



Exploring cardiovascular disease risk evaluation in patients with inflammatory joint diseases



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ABSTRACT

Objectives: Cardiovascular disease (CVD) risk calculators developed for the general population have been shown to inaccurately predict CVD events in patients with inflammatory joint disease (IJD). European guidelines for CVD prevention recognize the presence of carotid plaques (CP) as a very high CVD risk factor, equivalent of coronary artery disease. Patients with IJD have a high prevalence of CP. We evaluated if CP resulted in reclassification of patients with IJD into a more appropriate CVD risk class and recommended lipid lowering treatment.

Methods: CVD risk evaluation was performed in patients with IJD using SCORE and ACC/AHA risk calculators to predict CVD events.

Results: Of the 335 IJD patients evaluated (including rheumatoid arthritis $n = 201$, ankylosing spondylitis $n = 85$ and psoriatic arthritis $n = 49$), 183 and 159 IJD patients had a calculated CVD risk by SCORE and ACC/AHA $< 5\%$, indicating no need of lipid lowering treatment (LLT). However, of patients with low to moderate risk calculated by SCORE and ACC/AHA, 67 (36.6%) and 48 (30.2%) had CP and should according to guidelines receive intensive LLT. For patients with high risk, in the LLT considered group, 54.9% and 58.1% were reclassified to correct treatment when adding information on the presence of CP. Our results reveal a considerable reclassification into correct CVD risk category when adding CP in female patients.

Conclusion: The high frequency of asymptomatic atherosclerosis in patients with IJD has a notable impact on CVD risk stratification. Identification of CP will reclassify patients into recommended CVD preventive treatment group, which may be clinically important.

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1. Introduction

Patients with inflammatory joint diseases (IJD), including rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA), have an increased risk of cardiovascular disease (CVD) compared to the general population [1–4]. Prevention of CVD is a cornerstone in cardiology and one of the important tools in this regard is CVD risk calculators. It has been shown that four CVD risk algorithms developed for the general population inaccurately predict CVD events in European RA patients [5]. Furthermore, the Framingham and Reynolds risk calculators underestimate CVD events in RA patients from the US [6].

We have started a preventive cardio-rheuma clinic, where patients are referred for CVD risk stratification. In this clinic, we experience a

challenge regarding CVD risk evaluation due to the high frequency of atherosclerotic carotid plaques (CP). The asymptomatic nature of the CP, in addition to the limited use of carotid ultrasound during CVD risk stratification, may result in an underestimation of CVD risk and underuse of CVD preventive measures as lipid lowering treatment (LLT), with possible consequences for clinical outcome in patients with IJD.

In Europe the most commonly used CVD risk algorithm in clinical practice is the Systematic COronary Risk Evaluation (SCORE) [7]. The latest European guidelines recognize for the first time CP as a very high CVD risk factor [8], equivalent of coronary artery disease. Thus, LLT as high dose statin treatment is indicated for patients with CP on the same level as for patients with diagnosed CVD. In the latest American guidelines on CVD prevention, a novel CVD risk algorithm was recommended, and the cut-off point of indication for LLT was reduced from 10% to 7.5% [9]. An issue of discussion was the abandonment of lipid treatment targets, which diverge from the European guidelines where dose adjustments of LLT are recommended to obtain specified low density lipoprotein cholesterol (LDL-c) goals. However, due to the

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lower treatment cut-off a considerably larger proportion of patients will be classified to be in need of LLT using the American College of Cardiology/American Heart Association (ACC/AHA) risk calculator compared to the European SCORE.

Our objective was to examine to what degree the SCORE and ACC/AHA risk calculators classify patients with IJD who had CP to the correct CVD risk group and to what extent having CP affected stratification into recommended lipid lowering treatment group. Furthermore, to evaluate if either applying a 1.5 multiplier to the calculated risk as recommended by the European League Against Rheumatism (EULAR) [10], or if optimizing the risk estimate cut-off points of indication for LLT provided by use of these CVD risk algorithms, would improve CVD risk stratification and reclassification into recommended LLT group.

2. Patients and methods

We report on 335 patients with IJD, including RA (n = 201), AS (n = 85) and PsA (n = 49) (aged 40–75 years) who was referred from either the rheumatology outpatient clinic at Diakonhjemmet Hospital, or from general practitioners, for a CVD risk evaluation in the time period 2009 to 2012. The patients did not have documented CVD disease and were not using LLT.

Referral criteria to the preventive cardio-rheuma clinic were as follows: 1) when a person with IJD asks for a CVD risk evaluation f. ex. during the consultation with a rheumatologist at the outpatient clinic, 2) when the physician or the patient has knowledge of one or more CVD risk factor(s), 3) presence of symptoms or signs of a CVD risk factor – i.e. headache due to hypertension, and 4) premature familial CVD.

