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IMPACT OF RHEUMATOID ARTHRITIS ACTIVITY ON CARDIOVASCULAR RISK PREDICTION AND STATIN ELIGIBILITY: A MULTI-SCORE STUDY FROM IRAQ

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ABSTRACT

Background: Cardiovascular disease risk is elevated in rheumatoid arthritis, which is a chronic inflammatory disorder affecting the entire body. Minimizing the occurrence of cardiovascular events in individuals with rheumatoid arthritis requires precise cardiovascular risk evaluation in addition to suitable statin treatment. However, because they do not account for rheumatoid arthritis specific variables, conventional cardiovascular risk calculators may understate risk. **Aim of study:** To evaluate the cardiovascular risk using several methods in rheumatoid arthritis patients, including determining the prevalence of patients who should be on statins and estimate the patients who achieve their lipids targets. **Methods:** A cross-sectional study was conducted on 430 rheumatoid arthritis patients in Baghdad Teaching Hospital during a period of two years from April 2024 till April 2026. Cardiovascular risk was assessed using QRISK-3, ASCVD, and Adjusted Framingham Score. Data on demographics, disease activity (DAS28), clinical, and laboratory variables were collected. Statin eligibility was determined according to each risk tool's thresholds. **Results:** In this study, total eligibility for statins was 33.5%, with percentages varying by risk calculator: 31.6% according to QRISK-3, 22.3% according to ASCVD, and 6.3% according to AFS. With rheumatoid arthritis disease activity, the percentage of patients indicated to take a statin shot grew dramatically, reaching 76.8% of the most active individuals. Female gender, obesity, smoking, corticosteroid use, and high cholesterol were independent predictors of statin therapy. **Conclusions:** Cardiovascular risk assessment in rheumatoid arthritis patients depends heavily on the risk tool used, with QRISK-3 showing greater sensitivity likely due to inclusion of rheumatoid arthritis as a risk factor. Rheumatoid arthritis disease activity is strongly associated with higher cardiovascular risk and statin eligibility. These findings support the need for rheumatoid arthritis specific risk assessment in clinical practice.

KEYWORDS: Rheumatoid arthritis; Cardiovascular risk; QRISK-3; ASCVD, AFS.

INTRODUCTION

In rheumatoid arthritis (RA), an autoimmune disorder that manifests as a systemic chronic inflammatory disease, synovial inflammation and hyperplasia, and an increase in autoantibodies like anti-cyclic citrullinated peptide (anti-CCP) cause destructive arthropathy that worsens over time.[1,2] It affects approximately 0.5–1% of the global population, with a female predominance and peak incidence between the fourth and sixth decades of life.[3] Despite RA's predominance in joints, it can cause a wide range of extra-articular symptoms, such as lethargy, subcutaneous nodules, involvement of the lungs, cardiovascular events, pericarditis, vasculitis, and hematologic abnormalities.[4]

Cardiovascular disease (CVS) is one of the most clinically important extra-articular complications of RA and a major contributor to premature death. Compared

with the general population, patients with RA carry an estimated 1.5- to 2-fold higher cardiovascular risk (CVR).[5] Chronic inflammation independently promotes endothelial dysfunction, oxidative stress, arterial stiffness, plaque instability, and atherogenesis. Higher disease activity, longer duration, seropositivity, glucocorticoid exposure, and cumulative inflammatory load further increased risk.[6] A practical challenge is selecting a cardiovascular risk tool that performs adequately in RA.[7] Many calculators were derived from general-population cohorts and may not fully reflect autoimmune inflammation or RA treatment exposure.[8] To reduce this limitation, EULAR has recommended a 1.5 multiplier for conventional scores in selected RA patients.[9] Experimental and clinical studies suggest that statins can reduce inflammatory cytokine activity, improve endothelial function, stabilize atherosclerotic plaque, reduce oxidative stress, and influence immune-cell activation. Effects on T cells, macrophages, TNF-alpha, and IL-6 have been described.[10] Some RA studies reported modest reductions in inflammatory markers or disease activity, but the most established indication remains CVR reduction.[11] Framingham, QRISK-3, atherosclerotic cardiovascular disease (ASCVD), and Systematic Coronary Risk Evaluation (SCORE) have all been used in RA research, but their performance differs between populations.[12] QRISK-3 is particularly relevant because RA is included as an independent risk variable. In contrast, Framingham and ASCVD do not directly include RA-related inflammation, which may partly account for differences in statin eligibility estimates.[13] In Iraq, even though the burden of RA becomes increasingly recognized due to improved diagnostic awareness and growing epidemiological studies, there is limited local data on the appropriateness of statin medication and CVR in RA patients.

