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ECHOCARDIOGRAPHIC ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT

Background: Rheumatoid arthritis is a systemic inflammatory disease that affects primarily joints in addition to multiple organ systems, including the cardiovascular system. **Patients and method:** A cross-sectional study was conducted on 50 patients with rheumatoid arthritis who attended the rheumatology outpatient clinic in Baghdad teaching hospital between October 2023 and October 2024. Echocardiographic examinations were performed for each patient. **Results:** 50 patients with rheumatoid arthritis were enrolled in the study. Men constituted 38% (n=19) of the sample, while females showed predominance (62%). The mean period since diagnosis of rheumatoid arthritis was 33.59 months, with a range between 1 month and 69 months. Mean age (higher in patients with rheumatoid arthritis for ≥ 60; 44.6 years vs 34.64 years, ***P-value*** less than 0.0001), gender proportions (females were 19 in patients with rheumatoid arthritis for ≥ 60 vs 12 for those with disease duration of < 60 months, ***P-value*** less than 0.04), and mean systolic blood pressure (lower in patients with rheumatoid arthritis for ≥ 60 months; 118.24 mm Hg vs 124 mm Hg, ***P-value*** less than 0.0016) were significantly different between patients with rheumatoid arthritis ≥ 60 months and those with disease duration of < 60 months. Diastolic dysfunction was significantly higher in those with longer disease duration. **Conclusion:** In the rheumatoid arthritis population, diastolic dysfunction is frequently encountered, and its prevalence is positively correlated with disease duration.

KEYWORDS: Rheumatoid arthritis, echocardiography, diastolic dysfunction.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease mainly affecting the synovial joints that is frequently brought on by the combination of genes and environmental factors, such as tobacco use.[1] It usually begins in small peripheral joints, is symmetrical, and if treatment is not received, progresses to involve proximal joints.[2-4] Untreated RA is a progressive illness that increases morbidity and mortality.[5,6] Cardiovascular disorders, such as pericarditis, cardiomyopathy, myocarditis, cardiac amyloidosis, coronary vasculitis, arrhythmias, valve disorders, and, most crucially, congestive heart failure (CHF) and ischaemic heart disease, are among those extra-articular features.[7] Diastolic dysfunctions can progress significantly on follow-up, reaching 57.9%, and is common in RA patients without clinical heart failure (40.7% at baseline).[8] LVDD includes typical structural ventricular abnormalities, typically with normal ejection fraction, including decreased distensibility, impaired relaxation, and abnormal diastolic filling.[9] There is a continuum of diastolic dysfunction, ranging from restricted filling with very elevated filling pressures to impaired relaxation with normal filling pressures.[10] The exact cause of LVDD in RA is still unknown. Some researchers have suggested that it may be due to chronic myocarditis and reduced blood flow, resulting in a decrease in LV mass, as shown in magnetic resonance studies.[11] Another possibility for the cause of aberrant ventricular diastolic function is amyloidosis.[12] RA patients with LVDD have lower rates of known cardiovascular (CV) risk factors than the general population, and their ejection fraction is preserved.[13] The degree of inflammation in the body may contribute to the stiffening of the heart muscle and the eventual development of moderate to severe LVDD.[14] Aim of the study to assess the prevalence of

diastolic dysfunction in patients with newly diagnosed rheumatoid arthritis (< 60 months) and those who were diagnosed 60 months ago or more.

