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Inflammation, Conventional Cardiovascular Risk Factors, and Cardiovascular Risk in Rheumatoid Arthritis

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Abstract

Multiple studies have shown that rheumatoid arthritis (RA) is linked to a higher likelihood of developing cardiovascular disease (CV) compared to the general population. However, it is important to note that common comorbidities associated with cardiovascular disease also have a significant role, even though long-term inflammation and other characteristics specific to rheumatoid arthritis seem to mitigate part of this risk. This section examines the results of prior research that explored the connection between rheumatoid arthritis (RA) and prevalent cardiovascular disease (CVD) comorbidities, including diabetes, insulin resistance, obesity, dyslipidemia, hypertension, smoking, and excessive physical inactivity. The prevalence of these risk variables, as well as the mechanisms by which RA medications and inflammation impact them, are examined. Three widely used cardiovascular risk estimators in individuals with rheumatoid arthritis (RA) include the Framingham Risk Score, the Reynolds Risk Score, and the Systematic Coronary Risk Evaluation. In this last section, we examine the efficacy of various risk estimators. There are notable disparities in conventional cardiovascular risk factors, such as insulin resistance, atypical fat distribution, smoking, and insufficient physical activity, between those with rheumatoid arthritis and those without the condition. Although the evidence is conflicting, there is a potential association between rheumatoid arthritis and

elevated levels of dyslipidemia, diabetes, and hypertension. The available knowledge on cardiovascular risk factors in rheumatoid arthritis primarily relies on data obtained as covariates for studies on cardiovascular disease. There is a dearth of evidence regarding specific risk factors for rheumatoid arthritis (RA), such as the prevalence of these risk variables and the alterations caused by inflammation or therapy. Further investigation is necessary to establish precise techniques for assessing cardiovascular risk in individuals with rheumatoid arthritis.

Key words: rheumatoid arthritis, traditional cardiovascular risk factors, cardiovascular disease, coronary artery disease, coronary heart disease, inflammation, C-reactive protein, Reynolds risk score/calculator, Framingham risk score/calculator, hypertension.

Introduction

Illustrative case

Below is a description of a fictional patient who is a 53-year-old man with hypertension and a diagnosis of erosive rheumatoid arthritis six years ago. This patient has tested positive for antibodies related to the disease. His father's cause of death was sudden cardiac death, which occurred when he passed away at the age of 58. The individual's total cholesterol (Tchol) is measured at 230 mg/dl (5.95 mmol/l), with high density lipoprotein (HDL) levels at 45 mg/dl (1.16 mmol/l), and low density lipoprotein (LDL) levels at 128 mg/dl (3.31 mmol/l). He does not smoke, but he takes medicine to regulate his hypertension, which has a systolic blood pressure of 137 mmHg. The hypothetical patient not only had rheumatoid arthritis (RA), but also possessed conventional risk factors for cardiovascular disease (CVD). Do you believe it would be advantageous for him to initiate treatment with a medication known as a statin or an HMG-CoA reductase inhibitor? The inflammation resulting from rheumatoid arthritis (RA) increases the risk of cardiovascular disease beyond what can be accounted for by conventional risk factors [14]. However, the present methodologies used to quantify cardiovascular (CV) risk do not consider this supplementary risk.

This research provides a summary of the frequency and consequences of common risk factors for cardiovascular disease in people with rheumatoid arthritis (RA). The risk factors encompass dyslipidemia, insulin resistance (IR) and diabetes, hypertension, obesity, smoking, and physical inactivity. When analyzing the impact of RA drugs and inflammation on the disease, a significant issue arises due to the potential simultaneous influence of both factors on

conventional cardiovascular risk factors. Once we have enough data, we will analyze the impact of risk factors for cardiovascular disease (CVD) on inflammation and treatment. To summarize, we will examine the existing methods used to assess the risk of cardiovascular issues in persons with rheumatoid arthritis (RA), and identify the specific areas that still need additional research.

