Cureus
Part of **SPRINGER NATURE**

Epicardial Adipose Tissue and Left Ventricular Systolic Function in Rheumatoid Arthritis Assessed by Two-Dimensional Speckle Tracking Echocardiography

Tinglin Wang [1], Gehong Peng [1], Hongyu Liang [1], Bingxu Zhao [1]

1. Department of Echocardiography, The Affiliated Hospital of Zunyi Medical University, Zunyi, CHN

Corresponding author: Gehong Peng, 1577386582@qq.com

Abstract

Introduction

Epicardial adipose tissue (EAT) is an emerging cardiovascular biomarker. Subclinical left ventricular (LV) systolic dysfunction is common in rheumatoid arthritis (RA). The aim of this study was to assess LV systolic function using two-dimensional speckle tracking echocardiography (2D-STE) and investigate its association with EAT in RA patients without clinical cardiovascular disease (CVD).

Methods

60 RA patients without manifestations of CVD and 60 age- and gender-matched healthy controls have been recruited for the study. We assessed LV systolic function and EAT in all subjects using conventional echocardiography and 2D-STE. EAT was measured as the relative echo-free region between the free wall of the right ventricle and the visceral layer of the pericardium at end-systole.

Results

Global longitudinal strain (GLS) was decreased and EAT was increased in the RA group compared to the control group. GLS was reduced as EAT increased in RA patients (r=-0.273, P=0.035). After adjusting for confounders, multivariate linear regression analysis revealed a weakened correlation between EAT and GLS. Age and disease activity scores28 were independent factors influencing GLS in RA.

Conclusion

RA patients have significantly thickened EAT compared with controls. 2D-STE can detect early LV myocardial systolic dysfunction in RA, as shown by lower GLS. Accumulation of EAT is associated with lower GLS, but older age and higher disease activity may play a greater role in LV myocardial systolic dysfunction in RA.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes damage to patients' tissues and organs, affecting 0.5-1 percent of the global population, and the prevalence and incidence of RA are still increasing [1]. Apart from joint symptoms such as swelling, pain, and deformity, RA can also affect extra-articular organs such as the lungs, gastrointestinal tract, and kidneys, among others, with the heart being a crucial target organ. Cardiovascular disease (CVD) is an important cause of premature death in RA, and RA patients have a higher risk of asymptomatic ischemic heart disease, heart failure, and sudden cardiac death than the general population [2]. Cardiovascular risk prediction algorithms derived from traditional cardiovascular risk factors, such as hypertension and hyperglycemia, have demonstrated limited predictive value for CVD risk in patients with RA [3].

Epicardial adipose tissue (EAT) has received increasing attention as an emerging quantifiable marker of cardiovascular risk [4]. Abnormal deposition of EAT disrupts the anti-inflammatory and pro-inflammatory balance, exacerbates oxidative stress, and leads to atherosclerosis; the lipotoxicity of EAT can also cause myocardial damage, resulting in fibrosis of atrial and ventricular muscle and ultimately causing adverse effects such as alterations in cardiac structure and function [5]. EAT was found to be independently associated with subclinical left ventricular (LV) systolic dysfunction in a large community-based population-based study, independent of other cardiovascular risk factors [6]. Several studies have reported that RA patients have more EAT [7-9]. However, the relationship between EAT and LV systolic function in RA

patients remains unclear. The two-dimensional speckle tracking technique (2D-STE) is a novel method for the early assessment of subclinical myocardial dysfunction. This study aimed to assess LV systolic function by 2D-STE in RA patients without clinical CVD and to investigate its relationship with EAT.

Materials And Methods

Study population

This study included 60 consecutive RA patients admitted to our hospital's rheumatology ward between November 2022 and December 2023 as well as 60 healthy volunteers matched by sex and age during the same period. The inclusion criteria for the RA group were between 40 and 70 years of age, and they met the 2010 American College of Rheumatology and European League Against Rheumatism classification criteria [10]. Exclusion criteria were congenital heart disease, coronary heart disease, cerebrovascular and peripheral artery disease, heart failure, cardiomyopathy, moderate to severe valvular disease, serious arrhythmia, pericardial effusion, chronic liver and kidney diseases, diabetes mellitus, hypertension, malignant tumors, severe infections, and combinations of other autoimmune diseases. Hypertension was defined as systolic blood pressure (SBP) ⩾ 140 mmHg and/or diastolic blood pressure (DBP) ⩾ 90 mmHg or the use of antihypertensive drugs. Diabetes mellitus was defined as fasting plasma glucose (FPG) ⩾7.0 mmol/L or treatment for diabetes. Ethical approval for this study was obtained from the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (approval number: KLLY-2022-115). Informed consent was obtained from the participants.

