Short Communication

Assessment of Right Ventricular Functions in Patients with Rheumatoid Arthritis by Tissue Doppler Imaging and 2D Speckle-Tracking Echocardiography

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Abstract

Background: Advanced echocardiographic techniques play a crucial role in evaluating right ventricular function and providing valuable information for the management of rheumatoid arthritis (RA)-related cardiovascular complications. **Objectives:** To investigate early signs of right ventricle dysfunction in patients with RA using tissue Doppler imaging and two- dimensional speckle-tracking echocardiography (GLS). **Materials and Methods:** This case–control study examined cardiac changes in 50 RA patients compared to 50 healthy controls. Echocardiography and anthropometric measurements were used to assess ejection fraction, ventricle systolic and diastolic function, and myocardial strain. **Results:** The study examined socio-demographic characteristics and echocardiographic parameters in RA patients (N = 50) compared to controls. RA patients had a mean age of 48.28 ± 11.06 years, with 74.0% females. No significant differences in age, BMI, and body surface area between RA patients and controls. There were no significant mean differences between the two study groups according to ejection fraction. There is a significant difference in right ventricular systolic function (TAPSE, S^ velocity, and MPI) observed in RA patients. There is a significant difference in right ventricular diastolic function (E/A ratio, IVRT) observed in RA patients. Global longitudinal strain (GLS) was also significantly reduced. The treatment strategy (single vs. combination therapy) did not significantly affect echocardiographic parameters. The findings emphasize the importance of monitoring cardiac health in RA patients. RA patients show cardiac function alterations, particularly in right ventricular systolic function (TAPSE, S^, and MPI), right ventricular diastolic function (E/A ratio, IVRT), and global function (GLS). **Conclusion:** Monitoring cardiovascular health in RA patients is crucial. Treatment regimens (combination or monotherapy) did not significantly affect the measured echocardiographic parameters.

Keywords: 2D echocardiography, rheumatoid arthritis, right ventricular diastolic function (RVDF), right ventricular systolic function (RVSF), tissue doppler imaging (TDI)

Introduction

Rheumatoid arthritis (RA) is the most prevalent form of chronic inflammatory autoimmune arthritis characterized by progressive symmetric inflammation of affected joints, leading to cartilage damage, bone erosion, and functional impairment, and can extend beyond joint involvement.[1]

The establishment of RA likely involves two distinct events,[2,3] the genetic predisposition of the individual (leading to the generation of autoreactive T and B cells) and the triggering event (such as viral and bacterial infections or tissue injury), which activates antigen-presenting cells to stimulate the preexisting autoreactive lymphocytes.

The incidence of RA rose from 1.1 (No. of patients = 201) in 2014, to 2.2 (No. of patients = 309) in 2019; notably,

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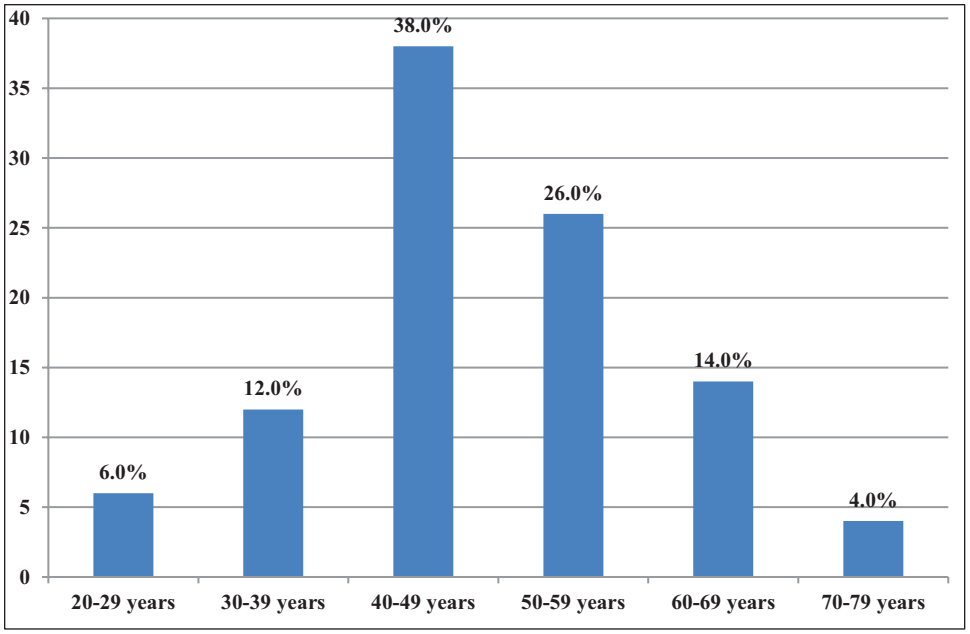

