

## Study of Cardiovascular Manifestations of Rheumatoid Arthritis and Correlation with Disease Duration and Severity

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### Abstract

**Aims and objectives:** Rheumatoid arthritis is a systemic chronic inflammatory disorder of unknown etiology that primarily involves synovial joint, and secondarily involves various organ systems. Involvement of cardiovascular system is well known but the disease is mainly subclinical. The study was conducted to see the prevalence of various cardiovascular manifestations in rheumatoid arthritis and correlate them with disease duration and severity.

**Material and methods:** In this cross-sectional study, 60 patients of rheumatoid arthritis attending outpatient and inpatient department at Rajindra Hospital and Government Medical College, Patiala were included. They were thoroughly investigated for cardiovascular abnormalities.

**Results:** The mean age of the patients was  $45.37 \pm 10.96$  years. Females outnumbered the males in this study. The mean duration of the disease was  $4.62 \pm 2.49$  years. Of all patients with cardiovascular abnormalities, 40% patients (24 cases) had echocardiographic abnormality, 40% had hypertension and 11.67% had ECG abnormality. The most common echocardiographic abnormality was LV diastolic dysfunction, followed by pericardial effusion. There was significant correlation of these manifestations with disease duration and severity.

**Conclusion:** The cardiovascular abnormalities showed a direct relationship with the increasing duration as well as severity of the disease. Hence, it is important to screen the patients of rheumatoid arthritis for these abnormalities so that early identification and treatment can be provided.

**Key words:** Echocardiography, ECG, Pericarditis, RA

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### I. Introduction

Rheumatoid arthritis is the most common autoimmune inflammatory arthritis in adults.<sup>1</sup> The disease is three times more frequent in women than men but sex difference diminishes in older age groups.<sup>2</sup> It primarily involves synovial joint, typically symmetrical in nature. The major clinical manifestations of RA are divided into, articular and extra-articular manifestations. Extra articular manifestations occur in about 40 percent of patients over a lifetime of disease.<sup>3</sup> The relationship between RA and cardiovascular disease has become a particular focus of attention because of the increased recognition of role of inflammation in the pathogenesis of atherosclerosis.<sup>4</sup> The various cardiovascular manifestations are pericarditis, myocarditis, coronary artery disease, heart failure, atrial fibrillation, arteritis and hypertension. Out of all, the most common cardiac complication of RA is pericarditis. It is found in 30–50% of autopsy cases and in up to 30% by echocardiography. Less than 10 percent of patients have a clinical episode of pericarditis.<sup>5,6</sup>

Subclinical myocardial disease is relatively common in patients of RA, despite the rarity of clinical myocarditis and infrequency of asymptomatic left ventricular dysfunction.<sup>7,8</sup> The RA-associated cardiomyopathy may be the result of focal non-specific, diffuse necrotizing or granulomatous myocarditis. These entities are histological diagnoses, which may be found in 3–30% of RA patients in postmortem studies.<sup>9</sup> They are usually associated with active articular disease and with other nonarticular manifestations.<sup>10</sup> It has been found that left ventricular diastolic dysfunction and pulmonary hypertension was more common in patients with rheumatoid arthritis.<sup>11,12</sup> Hypertension is an important cardiovascular risk factor in RA. The reported prevalence of HT among patients with RA varies from 3.8% to 73%. Several studies have demonstrated that it associates with subclinical atherosclerosis.<sup>13,14</sup> Chronic inflammation promotes the endothelial dysfunction, leading to decreased

blood vessel compliance and atheroma formation. Patients with RA who are positive for anti-cyclic citrullinated peptide antibodies (anti-CCP) have higher subclinical atherosclerosis than those who are not.<sup>15</sup> Markers of systemic inflammation confer a statistically significant additional risk for cardiovascular death among patients with RA, even after controlling for traditional CV risk factors and comorbidities.<sup>16,17</sup> The C-reactive protein concentration at baseline is an important predictor of subsequent death from cardiovascular events in patients with new onset inflammatory polyarthritis, and is independent of other factors of disease severity.<sup>18</sup> Since sub-clinical manifestations occur many years before their clinical presentation, hence the need for early recognition and more aggressive management of the disease, with a view to prevent the aforementioned complications is very important. The study was conducted to see the cardiovascular manifestations in rheumatoid arthritis and correlate them with the disease duration and severity.

## II. Aims And Objectives

- 1) To study cardiovascular manifestations of rheumatoid arthritis.
- 2) To correlate cardiovascular manifestations with duration and severity of rheumatoid arthritis.

## III. Materials And Methods

In this cross-sectional study, 60 cases of rheumatoid arthritis both from outpatient and inpatient department at Government Medical College and Rajindra Hospital, Patiala were included.

### Inclusion criteria:

Patients more than 18 years of age who fulfilled the revised ACR/EULAR criteria for RA were included in the study.

### Exclusion criteria:

1. Patients with age <18 years.
2. Patients suffering from congenital heart disease, ischaemic heart disease, valvular heart disease with rheumatic etiology, hypertension, pregnant females.
3. Patients with serum creatinine > 3.0 mg/dl or creatinine clearance < 30 ml/minute.
4. Patients with any immunosuppressive conditions or active infection.