Clinical data collection

Sex, age, height, weight, waist circumference (WC), body mass index (BMI), SBP, and DBP were obtained for all subjects. WC was measured while the subject was in the standing position, from the narrowest level between the lower edge of the ribs to the anterior superior iliac spine. BMI was calculated as weight in kilograms divided by the square of height in meters. Blood samples were collected from all subjects after fasting for at least eight hours, and FPG, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were recorded. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACCP) were also obtained in RA patients. RF positivity was defined as RF ⩾20 IU/mL, and ACCP positivity was defined as ACCP ⩾17 U/mL. Disease activity was calculated based on disease activity score 28 joints (DAS28) using CRP in RA patients [11].

Conventional echocardiography examination

All subjects underwent transthoracic echocardiography examination connected to a limb-lead electrocardiogram in the left lateral decubitus position. A qualified sonographer, who was unaware of the subjects' data, used an S5-1 probe and a Philips EPIQ CVx ultrasound machine (Philips Medical Imaging, Andover, MA) to examine patients. LV interventricular septal thickness in end-diastolic period (IVSD), LV posterior wall thickness in end-diastolic period (LVPWD), LV end-diastolic diameter (LVEDD), and LV end-systolic diameter (LVESD), mitral annular peak systolic velocity (S′), and LV ejection fraction (LVEF) were measured according to standardized measurement methods [12].

Echocardiographic measurement of EAT thickness

Measurements were taken from both the parasternal long-axis view (Figure *1A*) and the parasternal short-axis view (Figure *1B*). The electrocardiogram used the T-wave endpoint as a marker of ventricular end-systole. The relatively echo-free area between the outer edge of the myocardium and the visceral layer of the pericardium was measured perpendicular to the free wall of the right ventricle at end-systole. Both views were measured three times, and the mean value was used for the analysis [13]

2024 Wang et al. Cureus 16(5): e60495. DOI 10.7759/cureus.60495
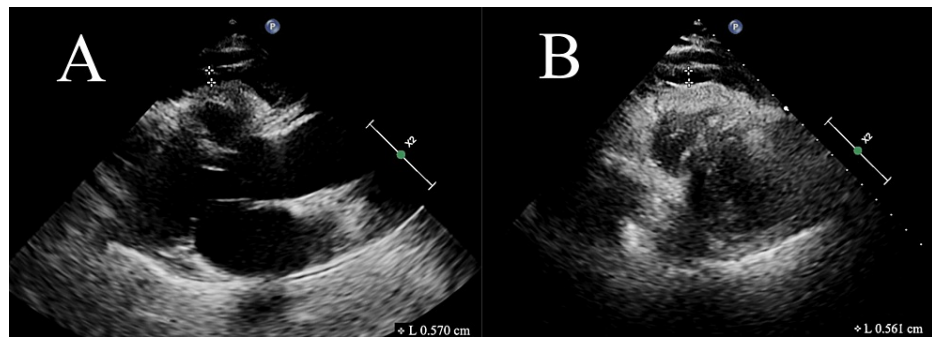
2 of 9

FIGURE 1: Echocardiographic measurement of EAT thickness in the parasternal long-axis view (A) and parasternal short-axis view (B) of the left ventricle at end-systole from an RA patient.

Abbreviations: EAT, epicardial adipose tissue; RA, rheumatoid arthritis

2D-STE examination

Subjects breathed calmly, and dynamic images of three cardiac cycles in apical two-chamber, apical long-axis, and apical four-chamber long-axis views were acquired and stored. The global longitudinal strain (GLS) was measured using the aCMQ technique (QLAB, version 13.0; Figure 53, Baltimore, MD). The dynamic images of the three sections were matched to the corresponding views in the software, which automatically recognized the cardiac cycle, mapped the region of interest, and adjusted the region of interest if necessary. If more than two myocardial segments were not tracked satisfactorily in a single section, the subject was excluded. The software automatically outputs PLS (peak longitudinal strains) of the apical four-chamber (Figure *2A*), apical long-axis (Figure *2B*), and apical two-chamber (Figure *2C*) views. GLS is the average of the PLS of the three views over two different cardiac cycles [14]. Because the LV myocardium shortens along its longitudinal axis during a period of contraction, and GLS describes the deformation of the myocardium in the longitudinal direction, the value is negative. To avoid confusing descriptions, it is expressed as an absolute value in this study, which means that lower absolute values of GLS represent weaker ventricular systolic function.

