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Coronary artery disease in rheumatoid arthritis : atypical symptoms and increased mortality

Recent epidemiologic studies have shown that rheumatoid arthritis (RA) itself, especially when it is rheumatoid-factor positive, confers a considerable risk for premature cardiovascular disease and early mortality.¹⁻³

Most traditional cardiovascular risk factors, including lipid and homocysteine levels, are similar in RA patients and well-matched population controls.⁴ Biomarkers of inflammation however, such as C-reactive protein (CRP), fibrinogen, soluble intracellular adhesion molecule (sICAM), soluble tumor necrosis factor receptors (sTNF) I and II, and osteoprotegerin, are increased in RA patients, as they are in coronary artery disease (CAD) patients.⁵ Similarly, markers for thrombosis, including fibrinogen, von Willebrand factor (vWF), tissue-type plasminogen activator (t-PA) antigen, and D-dimer, also have been found to be increased in RA patients.⁶ The general well-established risk factors for CAD in patients with RA include the chronic systemic inflammatory state caused by the underlying immunologic process. Other causes of cardiovascular disease progressions are: use of corticosteroids which may accelerate atherosclerosis, and possibly the use of methotrexate, which can elevate the level of circulating homocysteine.

On the other hand, autopsy studies have indicated frequent involvement of cardiac valves and aorta in RA, and a rapidly progressive valvulitis of the aortic valve advancing to the need for valve replacement over less than 5 years.⁵ Rheumatoid arthritis patients have a greater incidence of vascular events and mortality, and atherosclerosis also appears at an accelerated rate. There is a strong correlation between the presence of inflammatory biochemical markers and carotid atherosclerotic plaques.⁶ Rheumatoid arthritis patients have twice the risk of developing heart failure (HF) compared with the general population—and the lethality of heart failure is markedly higher. A rheumatoid factor-positive RA patient's relative risk of HF is

as high as 2.6. The RA patients' mortality compared with standard heart failure patients was similarly higher following the diagnosis of HF; 15.5% in the first 30 days following the diagnosis of HF, compared with 6.6% of the controls. Another distinguishing feature, the fact that the HF of RA patients is far more likely to involve diastolic function and the left ventricular ejection fraction, is generally preserved.⁷

According to a recent survey, CAD in patients with RA, is characterized by less extensive atherosclerosis but more inflammation and unstable atherosclerotic plaques compared with CAD in arthritis-free matched controls. In this study,⁸ only 32% of RA patients with unstable plaques with multivessel disease were found at autopsy, compared with 61% of controls. However, unstable plaques were found in the left anterior descending arteries of 48% of RA patients, and only in 22% of controls. Inflammation signs and markers were also significantly more common in the adventitia of the left anterior descending artery of RA patients. In an other study, during a mean 15-year follow-up of RA patients, the rate of sudden cardiac death was 35 cases per 10 000 person-years in the RA group, and 18 per 10 000 in controls. The rate of silent MI was also higher in the RA group; however, the cumulative incidence of angina remains less than in controls.⁹

In conclusion, population-based studies and finer laboratory analyses of RA consistently show a roughly twofold increased risk of ischemic heart disease in association with rheumatoid arthritis.

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