Rheumatoid arthritis was diagnosed by using 2010 American College of Rheumatology/ European League Against Rheumatism Criteria.<sup>19</sup> Severity of the disease was assessed according to American College of Rheumatology revised criteria for classification of functional status in rheumatoid arthritis.<sup>20</sup>

Various investigations like hemoglobin, total leukocyte count, differential leukocyte count, random blood sugar, urine examination, renal function tests, ESR, CRP, RA factor, X-ray of hands, Chest X-ray, ECG and echocardiography were done in the patients. ECG was examined specifically for the presence of ST-T changes, QT interval, prolonged PR interval, atrial fibrillation, right bundle branch block, Sinus Tachycardia and Sinus bradycardia. Transthoracic echocardiography was performed according to a standardized protocol and scan planes including the 4-chamber apical view, 2-chamber apical view, left parasternal long-axis view, and left parasternal short-axis view, recording the four cardiac valves, the great vessels, the cardiac chambers, and the interventricular and interatrial septa. It was done to look specifically for the presence of left ventricular diastolic dysfunction, pericardial effusion, mitral regurgitation, tricuspid regurgitation, pulmonary hypertension, and rheumatoid nodules. Any other abnormality when present was also taken into account.

## IV. Results

In the present study, the range of age was 21-70 years with the mean age of  $45.37 \pm 10.96$  years. Majority of the cases were in the age group of 41-50 years. Out of 60 patients, 50 were females constituting 83.33% of all. Males comprised of 16.67% of cases. The mean duration of the disease was  $4.62 \pm 2.49$  years. 30% of patients (18 cases) had duration of RA in the range of 5-10 years. The mean number of large joints involved was  $1.42 \pm 1.19$ . Average number of small joints involved was  $21.97 \pm 6.19$ . Majority of the patients 46.67% (28 cases) had class 2 functional status, whereas 17 patients (28.33%) had class 1 functional status. 25% of the patients had class 3 functional status.

ECG changes were present in 11.66% patients (7 cases), of which non-specific ST-T changes were present in majority (5 cases) of the patients, followed by right bundle branch block which was present in 3.33% of patients. 53 patients (88.34%) had a normal ECG.

**Table 1** shows distribution of cases on the basis of ECG findings

ECG	Number of cases (n=60)	Percentage (%)
RBBB	2	3.33%
Sinus Bradycardia	0	0%
Sinus Tachycardia	0	0%

First Degree Heart Block	0	0%
ST-T Changes	5	8.33%
Normal	53	88.34%
Total	60	100%

Echocardiography was normal in 32 (53.33%) cases. In rest of the patients the most common echocardiographic abnormality was Left Ventricular diastolic dysfunction, present in 15 (25%) patients, followed by pericardial effusion in 8 (13.33%) patients. Among the 8 cases with pericardial effusion, 2 had moderate pericardial effusion and 6 had minimal pericardial effusion. 1 patient had pulmonary hypertension.

**Table 2** shows distribution of cases on the basis of echocardiographic findings

Echo findings	Number of cases (n=60)	Percentage (%)
Normal	32	53.33%
LV Diastolic Dysfunction	15	25%
Pericardial Effusion	8	13.33%
Pulmonary Hypertension	1	1.67%
Valvular abnormality	0	0%
Total	60	100%

Majority of the patients with ECG and echocardiographic abnormalities were in the age group of 41-50 years, of which majority were females 26.67% and 3.33% were males. 24 patients out of 60 had hypertension accounting for 40% of the patients.

Among all patients with cardiovascular involvement, 40% patients (24 cases) had echocardiographic abnormality. Hypertension was present in 24 cases, whereas ECG abnormality was present in 11.67% (7 cases) patients.

**Table 3** shows distribution of cases on the basis of cardiovascular involvement

Cardiovascular involvement	Number of cases	Percentage
Echo abnormality	24	40%
HTN	24	40%
ECG abnormality	7	11.67%

The mean systolic and diastolic blood pressure in the patients was 138.07mmHg and 87.83mmHg, respectively. The mean value of different variables of echocardiography was depicted. The mean ejection fraction was 65.95% and the mean E/A ratio was 1.07.