FIGURE 2: The measurement of PLS in the apical four-chamber (A), apical long-axis (B), and apical two-chamber (C) views from an RA patient.

Abbreviations: PLS, peak longitudinal strain; RA, rheumatoid arthritis

Repeatability analysis

Two physicians repeatedly measured GLS and EAT in 15 randomly selected subjects. One of the observers took two measurements with a one-week interval between measurements, while the second observer was unaware of the first observer's results to analyze intraobserver and interobserver variability.

Statistical analysis

Statistical Product and Service Solutions (SPSS, version 29.0; IBM SPSS Statistics for Windows, Armonk, NY) software was used for analysis. Normal distribution was expressed as mean ± standard deviation, non-normally distributed data were expressed as median (interquartile range), and categorical variables were expressed as frequencies and percentages. Comparisons between groups were made using the student t-test, Wilcoxon rank sum tests, and chi-square tests, where appropriate. Pearson and Spearman correlations were used to assess the correlation between GLS and other parameters in RA patients. Variables that were statistically significant in univariate analyses were used in multivariate linear regression analyses to explore

2024 Wang et al. Cureus 16(5): e60495. DOI 10.7759/cureus.60495

3 of 9

independent associations of GLS in RA. The intraclass correlation coefficient (ICC) was used to assess the intraobserver and interobserver variability of GLS and EAT, and ICC ≥0.75 means good reliability. A two-tailed P value <0.05 was statistically significant.

Results

Approximately 258 RA inpatients were screened, of whom 64 were initially recruited, but four were later excluded from the final analysis because unclosed patent foramen ovale was found on echocardiography in one patient, lung cancer was found during the study in one patient, and two other patients had poor image quality.

The clinical and laboratory characteristics of all subjects are shown in Table *1*. There were no statistical differences between the RA group and the control group in terms of Gender, Age, BMI, SBP, DBP, FPG, TG, TC, HDL-C, and LDL-C (all P>0.05). WC, ESR, and CRP were higher in the RA group compared to the control group (all P<0.05).

	Control group	RA group	P value
Woman (n/%)	48 (80.0)[a]	47 (78.3)[a]	0.822
Age (years)	54.0±7.5	53.9±5.8	0.924
BMI (kg/m^2)	22.9±2.1	23.7±4.0	0.143
WC (cm)	80.8±4.8	85.7±9.8	0.001[*]
SBP (mm/Hg)	121.4±8.2	123.6±8.6	0.165
DBP (mm/Hg)	74.2±6.6	75.2±6.6	0.439
FPG (mmol/L)	4.9±0.4	4.9±0.5	0.950
TG (mmol/L)	1.3±0.4	1.2 (0.86)[b]	0.702
TC (mmol/L)	4.7±0.6	4.5±0.9	0.171
HDL-C (mmol/L)	1.2±0.2	1.1±0.3	0.067
LDL-C (mmol/L)	2.8±0.5	2.7±0.7	0.543
ESR (mm/h)	8.8±3.6	80.5 (53.7)[b]	<0.001[**]
CRP (mg/L)	1.4 (2.0)[b]	34.8 (76.5)[b]	<0.001[**]
DAS28	-	4.3±0.9	-
RF positive	-	53 (88.3)[a]	-
ACCP positive	-	49 (81.7)[a]	-

TABLE 1: Comparison of clinical and laboratory characteristics in two groups (N=60)

Data were expressed as Mean ± SD unless stated otherwise. [a]Data were expressed as a number with percentage inside the bracket. [b]Data were expressed as median (IQR). *P value<0.05; **P value <0.001

Abbreviations: RA, rheumatoid arthritis; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28, disease activity score 28 joints; RF, rheumatoid factor; ACCP, anti-cyclic citrullinated peptide antibody; SD, standard deviation; IQR, interquartile range

The echocardiographic parameters of all subjects are shown in Table *2*. EAT thickness was higher and GLS was lower in the RA group than in the control group (all P<0.05). There were no differences in IVSD, LVEDD, LVPWD, LVESD, S′, or LVEF between the RA group and the control group (all P>0.05).

