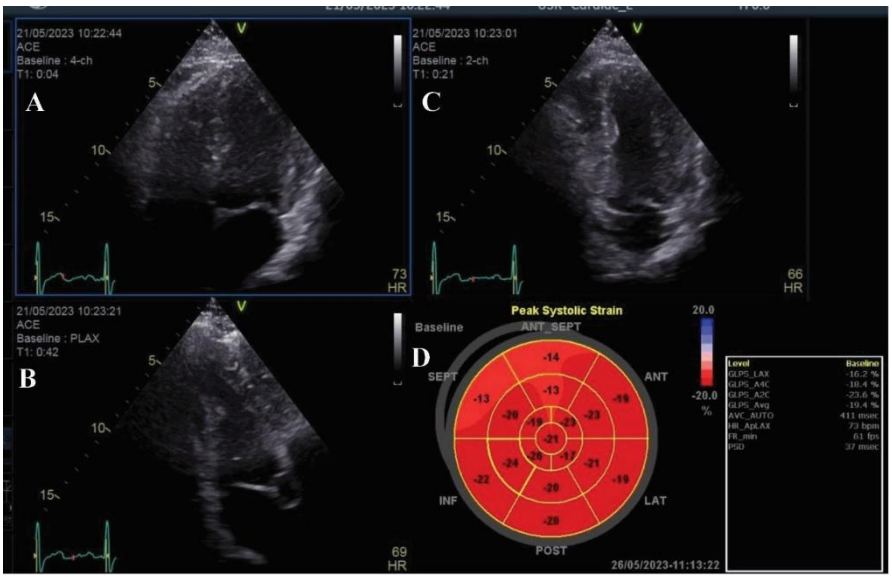

Figure S 2: LV STE case demonstration of the inactive group; **A** image: shows apical 4 chamber, **B** shows apical 3 chamber , **C** images shows apical 2 chamber view and the **D** image shows Bull's Eye Map of average global longitudinal strain = -19.4%.

GLPS-LAX: global longitudinal peak strain –long axis;GLPS-A4C: global longitudinal peak strain-apical 4 chamber;GLPS-A2C: global longitudinal peak strain-apical 2 chamber; GLPS-Avg: global longitudinal peak strain-average; AVC: aortic valve closure; ANT: anterior; POST: posterior; SEPT: septal; LAT: lateral; INF: inferior; ANT-SEPT: antroseptal.

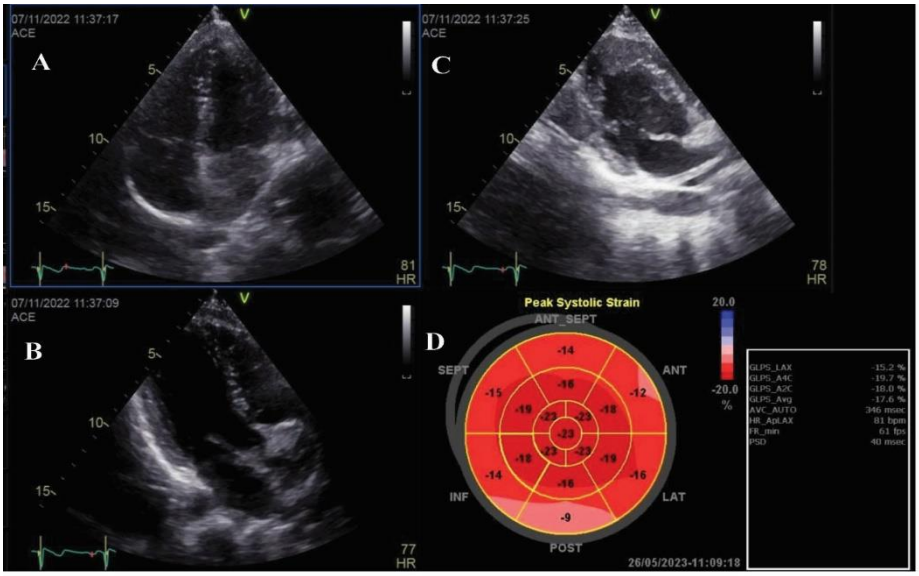

Figure S 3: LV STE case demonstration of the active group; **A** image: shows apical 4 chamber, **B** shows apical 3 chamber, **C** images shows apical 2 chamber view and the **D** image shows Bull's Eye Map of average global longitudinal strain = -17.6%.