**Table 4** shows distribution of clinical and echo variables in patients of RA

		RANGE	MINIMUM	MAXIMUM	MEAN±SD
Systolic Blood Pressure	SBP	<140	122.00	152.00	138.07±8.60
Diastolic Blood Pressure	DBP	<90	80.00	98.00	87.83±5.74
Left Atrial Diameter	LAD	2-4	2.20	3.90	3.15±0.39
Aortic Root Diameter	Aortic Root Diameter	2-3.7	2.30	4.30	2.99±0.40
Left Ventricle Internal Diameter in Diastole	LVIDDd	3.5-5.5	3.40	5.20	4.23±0.40
Left Ventricle Internal Diameter in systole	LVIDs	2.4-4.2	2.20	4.10	3.37±0.49
Inter Ventricular Septum Thickness	IVST	0.7-1.1	.50	1.10	0.84±0.14
Left Ventricular Posterior Wall Diameter	LVPWD	0.7-1.0	.60	1.30	0.81±0.18
Ejection Fraction	EF%	62-80%	54.00	84.00	65.95±7.01
E-M- Mode Measurement of Peak Early Flow	E	0.6-1.3	.48	1.18	0.66±0.11
A- M- Mode Measurement of Peak Early Flow Due to Atrial Contraction	A	0.6-1.3	.36	1.18	0.65±0.19
E/A	E/A		.53	1.70	1.07±0.31

Statistical analysis showed a significant (p=0.029) correlation of echocardiographic findings with duration of disease as well as with severity of the disease(p=0.032). The current study also showed a significant (p <0.05) correlation of ECG abnormalities with the duration of the disease and severity of the disease (p=0.037). The mean duration of disease in patients with echocardiographic abnormalities was 6.42±2.19

whereas in patients without echo abnormality was  $3.42 \pm 1.90$ , which was statistically highly significant ( $p=0.001$ ). Statistical analysis showed that the mean functional stage, mean systolic and diastolic blood pressure was statistically highly significant ( $p=0.001$ ) in patients with echo abnormalities as compared to patients without echo abnormality. Various variables of echocardiography were compared in patients with and without abnormalities. The only variable that was found to be statistically significant was E/A ratio ( $p=0.001$ ), the mean of which was  $0.91 \pm 0.3$  in patients with echo abnormalities and  $1.19 \pm 0.26$  in patients without echo abnormalities.

## V. Discussion

The present study was undertaken to study various cardiovascular manifestations in the patients of rheumatoid arthritis who attended outdoor or were admitted in the Department of Medicine, Rajindra Hospital, Patiala. They were evaluated clinically, along with relevant investigations. The mean age of the study participants was  $45.37 \pm 10.96$  years which was comparable to study conducted by Masooleh SI et al<sup>21</sup> i.e.  $49.7 \pm 11.56$ . In the studies conducted by Vizzardiet al<sup>22</sup>, Liang KP et al<sup>23</sup> and Raof RM et al<sup>24</sup>, the mean age was  $60.4 \pm 12.2$ ,  $60.5$  and  $53.31 \pm 2.14$ , respectively. The male: female ratio in the present study was 1: 5. The sex ratio in the studies conducted by Masooleh SI et al<sup>21</sup>, Vizzardi E et al<sup>22</sup>, Raof RM et al<sup>24</sup>, and Guedes et al<sup>25</sup> was 1:3.34, 1:3.4, 1:6.8, and 1:6.5, respectively. The mean duration of disease was  $4.62 \pm 2.49$  years. The mean disease duration in studies conducted by Vizzardi E et al<sup>22</sup>, Guedes et al<sup>25</sup> and Dawson et al<sup>26</sup> was found to be  $10.6 \pm 7.1$ ,  $11 \pm 8.7$ , and  $12.7 \pm 7.99$  respectively. The number of hypertensive patients in the current study was found out to be 40% which is comparable to study conducted by Vizzardi E et al<sup>22</sup> in which it was 51%. The study conducted by Raof RM et al<sup>24</sup> showed lesser number of hypertensive patients, accounting 20% of all.

In our study, a normal ECG was present in 88.34% cases. In the studies conducted by Masooleh et al<sup>21</sup> and Asai K et al<sup>27</sup>, a normal ECG was seen in 68% and 56.32% cases, respectively. The most common electrocardiographic abnormality detected in our study was non-specific ST-T changes, which was present in 8.33% cases which was comparable to Masooleh SI et al<sup>21</sup> in which 15% cases had ST-T changes. In the study by Asai K et al<sup>27</sup>, 20.9% cases had the same change. Second most common finding in our study was right bundle branch block which was found in 2.33% cases compared to Masooleh SI et al<sup>21</sup>, in which it was 4% cases.

In our study, echocardiographic abnormality was present in 40% cases. The most common abnormality was Left Ventricular diastolic dysfunction which was present in 25% cases, comparable to 14.54% in study conducted by Raof RM et al<sup>24</sup>. Second most common abnormality in our study was pericardial effusion which was found in 13.33% which was comparable to the study conducted by Selcuket al<sup>28</sup> in which it was 15%. High prevalence of this complication (47%) was found in study done by Masooleh SI et al<sup>21</sup>. Pulmonary hypertension was present in 1.67% cases in our study, whereas it was as high as 31% in the study by Dawson et al.<sup>26</sup>

## VI. Conclusion

The present study unmasked some important and relevant information about the impact of rheumatoid arthritis on cardiovascular system. The study is in concordance with the previous studies done on similar subject. A positive correlation between ECG and echocardiography findings with the duration and the severity of the disease is found. Hence, it is advisable to screen the patients of rheumatoid arthritis for cardiovascular abnormalities so that early identification and treatment can provide a healthier life ahead.

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