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# Estimation of Ten - Year Cardiovascular Disease Risk in Patients with Rheumatoid Arthritis using QRISK 3

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**Abstract:** ***Aim**: This study was initiated to assess the 10 - year cardiovascular disease risk in patients with Rheumatoid arthritis attending Rheumatology outpatient department in a tertiary care hospital in Kerala by using QRISK 3. **Methods**: 80 Rheumatoid arthritis patients between 25 to 84 years of age were selected from rheumatology outpatient department (OPD) at SK Hospital, Trivandrum. After 12 hours of fasting, venous blood was taken for total serum cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL), high density lipoproteins (HDL) and ESR. The disease outcome measure in RA patients was assessed by most validated composite tool entitled DAS 28. Much attention has been drawn to assess the cardiovascular risk in RA patients and was estimated using QRISK 3 online calculator. This gave us 10 - year cardiovascular risk in RA patients. The study appraised the involvement of disease activity in cardiovascular risk in RA patients and was carried out by multiple regression analysis. **Results**: The study included 80 rheumatoid arthritis patients with a mean age (in years) of 60±11. It has been found that 86.25% of the study population were female and the remaining were male. Presence of autoantibodies in RA patients were examined and the results showed that 73.7% of them were seropositive (either ACCP or RF positive). The study considered various comorbidities among the study population and the commonest comorbidity in RA patients was hypertension found in 41 (51.2%) patients.31 (38.7%) patients were overweight with mean body mass index (BMI) of 24.99 ± 3.45. Diabetes was found in 28 (35%) patients.53 (66.3%) had high low - density lipoprotein (LDL) whereas 33 (41.3%) had high total cholesterol (TC) and 11 (13.8%) had high triglyceride levels.8 (10%) patients were smokers. The current research confirmed the findings about cardiovascular risk in RA patients by means of QRISK 3 and stated that 36 (45%) patients had high cardiovascular risk, 21 (26.3%) had moderate risk and 23 (28.7%) had low cardiovascular risk. Multiple regression analysis accomplished the aim of examining the involvement of disease activity in QRISK 3 score and the results outlined the influence of high disease activity in increasing the cardiovascular risk. **Conclusion**: Rheumatoid arthritis patients encounter high cardiovascular risk and the high disease activity in RA patients intensify their cardiovascular risk in a significant level. Therefore, interventions to manage the conventional cardiac risk factors must be combined with the remedies to handle the disease activity. Consequently, attainment of satisfiable range of disease outcome could bring down a remarkable change in the cardiovascular risk outcome.*

**Keywords:** Cardiovascular disease; QRISK 3; Rheumatoid Arthritis (RA)

## 1. Introduction

Rheumatoid arthritis (RA) is an autoimmune disease, which mainly affects small and large joints, causing progressive damage and permanent disability, if not treated on time. In addition to this, extra articular manifestations like interstitial lungs disease, vasculitis, cardiovascular events etc. are the remaining key features associated with the disease. Treatment during the window period aids in reversing the signs and symptoms and prevents additional damages. So, early diagnosis and initiation of treatment is the main key in RA management.

The worldwide prevalence of RA is about 0.24% and its annual incidence in the United States and other western nations of northern Europe are about 40 per 100, 000 persons. ([5, 20, 38]) Prevalence of RA in adult Indian population is about 0.75%.

Several studies agree that patients with RA compared with the general population have an increased risk of cardiovascular events. Study by Sunjoo Boo et al., detailed that the RA patients are twice as likely to develop CVD as those without RA. Additional researches fabricated by Muhammed et al., and Alper et al., shared similar findings in their works.

Even though the risk of CVD is higher in RA patients, calculating their CVD risk is quite impractical in a busy Rheumatology OPD. Usually, the risk of CVD is assessed by conventional cardiovascular risk factors like lipid profile. This set of conventional risk factors can't be considered as a functional marker in rheumatoid arthritis patients. This is because of the motive that RA patients undergo a phenomenon titled lipid paradox, attributable to standard lipid profile.