This study is novel because it evaluates cardiovascular risk and the appropriateness of statin therapy in Iraqi patients with rheumatoid arthritis using and comparing multiple validated cardiovascular risk scores. The aim of this study is to evaluate the CVR using several methods in RA patients, including determining the prevalence of patients who should be on statins and estimate the patients who achieve their lipids targets.

PATIENTS AND METHODS

Study design and setting: A cross-sectional study with analytical components was conducted at Rheumatology Clinic in Baghdad Teaching Hospital during a period of two years from April 2024 till April 2026.

Study population and sample size: The study included adult patients attending rheumatology clinic during the study period, diagnosed as RA according to 2010 ACR/EULAR criteria.[14] for six months duration or more, with positive RF and/or anti-CCP antibodies. Patients with a history of diabetes, heart failure, myocardial infarction, stroke/TIA, peripheral arterial disease, ischemic heart disease, chronic kidney disease, and coronary revascularization; Also, those with hypothyroidism, dyslipidemia requiring statin, familial hypercholesterolemia or patients with clinical features suggestive of hyperlipidemia (xanthoma, xanthelasma, tendon xanthoma, corneal arcus, etc.), and those who refuse to participate were excluded from this study.

Sample size calculation: The sample size was calculated using the following equation: $n= (z^2pq)/d^2$ in which n= sample size, z= 1-α/2 percentile of a standard normal distribution = 1.96, p= expected proportion (unknown, so we assume 0.5), q= 1-p, and d= absolute precision = 0.05. The estimated sample was 384, but we included 430 patients to consider about 10% non-response and to increase the power of this study (Figure 1).

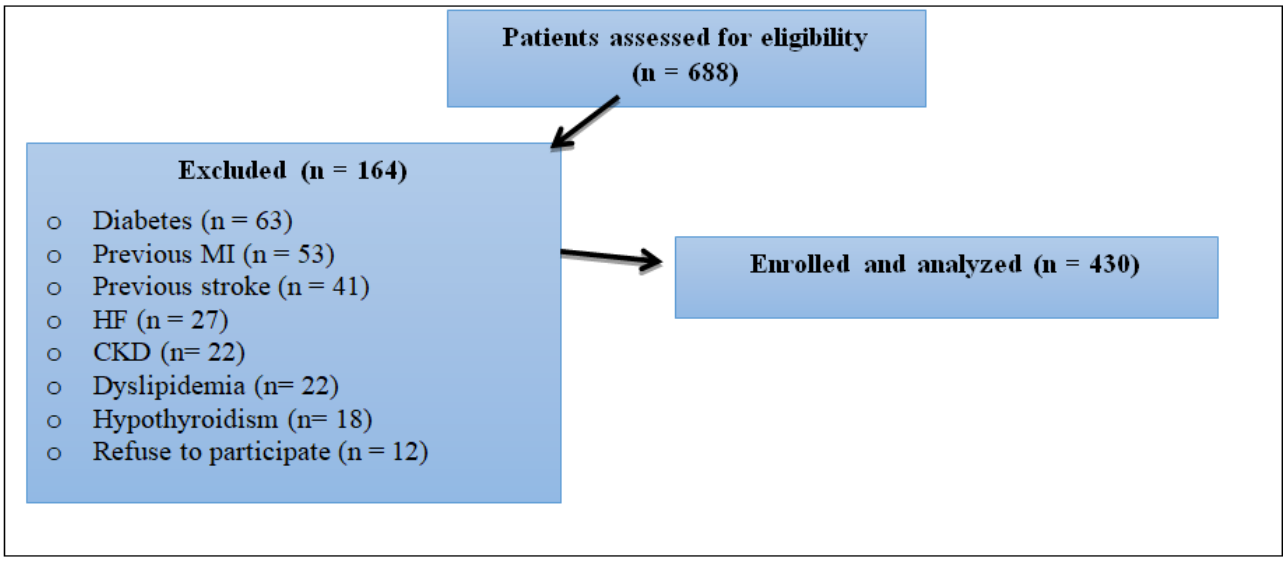

Figure 1: Patient Flow Diagram.

