

Original Research Article

Cardiac function abnormalities in rheumatoid arthritis and its association with duration of disease: a hospital-based case control study

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ABSTRACT

Background: Rheumatoid Arthritis is associated with many extra-articular manifestations including cardiac abnormalities, which increases the risk of morbidity and premature death. Sub-clinical cardiac abnormalities occur many years before their clinically overt manifestations. The objective of the present study is to compare cardiac function abnormality in rheumatoid arthritis patients and healthy controls by echocardiography and to determine its relation with duration of disease.

Methods: A hospital based case control study was conducted at a tertiary care centre of northern India including 70 rheumatoid arthritis patients and 70 controls. All subjects were evaluated by Electrocardiography and Trans-thoracic Echocardiography to determine cardiac function abnormalities.

Results: ECG abnormalities were detected in 30% of RA cases as compared to only 7.1% of controls. Most common ECG abnormality was LV diastolic dysfunction ($p=0.001$), followed by pericardial effusion. A weak positive correlation was found between duration of disease and IVRT ($r=0.329$, $p=0.005$) indicating worsening of cardiac function with increasing duration of disease.

Conclusions: Echocardiographic abnormalities are fairly common among RA patients with LV diastolic dysfunction being most common. Cardiac abnormalities increase with duration and severity of disease.

Keywords: Rheumatoid arthritis, Echocardiography, Diastolic dysfunction, Pericardial effusion

INTRODUCTION

Rheumatoid arthritis (RA) is a progressive, multi-systemic autoimmune disease characterized by chronic inflammation of multiple joints with associated systemic manifestations.¹ Rheumatoid arthritis is known to be the commonest autoimmune inflammatory arthritis among adults.² RA has an estimated worldwide prevalence of 1% among adult population and is an important cause of chronic morbidity.³ In adult Indian population, it has a prevalence of about 0.75%.^{4,5}

RA is associated with many extra-articular manifestations involving multiple organ systems.⁶ Extra-articular manifestations of RA occur in about 40% of patients, either at the beginning or during the course of their disease.⁷ The presence of extra articular manifestations in RA is marker of severe active disease and is associated with increased risk of premature mortality.⁸⁻¹⁰ Long-term survival of patients with rheumatoid arthritis (RA) is shorter than that of the general population.¹¹ Patients of RA have a high risk of morbidity and premature death related to cardiovascular, lung diseases and malignancies.^{12,13}

Occurrence of cardiovascular disease in patients with RA has become a specific focus of attention because of the recognition of role of inflammation in the pathogenesis of atherosclerosis.¹⁴ There is an increased risk of cardiovascular disease in patients with RA, and there may be an increased risk of heart failure and of atrial fibrillation.^{15,16} Among the different causes of death, increased mortality from heart disease has been reported in many studies in patients of RA with high prevalence of congestive cardiac failure.¹⁷

Though clinical myocarditis is infrequent, subclinical myocardial disease is relatively common in patients of RA.¹⁸⁻²⁰ Knowledge of this complication in patients with RA without clinically evident cardiac disease may be important to improve patient survival.

The cardiovascular involvement in rheumatoid arthritis is well-known but there are only few studies available from our country to assess the cardiovascular parameters in RA patients. Since sub-clinical manifestations occur many years before their clinical presentation in the disease, hence the need for early recognition and more aggressive management of the disease, with a view to prevent the aforementioned complications is very important. Hence present study was conducted with the objective to compare cardiac function abnormality in rheumatoid arthritis patients and healthy controls by echocardiography and to determine its relation with duration of disease.

METHODS

A hospital based case control was conducted from April 2017 to April 2019 in the department of General Medicine at one of the tertiary care referral centre of northern India. A total of 70 rheumatoid arthritis patients and 70 controls aged 20 to 60 years were included into the study. Sample size was calculated at 95 % confidence interval and 80% power assuming standard deviation of 0.23 and mean difference of 0.11 of E/A (Early diastolic flow velocity /Late diastolic flow velocity) ratio between rheumatoid arthritis patient and controls.

Patients were classified as having Rheumatoid arthritis based on 2010 American College of Rheumatology/ European League against Rheumatism criteria (cases). 21 Age and gender matched controls were selected from the other hospital attendants. Subjects with Diabetes, hypertension, pre-existing cardiac disease, current pregnancy was excluded from the study. Eligible cases were recruited consecutively till sample size was achieved. An eligible control was recruited after each recruited case.

All subjects were evaluated by a detailed clinical history and clinical examination and were subjected to various lab tests to decide for their eligibility. Electrocardiography (ECG) and Trans-thoracic Echocardiography (TTE) was done for all subjects using the same device and technique under similar standard condition. The pericardial space was evaluated in the parasternal longitudinal axis and sub

costal views and dimensions assessed using 2D echocardiograph.