Figure 1: Distribution of rheumatoid arthritis patients according to age ($N = 50$)

75% of RA patients in Iraq are women.[4] One of the leading causes of early mortality in RA patients is an extra articular complication of cardiovascular system (pericarditis, myocarditis coronary vasculitis nodules on valves, and heart failure [HF])[5] Cardiovascular diseases (CVD) are highly prevalent in patients with RA, affecting over one-third of individuals aged ≥40 years[6]

Congestive HF is the second leading cause of death in RA patients after myocardial infarction, with up to a two-fold increase in HF incidence among RA individuals.[7] Elevated circulating pro-inflammatory cytokines in RA patients are likely determinants for the pathogenesis of HF, such as TNF-alpha and interleukin-6, leading to endothelial activation, nitrosative and oxidative stress, increased myocardial stiffness, and fibrosis, ultimately resulting in diastolic dysfunction because of impaired relaxation of the myocardium[8]

Additionally, specific autoantibodies developed against antigens present in the myocardium might provoke local inflammation via their interaction with activating Fc receptors[9] and, as such, contribute to the development of HF.

HF diagnosis involves assessing ventricular systolic and diastolic functions, and decreased echocardiographic parameters of systolic and diastolic function are highly indicative, especially in RA patients.[10] Echocardiography, specifically tissue Doppler imaging (TDI) and strain, is used to detect subclinical ventricular dysfunction in RA patients without established heart illness.[11]

At least one of these four metrics should be routinely reported when assessing RV systolic function[12]:

1. Tricuspid annular plane systolic excursion (TAPSE).
2. Right ventricle systolic annular velocity (S^ wave) cm/s.
3. Fractional area change (FAC).
4. Myocardial performance index (RIMP or Tei index).

Assessment of RV diastolic function requires the integration of data from different echocardiographic views and modalities [Figure 1] (primarily 2-dimensional, PW, and tissue Doppler)[12]

Right ventricular global longitudinal strain (RV GLS) is a measure of myocardial deformation and it is an important indicator of RV function. In patients with RA, RV GLS may reduce due to the chronic inflammation, systemic involvement, and increased risk of cardiovascular complications associated with this condition.[13]

The aim of this study was to investigate early signs of right ventricle dysfunction in patients with RA using TDI and two-dimensional speckle-tracking echocardiography (2D STE).

Materials and Methods

Study design and patients

A case–control study that conducted from March to July 2023. The data collection was carried out in the echocardiography unit in Medical Department of Marjan Medical City in Babylon City, Iraq, and among patients who attended the rheumatology unit in the same hospital. Sample size calculated using the formula:[14]

$N = \{(z)^2 * p\ q/d^2\}$

$N = \{(1.96)^2 * 0.022 * 0.978/(0.05)^2\}$

$N = 33.1$

A sample size of 50 patients was included in this study. Other 50 apparently healthy volunteers homogenous in terms of age and gender who attended the Marjan Medical City were selected as the control group. Take all the patients and control cases in sinus rhythm condition, not smokers not alcoholics, and patients diagnosed by rheumatologists according to American College of Rheumatology criteria).[15]

Exclusion criteria

Coronary artery diseases and HF (ejection fraction less than 52%), valvular heart diseases, hypertension, diabetes mellitus, chronic obstructive airway diseases, arrhythmia, hyperlipidemia, cardiomyopathy, chronic kidney diseases, liver diseases, thyroid diseases and anemia, history of stroke, cases with poor echogenic windows that affect TDI and STE, systemic lupus erythematosus, ankylosing spondylitis, and other inflammatory arthritis.