This is an observational report, and ethical approval and informed patient consent is therefore not required. The data collection/publication has been recommended and approved by the Office of the Oslo University Hospital's Privacy and Data Protection Officer (2011/7318).

2.1. CVD risk factors

Information regarding smoking status, diabetes mellitus, medication use and family history of premature CVD (male <55 years, female <65 years) was recorded.

Total cholesterol (TC), high density lipoprotein cholesterol (HDL-c) and triglycerides (TG) were measured at the hospital laboratory (European Standard Accredited 2009) by routine procedures in a COBAS 600 [11]. LDL-c was calculated according to Friedewald's formula [12].

Brachial blood pressure (BP) was measured 3 times if >140/90 mm Hg, using an Omron M7, after a 5-minute rest in a supine position. A mean of the 2 last measurements was calculated. Further CVD risk factors were recorded: a history of smoking (ever/never) was obtained. Body mass index (BMI, kg/m²) was calculated as weight divided by height². Waist circumference was measured in a supine position during expiration, mid between the anterior superior iliac crest and the lower rib margin. The patient was asked about family history of CVD in first-degree relatives (males <55 years and females <65 years).

Bilateral B-Mode ultrasonography of the carotid arteries was performed with a Vivid-7 ultrasound scanner (General Electric's Vingmed Ultrasound, Horten, Norway) using a 12 MHz probe (9–14) linear matrix array transducer. The ultrasonography examinations were all performed in accordance to recommendations by an experienced sonographer (ASE), supervised by a cardiologist (AGS) [13], and as previously described [14]. Plaque(s) in the common-, bulb- and internal carotid arteries was identified in the longitudinally view as protrusions ≥ 1.5 mm into the lumen when both the far and near walls had sharp edges, or when the protrusion was ≥ 2 times the nearby intima-media thickness. Patients included in the study had CP that were asymptomatic and with a stenosis degree <50%.

2.2. CVD risk calculators

To compare the risk of future CVD events calculated by the ACC/AHA and SCORE algorithms, we divided estimated risk into 3 categories: 1) No treatment recommended (with lipid lowering medication) when the risk was <5%, which was similar for both calculators; 2) Consider treatment when the calculated CVD risk by either ACC/AHA was 5–7.4% or by SCORE at 5–9.99% + LDL ≥ 2.5 mmol/L; and 3) Treatment recommended when estimated risk by ACC/AHA $\geq 7.5\%$, and/or age 40–75 years with diabetes and/or LDL-c ≥ 4.9 mmol/L and/or diagnosed CVD, or by SCORE $\geq 10\%$ + LDL-c > 1.8 mmol/L and/or diagnosed CVD (Table 1).

The impact of CP on CVD risk stratification was evaluated. The CVD risk calculated by SCORE and ACC/AHA was used as continuous variables. We used 2 methods to optimize the cut-off point of the SCORE and ACC/AHA algorithms, to evaluate if this would increase the classification of IJD patients with CP to the correct CVD risk group. Firstly, we evaluated the closest point (0.1) at the receiver operating characteristic (ROC) curve. Secondly, since it is more important to identify than not to identify the CP, we also evaluated 80% sensitivity for optimizing the CVD risk classification of IJD patients with CP. The sensitivity represents the true positive CP, which equals the ratio of true positive CP to (true positive + false negative) CP.

For RA patients we applied the EULAR recommended 1.5 multiplier to the calculated CVD risk and termed this the modified-SCORE (M-SCORE). The 1.5 multiplier is recommended used if RA patients have at least 2 of the following: disease duration >10 years, anti-cyclic citrullinated peptide antibodies/rheumatoid factor positivity or presence of certain extra-articular manifestations. Although, disease duration was known, the other factors were not available at the time of CVD risk evaluation in the preventive cardio-rheuma clinic at Diakonhjemmet Hospital. Therefore, the 1.5 multiplier was applied for all RA patients.

2.3. Statistics

Demographic characteristics of patients with IJD are presented as crude data, and the results are expressed as mean \pm SD or median (IQR) for normally and non-normally distributed continuous variables, respectively. Categorical variables are presented as numbers and

Table 1
Cardiovascular disease risk categories and recommended preventive treatment.

Recommended lipid lowering treatment	CVD risk categories	
	ACC/AHA	SCORE
No treatment	Risk <5%	Risk <5%
Treatment considered	Risk 5 to <7.5%	Risk 5 to <10% and LDL-c ≥ 2.5 mmol/L
Treatment recommended	Risk $\geq 7.5\%$ and/or age 40–75 with diabetes and/or LDL-c > 4.9 mmol/L and/or diagnosed CVD	Risk $\geq 10\%$ and LDL-c > 1.8 mmol/L and/or diagnosed CVD

CVD: cardiovascular disease, ACC/AHA: American College of Cardiology/American Heart Association, SCORE: Systematic COronary Risk Evaluation, LDL-c: low density lipoprotein cholesterol.

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