Systolic function was determined by calculating the left ventricular fractional shortening and ejection fractions according to standard American Society of Echocardiography (ASE) guidelines. In M-mode, LV diameter in end diastole and end systole was determined using the two chamber views. 22 Systolic Dysfunction was defined as Fractional shortening less than 29% and/or ejection fraction less than 50%. Diastolic function indices were determined by pulsed Doppler recording across the anterior leaflet of the mitral valve; with the sample volume located between the tips of the mitral valve leaflets. Primary measurements of mitral inflow included the peak early filling (E-wave) and late diastolic filling (A-wave) velocities, the E/A ratio, deceleration time (DT) of early filling velocity, and the Isovolumetric Relaxation Time (IVRT). Other Parameters seen on Echocardiography were left atria size, left ventricular end systolic and end diastolic dimensions. Ethical clearance was obtained from Institute's Ethical committee prior to initiation of study. Written informed consent was obtained from all subjects prior to initiation of study.

Statistical analysis

Categorical variables were presented as frequency and percentages and were analyzed using Chi square test / Fischer Exact test as applicable. Continuous variables were expressed as mean and standard deviation and were analyzed using unpaired t test. The correlation between two variables was analyzed using Pearson's correlation coefficient and scatter plot. A "p" value less than 0.05 was considered to be statistically significant. All statistical analysis was done using Epi info version 7.2.1.0 statistical software.

RESULTS

A total of 70 RA patients and 70 controls were enrolled in the study. The mean age of RA cases was 45.71 ± 7.54 years. Most of the RA patients were females (72.8%). Most of the patients (91.4%) had disease for <10 years duration (Table 1).

ECG abnormalities were detected in 30% of RA cases as compared to only 7.1% of controls. Left atrium diameter, left ventricular end diastolic / systolic dimension were significantly larger in RA cases as compared to controls. Late diastolic flow velocity (A) was significantly more in RA cases. E/A ratio as well as E/e' ratio was both significantly lower in RA cases. Deceleration time (DT) was significantly more in RA cases as compared to controls. IVRT was significantly longer in RA cases as compared to controls ($p=0.04$). Left ventricular internal diameter end diastole (LVIDes) and Left ventricular internal diameter end systole (LVIDed) were both significantly more in RA patients.

Table 1: Demographic characteristics of study subjects.

	Case	Control	P value
Age (years)	45.71±7.54	45.63±8.26	0.680 (NS)
Gender			
Female	51 (72.8%)	51 (72.8%)	0.849
Male	19 (27.1%)	19 (27.1%)	(NS)
Duration of disease			
<5 years	31 (44.3%)		
>5-10 years	33 (47.1%)		
>10 years	6 (8.5%)		

Mean pulmonary artery pressure was also significantly more in RA case with five RA cases showing pulmonary artery hypertension Left ventricular diastolic dysfunction was significantly more in RA patients. (Table 2). Among RA patients, ST changes was the most common ECG abnormality (12.4%) followed by Right bundle branch block (Table 3).

A weak positive correlation was found between duration of disease and IVRT ($r=0.329$, $p=0.005$) indicating worsening of cardiac function with increasing duration of disease (Figure 1). Significant association was seen between higher LVDD grade and duration of disease (Table 4). LV Diastolic dysfunction was the most common echocardiographic finding among RA patients (44.2%) followed by pericardial effusion (15.2%). Pulmonary hypertension was seen in 7.1% RA patients. (Table 5)

Table 2: Comparison of echocardiographic and ECG findings.

	Case	Control	P value
Left Atrium Diameter (mm)	25.8±4.8	27.7±5.3	0.03 (S)
Left Ventricular end Diastolic Dimension (mm)	44.2±6.9	42.1±2.4	0.02 (S)
Left Ventricular end Systolic Dimension (mm)	29.3±5.9	26.2±5.2	0.001 (S)
Ejection Fraction (%)	56.6±3.1	57.2±2.8	0.24 (NS)
Early Diastolic Flow Velocity, E (cm/sec)	83.68±16.52	87.95±9.7	0.06 (NS)
Late Diastolic Flow Velocity, A (cm/sec)	81.19±11.9	75.43±9.6	0.002 (S)
e' Velocity (cm/sec)	9.167±1.04	9.486±0.87	0.045 (S)
E / e' Ratio	9.04±1.59	9.56±0.89	0.02 (S)
E/A Ratio	1.048±0.27	1.344±1.19	0.044 (S)
DT (msec)	190.6±27.3	182±21.6	0.04 (S)
Isovolumic Relaxation Time (ms)	79.6±7.9	77.3±5.3	0.04 (S)
LVIDes (mm)	29.3±5.9	26.2±5.2	0.001 (S)
LVIDed (mm)	44.2±6.9	42.1±2.4	0.025 (S)
Pulmonary Artery Pressure (mmhg)	25.6±5.54	20.1±20.1	0.001 (S)
PAH	5 (7.1%)	0	0.755 (NS)
LVDD Absent	39 (55.7%)	67 (95.7%)	
1st grade	25 (35.7%)	3 (4.3%)	<0.001 (S)
2nd grade	6 (8.6%)	0	
ECG			
Normal	49 (70%)	65 (92.9%)	0.001 (S)
Abnormal	21 (30%)	5 (7.1%)	

Table 3: ECG abnormalities in rheumatoid arthritis patients.