Dyslipidaemia

Cholesterol, especially low-density lipoprotein (LDL), is accountable for the formation of fatty streaks in the coronary arteries. These streaks have the potential to eventually develop into atherosclerotic plaques that restrict blood flow [5]. There is a potential for these plaques to rupture, leading to the formation of blood clots that can block the coronary arteries and cause a heart attack (myocardial infarction). According to ATP III guidelines, there is no significant difference in the prevalence of dyslipidemia, characterized by high levels of LDL and Tchol and low levels of HDL, between those with rheumatoid arthritis (RA) and those without the condition. Despite the fact that individuals with rheumatoid arthritis have an elevated risk of cardiovascular disease compared to the whole population. A study discovered that dyslipidemia raised the likelihood of cardiovascular disease in individuals with rheumatoid arthritis (RA), similar to the effect observed in the control group [3]. There seems to be a correlation between the lipid profiles of individuals with rheumatoid arthritis (RA) and controls, along with the degrees of inflammation and treatment.

Our focus will be on three specific forms of cholesterol—LDL, HDL, and Tchol—which have been strongly correlated with the risk of cardiovascular disease [8]. The lipid profiles of patients were determined through two exams conducted prior to the administration of medication for rheumatoid arthritis. Before the diagnosis of rheumatoid arthritis (RA), a study conducted using blood bank samples found that individuals with RA had a higher total cholesterol (Tchol) and a lower high-density lipoprotein (HDL) compared to age- and gender-matched controls. These findings indicate an unfavorable atherogenic profile [9]. Based on the results of a second study that looked at past data from a large group of people, it was determined that the levels of total cholesterol (Tchol) in individuals with rheumatoid arthritis (RA) were lower compared to those without the condition (controls). Furthermore, the study cited earlier discovered that individuals with rheumatoid arthritis exhibited reduced levels of LDL compared to the control group.

Furthermore, the researchers discovered a notable decrease in LDL levels in the five years leading up to the diagnosis of rheumatoid arthritis [10]. However, there was an association observed between the decreased levels of Tchol and LDL and a potential rise in the risk of cardiovascular disease [11]. Most lipid studies conducted in individuals with rheumatoid arthritis (RA) primarily examine the alterations in lipid profiles resulting from RA treatment. Tocilizumab and tumor necrosis factor (TNF) blockade have the most pronounced association with alterations in lipid levels among the several therapies for rheumatoid arthritis (inflammatory arthritis). TNF inhibitors have been observed to elevate levels of HDL (high-density lipoprotein) and Tchol (total cholesterol), but there is no evidence to suggest that they increase levels of LDL (low-density lipoprotein) [12]. TNF blockers influenced both Tchol (total cholesterol) and HDL (high-density lipoprotein), leading to the development of a consistently atherogenic profile (Tchol/HDL) [1322]. The lipid profiles of individuals who respond to RA therapy undergo significant modifications, but non-responders do not see any alterations. The presence of this phenomenon indicates that the alterations in lipid levels were not induced by a particular intervention, but rather by a decrease in inflammation [19-24]. Studies have demonstrated that tocilizumab, a humanized antibody that attaches to the IL-6 receptor, leads to elevated levels of LDL and Tchol [24].

However, the effect of these changes on the probability of developing cardiovascular disease is not fully comprehended and is now being investigated [25, 26]. There has been a scarcity of study on the impact of DMARDs, except from TNF and IL-6 R blockers, on lipid profiles in individuals with rheumatoid arthritis (RA). There is little evidence to suggest that MTX has any impact on lipid profiles, regardless of inflammation [27, 28–29]. Hydroxychloroquine, in contrast, has the potential to enhance atherogenic characteristics in individuals with rheumatoid arthritis (RA). Inflammation induces alterations in both the functionality and concentrations of lipids. One can investigate the relationship between inflammation and changes in cholesterol levels by doing research on the effects of RA medication on cholesterol levels. There seems to be an inverse relationship between the levels of HDL and the levels of disease activity in rheumatoid arthritis [16, 17, 21]. A comparative study was conducted to examine the differences between untreated rheumatoid arthritis patients aged 60 and above, and a control group without rheumatoid arthritis.