This study used GE medical system Vividiq echocardiography machine (General Electric Company (GE), Shanghai, China) with transducer M5Sc phased array transducer frequency of 1.5–4.5 MHz. The participants were put in left lateral decubitus positioned and monitored using an electrocardiographic lead, the following echocardiographic cuts were performed in long parasternal, apical two, and four chambers to evaluate cavities systolic and diastolic functions of ventricles. All measurements were performed in accordance with the guidelines/recommendations of American Society of Echocardiography/European Association of Echocardiography.[16]

The following echocardiographic variables were assessed:

1. Ejection fraction (EF), calculated by use of biplane modified Simpson's method, considering the normal value of EF as 54%–74% [2 standard deviation (S-D)] range for the female, and 52%–72% (2 S-D) range for male according to the current recommendations.[17]
2. Right ventricle systolic annular velocity (S^ wave) cm/s, by TDI placing the sample volume of the pulse wave Doppler at the lateral sides of the tricuspid valve annulus to measure the maximal systolic velocity of the myocardium of basal lateral wall (normal S^ wave velocity = 14.1 ± 2.3 cm/s, cutoff value ≥ 10 cm/s).[17]
3. TAPSE in apical 4-chamber view. The M-mode cursor should be aligned along the RV free wall as perpendicular to the lateral tricuspid annulus as possible (and as parallel as possible to the movement of the TV annulus). The distance moved by the leading edge of the annulus from end-diastole toward the apex at end-systole is measured (normal range TAPSE = 24 ± 3.5 mm, cutoff value > 17mm)[17]
4. Myocardial performance index (MPI) measured in apical 4-chamber view Obtained by applying TDI pulse wave to the lateral tricuspid annulus. MPI = (IVCT + IVRT)/ET (normal range 0.38 ± 0.08, cutoff value > 0.54).[17]
5. Diastolic function of RV,[12] evaluated by use of:
   - Index right atrium in the apical 4-chamber view, RA area is traced at the end of ventricular systole then Index RA area = RA area/BSA cm^2/m^2 (cutoff value ≤ 11 cm^2/m).[16]
   - RV wall thickness. By M-mode or 2D echocardiography, from the subcostal window at end-diastole preferably at the level of the tip of the anterior tricuspid leaf*let al*ign the ultrasound beam perpendicular to the RV free wall (normal value ≤ 5 mm).[16]
   - Inferior vena cava (IVC) diameter and collapsibility by 2D echocardiography and M-mode in subcostal view. The M-mode cursor placed through the IVC was approximately 1.0–2.0 cm distal from the right atrium and just proximal to the junction of the hepatic veins that lie approximately 0.5–3.0 cm proximal to the ostium of the right atrium. The IVC diameter was measured at rest and during normal respiration (diameter ≤ 2.1 cm and collapsibility ≥ 50%).[16]
   - E/A ratio by measuring Tricuspid valve early diastolic filling velocity (E wave) and Tricuspid valve late diastolic filling velocity (A wave) by pulse wave Doppler (normal value 0.8–2.1).[16]
   - E/e^ ratio by measuring Tricuspid valve early diastolic filling velocity (E wave) by pulse wave Doppler and RV Early diastolic velocity (e^ wave) by TDI, (normal value ≤ 6).[16,17]
   - Isovolumic relaxation time (IVRT) by TDI (normal value ≤ 73 ms).[17]
6. Global longitudinal strain (GLS) of the right ventricle through RV-focused apical 4-chamber view in breath-hold. Image acquisition (frame rate between 40 and 70 f/s), appropriate depth, sector width, and slight over-gain help checking endocardial tracking designating region of interest (ROI) and avoid the pitfalls. ECG tracing (normal range of GLS is 23.6%–31.9%).[18]

