Cardiovascular Disease Risk in Patients with Rheumatic Diseases

Rachel H. Mackey, PhD, MPH[a,*], Lewis H. Kuller, MD, DrPH[b], Larry W. Moreland, MD[c]

KEYWORDS

• Rheumatoid arthritis • Cardiovascular • Lipids • Lipoproteins • Myocardial fibrosis

KEY POINTS

- Adults with rheumatoid arthritis (RA) have an ~1.5 times higher risk of cardiovascular disease (CVD) even with no traditional CVD risk factors, and incidence rates increase substantially with number of CVD risk factors.
- Low-density lipoprotein (LDL) or high-density lipoprotein (HDL) particles or apolipoproteins (apoB or apoA1) may be more reliable CVD risk factors than cholesterol (total, LDL-cholesterol, or HDL-cholesterol) concentrations because of chronic inflammation.
- In RA, current CVD risk factors likely underestimate the extent of subclinical atherosclerosis.
- Inflammation may directly cause myocardial injury and heart failure.
- Disease activity is a strong risk factor for CVD and mortality and key target for CVD risk reduction.

INTRODUCTION

Increased cardiovascular disease (CVD) risk has been reported for rheumatoid arthritis (RA) and other inflammatory autoimmune rheumatic diseases, which have a lifetime risk of adult onset of 1 in 12 for women and 1 in 20 for men.[1] This review focuses on the most common, RA, which occurs 2 to 3 times more often in women than men. The risk for CVD and total mortality is greater than 1.5 times higher in RA patients

Disclosure statement: Dr R.H. Mackey has received honoraria from the National Lipid Association related to educational, not promotional, endeavors. Dr L.W. Moreland serves on data safety monitoring boards for Boeringher-Ingelheim, Pfizer, and Acerta. None (Dr L.H. Kuller).

[a] Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, University of Pittsburgh, 542 Bellefield Professional Building, 130 North Bellefield Avenue, Pittsburgh, PA 15213, USA; [b] Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Room 550, Bellefield Professional Building, 130 North Bellefield Avenue, Pittsburgh, PA 15213, USA; [c] Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, 3500 Terrace Street, Thomas E. Starzl Biomedical Science Tower South 711, Pittsburgh, PA 15261, USA
* Corresponding author.
E-mail address: mackey@edc.pitt.edu

Clin Geriatr Med 33 (2017) 105–117
http://dx.doi.org/10.1016/j.cger.2016.08.008
0749-0690/17/

and 10-year CVD risk scores underestimate risk. CVD is more likely to be fatal, and unrecognized myocardial infarctions (MI), sudden death, and heart failure (HF) are increased. More aggressive primary and secondary prevention of CVD is needed in RA patients,[2–4] many of whom are postmenopausal women. The current review focuses on the following (1) the role of dyslipidemia in RA-related CVD risk; (2) risk of inflammation-related myocardial disease and eventual HF; (3) the emergence of RA disease activity as a key focus for CVD risk prediction and CVD risk reduction in RA.

RA is associated with greater than 1.5-fold higher risk of coronary heart disease (CHD), CVD, HF,[5,6] venous thrombosis,[7,8] fatal CVD, and total mortality,[9–12] and other CVD outcomes (**Box 1**). Unrecognized MI, sudden death,[13] and asymptomatic HF[14,15] are all increased among RA patients.

The greater than 1.5-fold higher risk of CVD exists at most levels of traditional CVD risk factors, even among individuals with no smoking, diabetes, hypertension, or history of hypercholesterolemia, as shown in the Women's Health Initiative (WHI) RA Study (crude relative risk = 10.75/6.35 = 1.69) (**Table 1**).[16] CVD risk in RA is strongly related to traditional CVD risk factors, for example, cigarette smoking, hypertension, diabetes, and hyperlipidemia.[11,17–19] The risk factor profile in RA (**Box 2**) includes higher prevalence of smoking, hypertension,[20] diabetes,[17] and obesity, although some RA patients have low body mass index (BMI).

The role of dyslipidemia in RA has been questioned due to a "lipid paradox." RA patients have lower levels of total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol (LDL-C) than adults without RA.[21] Increased CVD risk is associated with low levels of TC and LDL-C.[22] Total and LDL-C levels decrease before RA diagnosis,[23] often increase in response to anti-inflammatory medications, and decrease in response to flares of RA disease activity. The paradoxically low total and LDL-C levels contribute to underestimation of CVD risk by CVD risk scores (eg, Framingham Risk Score, Reynolds Risk Score,[24] and SCORE [Systematic COronary Risk Evaluation][25]), which have been shown to incorrectly classify as "low risk" approximately 60% of RA patients with coronary artery calcification greater than 300,[26] and approximately one-third of those who subsequently had CVD events.[25]

WHAT EXPLAINS THE EXCESS CARDIOVASCULAR DISEASE RISK IN RHEUMATOID ARTHRITIS?

Active RA is characterized by systemic inflammation that is credited with much of the excess risk of CVD and mortality in RA. The contribution of inflammation to

Box 1
Cardiovascular diseases increased in rheumatoid arthritis

- Myocardial infarction (often unrecognized)[13]
- Sudden death[13]
- Stroke[9]
- Venous thrombosis[7,8]
- Heart failure[5,6]
- Diastolic dysfunction[65]
- Peripheral vascular disease[78]
- Subclinical atherosclerosis[72,79,80]
- Endothelial dysfunction[81]