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EDITORIAL

The increased cardiovascular risk in rheumatoid arthritis: when does it start?

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See related research by Södergren *et al*., http://arthritis-research.com/content/12/4/R158

Abstract

Established rheumatoid arthritis (RA) is associated with a doubled cardiovascular risk. However, data about the cardiovascular risk in early RA are scarce. Preclinical atherosclerosis can be reliably assessed with the carotid intima media thickness (cIMT), and the cIMT is a well-validated predictor of cardiovascular events. The cIMT was therefore used in a recent controlled, prospective study in patients with early RA. Surprisingly, an increased cardiovascular risk at baseline could not be demonstrated whereas cIMT progression appeared to be comparable with the general population. Obviously, this study underscores the need for further large-scale investigations to solve the emerging discrepancy with the existing literature.

Nowadays it is well known that patients with established rheumatoid arthritis (RA) suffer from an increased cardiovascular risk in comparison with the general population, and both traditional cardiovascular risk factors as well as the underlying chronic inflammatory process contribute to this excess cardiovascular risk. Little is known, however, about the cardiovascular risk in early RA patients – hence the recent article by Södergren and colleagues could be an important contribution to the field [1].

The increased cardiovascular risk in RA is mainly due to atherosclerotic events. Until recently atherosclerosis was considered an accumulation of lipoproteins within the arterial wall. During the past decade, however, atherosclerosis has been recognized as a chronic inflammatory process in the artery. The first step in the process is endothelial dysfunction caused by traditional cardiovascular risk factors such as smoking. The endothelium becomes more permeable – to lipids, for example – and becomes procoagulant instead of anti-coagulant. The inflammatory response further results in an entry of inflammatory cells and muscle cells. Foam cells are formed and result in fatty streaks. This lesion progresses and a fibrous cap is formed, consisting of smooth muscle cells and a collagen matrix that separates this atherosclerotic plaque from the arterial lumen. Ultimately, the plaque may rupture and the subsequent thrombosis causes a myocardial infarction.

In the study by Södergren and colleagues, the carotid intima media thickness (cIMT) (a marker of preclinical atherosclerosis) and flow-mediated dilatation of the brachial artery (a marker of endothelial dysfunction) were assessed in 79 early RA patients and in 44 age-matched and sex-matched controls. In a subgroup of 27 RA patients (and controls), the assessments were repeated after 18 months. Carotid plaques, another feature of preclinical atherosclerosis that can be assessed during cIMT measurement, were not reported. The flow-mediated dilatation and the cIMT at baseline were not significantly different between the two groups. This observation is remarkable particularly for the cIMT, as RA patients had significantly more cardiovascular risk factors (hypertension, smoking and dyslipidemia) – important determinants of the cIMT [2] – than the controls, and one would expect at least a tendency for an increased cIMT in RA patients, whereas an opposite trend was seen. Moreover, these results contradict findings from other studies that indicate an increased rate of cardiovascular events as well as cardiovascular risk factors before the clinical onset of RA.

The cIMT thickness in both groups was, as expected, associated with the traditional cardiovascular risk factors, and no relationship with disease activity markers was found in the RA group. This latter finding is in line with the results of our recent meta-analysis of cIMT in established RA patients, where also no relationship with disease activity could be demonstrated [3]. Perhaps using a cumulative disease activity marker (for example, number of erosions) would have been more appropriate

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in view of the observed relationships between disease duration/severity and cardiovascular risk. Moreover, this meta-analysis revealed a cIMT difference of 0.09 mm between RA patients and controls, indicating an approximately 15% increased cardiovascular risk [4]. This value is far less than expected in view of the 50 to 100% increased cardiovascular risk demonstrated in early RA and established RA patients [5,6]. The majority of the cardiovascular events are caused by plaque ruptures, which must imply that plaques rupture earlier in an inflammatory situation than in a non-inflammatory situation [7].

The observed increase in cIMT for RA patients in the study by Södergren and colleagues was 0.05 mm in 18 months, and was significantly larger than that in the control group. This value fits within the increase observed in a much larger investigation in the general population [8], however, so it is tempting to speculate that this normal cIMT progression in RA patients was due to effective antirheumatic treatment, nowadays aimed at remission, even though prospective data about disease activity were not provided.

Although there remain some methodological issues, the study by Södergren and colleagues clearly underscores two pivotal aspects about the cardiovascular risk in RA: an increased prevalence of cardiovascular risk factors in RA, and that effective antirheumatic treatment probably decreases the cardiovascular risk in RA. Their study therefore supports the recently published European League Against Rheumatism recommendations for cardiovascular risk management in inflammatory arthritis patients, which advocate that cardiovascular risk management should be aimed at disease activity suppression as well as at cardiovascular risk factor screening and treatment [9].

As the present findings are in contradiction with the existing literature, larger prospective, controlled investigations with a rigorous methodological design are necessary. Another challenging topic for future studies is how to identify the patients with a high risk for plaque rupture. Such studies may hopefully become redundant when it is demonstrated that effective antirheumatic therapy, aimed at disease remission, normalizes the change of plaque rupture.

Abbreviations

cIMT, carotid intima media thickness; RA, rheumatoid arthritis.

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Competing interests

The author declares that he has no competing interests.

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