Statistical analysis

The statistical analysis was carried out using SPSS version 27 (SPSS, IBM Company, Chicago, IL, USA). Continuous variables were presented as (Means ± SD) and the Student's *t* test was used to compare means between the two groups. Categorical variables were presented as frequencies, percentages, and the Pearson Chi-Square test was used to find the association between categorical variables. *P* value of ≤0.05 was considered significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of

Helsinki.[19] It was carried out with patients verbal and analytical approval before conducting the study. Informed consent was obtained from all patients, ensuring they were fully aware of their participation in the study and its potential implications. The study protocol and the subject information and consent form were reviewed and approved by a local committee on publication ethics at Babil Health Directorate under reference No. 360 on July 15, 2022.

Results

The results of the distribution of RA patients according to sex ($N = 50$), most of the patients ($N = 37$, 74.0%) were females. The mean age of patients was 48.28 ± 11.06 years, majority of patients ($N = 19$, 38.0%) presented with the age group (40–49 years) [Figure 1].

Mean body mass index of patients was 25.4 ± 2.6 kg/m², obese patients represent ($N = 2$, 4.0%) of patients, overweight patients represent ($N = 28$, 56%) of patients [Figure 2].

The results found that there is no significant difference between two the study groups according to body mass index ($P = 0.36$). There were no significant mean differences between the two study groups according to EF (62.46 ± 4.87 vs. 61.62 ± 3.69, P value = 0.34). This study showed that patients with RA have significantly lower values of TAPSE (18.84 ± 2.45 vs. 20.34 ± 2.28) than the control group and there was a significant difference between the two study groups (P value = ***0.002***).

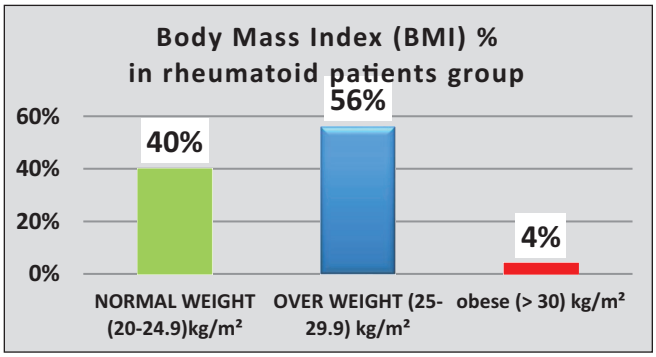

Figure 2: Distribution of rheumatoid arthritis patients according to body mass index (kg/m²) ($N = 50$)

This study also showed that the patients with RA have significantly lower values of S^ (11.21 ± 1.86 vs 12.29 ± 2.3) and there were significant mean differences between the two study groups (P value = **0.01***). There was significant mean differences between two study groups according to MPI (0.53 ± 0.06 vs. 0.5 ± 0.04, P value = **0.02***).

This study revealed that the patients with RA have a significantly lower E/A ratio than the control group (**0.9 ± 0.15** vs. **1.05 ± 0.15**, P value = **0.0001***). The results also found that the patients with RA have a significant mean difference in IVRT in comparison with control group (66.6 ± 6.5 ms vs. 61.7 ± 5.6 ms, P = **0.0001***). There was a significant mean reduction in GLS among patients with RA in comparison to control group (−22.28 ± 2.68 vs. −24.26 ± 2.35, P value = **0.0001***).

There were no significant mean differences between RA patients on monotherapy protocol (DMARDs) and RA patients on the combination-therapy protocol (DMARDs+Biological therapy) regarding the following parameters (TAPSE, S^, MPI, E/A ratio, IVRT, GLS) ($P > 0.05$) [Table 1].

Discussion

This study was conducted to compare the echocardiographic features between RA patients and healthy individuals. After excluding every patient with clinical evidence of cardiovascular diseases that may act as a confounder for results, the study examined socio-demographic characteristics and echocardiographic parameters in RA patients ($N = 50$) compared to control group ($N = 50$). RA patients had a mean age of 48.28 ± 11.06 years, with 74% females, No significant differences in age, BMI, and body surface area between RA patients and controls ($P > 0.05$).