The study revealed a noteworthy decrease in HDL values among patients with rheumatoid arthritis compared to the control group [30]. When there is inflammation, high-density lipoprotein (HDL) can change into a particle that promotes inflammation. This particle has the ability to speed up the development of atherosclerosis [31, 32]. The given sequence is [16, 17, 21, 30]. There is no noticeable correlation between the levels of LDL and the inflammation linked to RA. Using statins as a standard treatment is an effective approach to specifically reduce LDL levels in patients with rheumatoid arthritis. Based on the results of a randomized placebo-controlled study [33], individuals with rheumatoid arthritis who were administered statin medication for a duration of six months demonstrated a notable decrease in both total cholesterol and low-density lipoprotein (LDL) levels. The study's findings indicate that the patients who received statin treatment showed a notable decrease in both inflammatory indicators (such as CRP and ESR) and disease activity. Based on these findings, statins possess the capacity to decrease cholesterol levels and exhibit a mild anti-inflammatory impact when employed in the treatment of rheumatoid arthritis (RA), thereby diminishing the likelihood of cardiovascular illness.

Insulin resistance and diabetes

The concept that RA and IR are connected to one another is well supported by epidemiological evidence. Initially, the research will focus on the literature pertaining to rheumatoid arthritis (RA) and inflammatory response (IR). Subsequently, the material about rheumatoid arthritis (RA) and diabetic mellitus (DM) will be examined. Several research [34] have employed the homeostatic model assessment (HOMA) calculation to measure insulin resistance, known as HOMA-IR analysis. A study discovered that 124 individuals diagnosed with rheumatoid arthritis (RA) exhibited indications of insulin resistance (IR) based on the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), with a prevalence of 54%. However, the estimated incidence rate (IR) in the general population is 40-45% according to reference [36]. A study was conducted to compare the HOMA-IR levels in persons with rheumatoid arthritis (RA) to a control group. It was found that all participants in both groups had co-existing thyroid dysfunction.

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was 1.65 for individuals with rheumatoid arthritis (RA), while it was 1.16 for the control group (P = 0.031) [37]. Two separate cross-sectional studies have examined the correlation between

inflammation and insulin resistance (IR) in individuals with rheumatoid arthritis (RA). A comparison between patients with rheumatoid arthritis (RA) who had low-grade and high-grade inflammation revealed that those with high-grade inflammation exhibited a notably elevated HOMA-IR [38]. The present steroid dosage did not have a substantial impact on predicting HOMA-IR. Nevertheless, the measured waist circumference, CRP, and ESR were all significant predictors. In a separate cross-sectional investigation, it was discovered that C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNFa) had a notable association with HOMA-IR.

Moreover, there was an inclination towards an increased HOMA-IR in correlation with the total amount of steroids administered. The correlation between diabetes and rheumatoid arthritis has not been definitively established in previous research. Multiple independent examinations have consistently found a positive correlation. After considering the administration of glucocorticoids, it was found that individuals with rheumatoid arthritis (RA) have a 50% increased likelihood of developing diabetes mellitus [95% confidence interval (CI) 1.4, 1.5]. This finding was uncovered in a study that utilized a considerably extensive administrative database sourced from Canada [39]. An earlier investigation of an administrative database [40] revealed a 40% (95% CI 1.3, 1.4) rise in diabetes mellitus linked to rheumatoid arthritis. These findings align with the analysis. Past investigations have consistently shown that patients with rheumatoid arthritis (RA) have a higher prevalence of diabetes mellitus. Lastly, a study conducted on a population indicated that there was a 1.3 odds ratio (OR) increase in the risk of diabetes mellitus (DM) associated with rheumatoid arthritis (RA). However, there were several occurrences, and the confidence interval (CI) included the value of 1 [44]. Multiple investigations were conducted, although none of them established any correlation between the two. A strong association was found between rheumatoid arthritis and type 1 diabetes, with an odds ratio of 4.9 (95% confidence interval: 1.8, 13). However, no significant association was observed between rheumatoid arthritis and type 2 diabetes, with an odds ratio of 1.1 (95% confidence interval: 0.7, 1.6) [45]. Based on the results of at least two prior studies that specifically examined the impact of cardiovascular illness on diabetes risk, it was shown that there was no disparity in the occurrence of diabetes between those with and without rheumatoid arthritis.