	Control group	RA group	P value
EAT (mm)	4.21±0.51	4.97±0.93	<0.001 [**]
IVSD (mm)	9.28±0.38	9.32±0.44	0.563
LVEDD (mm)	44.54±2.32	45.14±2.67	0.187
LVPWD (mm)	9.04±0.41	9.08±0.48	0.624
LVESD (mm)	28.31±1.97	28.95±2.54	0.128
S′ (cm/s)	10.85±1.45	10.47±1.65	0.187
LVEF (%)	64.30±2.32	63.62±2.58	0.130
GLS (%)	20.16±1.04	18.92±1.72	<0.001 [**]

TABLE 2: Comparison of echocardiographic parameters in two groups (N=60)

Data were expressed as mean ± SD. **P value <0.001

Abbreviations: RA, rheumatoid arthritis; EAT, epicardial adipose tissue; IVSD, interventricular septal thickness in end-diastolic period; LVEDD, LV end-diastolic diameter; LVPWD, LV posterior wall thickness in end-diastolic period; LVESD, LV end-systolic diameter; S′, mitral annular peak systolic velocity; LVEF, LV ejection fraction; GLS, global longitudinal strain; SD, standard deviation

Table *3* represents the correlation analysis between GLS and other variables in the RA group. In RA patients, bivariate correlation analysis showed that EAT, age, SBP, ESR, and DAS28 were negatively associated with GLS (all P<0.05).

	r	P value
EAT	-0.273	0.035 [*]
Age	-0.355	0.005 [*]
BMI	-0.108	0.411
WC	-0.155	0.237
SBP	-0.258	0.047 [*]
DBP	-0.212	0.104
FPG	0.034	0.797
TG	0.140	0.285
TC	0.069	0.602
HDL-C	0.021	0.875
LDL-C	0.101	0.441
ESR	-0.314	0.014 [*]
DAS28	-0.420	0.001 [*]

TABLE 3: Correlation of GLS with different factors in RA patients

*P value<0.05

Abbreviations: GLS, global longitudinal strain; RA, rheumatoid arthritis; EAT, epicardial adipose tissue; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; DAS28, disease activity score 28 joints

Table *4* represents a multivariate linear regression analysis of GLS in the RA group. Multivariate linear regression analysis showed that EAT and GLS correlations weakened (P>0.05), whereas age and DAS28 were independently associated with GLS in RA patients (all P<0.05).

2024 Wang et al. Cureus 16(5): e60495. DOI 10.7759/cureus.60495

5 of 9

	Nonstandardized coefficients		Standardized coefficients (β)	t	P value
	B	SE			
EAT	-0.358	0.205	-0.192	-1.746	0.087
Age	-0.098	0.033	-0.331	-2.964	0.005[*]
SBP	-0.034	0.024	-0.169	-1.428	0.159
ESR	-0.008	0.007	-0.141	-1.139	0.260
DAS28	-0.485	0.234	-0.265	-2.072	0.043[*]

TABLE 4: Multiple linear regression analysis of GLS in RA patients

*P value<0.05

Abbreviations: GLS, global longitudinal strain; RA, rheumatoid arthritis; EAT, epicardial adipose tissue; SBP, systolic blood pressure; ESR, erythrocyte sedimentation rate; DAS28, disease activity score 28 joints

The ICCs of GLS and EAT in intraobserver and inter-observer were 0.94, 0.92, and 0.90, 0.87, respectively, which means good reliability for both intraobserver and interobserver readings (all P<0.05).

Discussion

In this study, we assessed EAT and LV systolic function by 2D-STE and, for the first time, explored the relationship between EAT and GLS in RA patients.

2D-STE has no angle dependence, and GLS is more sensitive than conventional echocardiographic parameters for detecting occult myocardial dysfunction and additionally provides prognostic information about adverse cardiovascular events [14,15]. Cioffi et al. have found that subclinical LV systolic dysfunction, as defined by GLS, independently predicted all causes and cardiovascular hospitalization in RA patients [15]. Although progress has been made in the prevention and treatment of CVD in RA in recent years, EULAR still recommends regular cardiovascular risk assessment in patients with RA [3]. Myocardial dysfunction is common in RA, with a reported 45% incidence of LV systolic dysfunction in RA patients without clinical evidence of CVD [16]. A recent meta-analysis showed reduced GLS in RA patients without cardiac disease and heart failure manifestations compared to controls [17].

