

Change in cardiovascular risk after initiation of anti-rheumatic treatment in early rheumatoid arthritis

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Ischaemic heart disease and stroke are the most common causes of death and rheumatoid arthritis (RA) is associated with an increased risk of these cardiovascular diseases (CVD) (1-2). Different cardiovascular (CV) risk models are used to estimate the 10-year risk of fatal and non-fatal CVD, and indicate if an antihypertensive and/or statin is necessary to lower the risk for a future CV event (3-4). To determine the influence of the risk model as well as the moment of CV risk screening, CV risk scores were calculated in 104 consecutive early RA patients before and four weeks after treatment with methotrexate escalated to 17.5 mg/week, combined with 30 mg/day prednisolone tapered to 10 mg in four weeks (5). Risk scores were assessed with two calculators, the Dutch Systematic Coronary Risk Evaluation (SCORE) (3) and the HeartSCORE (4).

The correlation between absolute values of the Dutch SCORE and HeartSCORE had a spearman coefficient of 0.79 with a *p*-value of 0.01. The agreement between the different risk categories (low, medium, high) was 62.4%, and had a slight correlation ($\kappa=0.13$, *p*<0.01) (6)). At baseline, 29.9% and 3.1% of the patients were classified as high risk according to the Dutch SCORE and HeartSCORE, respectively. According to the Dutch CV-risk management guidelines that use the Dutch SCORE, all high risk patients had at baseline an indication for (adaptations of) preventive treatment. After four weeks of RA treatment, the mean DAS44 decreased with 1.9 points. Blood pressure and total cholesterol: high-density lipoprotein (TC:HDL) ratio decreased during anti-rheumatic treatment. According to the Dutch SCORE nine (9.3%) patients switched from risk category, of which five patients went to a lower category and four patients to a higher category. In the HeartSCORE four (4.1%) patients changed from category. In 13.4% patients the advice for (adaptations of) preventive treatment changed during the first four weeks of anti-rheumatic treatment. If baseline CV risk assessment would be applied, this would lead to potential overtreatment in 10% of all patients. The change in CV risk score and hence the advice about preventive treatment is thus correlated with the reduction of disease activity or the initiation of anti-rheumatic treatment. This is in line with previous literature that, e.g., described a reduction in acute myocardial infarction with the use of methotrexate (RR 0.81) (7-8). Furthermore, risk estimation depends on the risk calculator that is used. Clinically this will have an impact on the therapy and prevention strategies chosen. The difference between the Dutch SCORE and the HeartSCORE is partially explained because the HeartSCORE only assesses the risk on mortality and does not take non-fatal CV events into account (3-4). The influence

Table I. Demographics and outcomes at baseline and after four weeks of anti-rheumatic treatment.

	Baseline	After 4 weeks
Demographics		
Age	48.5 (12.4)	
Gender (females)	70 (67.3%)	
Symptom duration (months)	7.0 [3.0-21.0]	
RF or ACPA positive	89 (86%)	
DAS44	3.5 (3.3)	1.6 (0.9)*
CV risk components		
History of CV events	7 (6.7%)	7 (6.7%)
Current smoking	26 (25.0%)	25 (24%)
Statin use	5 (4.8%)	5 (4.8%)
Antihypertensive use	16 (15.4%)	16 (15.4%)
Syst RR [‡]	130.8 (22.5)	127.8 (17.7)
LDL [†]	3.2 (0.8)	3.3 (0.9)*
TC:HDL ratio [†]	3.9 (1.3)	3.2 (1.0)*
CV risk scores		
Dutch SCORE linear risk score ^Δ	11.0 [3.5-23.5]	10.0 [3.0-22.0]*
Dutch SCORE low risk score ^Δ	43 (44.3%)	46 (47.4%)
Dutch SCORE medium risk score ^Δ	25 (25.8%)	20 (20.6%)
Dutch SCORE high risk score ^Δ	29 (29.9%)	31 (32.0%)
HeartSCORE linear risk score ^Δ	0.0 [0.0-1.5]	0.0 [0.0-1.5]*
HeartSCORE low risk score ^Δ	90 (92.8%)	94 (96.9%)
HeartSCORE medium risk score ^Δ	4 (4.1%)	1 (1.0%)
HeartSCORE high risk score ^Δ	3 (3.1%)	2 (2.1%)
Indication for preventive CV treatment, according to the Dutch CV-risk management guidelines		
Statin indication (high risk and LDL>2.5)	28 (28.9%)	27 (27.8%)
Antihypertensive indication (high risk and syst RR>140)	19 (19.6%)	13 (13.4%)

Numbers are presented as frequency (percentage), mean (SD) or median [IQR].

^ΔPatients without cardiovascular events, n=97; [†]Patients without antihypertensives, n=88; [‡]Patients without statins, n=99; *Statistical difference (*p*<0.05) between baseline and after four weeks.

ACPA: anti-citrullinated protein antibody; CV: cardiovascular; DAS: disease activity score; HDL: high-density lipoprotein; IQR: interquartile range; LDL: low-density lipoprotein; RA: rheumatoid arthritis; RF: rheumatoid factor; SCORE: Systematic Coronary Risk Evaluation; SD: standard deviation; Syst RR: systolic blood pressure; TC: total cholesterol.

of fluctuations in disease activity over time in RA patients is difficult to incorporate in risk prediction models; single disease activity measurements (as disease activity score or C-reactive protein) appear not to be adequate (9). Therefore, it is important to realise the limitations of the CV risk calculator.

In conclusion, CV risk management is important early in the course of RA. However, the timing of CV risk assessment, as well as the applied CV risk model, have an impact on the advice regarding the need for (adaptations of) CV preventive treatment. In our study, many patients were classified in a different risk category after the first month of anti-rheumatic treatment, which led in 13% of the patients to a change of the CV preventive treatment advice. It seems wise to perform CV risk assessment early in the course of RA, but not in the phase of active disease. Further research is needed to determine which risk model is optimal and when in the course of RA it should be applied.

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Competing interests: none declared.

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