METHOD

This cross-sectional study was conducted on 50 patients with clinically confirmed rheumatoid arthritis (RA) who attended the rheumatology outpatient clinic at Baghdad Teaching Hospital between October 2023 and October 2024. The study was approved by the Department of Internal Medicine, College of Medicine, University of Baghdad. Informed consent was obtained from all participants before enrollment. Inclusion criteria required patients to be between 20 and 55 years old with a clinical diagnosis of RA based on established diagnostic criteria. Patients were excluded if they were younger than 20 or older than 55 years, or if they had comorbid conditions such as hypertension, ischemic heart disease, diabetes mellitus, renal insufficiency, hyperlipidemia, or a BMI ≥ 30 kg/m². Additional exclusion criteria included a history of abnormal electrocardiogram (ECG), low ejection fraction (<60%), moderate to severe RA disease activity, disease duration longer than 7 years, or current use of biological therapy. All enrolled participants underwent detailed clinical evaluation, physical examination, 12-lead ECG, and transthoracic echocardiography. RA disease activity was quantified using the DAS28 (28-joint Disease Activity Score) calculator available online (https://www.4s-dawn.com/DAS28/). Based on DAS28 scores, disease activity was categorized as remission (<2.6), low (2.6–3.1), moderate (3.1–5.1), or severe (>5.1). Echocardiographic assessments were conducted using a GE Vivid E9 XD Clear machine with a 5 MHz transducer. Examinations were performed in left-up and semi-lateral positions using standard parasternal and apical views. Measurements were taken across three consecutive cardiac cycles for accuracy. Two-dimensional echocardiography included measurements of interventricular septal thickness, posterior wall thickness, LV end-diastolic and end-systolic diameters, ejection fraction (using biplane Simpson's method), and left atrial volume index (LAVI). LAVI was indexed to body surface area using the Mosteller formula. Doppler echocardiography measured mitral inflow velocities (E and A waves), deceleration time, lateral and septal early diastolic tissue velocities (e′), E/e′ ratio, and peak tricuspid regurgitation (TR) velocity. Diastolic dysfunction was diagnosed if at least three of the following criteria were present: septal e′ < 7 cm/s or lateral e′ < 10 cm/s, average E/e′ > 14, LAVI > 34 mL/m², or TR velocity > 2.8 m/s. Data analysis was carried out using SPSS version 26 and Microsoft Excel 2010. Means and ranges were used for continuous variables, while categorical variables were summarized using frequencies and percentages. Depending on data distribution, comparisons were made using t-tests, Mann-Whitney U tests, Chi-square, or Fisher's exact test. Correlations were assessed using Pearson's correlation, with significance set at $p < 0.05$.

RESULTS

Fifty patients with rheumatoid arthritis were enrolled in the study. The mean age was 39.62 years and mean body mass index and body surface area were 28.17 kg/m and 1.92 m^2 respectively. Men constituted 38%(n=19) of the sample while females showed predominance (62%). Thirty-one (62%) patients had positive family history for rheumatoid arthritis. Blood pressure measurements showed that mean systolic and diastolic blood pressure were 121.12 mmHg and 78.2 mmHg respectively. Mean period since diagnosis of rheumatoid arthritis was 33.59 months with a range between 1months and 69 months. Demographic and echocardiographic parameters for the sample are illustrated in table 1 and 2 respectively.

Table 1: Demographics of the study population.

Parameter	Study population (n=50)
Age(years)	Mean (SD) 39.62 (7.96)
Sex: **Male** **Female**	No. (%) 19 (38%) 31 (62%)
BMI(kg/m^2)	Mean (SD) 28.17(4.87)
BSA(m^2)	Mean (SD) 1.92 (0.16)
Family history of RA; **Positive** **Negative**	No. (%) 31 (62%) 19 (38%)
Blood pressure (mm Hg) **Systolic** **Diastolic**	Mean (SD) 121.12 (6.69) 78.2 (6.84)
RA duration(months)	Mean (SD) 33.59 (30.96)

**SD; standard deviation, BMI; body mass index, BSA; body surface area, RA; rheumatoid arthritis.*

Table 2: Echocardiographic parameters of the study population.

Parameter	Study population (n=50) Mean (SD)
LV IVS thickness D (mm)	8.49 (0.77)
LV PW thickness D (mm)	8.09 (0.81)
LVEDd (mm)	46.62 (3.64)
LVESd (mm)	35.12 (3.45)
EF %	64.58 (2.53)
LAVI (ml/m^2)	21.86 (3.73)
Mitral A velocity (cm/s)	76.66(17.47)
Mitral E velocity (cm/s)	72.36 (17.60)
E/A ratio	0.98 (0.31)
Deceleration time (m/s)	195.8 (39.86)
Lat. E` velocity (cm/s)	9.39 (4.10)
Septal e` velocity (cm/s)	7.72 (3.38)
Average E/e` ratio	10.17 (4.30)
TR velocity (m/s)	3.42 (0.62)

*SD; standard deviation, LV IVS; left ventricle interventricular septum, LV PW; left ventricle posterior wall, LVEDd; left ventricular end-diastolic diameter, LVESd; left ventricular end-systolic diameter, EF; ejection fraction, LAVI; left atrial volume index, mitral A velocity; peak late diastolic mitral inflow velocity, mitral E velocity; peak early diastolic mitral inflow velocity, lat. E` velocity; early diastolic velocity of lateral mitral annulus, Septal e` velocity; early diastolic velocity of septal (medial) mitral annulus, TR velocity; tricuspid regurgitation peak velocity.