This phenomenon brings about a paradoxical association between TCh and LDL levels, as well as TCh/HDL and LDL/HDL ratios and cardiovascular disease in rheumatoid arthritis. Despite the standard lipid profile, this paradoxical association specifies the increased cardiovascular events in the rheumatoid arthritis patients. Significant interactions between LDL and ESR is considered as the core reason for the cardiovascular risk in rheumatoid arthritis and is thought to be confounded by the inflammation in rheumatoid arthritis. [(5)]

As these conventional risk factors are ineffective in assessing the cardiovascular risk in rheumatoid arthritis patients, composite risk assessment tools have to be exploited to appraise their risk of cardiovascular events. Distinct composite risk assessments tools are accessible to assess the cardiovascular risk. In particularly, SCORE, Framingham risk score, Reynolds risk score, QRISK 3 etc. Selection of the most accurate risk assessment tool influences the CVD risk stratification in patients with RA. For that reason, our study has employed QRISK 3 for the cardiovascular risk evaluation in RA patients. QRISK 3 is a validated risk assessment tool and its usefulness in risk estimation was proven by several studies and thus we decided to estimate the cardiovascular

risk in current study population through QRISK 3. [45] Risk scores assessed by QRISK 3 give information on CVD risk of an individual RA patient along with their relative risk.

Several studies have assessed the cardiovascular risk in RA patients, but the estimated risk was not quantified in any of the studies and thus the current investigation has tried to compute it. Estimation of the cardiovascular disease risk at an early stage could help us to construct interventions to avert the risk and this could enable us to change the final outcome. By taking all these objectives into consideration, our study was defined to determine the 10 - year cardiovascular disease risk in Rheumatoid Arthritis patients, attending Rheumatology outpatient department in a tertiary care hospital by using QRISK 3.

## 2. Subjects & Methods

This is a cross sectional observational study conducted in the Rheumatology department of SK Hospital, Kerala. Approval was obtained from the institutional review board. Patients were selected randomly and informed written consent was collected from them. The duration of the study was six months (from 1st Jan 2022 to 30th Jun 2022).80 patients diagnosed as case of RA based upon ACR 2010 criteria and between 25 to 84 years were investigated. Patients with other inflammatory diseases, female patients on oral contraceptives, pregnant women, patients with familial dyslipidaemia or diseases known to cause dyslipidaemia and patients with moderate to severe CKD were kept out from the study. Patients were evaluated at baseline and followed up at their review period. Demographic details of the patients including age, gender, duration of the disease, medications used were enumerated in the study proforma. Previous history of hypertension, diabetes, CAD, smoking, dyslipidaemia and stroke was gathered from the patients. Blood pressure was measured using digital blood pressure monitor.

Assessment of disease activity in RA patients is a nationally endorsed quality measure, which interprets how well the RA is being controlled. Wide varieties of composite tools are available to estimate the disease activity. Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS), Disease Activity Score 28 Joints (DAS28 - ESR/CRP), Patient - Derived DAS28 are some of the examples of the disease activity assessment tools. Current study tested the disease activity in RA patients using the most validated tool, i. e., DAS - 28. DAS stands for the disease activity score and the number 28 refers to the 28 joints that are examined in the disease activity assessment. At first visit, disease activity was assessed clinically by noting number of tender joints (TJ), swollen joints (SJ) and patient global health (PGH). Blood sample was drawn for fasting lipid profile and erythrocyte sedimentation rate (ESR).

Body mass index was measured using the BMI formula i. e., weight in kilograms/height in meter. Cardiovascular risk prognosis was done by means of QRISK 3. QRISK 3 score was calculated by using patient's age, sex, ethnicity and other clinical information like smoking status, diabetes status, atherogenic ratio, systolic blood pressure, BMI etc. This gave a 10 - year cardiovascular risk in each RA patient (low risk: less than 10%, moderate risk: 10% to 20% or high risk more than 20%).