There is an inconsistency in the understanding of how immunosuppressives affect immune response in rheumatoid arthritis (RA). Three separate study teams conducted investigations into the impact of TNF inhibition on insulin resistance (IR). In research involving 45 individuals who had initiated therapy with infliximab, the insulin resistance (IR) did not diminish over a period of six months. However, the group with the greatest initial IR experienced a drop in IR during the study [47]. The experiment investigating adalimumab [48] found that IR did not decrease in any of the nine patients with rheumatoid arthritis who participated.

In a subsequent trial, a group of 19 patients diagnosed with rheumatoid arthritis were administered infliximab for a duration of fourteen weeks. The results of this treatment demonstrated a notable enhancement in the patients' immune response [20]. Although this publication [49] lacks significant information, a recent study conducted on eleven individuals with rheumatic conditions revealed that tocilizumab significantly diminished the intensity of HOMAI-IR. A concise study with 22 participants revealed that 14 persons diagnosed with rheumatoid arthritis (RA) observed a decrease in HOMA-IR levels after initiating treatment with MTX within the initial eight weeks [43]. Patients diagnosed with rheumatoid arthritis who undertake therapy have also been linked to a decreased probability of developing diabetes. Unlike other non-biologic diabetes management tools, a study conducted on a large administrative database indicated that TNFa blockers and HCQ significantly decreased the chance of getting diabetes in the future by a factor of 30 to 50%. The results of this analysis corroborated the findings of a previous study that utilized HCQ and showed a reduced occurrence of diabetes in a cohort of individuals with rheumatoid arthritis [51].

Obesity

The Centers for Disease Control and Prevention in the United States estimate that individuals with arthritis have a 54% greater obesity rate compared to those without the condition. The World Health Organization defines obesity as having a body mass index (BMI) of 30 kilograms per square meter or higher. However, among Asians, the threshold is lower at 25 kilograms per square meter [53]. The existing research on the correlation between rheumatoid arthritis and body mass index (BMI) in comparison to the general population is inconclusive [1, 3, 54]. A study assessing the impact of different cardiovascular risk factors on patients with rheumatoid arthritis (RA) compared to a control group found that obesity had a comparable

effect on the risk of cardiovascular disease in both RA patients and controls [3]. The body mass index (BMI) was created as a scientifically measured alternative to quantify the level of body fat [55]. Research utilizing bioelectrical impedance, a technology that assesses body fat composition, found that individuals with rheumatoid arthritis (RA) had elevated body fat percentages relative to healthy controls, even after accounting for body mass index (BMI). A study utilizing abdominal CT scans found that female RA patients had a greater proportion of subcutaneous fat compared to controls with the same body mass index and waist circumference.

On the other hand, male RA patients had a higher percentage of visceral fat. These data suggest that the body fat content of RA patients may be overestimated when calculating BMI, relative to controls. This would lead to an underestimate of their susceptibility to cardiovascular disease. Obesity is considered a causative factor in the development of low-grade inflammation [5860]. This is because it has been proven that adipose tissue releases pro-inflammatory cytokines like IL-6 and adiponectin. Higher body mass indexes in the general population are linked to elevated CRP levels [61, 62], which in turn are related with an augmented risk of cardiovascular disease. A association exists between modified body fat composition and elevated CRP levels, as well as more severe rheumatoid arthritis [63, 64].