On comparison of demographics for patients with rheumatoid arthritis ≥ 60 months and those with disease duration of < 60 months, age (higher in patients with rheumatoid arthritis for ≥ 60; 44.6 years vs 34.64 years, ***P-value*** less than 0.0001), gender proportions(females were 19 in patients with rheumatoid arthritis for ≥ 60 vs 12 for those with disease duration of < 60 months, ***P-value*** less than 0.04), and systolic blood pressure(lower in patients with rheumatoid arthritis for ≥ 60 months; 118.24 mm Hg vs 124 mm Hg, ***P-value*** less than 0.0016) were significantly different. Other demographic parameters were not significantly different between the two groups. On comparison of echocardiographic variables for patients with rheumatoid arthritis for ≥ 60 months and those with disease duration of < 60 months, diastolic dysfunction was significantly higher in those with longer disease duration (14 patients with diastolic dysfunction, 6 patients with indeterminate diastolic function, and 5 patients with normal diastolic function vs all patients with normal diastolic function, ***P-value*** less 0.05). In addition, mitral E velocity, E/A ratio, E deceleration time, lat. E` velocity, and septal e` velocity were significantly lower in patients with rheumatoid arthritis duration of ≥ 60 months in comparison with patients group with shorter disease duration (61.73 cm/s vs 83 cm/s; ***P-value*** < 0.0001, 0.7 vs 1.25; ***P-value*** < 0.0001, 177.88 m/s vs 213.72 m/s; ***P-value*** 0.0009, 5.7 cm/s vs 13.09 cm/s; ***P-value*** < 0.0001, and 4.7 cm/s vs 10.76 cm/s; ***P-value*** < 0.0001 respectively) while Mitral A velocity, E/e` ratio, and tricuspid velocity were significantly higher in patients with longer disease duration (87.67cm/s vs 65.65cm/s; ***P-value*** < 0.000113.24 vs 7.10; ***P-value*** < 0.0001 and 2.88 m/s vs 1.85 m/s; ***P-value*** < 0.0001 respectively). Other echocardiographic findings were not significantly different between patients with longer disease duration and those with duration less than 60 months. Table 4 explains the comparison between patients with rheumatoid arthritis for ≥ 60 months and those with disease duration of < 60 months with respect to demographics and echocardiographic measurements. As in table 3.

Table 3: Comparison of parameters between patients with rheumatoid arthritis for ≥ 60 months and those with disease duration of < 60 months.

Parameter	Patients with RA for ≥ 60 months(n=25)	Patients with RA for < 60 months(n=25)	*P-value*
Sex; No. (%) Male Female	 6(24%) 19(76%)	 13(52%) 12(48%)	0.041
BMI(kg/$m^{2)}$ Mean(SD)	28.99(4.67)	27.36(5.02)	0.24
BSA(m^2) Mean(SD)	1.9(0.14)	1.94(0.17)	0.28
Family history of RA; No. (%) Positive Negative	 15(60%) 10(40%)	 16(64%) 9(36%)	0.77

Blood pressure (mm Hg) Mean(SD) Systolic Diastolic	 118.24(5.87) 77.72(7.48)	 124(6.30) 78.68(6.25)	 0.0016 0.62
Diastolic function; No. (%) Normal Decreased Indeterminate	 5(20%) 14(56%) 6(24%)	 25(100%) 0(0%) 0(0%)	 < 0.00001 < 0.00001 0.02
LV IVS thickness D (mm) Mean(SD)	 8.5(0.76)	 8.46(0.80)	 0.83
LV PW thickness D (mm) Mean(SD)	 8.05(0.84)	 8.12(0.79)	 0.77
LVEDd (mm) Mean(SD)	 45.89(3.62)	 47.36(3.59)	 0.15
LVESd (mm) Mean(SD)	 34.86(4.03)	 35.37(2.82)	 0.60
EF % Mean(SD)	 64.32(2.33)	 64.84(2.73)	 0.47
LAVI (ml/m2) Mean(SD)	 22.23(3.93)	 21.49(3.55)	 0.49
Mitral A velocity (cm/s) Mean(SD)	 87.67(14.91)	 65.65(12.17)	 <0.0001
Mitral E velocity(cm/s) Mean(SD)	 61.73(11.21)	 83(16.47)	 < 0.0001
E/A ratio Mean(SD)	 0.7(0.09)	 1.25(0.15)	 < 0.0001
E deceleration time (m/s) Mean(SD)	 177.88(39.63)	 213.72(31.69)	 0.0009
Lat. E` velocity (cm/s) Mean(SD)	 5.7(1.98)	 13.09(1.36)	 < 0.0001
Septal e` velocity (cm/s) Mean(SD)	 4.7(1.77)	 10.76(1.04)	 < 0.0001
Average E/e` ratio Mean(SD)	 13.24(4.04)	 7.10(1.38)	 < 0.0001
TR velocity (m/s) Mean(SD)	 2.88(0.37)	 1.85(0.35)	 < 0.0001