ECG	Number of cases (n=70)	Percentage
Right axis deviation	1	0.7
Left axis deviation	2	2.9
RBBB	5	7.1
Sinus bradycardia	0	0
Sinus tachycardia	4	5.7
First degree heart block	0	0
ST-T changes	8	12.4
Normal	50	71.4
Total	70	100

Table 4: LVDD grade in relation to duration of disease.

Duration of disease	LVDD grade					
	Absent		Grade I		Grade II	
	N	%	N	%	N	%
<5 years	12	30.8	1	4	0	0.0
5-9 years	27	69.2	22	88	1	16.7
≥10 years	0	0.0	2	8	5	83.3
Total	39	100.0	25	100	6	100

Chi-square = 46.870 with 4 degrees of freedom; $p < 0.001$ (S)

Table 5: Frequency of echocardiographic findings among RA patients.

Echo	Number of cases (n=70)	Percentage
Normal	39	55.7
LV diastolic dysfunction	31	44.2
Pericardial effusion	10	15.2
Pulmonary hypertension	5	7.1
Valvular abnormality	0	0

DISCUSSION

Present study included RA patients ranging from 21 years to 60 years with mean age of 45.71 ± 7.54 years which was comparable to other studies.²³⁻²⁵ most patients with rheumatoid arthritis were females with a male to female ratio of 1:3. This female preponderance was supported by findings of other studies reporting female patients to be 3.3 to 6.5 times higher as compared to male patients.²⁴⁻²⁸

Most of the rheumatoid arthritis patients had normal ECG findings (70%). Various past studies also reported normal ECG in most RA patients.^{29,30} Most common ECG abnormality was non-specific ST-T changes present in 12.4% cases which was comparable to findings of Raminderpal Singh et al in which 8.33% cases had ST-T changes.²⁹ Masooleh et al and Asai K et al found 15% and 20.9% had ST changes respectively.^{25,30} Second most common finding in our study was right bundle branch block (7.1%) which was comparable to findings of other studies.^{25,29,30} Sinus bradycardia was not found in any patient as was similarly reported by other studies.^{25,29}

Most common echocardiographic abnormality was LV diastolic dysfunction found in 42.2% cases of rheumatoid arthritis as compared to only 4.3% among controls. Maoiné et al and Juanatey et al also revealed significantly higher proportion of diastolic dysfunction in RA patients as compared to controls.^{31,32} Left ventricular diastolic dysfunction is usually attributable to common structural abnormalities, such as hypertrophy or interstitial fibrosis, and impaired myocyte relaxation resulting from ischemia.³³ Various other past studies have reported proportion of LVDD ranging from 25% to 57% in rheumatoid arthritis patients.^{23-25,34} Higher proportion of

LVDD in some studies could be due to longer duration of disease among cases. LVDD was found to be significantly associated with duration of disease in present study.

Also, severity of LVDD was significantly associated with duration of disease. Effect of duration of disease was also indicated by the positive correlation between duration of disease and IVRT seen in present study ($p < 0.001$). Levendoglu et al and Kumar also reported significant correlation between IVRT and disease duration ($p < 0.001$).^{27,35}

Second most common finding in present study was pericardial effusion present in 15.2% of rheumatoid arthritis cases which was comparable to findings of other studies.^{29,34} Pulmonary hypertension was present in 7.1% cases and none of the control subjects in our study. Past studies have also reported that pulmonary hypertension was more common in patients with rheumatoid arthritis.³⁶ It was as high as 31% in the study by Dawson et al, probably because of inclusion of patients with longer disease duration in their study.³⁷

Left ventricular diastolic diameter was significantly larger in RA cases in present study. Rudominer et al also reported similar findings. IVRT was significantly longer in RA cases as compared to controls as was similarly reported by Mustonen et al.^{38,39} Kumar et al also reported significantly longer IVRT among RA cases as compared to controls. E/A ratio was also significantly lower in RA cases as compared to controls.²⁷ Franco et al and Kumar et al also reported E/A ratio to be significantly lower in RA cases.⁴⁰ Late diastolic flow velocity was significantly higher in RA cases as compared to controls. Findings of study by Kumar et al support these results.⁴¹

Cardiac disease is often clinically silent and is rarely a severe life-threatening complication in RA. Still, studies like Rincon et al observed that the higher incidence of cardiovascular complications in these patients was independent of the influence of traditional cardiovascular risk factors.⁴²

CONCLUSION

About half of the patients with Rheumatoid arthritis had echocardiographic abnormality or ECG changes. Most common echocardiographic abnormality was LV diastolic dysfunction, followed by pericardial effusion and most common ECG change was ST-T changes. A positive correlation was seen between echocardiography findings with the duration and severity of disease. Periodic screening the patients of rheumatoid arthritis specially for those with longer duration of disease could be useful for early identification and treatment of any cardiovascular abnormalities and thus reduce chronic morbidity and premature mortality associated with rheumatoid arthritis.

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