Several studies in different RA cohorts have observed that higher disease severity is associated with lower LV systolic function [12,14,18]. One of the studies from Asia also confirmed that disease activity assessed by DAS28 was a major predictor of LV myocardial strain injury in RA, consistent with the results of our study [14]. Furthermore, myocardial protection by reducing the degree of disease activity and controlling the inflammatory state has also been observed in the treatment of RA [19]. EULAR also recommends controlling disease activity to reduce cardiovascular risk in RA [3]. However, age as a determinant of GLS in RA was not found in a study evaluating subclinical LV systolic dysfunction in very early RA patients, which may be because the study included outpatient RA with newly diagnosed and treatment-naive compared with ours [18].

The pathophysiological mechanism of cardiovascular involvement in RA has not been clarified, but it is currently believed that chronic inflammation leads to damage of vascular endothelial cells, accelerated atherosclerosis, microcirculatory dysfunction affects myocardial function, persistent inflammation causes oxidative stress, and the increase in pro-inflammatory cytokine-induced fibroblast activity can lead to myocardial collagen deposition and interstitial fibrosis, which affects LV function [2]. It has also been suggested that changes in adipocytokine secretion patterns could intensify the inflammatory response, worsen tissue damage, and potentially link RA to CVD [20].

EAT is a specific form of visceral fat around the heart and is metabolically active, secreting adipocytokines (e.g., leptin, resistin, interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α)) [4]. The pathogenic role of adipocytokines such as leptin, resistin, IL-6, and TNF-α in atherosclerotic CVD has been suggested [21]. Previously, an animal experiment has confirmed that leptin from pericardial adipose tissue in obese rats can induce fibrosis in cardiomyocytes [22]. Because of the lack of anatomical barrier between EAT and the myocardium and coronary arteries and the sharing of the same microcirculation, the biologically active substances secreted by EAT can act on coronary arteries and myocardial tissues through paracrine and vascular secretion, aggravating inflammatory reactions and affecting vascular and myocardial structure and function [5]. An animal experiment has confirmed that changes in the secretory products of EAT can inhibit

2024 Wang et al. Cureus 16(5): e60495. DOI 10.7759/cureus.60495

6 of 9

the contractile function of cardiomyocytes in experimental rats [23].

Several previous studies have compared the thickness of EAT in RA patients with controls and found that RA patients have a higher EAT, consistent with our results [7-9]. However, there are no studies on the correlation between EAT and LV systolic function in RA patients without significant CVD. In the present study, we found a negative correlation between the thickness of EAT and LV systolic function in RA patients.

The link between EAT and atherosclerosis has been observed in RA, with a significant positive correlation between EAT and arterial stiffness, and EAT was an independent predictor of elevated aortic pulse wave velocity [24]. Significantly elevated levels of leptin and resistin have been observed in RA patients, especially those with high disease activity [25,26]. A study including 192 RA patients suggests that leptin is associated with the degree of atherosclerosis and plaque formation, independently of other cardiovascular risk factors [27].

Exploring the relationship between EAT and LV systolic function in RA patients is of great clinical value. The correlation between impaired LV systolic function and EAT suggests that EAT may be an imaging marker for assessing subclinical LV systolic insufficiency in RA. A case-control study found less EAT in RA patients treated with TNF-α inhibitors [7]. Additionally, TNF-α inhibitors have been shown to play a positive role in CVD in RA [19]. However, further studies are needed to confirm whether the beneficial effects of TNF-α inhibitors on cardiovascular function are mediated through EAT. Although the accumulation of EAT was associated with reduced GLS in RA patients in the present study, the correlation was attenuated after adjustment for confounders. Age and RA disease severity may play a greater role in LV myocardial dysfunction.

Our study also has several limitations. First, the present study was a single-center cross-sectional study with a small sample size, which did not allow us to infer a causal relationship between EAT and GLS, and the results could not be extrapolated. Second, the gold standard for EAT assessment is cardiac magnetic resonance, not echocardiographic measurements, but a recent study reported a good correlation between echocardiographic and magnetic resonance measurements of EAT [28]. Moreover, there are still many limitations of 2D-STE (e.g., image quality, frame rate, and chest wall conformation), which may account for the increased intra- and interobserver variability of GLS measurements [29]. Third, because of the mostly incomplete medical records of RA patients, it was not possible to accurately obtain the duration of the disease and therapeutic medications; therefore, the impact of these factors on the study results could not be considered. Finally, limited by the conditions of the laboratory, adipokines, and cytokines were not measured in RA patients.