Data Collection Tools: Data was gathered retrospectively by a questionnaire which was applied to all study patients to collect needed information such as: Sociodemographic characteristics (Age, gender, occupation, smoking status, residence, educational level, BMI level, and duration of RA), statin use and perception, disease activity which was determined by DAS28 score. It includes evaluation of 28 swollen joints (SJC28) and tender joints counts (TJC28), ESR, and patient's global health (GH) status on a 0–100 VAS to calculate a score. We used an online DAS28 calculator, which uses an equation to compute a score for disease activity.[15] cardiac symptoms and evaluation (Symptoms as cardiac chest pain, palpitation, shortness of breath, fatigue, leg edema, dizziness and intermittent claudication, history of CVD as CAD, hypertension, heart failure, ACS, pericarditis, and PAD, and previous cardiac investigations as ECG, Echo, stress test, CT Angio, Holter, and prior vascular intervention), and additional assessments (Blood pressure, lipid profile, DM status, anemia, thyroid function, and eGFR). BMI was calculated from the equation Weight (Kg)/Square height (m^2). So, patients were classified as: Normal (≤ 24.99 kg/m^2), overweight (25 - 29.99 kg/m^2), and obese (≥ 30 kg/m^2).

Risk Scores assessment

- ✓ QRISK3, the third iteration of the QRESEARCH risk estimator algorithm: You can use it to predict how likely it is that you will have a heart attack or stroke, either fatal or non-fatal, in the next decade. The following factors are used to determine it: Considerations such as age, ethnicity, smoking status, weight, height, body mass index (BMI), diabetes, treatment-related hypertension, blood pressure (both systolic and diastolic), family history involving first-degree relatives under 60 years old, cholesterol/HDL ratio, and other co-morbidities should be taken into account. Severe mental illness, erectile dysfunction, atypical anti-psychotic use, migraines, rheumatoid arthritis, systemic lupus erythematosus, chronic kidney disease, steroid use.[16]
- ✓ Adjusted Framingham Score (AFS): It tends to overestimate the risk of CV events in high-risk individuals and undervalue them in low- and intermediate-risk patients. It takes information from eight different sources, including the patient's age, blood pressure, cholesterol, smoking status, and diabetes status, among other things. If a patient has RA for more than ten years, tests positive for RF and/or anti-CCP (ACPA) and has symptoms outside of the joints (such as vasculitis, nodules, pleuritis, pericarditis, etc.), the original advice from EULAR applies to a 1.5 multiplication factor. Patients were categorized as low risk (<10%), intermediate risk (10-20%), or high risk (>20%) based on AFS classification.[17]
- ✓ ASCVD Score. It is used by the ACC/AHA guidelines, defining low, borderline, moderate and high risk as values < 5%, between 5% and 7.5%, between 7.5% and 19% and ≥ 20%, respectively.[18]

Ethical considerations and official approvals: As well as the 1975 Declaration of Helsinki, as revised in 2013, the research was carried out in accordance with ethical standards. Everyone who took part in the study was given the green light orally and asked for permission to take part. No identifiable information was ever shared. This investigation was the only use of the data.

Statistical analysis: For data analysis, SPSS version 28 was utilized. Mean, standard deviation, and ranges are the ways the data is presented. Numbers shown as percentages and frequencies for categorical data. To determine whether there was a correlation between statin eligibility and disease activity, a chi-square test was employed. The dependent variable of the logistic regression analysis was whether or not RA patients had a statin therapy indication, and the independent factors that had been determined to be significant in the binary analysis. For statistical significance, a P-value of less than 0.05 was used.

RESULTS

In this study, mean age of patients was 54.32 ± 8.41 years and most of them were aged 40–59 years (53.7%) and were females (85.1%). The majority were living in urban areas (75.1%); 48.4% of them had finished primary/secondary education; 39.1% were employers; 44.4% of them were obese; 38.8% were current smokers; and most patients had RA duration of less than 10 years (63.7%). According to DAS28, 56% of patients had low disease activity and 13.1% had high disease activity (Table 1).

Table 1: Socio-demographic and clinical characteristics (n= 430).

Variable		Frequency (n= 430)	Percentage (%)
Age group (years)	**< 40**	112	26.1
	40 – 59	231	53.7
	≥ 60	87	20.2
Gender	**Male**	64	14.9
	Female	366	85.1
Residence	**Urban**	323	75.1
	Rural	107	24.9
Educational level	**Illiterate**	42	9.7
	Primary/Secondary school	208	48.4

	Higher education	180	41.9
Occupation	**Employee**	168	39.1
	Housewife	104	24.2
	Private work	92	21.4
	Retired	66	15.3
BMI Level	**Normal**	93	21.6
	Overweight	146	34.0
	Obese	191	44.4
Smoking	**Yes**	167	38.8
	No	263	61.2
Duration of RA (years)	**< 10**	274	63.7
	≥ 10	156	36.3
Disease activity (DAS28)	**Low**	241	56.0
	Moderate	133	30.9
	High	56	13.1

Measuring blood pressure showed that the mean systolic and diastolic blood pressures were 134.37 ± 10.68 and 83.11 ± 5.15 mmHg, respectively. The laboratory investigation results showed that the mean total cholesterol level was 191.6 ± 26.14 mg/dl, while the mean triglyceride level was 176.1 ± 31.24 mg/dL, and the mean ESR was 26.77 ± 10.75 mm/hr (Table 2).