The database was developed in Excel and exported to SPSS 19.0 program. Statistical analysis involved the evaluation of normality of quantitative variables. All the categorical variables like gender, DM, hypertension etc., were summarised using frequency and percentages. Correlation between QRISK 3 and lipid profile was studied to analyse the influence of lipid profile in QRISK 3. QRISK 3 risk score was computed by enumerating several parameters into the QRISK 3 online calculator. Consequently, it is strenuous to address the individual involvement of these parameters in computed QRISK 3 score. But the current study has to acknowledge the influence of RA associated parameters like disease activity in QRISK 3 score. Thus, the proposed study performed multiple regression analysis to assess the involvement of disease activity in augmenting the cardiovascular risk.

## 3. Results

The study evaluated 80 RA patients with a mean age (in years) of 60±11. It has been found that 86.3% of the study population were female and the remaining were male. Presence of autoantibodies in RA patients were examined and the results showed that 73.7% of them were seropositive (either ACCP or RF positive).10% of the patients had an extra - articular manifestation (pulmonary involvement – interstitial lungs disease). Disease outcome measure was assessed by DAS - 28 and patients were stratified into 3 categories and the findings demonstrated that 59 (72.5%) patients had moderate to severe disease activity, 7 (8.7%) had mild disease activity and 14 (17.5%) were in remission.36.25% of the study population had a disease duration of more than 6 years. In addition to the basic characteristics of the study population the data derived co - morbidities established in RA patients (table 1). The commonest comorbidity in RA patients was hypertension found in 41 (51.2%) patients.31 (38.7%) patients were manifested as overweight. Another exceptional comorbidity was Diabetes and was detected in 28 (35%) patients. The study had underlined lipid profile alterations seen in RA patients and the atypical changes were derived in the analysis. According to which 53 (66.3%) had high low - density lipoprotein (LDL) whereas 33 (41.3%) had high total cholesterol (TC) and 11 (13.8%) had high triglyceride levels. Smoking being one of the most puzzling and complex risk factors for CVD, the proposed study yielded 8 (10%) patients as smokers.

**Table 1:** Co - morbidities in RA patients

| Variables | Number and percentages |
|---|---|
| HTN | 41 (51.2%) |
| DM | 28 (35%) |
| CAD | 15 (18.8%) |
| DLP | 27 (33.8%) |
| Stroke | 3 (3.8%) |
| Smoking | 8 (10%) |
| **HIGH BMI** | |
| Overweight = 25 - 30 | 31 (38.7%) |
| Obese = above 30 | 6 (7%) |
| **LIPID PROFILE** | |
| LDL (High) | 53 (66.3%) |
| TC (High) | 33 (41.3%) |
| TG (High) | 11 (13.8%) |
| HDL (Low) | 15 (18.75%) |

Another promising finding of the study deals with risk quantification in RA patients. Table 2 enlists the risk stratification associating QRISK 3. This prominent finding stratified 36 (45%) patients under high cardiovascular risk category, 21 (26.3%) under moderate risk and 23 (28.7%) under low cardiovascular risk category.

**Table 2:** Stratification of risk associating QRISK 3

| Cardiovascular risk | Number (Percentage) |
|---|---|
| Low (<10%) | 23 (28.7%) |
| Moderate (10 - 20%) | 21 (26.3%) |
| High (>20%) | 36 (45%) |

Table 3 highlights the Comparison of Lipid parameters between different disease activity score categories (DAS 28). These findings were assessed to evaluate the lipid profile alterations confounded by the inflammation, being a marker of disease activity in RA patients. No significant difference was observed in the lipid parameters between different disease activity categories, except for the TC/HDL ratio showing a negative correlation.

