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Letter to the Editor

Skin autofluorescence as a tool for cardiovascular risk estimation in patients with rheumatoid arthritis

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Rheumatoid arthritis (RA) is associated with increased cardiovascular mortality and morbidity [1,2]. Most studies among RA patients were performed in an era in which RA could only be suboptimally managed. With current available therapeutics for RA and treatment guidelines aiming at remission in a relatively short time, we assume that the cardiovascular risk (CVR) will be lower because of the shorter duration of systemic inflammation.[3]

To assess the CVR in RA patients, Dutch guidelines recommend to use the SCORE tool [4,5]. According to this tool, 15 years should be added to the actual age in order to estimate the CVR in RA patients. Almost all patients of 55 year and older are therefore classified as having a high CVR except for non-smoking women with normal blood pressure and lipid profile. To minimize the risk of over-treatment, there is a need to assess the CVR in RA patients in another objective manner.

The study objective was to assess whether skin autofluorescence (SAF) measurement is a better tool to estimate the CVR in RA patients compared to using the SCORE tool. With SAF measurement the amount of tissue Advanced Glycation End products (AGEs) are measured non-invasively with the AGE reader standalone type 214-B00102 [6]. AGEs are a divers set of compounds that accumulate in tissues during normal ageing. The amount of AGEs are indicative for vascular damage and predictive for future cardiovascular events [7,8].

A prospective cohort study was undertaken in a teaching hospital in the Netherlands from 2014 to 2016. Consecutive adult patients diagnosed with RA and treated at the outpatient clinic of the department of rheumatology of Gelre hospital were included. Excluded were patients with a history of cardiovascular disease, diabetes, or kidney failure, patients in class V and VI of the Fitzpatrick scale, as well as patients with skin diseases, scars or tattoos on forearms.

All patients had a CVR assessment which included the SCORE tool, SAF measurement, clinical history, physical examination, lipid profile, blood glucose, and kidney function. All study activities are standard usual care in line with national guidelines. As data were collected as part of usual care, this study falls outside the scope of the Dutch Medical Research Involving Human Subjects Act. The local Medical Ethics Committee of Gelre Hospital, Apeldoorn, the Netherlands approved verbal informed consent that was noted in the patients' file. No written informed consent was required.

The outcome of SAF measurement was categorized as normal, increased or high CVR [6,7]. The outcome of SCORE tool was categorized as normal (< 10% cardiovascular mortality and morbidity in the next 10 years), increased (10–20%), or high CVR (> 20%). Three by three tables were computed to compare the different risk assessment tools. The percent agreement between SAF and SCORE with and without adjustment of 15 years was calculated. Correlation was evaluated using the Spearman correlation coefficient (Rho).

A total of 79 patients were included (Table 1). Fifty-two patients (66%) had a normal CVR with the SAF risk assessment. Nineteen patients (24%) had a normal CVR using the SCORE risk assessment with age adjustment of 15 years, whereas 48 patients (61%) had a normal CVR without age adjustment.

Eleven patients (14%) had a high CVR with the SAF risk assessment and 50 patients (63%) had a high CVR with the SCORE risk assessment with age adjustment of 15 years. When using the SCORE risk assessment without age adjustment, 15 patients (19%) had a high CVR. Agreement between the SAF outcome and SCORE with 15 years added was 29% (23/79). Agreement between SAF outcome and SCORE without 15 years added was 48% (38/79). For the correlation between SAF outcome and SCORE with 15 years adjustment the Spearman's Rho coefficient was 0.525 ($P < 0.001$). For the correlation between SAF outcome and SCORE without 15 years adjustment the Spearman's Rho coefficient was 0.925 ($P < 0.001$).

A sub-analysis was performed in RA patients of 55 years and older, because this group will be classified as 70 years or older using the SCORE tool. Of 49 patients, 45 were classified as high CVR using SCORE risk assessment compared to 9 patients using SAF risk assessment.

SCORE risk assessment with age adjustment of 15 years, is more likely to overestimate the number of RA patients with a high CVR compared to risk assessment by means of SAF measurement, especially in RA patients aged 55 years and older. SCORE assessment with actual age combined with SAF risk assessment might be a better strategy to identify RA patients with a high CVR. This is one of the first studies to assess SAF measurement in RA patients. Although our study population is small, the promising results warrant further investigation.

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Table 1
Characteristics of study population.

Variable	Number (%)
Gender	
Male	18 (23)
Female	61 (77)
Median age (range)	58 (27–77)
Duration RA since diagnosis	
< 5 years	28 (36)
5–10 years	20 (25)
10–20 years	23 (29)
> 20 years	8 (10)
Rheumatoid factor	
Positive	54 (68)
Negative	23 (29)
Unknown	2 (3)
Median C-reactive protein (range)	2,7 mg/L (0,2–35,0)
Median Erythrocyte sedimentation rate (range)	10 mm/h (2–57)
Disease Activity Score	
< 3,2	61 (77)
3,2-5,1	11 (14)
> 5,1	1 (1)
Unknown	6 (8)
Smoking status	
Smoker	19 (24)
Ex-smoker	32 (40)
Never smoked	26 (33)
Unknown	2 (3)
New diagnoses	
Hypercholesterolemia	34 (43)
Hypertension	27 (34)
Hypercholesterolemia AND hypertension	8 (10)
Does not apply	2 (3)
Other	5 (6)
Unknown	3 (4)

Competing interests

None to declare.

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