Table 2: Clinical and laboratory profile.

Variable	Mean ± SD	Range (Min-Max)
Systolic BP (mmHg)	134.37 ± 10.68	107.6 – 178.0
Diastolic BP (mmHg)	83.11 ± 5.15	74.3 – 99.2
Total Cholesterol (mg/dL)	191.6 ± 26.14	126.2 – 260.7
Triglycerides (mg/dL)	176.1 ± 31.24	83.6 – 195.5
ESR (mm/hr)	26.77 ± 10.75	11.3 – 77.4

As shown in table 3, proportion of patients classified as requiring statin therapy varied across CVR assessment tools. According to QRISK3, statin therapy was indicated in 31.6% of patients compared with 22.3% according to ASCVD and 6.3% according to the AFS. Overall, statin therapy was indicated in 33.5% of the patients.

Table 3: CVR assessment and indication of statin therapy.

Variable		Frequency (n= 430)	Percentage (%)
ASCVD score	**Indicated**	96	22.3
	Not	334	77.7
QRISK-3 score	**Indicated**	136	31.6
	Not	294	68.4
AFS	**Indicated**	26	6.3
	Not	403	93.7
Overall statin indication	**Indicated**	144	33.5
	Not	286	66.5

Table 4 showed that there is a significant association observed between RA disease activity and statin eligibility (P=0.001) as the proportion of patients requiring statin therapy increased progressively with disease activity, from 17.4% among those with low disease activity to 44.4% among those with moderate disease activity and 76.8% among those with high disease activity.

Table 4: Disease activity and statin eligibility.

Disease activity	Statin indication		Total (%) n= 430	P - Value
	Indicated (%) n= 144	Not indicated (%) n= 286		
Low	42 (17.4)	199 (82.6)	241 (56.0)	**0.001**
Moderate	59 (44.4)	74 (55.6)	133 (30.9)	
High	43 (76.8)	13 (23.2)	56 (13.0)	

Logistic regression analysis was applied (table 5) using results of indication of statin therapy as the dependent variable. Five factors were found to be important independent predictors for indication of statin therapy. These factors were female gender is 2.21 more likely increase the rate of indication of statin therapy (OR= 2.21 with 95% CI: 1.29 – 5.6), obese patient is 2.44 more likely increase the rate of indication of statin therapy (OR= 2.44 with 95% CI: 1.22 to 6.1), smoking is 4.81 more likely increase the rate of indication of statin therapy (OR= 4.81 with 95% CI: 2.13 to 9.33), steroid use is 3.37 more likely increase the rate of indication of statin therapy (OR= 3.37 with 95% CI: 1.88 to 7.32), and increment in total cholesterol level is 1.38 more likely increase the rate of indication of statin therapy (OR= 1.38 with 95% CI: 1.14 to 2.7).

Table 5: Logistic regression analysis of possible predictors for indication of statin therapy.

Variables		Odd's ratio	95% CI for odd's ratio
Gender	**Female**	2.21	1.29 – 5.6
BMI Level Reference: Normal	**Obese**	2.44	1.22 – 6.1
Smoking status	**Smokers**	4.81	2.13 – 9.33
Steroid use	**Yes**	3.37	1.88 – 7.32
Total cholesterol Level	**Increase**	1.38	1.14 – 2.7

DISCUSSION

The current research shows that the projected requirement for statin medication differs greatly depending on the risk assessment tool utilized, shedding light on a significant yet possibly unacknowledged CV burden among RA patients in Iraq. Importantly, whereas one third of patients were found to be eligible for statins, that number rose dramatically with increasing RA disease activity, reaching over 75% of patients with high disease activity. These results show that CVR assessments for RA should take the disease's systemic inflammatory nature into account, and that using only one traditional risk calculator can cause people to make different, potentially life-threatening choices about preventative treatment.