GLPS-LAX: global longitudinal peak strain –long axis;GLPS-A4C: global longitudinal peak strain-apical 4 chamber;GLPS-A2C: global longitudinal peak strain-apical 2 chamber; GLPS-Avg: global longitudinal peak strain-average; AVC: aortic valve closure; ANT: anterior; POST: posterior; SEPT: septal; LAT: lateral; INF: inferior; ANT-SEPT: antroseptal.

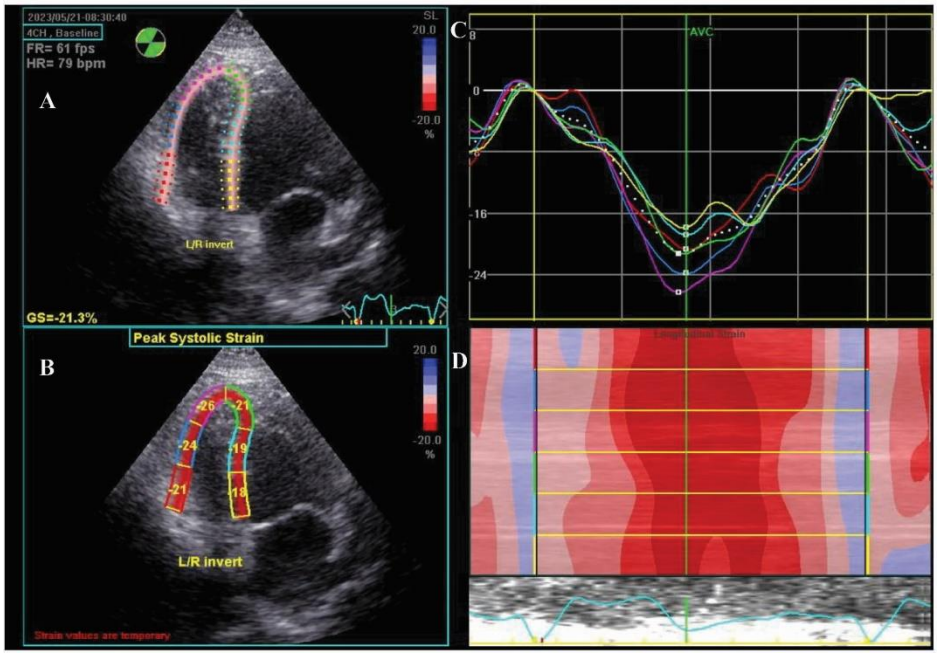

Figure S 4: RV STE case demonstration of the control group: **A** image shows parametric color-coded display of end-systolic strain with GS of RV= -21.3 %, **B** image shows segmental end-systolic strain of both interventricular septum (IVS) and (free wall strain). FWS was calculated manually by averaging (the basal, mid, and apical free wall segments 21+24+26 divided by3= -23.6%, **C** image shows strain–time curves. The RV global strain variations during the cardiac cycle are shown by the white dotted line, while the colored curves indicate the segmental strain changes, **D** image shows an anatomical color-coded M-mode display of segmental strain variations during the cardiac cycle.
GS: global strain; L\R: left\right; AVC: aortic valve closure.