**Table 3**

| | TC | HDL - C | LDL - C (mg/dl) | VLDL (mg/dl) | TG (mg/dl) | TC/HDL | DAS - 28 |
|---|---|---|---|---|---|---|---|
| TC | 1.000 | 0.253 | 0.795 | 0.228 | 0.223 | 0.336 | 0.053 |
| HDL - C | 0.253 | 1.000 | - 0.121 | - 0.142 | - 0.328 | - 0.766 | 0.061 |
| LDL - C (mg/dl) | 0.795 | - 0.121 | 1.000 | 0.169 | 0.116 | 0.538 | 0.067 |
| VLDL (mg/dl) | 0.228 | - 0.142 | 0.169 | 1.000 | 0.528 | 0.256 | - 0.052 |
| TG (mg/dl) | 0.223 | - 0.328 | 0.116 | 0.528 | 1.000 | 0.487 | - 0.064 |
| TC/HDL | 0.336 | - 0.766 | 0.538 | 0.256 | 0.487 | 1.000 | - 0.028 |
| DAS - 28 | 0.053 | 0.061 | 0.067 | - 0.052 | - 0.064 | - 0.028 | 1.000 |

**Correlation between lipid profile and disease activity**

Table 4 shows the relationship between QRISK 3 and various other independent variables. Distinct independent variables make it hard to analyse the individual participation of each variable in QRISK 3 score. For that reason, multiple regression analysis was performed to address the difficulty in evaluating the role of RA associated parameters like disease activity in QRISK 3. Multiple regression analysis was used to accomplish the aim of examining the involvement of disease activity in QRISK 3 score and the results outlined the evidence to depict the involvement of high disease activity in augmenting the cardiovascular risk in RA patients with a p value =0.05

**Table 6:** Multiple regression (Significant codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '. ' 0.1 ' ' 1)

| Coefficients | Estimate | Std. Error | t value | P value | |
|---|---|---|---|---|---|
| Intercept | -47.54522 | 12.44958 | -3.819 | 0.000328 | *** |
| Age (years) | 0.94129 | 0.09273 | 10.151 | 1.78e - 14 | *** |
| Gender | 7.95248 | 2.70158 | 2.944 | 0.004659 | ** |
| BMI | -0.08974 | 0.26088 | -0.344 | 0.732088 | |
| Systolic blood pressure | 0.12077 | 0.05233 | 2.308 | 0.02459 | * |
| Diastolic blood pressure | -0.1083 | 0.07721 | -1.403 | 0.166076 | |
| Diabetes mellitus | 10.25801 | 1.99772 | 5.135 | 3.44e - 06 | *** |
| Hypertension | 1.89264 | 1.79984 | 1.052 | 0.297364 | |
| Dyslipidaemia | -3.45531 | 1.81838 | -1.9 | 0.06238 | . |
| Coronary artery disease | 8.36622 | 2.66919 | 3.134 | 0.002702 | ** |
| Stroke | -1.97906 | 4.91663 | -0.403 | 0.688779 | |
| DRA | 0.03925 | 0.10479 | 0.375 | 0.709364 | |
| DAS - 28 Mild disease activity | 2.83778 | 3.40055 | 0.835 | 0.407419 | |
| DAS - 28 Moderate disease activity | 2.34798 | 2.30958 | 1.017 | 0.313555 | |
| DAS - 28 High disease activity | 4.42362 | 2.3895 | 1.851 | 0.069223 | . |
| TC | -0.54202 | 1.9155 | -0.283 | 0.778212 | |
| HDL - C | -1.59797 | 2.12978 | -0.75 | 0.456106 | |
| LDL - C | -0.69079 | 2.29542 | -0.301 | 0.764535 | |
| VLDL | 2.57789 | 4.43377 | 0.581 | 0.56321 | |
| TG | 2.64989 | 4.45842 | 0.594 | 0.554586 | |
| TC/HDL | -4.05516 | 2.45765 | -1.65 | 0.104345 | |
| Seropositive | 0.69049 | 1.81898 | 0.38 | 0.705624 | |

## 4. Discussion

In this study, 10 - year cardiovascular risk in patients with RA was assessed by using QRISK 3. At first, we identified several co - morbidities often present in studied group and that definitely are related to a worse cardiovascular prognosis.