Hypertension

A prior study investigating the prevalence of hypertension in individuals with rheumatoid arthritis, within the context of cardiovascular disease investigations, did not show a clear increase in risk when compared to individuals without rheumatoid arthritis. Based on a meta-analysis of seven case-control studies on rheumatoid arthritis (RA), it was found that there is no significant difference in the occurrence of hypertension between patients with RA and the control group [7]. Conversely, some other research have found a correlation between rheumatoid arthritis and higher blood pressure or a greater occurrence of hypertension. These investigations took into account hypertension as a starting point for comparison [65]. A long-term analysis has not yet examined the relative risk of hypertension in patients with rheumatoid arthritis (RA) compared to controls. A study discovered that the risk of hypertension had a similar impact on cardiovascular risk in individuals with rheumatoid arthritis (RA) as it did in the general population [3]. Several studies have found a correlation

between RA and heightened stiffness, as evidenced by comparing the flexibility of the artery wall in individuals with RA to that of control subjects [66].

Regarding BP, these investigations have largely been fulfilled. Therefore, although these studies do not allow us to directly compare the risk of hypertension in RA patients to that of controls, the results nonetheless indicate that RA patients have a reduced ability of their arterial system to adapt to changes in blood volume. Several experimental treatments have shown significant efficacy in reducing blood pressure (BP), but most disease-modifying anti-rheumatic medicines now available on the market do not have this effect [67]. Moreover, studies have shown that glucocorticoids and non-steroidal anti-inflammatory medications (NSAIDs), both selective and non-selective, might increase blood pressure [6871]. Some individuals may experience a significant increase in blood pressure as a result of taking these medications, requiring them to seek medical help.

Cigarette smoking

Smoking is often regarded as the primary environmental risk factor for rheumatoid arthritis [72, 73]. Although smoking rates are declining in society, it remains one of the most modifiable risk factors for cardiovascular disease [74]. Individuals who have been diagnosed with rheumatoid arthritis (RA) had a greater likelihood of smoking cigarettes, with an odds ratio of 1.56 and a 95% confidence range ranging from 1.34 to 1.80 [7]. Furthermore, three independent investigations, which were not incorporated into the meta-analysis, revealed that individuals afflicted with rheumatoid arthritis had a greater incidence of past and current smoking in comparison to those without the ailment [3, 4, 75]. A population-based RA case-control study evaluated the impact of cigarette smoking on the risk of cardiovascular disease (CVD). The study found that current smoking status increased the risk of CVD, although the increase was significantly lower in RA cases compared to controls. Research [76, 77] indicates that smoking cigarettes is linked to a more severe manifestation of rheumatoid arthritis (RA), especially in males with seropositive illness.

Physical activity

Including more physical exercise in one's lifestyle is an important component for reducing the risk of cardiovascular disease (CVD). A concise investigation utilizing questionnaires revealed that individuals suffering from rheumatoid arthritis (RA) had considerably lower levels of physical activity compared to individuals from the general community [78]. In a separate small

pilot study [79], scientists discovered that individuals with rheumatoid arthritis (RA) and those without RA had similar levels of energy expenditure. When the researchers reviewed the actual activities of the study, they found that individuals with rheumatoid arthritis (RA) walked significantly less than the control group. In comparison to individuals who maintain active lifestyles, patients suffering from rheumatoid arthritis who do not participate in physical activity exhibit elevated blood pressure, increased cholesterol levels, and higher levels of low-density lipoprotein (LDL), which are similar to those observed in the general population [80]. Exercise therapy have been demonstrated to be beneficial in maintaining and enhancing functional status in individuals with rheumatoid arthritis (RA) [81]. Thus, it is probable that exercise therapy would likewise be highly beneficial for reducing cardiovascular risk.