In this study, the QRISK-3 score outperformed all other tools in terms of sensitivity, determining that 31.6% of patients met the requirements for statin treatment using a cutoff of 10% or above. While the AFS was the most cautious tool, determining that just 6.3% of patients were suitable for statin medication, the ASCVD score categorized 22.3% of patients as high-risk (≥7.5%). In the end, 33.5% of patients were eligible for statin treatment. These results are consistent with studies conducted by Alnefaie SA et al.[12] and Hughes DM et al.[13] which demonstrated that QRISK-3 was the most sensitive calculator with its design to capture a broader range of high-risk individuals by including RA-specific risk enhancement. By specifically including RA as a risk factor, QRISK-3 captures the increased CV load associated with chronic inflammation and may thus detect more RA patients. On the other hand, AFS takes a more cautious approach, especially when the risk augmentation for RA is not enough to surpass its treatment threshold.[19]

The resulting discrepancy highlights how statin eligibility in RA patients can be significantly impacted by the choice of risk calculators.

This study showed that the most significant predictors of statin indication were smoking (The most significant independent predictor in the multivariate analysis), female gender, obesity, steroid use, and elevated total cholesterol level. Agreement showed by Spitz JA et al study when found that smoking was independently associated with increased likelihood of becoming statin-eligible, along with higher BMI, and higher total cholesterol.[20] The atherosclerotic CVR is greatly amplified by smoking due to its effects on endothelial dysfunction, inflammation, oxidative stress, platelet activation, and unfavorable lipids.[21] The preexisting chronic inflammatory condition in RA patients may make these consequences worse. Smokers are also more prone to exceed the risk threshold for statin treatment because smoking is explicitly included in key CVR calculators like QRISK3 and ASCVD.[22] Disagreement found regarding female gender in studies conducted by Kuriya B et al.[23] and others who found higher statin eligibility among men than women. Although women generally have lower conventional CVR than men, the predominance of women in RA and the substantial inflammatory and metabolic burden associated with the disease may partly explain this finding in this study. According to this research, steroid use is a strong independent predictor of statin indication. Hypertension, dyslipidemia, insulin resistance, weight gain, and direct vascular effects are some ways that glucocorticoids might negatively impact CVR.[24] The CVR linked to persistent systemic inflammation may be exacerbated in RA, compounding this effect. Obesity was an independent predictor of statin indication in this study which is consistent with larger evidence linking a higher BMI to an increased probability of statin eligibility and start. The fact that obesity is associated with a host of CVR factors such as high blood pressure, bad cholesterol, insulin resistance, and inflammation throughout the body may explain this correlation.

Study limitations

This study has several limitations

- ✓ This study's design makes it difficult to draw any conclusions about the links between RA features, cardiovascular risk factors, and statin eligibility based on their temporal or causative nature.

- ✓ The results may not be applicable to other Iraqi communities or RA patients treated in community settings because the study only involved one rheumatology center in Baghdad.
- ✓ The risk of CV events was assessed using preexisting risk calculators instead of being tested against real occurrences; thus, variations in statin eligibility should not be taken as indications of genuine differences in the prediction accuracy of the tools.
- ✓ The study didn't include individuals who had preexisting conditions like diabetes, CVD, or any of numerous other major comorbidities; this could have led to a healthier RA population overall, but it also reduced the generalizability of the results.
- ✓ It is possible that not all relevant RA-related parameters, such as the total amount of inflammation, the length of time people were exposed to glucocorticoids, and the total amount of these drugs, as well as other possible CVR, were considered.

CONCLUSION

The evaluation of CVR in Iraqi RA patients varies significantly across risk calculators. Statin medication was appropriate for around a third of patients; eligibility increased dramatically with rising disease activity levels, reaching over 75% of patients with high RA activity. Traditional techniques such as ASCVD and AFS tend to estimate lower eligibility for statins, whereas QRISK-3, which includes RA as a risk factor, was the most sensitive tool in identifying patients who needed statins. The use of steroids, high cholesterol, being a woman, being overweight, and smoking were important independent predictors of statin prescription. RA should be regarded as a CVR enhancing condition and that regular CVR evaluation should be part of RA treatment plans and follow up because persistent inflammation is associated with an elevated risk of CVD.

Future work

To validate risk calculators for the Iraqi RA population, conduct longitudinal studies to assess actual CV outcomes correlated with RA activity and statin use, expand research across multiple centers to ensure a more representative sample, and refine CVR prediction by incorporating detailed RA-related inflammation markers and treatment exposure data. Patients with RA who are at high risk for CV complications must also receive interdisciplinary care that incorporates individualized risk management plans.

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