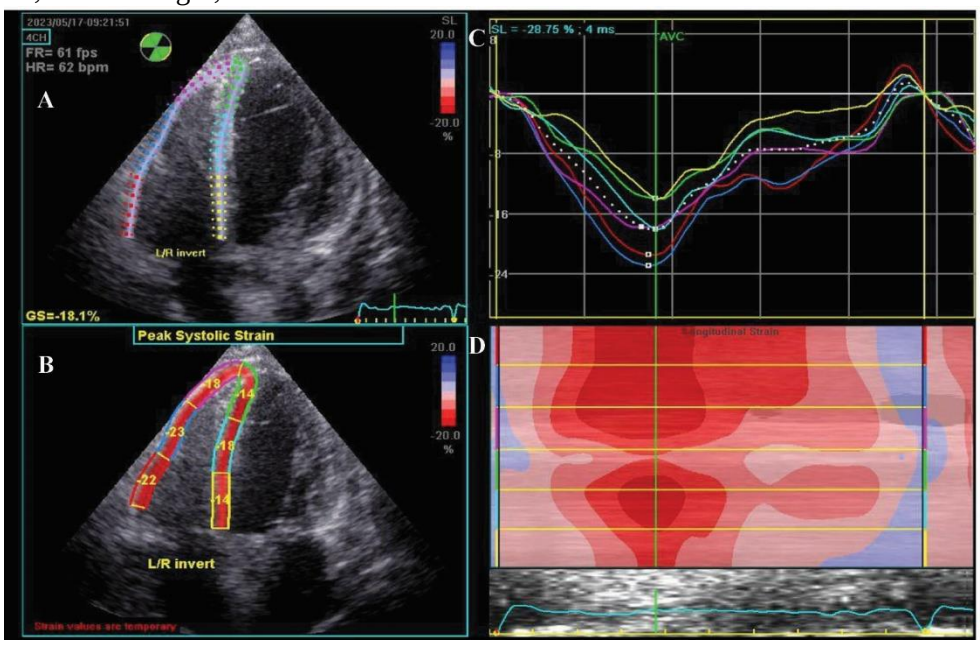

Figure S 5: RV STE case demonstration of the inactive group: **A** image shows parametric color-coded display of end-systolic strain with GS of RV= -18.1 %, **B** image shows segmental end-systolic strain of both interventricular septum (IVS) and (free wall strain). FWS was calculated manually by averaging (the basal, mid, and apical free wall segments 22+23+18 divided by 3= -21%, **C** image shows strain–time curves. The RV global strain variations during the cardiac cycle are shown by the white dotted line, while the colored curves indicate the segmental strain changes, **D** image shows an anatomical color-coded M-mode display of segmental strain variations during the cardiac cycle.
GS: global strain; L\R: left\right; AVC: aortic valve closure.

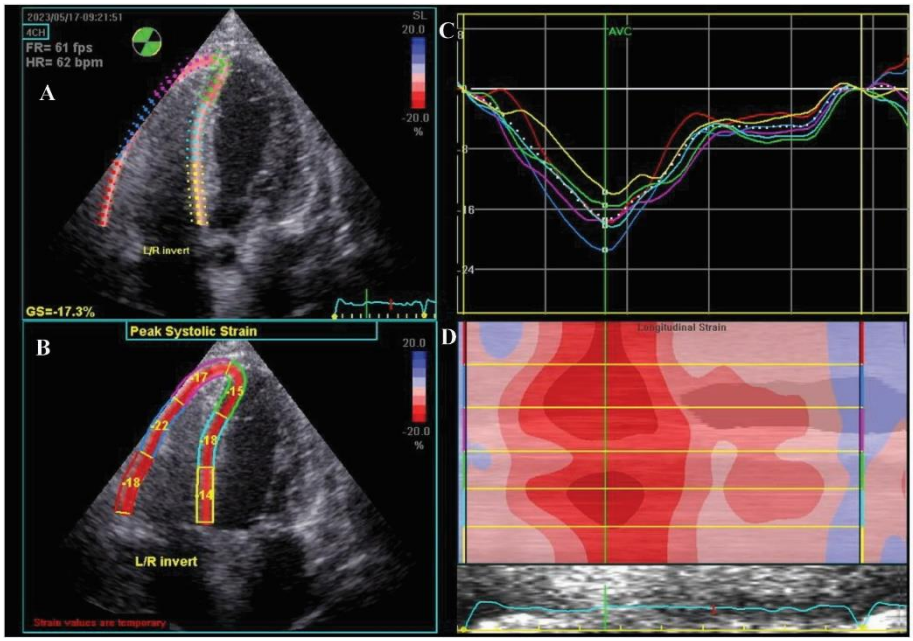

Figure S 6: RV STE case demonstration of the active group: **A** image shows parametric color-coded display of end-systolic strain with GS of RV= -17.3 %, **B** image shows segmental end-systolic strain of both interventricular septum (IVS) and (free wall strain). FWS was calculated manually by averaging (the basal, mid, and apical free wall segments 18+22+17 divided by 3= -19%, **C** image shows strain–time curves. The RV global strain variations during the cardiac cycle are shown by the white dotted line, while the colored curves indicate the segmental strain changes, **D** image shows an anatomical color-coded M-mode display of segmental strain variations during the cardiac cycle.
GS: global strain; L\R invert: left\right invert; AVC: aortic valve closure