Conclusions

We conclude that significant differences in the thickness of EAT were observed among participants, with increased EAT thickness in the RA group. A 2D-STE can detect early LV myocardial systolic dysfunction in RA patients, as shown by lower GLS. The bivariate correlations further illuminate the negative correlation between GLS and EAT in RA patients, as evidenced by the accumulation of EAT associated with lower GLS. However, the predictive value of EAT in GLS of RA patients does not emerge as a robust independent predictor. Subclinical LV systolic dysfunction in patients with RA seems to be more influenced by age and disease activity rather than the thickness of EAT.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Tinglin Wang, Hongyu Liang, Gehong Peng

Acquisition, analysis, or interpretation of data: Tinglin Wang, Hongyu Liang, Bingxu Zhao

Drafting of the manuscript: Tinglin Wang, Bingxu Zhao

Critical review of the manuscript for important intellectual content: Tinglin Wang, Hongyu Liang, Bingxu Zhao, Gehong Peng

Disclosures

2024 Wang et al. Cureus 16(5): e60495. DOI 10.7759/cureus.60495

7 of 9

References

1. Safiri S, Kolahi AA, Hoy D, et al.: Global, regional and national burden of rheumatoid arthritis 1990-2017: a systematic analysis of the Global Burden of Disease study 2017. Ann Rheum Dis. 2019, 78:1463-71. 10.1136/annrheumdis-2019-215920

2. Pan SY, Tian HM, Zhu Y, et al.: Cardiac damage in autoimmune diseases: target organ involvement that cannot be ignored. Front Immunol. 2022, 13:10.3389/fimmu.2022.1056400

3. Agca R, Heslinga SC, Rollefstad S, et al.: EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis. 2017, 76:17-28. 10.1136/annrheumdis-2016-209775

4. Fang W, Xie S, Deng W: Epicardial adipose tissue: a potential therapeutic target for cardiovascular diseases . J Cardiovasc Transl Res. 2024, 17:322-33. 10.1007/s12265-023-10442-1

5. Iacobellis G: Epicardial adipose tissue in contemporary cardiology . Nat Rev Cardiol. 2022, 19:593-606. 10.1038/s41569-022-00679-9

6. Yao F, Zeng L, Hua M, et al.: Association of epicardial and visceral adipose tissue in relation to subclinical cardiac dysfunction in Chinese: Danyang study. BMJ Open. 2023, 13:10.1136/bmjopen-2023-075576

7. Lima-Martínez MM, Campo E, Salazar J, et al.: Epicardial fat thickness as cardiovascular risk factor and therapeutic target in patients with rheumatoid arthritis treated with biological and nonbiological therapies. Arthritis. 2014, 2014:10.1155/2014/782850

8. Fatma E, Bunyamin K, Savas S, et al.: Epicardial fat thickness in patients with rheumatoid arthritis . Afr Health Sci. 2015, 15:489-95. 10.4314/ahs.v15i2.23

9. Saha S, Singh R, Mir IA, Bansal N, Singh PK, Nadeem M: Epicardial fat thickness: a cardiometabolic risk marker in rheumatoid arthritis. Cureus. 2022, 14:10.7759/cureus.21397

10. Aletaha D, Neogi T, Silman AJ, et al.: 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2010, 69:1580-8. 10.1136/ard.2010.138461

11. Anderson J, Caplan L, Yazdany J, et al.: Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. Arthritis Care Res (Hoboken). 2012, 64:640-7. 10.1002/acr.21649

12. Midtbø H, Semb AG, Matre K, Kvien TK, Gerdts E: Disease activity is associated with reduced left ventricular systolic myocardial function in patients with rheumatoid arthritis. Ann Rheum Dis. 2017, 76:371-6. 10.1136/annrheumdis-2016-209223

13. Iacobellis G, Assael F, Ribaudo MC, Zappaterreno A, Alessi G, Di Mario U, Leonetti F: Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction. Obes Res. 2003, 11:304-10. 10.1038/oby.2003.45

14. Hanvivadhanakul P, Buakhamsri A: Disease activity is associated with LV dysfunction in rheumatoid arthritis patients without clinical cardiovascular disease. Adv Rheumatol. 2019, 59:56. 10.1186/s42358-019-0100-x