Although most of the patients (56%) were overweight and only 4% were obese, there is no association found between RA and body mass index.[20] The result of the conventional echocardiographic parameter (EF) showed that there

Table 1: Comparison between patients with rheumatoid arthritis group and control group according to EF, TAPSE, S ^ , MPI, E/A ratio, IVRT, GLS ($N = 100$)

Parameters	Study group		*P* value
	Rheumatoid arthritis ($N = 50$)	Control group ($N = 50$)	
Ejection fraction (%) by Simpsons method	62.46 ± 4.87	61.62 ± 3.69	0.334
TAPSE (mm)	18.84 ± 2.45	20.34 ± 2.28	0.002*
S^ (cm/s)	11.21 ± 1.86	12.29 ± 2.3	0.01*
MPI	0.53 ± 0.06	0.5 ± 0.04	0.02*
E/A	0.9 ± 0.15	1.05 ± 0.15	0.0001*
IVRT cm²/m²	66.6 ± 6.5	61.7 ± 5.6	0.0001*
GLS (%)	−22.28 ± 2.68	−24.26 ± 2.35	0.0001*

*mean significant *P* value

were no significant differences between RA patients and control group and this result agreed with another study like Ji *et al*.[21]

This study shows that patients with RA have generally lower values of TAPSE, S^, and MPI than the control group and there was a significant difference between patients with RA group and control group indicating that they may have related to cardiovascular involvement in patients with rheumatic diseases. The study's findings were compatible with several authors worldwide. Norouzi *et al*. (n = 10)[22] revealed significantly lower values of TAPSE and S^ between patients in RA group and control group (25.10 ± 2.28 vs. 20.90 ± 3.32, P = 0.004) (15.10 ± 2.02 vs. 12.50 ± 1.51, P = 0.004), respectively.

This study showed that the patients with RA have significantly lower E/A ratios than the control group, and also have a significantly mean difference in IVRT in comparison with control group. This suggests that RA patients may have impaired RV diastolic function compared to control group. This study's findings are similar to those of Vizzardi *et al*. (n = 93)[23] which show a decrease E/A ratio, and another study done by Seyfeli *et al.* (35 RA patients)[24] which reported that RA patients may have impaired RV diastolic function, as measured by TDE, which reflects the relaxation and impaired filling of the RV.

The abnormalities observed in RV systolic and diastolic functions in RA patients could be attributed to various factors, such as systemic inflammation, myocardial involvement (myocarditis or fibrosis), pulmonary involvement (interstitial lung disease or pulmonary hypertension), pericardial involvement (pericarditis or effusion), or coronary artery disease. Some of these factors may be modifiable with anti-inflammatory or disease-modifying drugs, while others might require specific interventions or therapies.[25]

In the current study, it seems that patients with RA have a lower GLS (percentage) than the control group, which means that their right ventricular global function is impaired. This study's findings are similar to those of Naseem *et al*. (120 patients with RA)[26] that revealed high state of systemic inflammation in RA could lead to a possible mechanism of myocardial dysfunction through myocardial fibrosis in the absence of coronary artery diseases.

Fine *et al.*[27] found that the global longitudinal RV strain was reduced in patients with RA compared with healthy patients and that strain abnormalities correlate with RA disease severity. In patients with RA, RV GLS may reduce due to the chronic inflammation, systemic involvement, and increased risk of cardiovascular complications associated with this condition.[28]

Conclusion

Right ventricular systolic function {TAPSE (P = 0.002), S' (P = 0.01), MPI (P = 0.02)} and right ventricular diastolic function and GLS show alterations in right ventricle function of RA patients, suggesting a potential impact of RA on the cardiovascular system, warranting further research and attention to cardiac health in patients with RA without other cardiovascular risk factors. No significant differences were found in the measured echocardiographic parameters between patients on a combination-therapy protocol, and patients on a monotherapy protocol.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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