Rheumatoid arthritis is a chronic autoimmune disease that affects the synovium and later it can progress into other organs including the cardiovascular system. Along with joint problems, cardiovascular involvement in RA is a major concern nowadays. In their study, Crowson et al, found that the majority of RA patients with angina went undetected, MI patients were less able to get reperfusion therapy, and there was a decreased incidence of primary and secondary cardiovascular disease prevention.

The EULAR recommendations for managing cardiovascular risk in RA patients may assist doctors to recognize that RA is linked to an elevated risk of cardiovascular events. Unfortunately, although being a major source of worry, cardiovascular risk in individuals with RA is frequently overlooked and undertreated.

The current study looked at how statins are used in RA patients and found that many high - risk patients who need statin medication are still left untreated. Estimation of QRISK 3 could help those RA patients with a high cardiovascular risk in receiving preventive therapy at an early stage. Traditional cardiovascular risk factors and RA itself should be actively managed in these individuals.

Our findings demonstrate that RA is more common in middle - aged women, which is verified by another study conducted by Dr. Jaya et al.

By analysing the presence of hypertension in the study subjects, the results showed that majority of the patients had a positive history of hypertension and had high systolic blood pressure values, which is suggestive of stage 2 hypertension, however most were kept untreated.

In a meta - analysis by Boyer et al., the frequency of DM in RA patients was higher than that in the control group (p=0.003); and other studies also found similar findings. [41 - 43] In the present study about 35% of the study population had DM.

Another important co - morbidity studied in this manuscript was dyslipidaemia and about 33.8% of the study population was presented with dyslipidaemia.

In comparison with the general population, patients diagnosed with RA are at a twofold increased risk to suffer a cardiovascular event; and the magnitude of this increase is comparable to the risk of cardiovascular events in patients with type 2 diabetes mellitus. [40] In this study, with an average disease duration of 7.26 years, about 45% of the study population fell into the high cardiovascular risk category.

High disease activity in RA patients is a factor which contributes to the high cardiovascular risk and its significance was confirmed by multiple regression analysis.

Salman et al., discussed that the risk of cardiovascular events increases considerably in patients with RA due to atherosclerosis. This increase in risk cannot be explained completely on the basis of traditional cardiac risk factors. It was an established belief that lipids accumulate in arterial wall to form plaque. But recent researches have clearly revealed that main cause of atherosclerotic plaque is inflammation. Preventive strategies for modifiable cardiac risk factors can help in lowering the chances of cardiovascular events by reducing the possibility of atherosclerosis and treatments to neutralize the immunologic response could reduce the chance of cardiovascular events in RA patients to a remarkable range.

It highlights the importance to create a high awareness of this risk among RA patients and the role of attaining target cholesterol and blood pressure levels in these high - risk patients. Further attention should be paid to optimal cardiovascular risk categorization and its management.

The tools designed to assess cardiovascular risk in the general population, such as the Framingham score, cannot predict the actual cardiovascular risk in RA patients, because, despite the key role of inflammation in the development of atherosclerosis, in clinical practice this factor is overlooked in many stratification tools. [24]

QRISK 3 is an appropriate tool to assess the cardiovascular risk in RA patients of any ethnicity as the calculator consider ethnicity and RA as factors in risk estimation and gives precisely exact score beyond 30% which is not the case with other calculator and could help the clinicians to identify those at risk of developing cardiovascular events and stroke. [7]

We would like to remark that our study is cross sectional which may be a limiting factor, because, it does not make it possible to investigate whether the use of the QRISK 3 accurately predicts the occurrence of future cardiovascular events.

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