

Cardiovascular risk estimation and management in rheumatoid arthritis: comment on the EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis

Sirs,

Cardiovascular disease (CVD) is still the major cause of mortality in rheumatoid arthritis (RA) after more than a decade of biologic agents in clinical practice. In 2010, EULAR published a cardiovascular (CV) risk management guideline in RA (1). Recommendations were based on the cumulated evidence derived from mostly observational and epidemiologic studies. While research regarding the increased CV morbidity and mortality in RA patients has advanced in recent years, there are certain issues that need to be further discussed:

EULAR recommends annual CV risk assessment using national guidelines or Systematic Coronary Risk Evaluation (SCORE) model, if national guidelines are absent. A further adaptation of the SCORE model is recommended in RA patients by multiplying the SCORE with a correction factor of 1.5, if the patient meets two of the following 3 criteria: disease duration >10 years, rheumatoid factor and/or anti-cyclic citrullinated peptide positivity, presence of extra-articular manifestations. The SCORE model predicts 10-year fatal-CVD based on traditional CV risks including age, gender, systolic blood pressure, total-cholesterol/HDL-cholesterol and smoking status. Although SCORE model performs well in predicting CV events in general European Caucasian populations, it is shown that it underestimates the true CV risk of RA patients (2-4). In a prospective study of early RA cohort 24% of patients with low CV risk according to SCORE developed CV events (2). Increased carotid intima-media thickness ($[cIMT]>0.9\text{mm}$) and/or carotid plaques in carotid ultrasonography (US) are good surrogate markers for atherosclerosis in RA patients and non-rheumatic individuals (5). When $cIMT>0.9\text{mm}$ and/or carotid plaques were considered as the gold standard for subclinical atherosclerosis, again SCORE failed to identify majority of the patients at high CV risk in two different European cohorts (3, 4). Even 1.5 multiplication factor did not improve

risk estimation that modified SCORE (mSCORE) failed to identify 88% of the patients with $cIMT>0.9\text{mm}$ and/or carotid plaques (3). This underestimation probably results from focusing solely on traditional CV risk factors in estimating CV risk in RA subjects. Data from several studies demonstrate that traditional risk factors account for only a small portion of the overall risk for CVD in RA (6). The rest of the risk is attributed to inflammation and genetic background. Furthermore, the relative impact of some of the traditional risk factors for CVD risk, such as male gender and smoking, differ in RA (6). Besides, not all traditional risk factors like under-treatment of hypertension, family history of early CVD and obesity (body mass index $[BMI]>30\text{kg/m}^2$), are involved in the SCORE risk algorithm. The BMI needs special emphasis here; $BMI>30\text{kg/m}^2$, obesity, is associated with both inflammation and increased CV mortality in RA similar to the general population, however, low BMI ($<20\text{kg/m}^2$) is also associated with increased CV mortality in RA (6). However, no correction of SCORE for BMI was recommended by EULAR. The SCORE risk model also does not involve any inflammatory or RA-related parameter. The number selected "1.5", to correct the SCORE by EULAR, somewhat comes from relevant standardised mortality ratios, but it does not improve CV risk assessment in RA patients as evident from the above studies. Those studies and data from our cohort (7) indicate that most of the patients are in the moderate risk group (SCORE 1-5%), multiplying the SCORE with 1.5 changes less than 5% of patients' risk status. Even, the mean mSCORE of a Spanish RA cohort ($2.16\pm2.49\%$) and our RA cohort ($1.70\pm2.95\%$) are far lower than the SCORE risk of the general population of Spain ($6.0\pm6.5\%$) and Turkey ($7.4\pm9.3\%$) (3, 7, 8). Although the data is controversial, certain other disease characteristics, such as use of corticosteroids and non-steroidal anti-inflammatory drugs may increase the CVD risk in RA as well. It is also shown that the increased CVD risk begins even prior to or within 1 year of the clinical onset of RA, not just after 10 years of disease duration (9). However, despite all shortcomings of SCORE/mSCORE, other risk algorithms like Framingham risk score or Reynolds risk score (involving high-sensitive CRP) do not offer any advantage and both seem to underestimate the true risk (2). Another risk algorithm that includes

RA as an independent risk factor, QRisk II, conversely, overestimates the risk (2). Although the increased risk in RA is well recognised, it is important to estimate the risk in the individual patient. All these CVD risk algorithms significantly correlated with vascular changes over time (10), however currently, neither SCORE and other traditional risk estimators nor their EULAR modified versions seem adequate to identify high-risk RA patients. RA-specific risk estimators, including parameters reflecting inflammatory burden and extended traditional/RA-specific risk factors, should be developed. Until then, considering the inadequate screening and management of CV risks in RA among rheumatologists, using an "overestimating" risk estimator (QRisk II or any other national risk estimator) or use of carotid US for identification of high-risk patients would be preferable. So far, there is no randomised-controlled trials evaluating the effects of aspirin or statins on CV mortality in RA patients when used as a primary/secondary preventive strategy. The number needed to treat or harm, treatment thresholds, goals or duration are all unknown. The effect of these strategies on overall CV risk should also be clarified. In conclusion, the majority of the EULAR recommendations focus on the risk estimation, recommending mainly the use of national guidelines for the management of traditional risk factors, along with adequate control of disease activity. Current EULAR recommendations are high-risk patient-oriented. Until the ideal risk estimator has been developed, optimum approach and frequency of risk assessment for low-to-moderate CV risk patients should be addressed. The importance of screening for CV risk factors and monitoring of adherence to primary/secondary preventive measures of CVD should be emphasised in RA. The role of non-pharmacologic strategies for CV risk reduction, including, exercise, weight control, reduction of salt intake, dietary modifications, should also be accentuated in EULAR recommendations for CV risk management in RA patients. Lastly, the optimum approach for screening of CVD in asymptomatic RA patients without previous CVD should also be determined.

G. OZEN
H. DİRESKENELİ
N. İNANC

*Marmara University School of Medicine,
Department of Internal Medicine, Division
of Rheumatology, Istanbul, Turkey.*

Address correspondence and reprint requests to: Dr Gulsen Ozen, Marmara University, School of Medicine, Division of Rheumatology, Mimar Sinan Street no. 41, Pendik, 34899 Istanbul, Turkey.

E-mail: ozengs@yahoo.com

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