Potential strategies for estimating CV risk

Ongoing research is focused on accurately predicting the risk of cardiovascular disease in individuals with rheumatoid arthritis. Currently, the Framingham Risk Score (FRS) [82] and the Reynolds Risk Score (RRS) [62] are the two methods used to assess the cardiovascular risk in the general population (Table 1). The FRS considers the standard risk factors, such as age, gender, and overall cholesterol levels, to determine the probability of a coronary event happening within a ten-year timeframe. The RRS utilizes the high-sensitivity CRP (hsCRP) measurement to evaluate the likelihood of developing inflammation-related conditions such as coronary events or strokes within a ten-year timeframe. The Systematic Coronary Risk Evaluation (SCORE) is widely utilized in Europe [83] (Table 1) to assess the probability of experiencing fatal cardiovascular disease during a ten-year timeframe.

Do these risk scores apply to those with rheumatoid arthritis?

Despite the presence of evidence linking a higher Framingham Risk Score (FRS) to an increased cardiovascular (CV) risk in rheumatoid arthritis (RA), it is important to note that both the FRS and Systematic Coronary Risk Evaluation (SCORE) would underestimate the CV risk in RA. This is because they only consider conventional CV risk factors and do not take into account inflammatory markers. The user's text is "[84]". This is because both of these risk factors solely encompass conventional cardiovascular risk variables. Multiple studies have found that inflammation is the main cause of the remaining risk of cardiovascular disease in individuals with rheumatoid arthritis (RA), whereas known risk factors only account for a part of the total risk [13]. A recent study conducted on a large group of people indicated that female patients

with rheumatoid arthritis had cardiovascular rates that were about fifty percent higher than what was expected based on the Framingham Risk Score (FRS). Despite adjusting for inflammation in the calculation, the RRS may still be an inaccurate measure of cardiovascular risk. This is because it was calibrated using a population with an average hsCRP level of around 2.0 mg/l, which is considerably lower than the usual amount seen in people with RA. As an illustration, the Brigham Rheumatoid Arthritis Sequential Study [86] was conducted on a group of 1100 patients receiving treatment for rheumatoid arthritis.

The study found that the average hsCRP level in this cohort was 9.7 mg/l. This value aligns with the findings of other established cohorts studying rheumatoid arthritis. Because C-reactive protein (CRP) levels can vary significantly in individuals with rheumatoid arthritis (RA) due to therapy modifications and disease flare-ups, its ability to accurately predict the risk of cardiovascular disease at any given time is uncertain. Furthermore, the RRS fails to consider any significant connections between the amount of inflammation and the variables linked to cardiovascular risk. Patients with elevated erythrocyte sedimentation rate (ESR) levels and multiple cardiovascular risk factors exhibited a carotid intima medium thickness (cIMT) that exceeded the expected value obtained by combining the cIMT values of each individual component [87].

IMT serves as an alternative measure for assessing cardiovascular risk. Indeed, a study discovered that incorporating CRP into the risk calculator revealed that both RRS and FRS underestimated the risk of cardiovascular disease [85]. The European League Against Rheumatism (EULAR) established an expert team to offer recommendations on enhancing the evaluation of cardiovascular risk in rheumatoid arthritis (RA). According to EULAR, if a patient exhibits two or more of the following: extra-articular symptoms, RF or antibodies to citrullinated peptide antibodies, or RA sickness duration greater than 10 years, a multiplier of 1.5 should be used to FRS or SCORE [88]. This recommendation is based on research of subpar quality. No validation has been conducted for this multiplier.