DISCUSSION

STE is a tool that holds promise for quantifying cardiac function which is a semi-automated assessment that increases the sensitivity of the assessment and allows for the detection of subclinical myocardial impairment [12]. Our study highlighted RV function assessment as being a neglected chamber in the routine assessment of AS patients. Due to the complex anatomy of the RV and the narrow acoustic window, evaluating RV function by echocardiography is to some extent challenging The drawbacks of traditional techniques like TAPSE, fractional area change (FAC), and lateral S' waves include angle dependence and one-dimensional analysis. Angle independence and 2D RV function assessment are made possible by 2D-STE [13]. Our results revealed that conventional assessments of RV TAPSE, RV (MPI), and RV lateral S wave by TDI were all non-statistically significant among the three groups and all were in the normal range in comparison to the control, this result proves that there was no RV systolic dysfunction by conventional methods. This finding was concordant with Zungur et al [7].With STE evolution our study found RV FWS was statistically significantly more impaired in the active group (II). This finding proves that although the presence of AS did not cause cardiac dysfunction in AS population by conventional assessment, cardiac impairment occurred sub-clinically. In addition, the potential causes of subclinical RV impairment include the exposure of the myocardium to inflammatory mediators, amyloid, and collagen deposition, all of which reduce RV compliance, and also the high PASP in AS population played a significant role in RV systolic pressure overload. This finding was concordant with Zungur et al [7] who found RVFWS was impaired in AS population. To our knowledge, our study is the first one in AS to correlate between RVFWS, ASDAS. Our result revealed that RVFWS correlate negatively with ASDAS, Mohamed et al [14] did a study using STE but used RVGLS instead of RVFWS in another inflammatory disease Rheumatoid Arthritis (RA) and found significant negative correlations between RA disease activity score level and RV GLS value. Pulmonary arterial hypertension (PAH) is frequently detected in different connective tissue diseases such as rheumatoid arthritis and systemic lupus erythematosus defined as Group1 PAH in ESC guidelines of pulmonary hypertension [13]. However, the occurrence of PAH in a patient with AS has not been reported with a detailed clinical description in the English literature [15] and our

result found; PASP was statistically significant higher in the active group (II). RVFWS in the current study correlate negatively with PASP. Karoli et al [16] reported a significant positive correlation between the right ventricular wall and pulmonary artery pressure (r=0.61, p <0.001) this might be explained by using conventional RV assessment of RV-free wall thickness in his study. We found that the independent predictor of impaired RVFWS in AS was PASP. This was concordant with Zungur et al [7] who found that PASP was a predictor on RV impairment in AS. With analysis the impact of drug treatment on RV function, RVFWS was statistically significantly impaired in the biological drug group (taking TNF-α inhibitor; Etanerecept). The pro-inflammatory cytokines induce the cardio-myocyte dysfunction on RV myocardium and The anti –TNF therapy; Etanerecept used in this biological group couldn't prevent or eliminate the impairment by controlling the inflammatory process [4], actually, our study is the first one to assess drug effect on RV function either by conventional methods or STE- derived RVFWS. By the way; our study showed that LV GLS was non-statistically significant among the three groups ; this was discordant with previous studies [17-18] which found that LV GLS was statistically significant in AS group this discrepancy with our study might be due to the longer disease duration in their AS population, their groups weren't not based on active or not active state. Actually, what makes RV impairment more obvious than LV was the presence of significant pulmonary hypertension (PH) which make a pressure overload on RV, and leads to RV thickening, hypertrophy, finally RV impairment [19].

CONCLUSIONS AND ECOMMENDATIONS

Subclinical impaired RVFWS was detected in AS patients and was associated high disease activity score. RVFWS was impaired in the biological drug subgroup meaning that drug therapy used in the management of AS couldn't prevent this cardiac impairment ,and so 2D –STE derived RVFWS in AS can be used to detect this impairment at an early disease stage being simple, non-invasive, and not time-consuming with available offline analysis. PASP was a significant predictor of impaired RVFWS, and so assessment of PASP is recommended side by side with 2D STE. Future multicenter large studies focusing on the relationship between drug type and the effect of ventricular systolic function in AS is highly recommended to confirm our results.

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