*SD; standard deviation, BMI; body mass index, BSA; body surface area, RA; rheumatoid arthritis, LV IVS; left ventricle interventricular septum, LV PW; left ventricle posterior wall, LVEDd; left ventricular end-diastolic diameter, LVESd; left ventricular end-systolic diameter, EF; ejection fraction, LAVI; left atrial volume index, mitral A velocity; peak late diastolic mitral inflow velocity, mitral E velocity; peak early diastolic mitral inflow velocity, lat. E` velocity; early diastolic velocity of lateral mitral annulus, Septal e` velocity; early diastolic velocity of septal (medial) mitral annulus, TR velocity; tricuspid regurgitation peak velocity, p-value was considered significant at less than 0.05.

DISCUSSION

In the present study, the average age of patients with rheumatoid arthritis (RA) was 39.62 years, aligning closely with the findings of Sharma et al. (41.7 years).[15] However, other studies reported older mean ages, including ABDUL MUIZZ et al. (48.19 years)[16] and Targońska-Stępniak et al. (53.9 years)[17], while Ghaleb et al. observed a younger mean age (33.4 years).[18] Our sample size of 50 RA patients is comparable to that of ABDUL MUIZZ et al.[16], while Crowson et al. included 231 patients[19] and Sitia et al. studied only 22.[20] Female predominance in our study (62%) reflects the well-established pattern seen in RA populations, as documented by Sharma et al., ABDUL MUIZZ et al., and Marasovic-Krstulovic et al.[15,16,21] The mean RA duration in our study was 2.8 years, comparable to that reported by Sitia et al.[23], but shorter than that found by Liang et al.[22] Notably, we found a 40% prevalence of abnormal or indeterminate diastolic function, which is markedly higher than in the general population. For instance, Jamiołkowski et al. reported only 5.4% prevalence in a cohort of 648 individuals using the same diagnostic criteria.[23] This reinforces the observation that diastolic dysfunction is more frequent among RA patients, consistent with other studies such as Almeida et al. and Prasad et al.[24,25] Previous RA studies have reported varying prevalence rates of diastolic dysfunction, ranging from 21% to 59%[8,26], largely due to differences in definitions, sample characteristics, and diagnostic methods. Park et al. used the same criteria as our study and reported a prevalence of 21% based on two or more abnormal parameters, which increased to 40%

when at least one abnormality was considered.[8] Our higher prevalence may reflect demographic or sample size differences. Importantly, our results showed a significant correlation between RA duration and diastolic dysfunction. This is in agreement with Arslan et al., Udayakumar et al., Ghaleb et al., Rexhepaj et al., Liang et al., and Sharma et al., who consistently found longer RA duration to be associated with impaired diastolic function.[15,18,22,27-29] Prospective studies further support these findings. Park et al. followed 158 RA patients and observed an increase in diastolic dysfunction prevalence from 40.7% to 57.9% over 4–6 years.[8] Similarly, Davis et al. noted worsening echocardiographic parameters over time in a comparable cohort.[30] This study has several limitations. First, the small sample size may reduce the statistical power and generalizability of the findings. Second, its cross-sectional design limits the ability to establish causal relationships and is prone to bias. Third, grading of diastolic function was not feasible in some cases due to indeterminate results under strict algorithmic criteria. Additionally, varying definitions of diastolic dysfunction across prior studies complicate comparisons. The potential influence of disease-modifying antirheumatic drugs (DMARDs) on cardiac function was not evaluated. The absence of a control group and the single-center setting also restrict broader applicability.

CONCLUSION

In rheumatoid arthritis population diastolic dysfunction is frequently encountered and its prevalence is positively correlated with disease duration. Further prospective studies with a bigger sample size are recommended to examine the prevalence of diastolic dysfunction and to better understand the relationship between diastolic dysfunction and rheumatoid arthritis duration. Screening for diastolic dysfunction is required in rheumatoid arthritis patients, particularly those with a prolonged illness duration.

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