Conclusion

Returning to our hypothetical patient, who does not smoke, has a systolic blood pressure of 137 mmHg (while taking medication to lower high blood pressure), a total cholesterol level of 230 mg/dl, high-density lipoprotein (HDL) level of 45 mg/dl, and low-density lipoprotein (LDL) level of 128 mg/dl. According to the Framingham Risk Score (FRS), this patient has a 10%

probability of being diagnosed with coronary heart disease or experiencing death from coronary heart disease within the next ten years (as shown in Table 2). His C-reactive protein level was 15 mg/dl on his latest appointment. Based on the RRS, his ten-year risk of developing cardiovascular disease was determined to be thirteen percent. Based on the SCORE, residing in high-risk European countries such as England carries a three percent probability of mortality due to cardiovascular disease within the next decade (Table 2).

Table 1 Comparison of clinical variables and predicted outcomes for the FRS, RRS and the SCORE

Clinical variable	FRS	RRS	SCORE
Age	✓	✓	✓
Gender	✓	✓	✓
Tchol	✓	✓	✓
HDL	✓	✓	
Current smoker	✓	✓	✓
Systolic BP	✓		✓
On medication for hypertension	✓		
hsCRP		✓	
Mother or father with heart attack or stroke before age 60		✓	
High-/low-risk European country			✓
Predicted 10-year risk	MI or coronary death	MI or stroke	Fatal CVD

Table 2 Comparison of predicted 10-year risk of CVD disease for hypothetical patient based on the FRS, RRS and the SCORE

Variables	FRS	RRS	SCORE
Age, years	53	53	53
Gender	Male	Male	Male
Tchol	230 mg/dl	230 mg/dl	5.95 mmol/l
HDL, mg/dl	45	45	-
Current smoker	No	No	No
Systolic BP, mmHg	137	-	137
On medication for hypertension	Yes	-	-
hsCRP, mg/l	-	15	-
Mother or father with heart attack or stroke before age 60	-	Yes	-
High-/low-risk European country	-	-	High
Predicted 10-year risk	10% MI or coronary death	13% MI or stroke	3% fatal CVD

If FRS were to receive the multiplier suggested by EULAR, his risk would rise to 15%. Applying the Adult Therapeutic Panel III guidelines [6], which establish LDL goals for statin treatment, to FRS (with or without the multiplier) and RRS, would indicate that the patient does not need any extra medication for his LDL level. This would be true irrespective of the presence of the multiplier. However, considering his chronic rheumatoid arthritis and the notable family history of heart disease, it would be prudent to explore adding a statin to his treatment plan. However, there is insufficient evidence to substantiate this argument. This hypothetical

situation highlights the significance of creating a data-driven and verifiable approach to assess the cardiovascular risk in persons with rheumatoid arthritis. Individuals with rheumatoid arthritis (RA) are most likely to have greater rates of cardiovascular disease risk factors such as insulin resistance (IR), fat mass distribution, physical activity, and smoking compared to the control group. The facts about comorbidities such as diabetes, hypertension, and dyslipidemia that contribute to cardiovascular disease are perplexing, while it is plausible that the prevalence of these disorders is elevated. Studies have shown that rheumatoid arthritis (RA) can alter the types and levels of risk factors linked with cardiovascular disease (CVD) when compared to the general population. This is due to the inflammation and treatment associated with RA. Therefore, we suggest reconsidering the conventional conceptual framework of cardiovascular risk in individuals with rheumatoid arthritis. Hence, to precisely measure cardiovascular risk, it is imperative to consider both conventional risk factors and the potential impact of inflammation on these factors, without making a clear distinction between the two groups (Fig. 1B). Contrarily, the method of treating established risk factors and inflammation as separate entities is not followed (Fig. 1A). In summary, precisely assessing the cardiovascular risk in patients with rheumatoid arthritis (RA) remains challenging. Additional study is necessary to investigate each cardiovascular risk factor individually and enhance the calculation of cardiovascular risk. This will help inform our judgments for the prevention of primary and secondary cardiovascular disease in individuals with rheumatoid arthritis.