15. Cioffi G, Ognibeni F, Dalbeni A, et al.: High prevalence of occult heart disease in normotensive patients with rheumatoid arthritis. Clin Cardiol. 2018, 41:736-43. 10.1002/clc.22926

16. Cioffi G, Viapiana O, Ognibeni F, et al.: Prevalence and factors related to left ventricular systolic dysfunction in asymptomatic patients with rheumatoid arthritis. A prospective tissue Doppler echocardiography study. Herz. 2015, 40:989-96. 10.1007/s00059-015-4320-5

17. Thallapally VK, Bansal R, Thandra A, et al.: Detection of myocardial dysfunction using global longitudinal strain with speckle-tracking echocardiography in patients with vs without rheumatoid arthritis: a systematic review and meta-analysis. J Echocardiogr. 2023, 21:23-32. 10.1007/s12574-022-00583-8

18. Lo Gullo A, Rodríguez-Carrio J, Aragona CO, et al.: Subclinical impairment of myocardial and endothelial functionality in very early psoriatic and rheumatoid arthritis patients: association with vitamin D and inflammation. Atherosclerosis. 2018, 271:214-22. 10.1016/j.atherosclerosis.2018.03.004

19. Ntusi NA, Francis JM, Sever E, et al.: Anti-TNF modulation reduces myocardial inflammation and improves cardiovascular function in systemic rheumatic diseases. Int J Cardiol. 2018, 270:253-9. 10.1016/j.ijcard.2018.06.099

20. Ruscitti P, Di Benedetto P, Berardicurti O, Liakouli V, Carubbi F, Cipriani P, Giacomelli R: Adipocytokines in rheumatoid arthritis: the hidden link between inflammation and cardiometabolic comorbidities. J Immunol Res. 2018, 2018:10.1155/2018/8410182

21. Liu L, Shi Z, Ji X, Zhang W, Luan J, Zahr T, Qiang L: Adipokines, adiposity, and atherosclerosis . Cell Mol Life Sci. 2022, 79:272. 10.1007/s00018-022-04286-2

22. Wang P, Luo C, Zhu D, et al.: Pericardial adipose tissue-derived leptin promotes myocardial apoptosis in high-fat diet-induced obese rats through Janus kinase 2/reactive oxygen species/Na+/K+-ATPase signaling pathway. J Am Heart Assoc. 2021, 10:10.1161/JAHA.121.021369

23. Greulich S, de Wiza DH, Preilowski S, et al.: Secretory products of guinea pig epicardial fat induce insulin resistance and impair primary adult rat cardiomyocyte function. J Cell Mol Med. 2011, 15:2399-410. 10.1111/j.1582-4934.2010.01232.x

24. Petra CV, Albu A, Pamfil C, Tamas MM, Vesa SC, Rednic S: The relationship between epicardial adipose tissue and arterial stiffness in patients with rheumatoid arthritis. Med Ultrason. 2019, 21:427-34. 10.11152/mu-2001

25. Lee YH, Bae SC: Circulating leptin level in rheumatoid arthritis and its correlation with disease activity: a meta-analysis. Z Rheumatol. 2016, 75:1021-7. 10.1007/s00393-016-0050-1

26. Huang Q, Tao SS, Zhang YJ, et al.: Serum resistin levels in patients with rheumatoid arthritis and systemic

lupus erythematosus: a meta-analysis. Clin Rheumatol. 2015, 34:1713-20. 10.1007/s10067-015-2955-5

27. Kang Y, Park HJ, Kang MI, Lee HS, Lee SW, Lee SK, Park YB: Adipokines, inflammation, insulin resistance, and carotid atherosclerosis in patients with rheumatoid arthritis. Arthritis Res Ther. 2013, 15:R194. 10.1186/ar4384

28. van Woerden G, van Veldhuisen DJ, Gorter TM, et al.: The value of echocardiographic measurement of epicardial adipose tissue in heart failure patients. ESC Heart Fail. 2022, 9:953-7. 10.1002/ehf2.13828

29. Sonaglioni A, Nicolosi GL, Granato A, Bonanomi A, Rigamonti E, Lombardo M: Influence of chest wall conformation on reproducibility of main echocardiographic indices of left ventricular systolic function. Minerva Cardiol Angiol. 2024, 72:111-24. 10.23736/S2724-5683.23.06475-X

2024 Wang et al. Cureus 16(5): e60495. DOI 10.7759/cureus.60495

9 of 9