Response to: 'Correspondence on 'Cardiovascular effects of biological versus conventional synthetic disease-modifying antirheumatic drug therapy in treatment-naive, early rheumatoid arthritis" by Georgiadis *et al*

We thank Athanasios *et al* for their interest in our original report entitled, 'Cardiovascular effects of biological versus conventional synthetic disease-modifying antirheumatic drug therapy in treatment-naive, early rheumatoid arthritis.[1]

Athanasios *et al* state that the findings of cardiovascular (CV) abnormalities in patients with new onset rheumatoid arthritis (RA) reported in the Coronary Artery Disease Evaluation in Rheumatoid Arthritis (CADERA) study are not surprising. While we agree that other studies, including the report by Athanasios that is quoted in the letter describe changes in early RA, there are no prospective randomised controlled trials of CV manifestations in very early RA cohorts. The trial cohort underpinning the 'CADERA' study had a median symptom duration of 20 weeks, with no history of CV disease (CVD) and a maximum of one traditional risk factor excluding diabetes mellitus. The results of CADERA, therefore, add to the existing evidence on CV abnormalities of very early RA.

In their letter, Athanasios *et al* assert that treat-to-target approaches would be expected to improve the observed vascular stiffness. Again, while this would appear intuitive, our results indicate that improvement was not linked to response status to the randomised treatment strategies or the disease activity state. As we discussed in the manuscript, these findings imply mechanisms beyond those of a generic inflammation paradigm the authors speak to.

The authors report on their own prospective, observational study in which 58 patients with treatment-naïve early RA were compared with 63 healthy individuals with no history of CVD or any risk factors.[2] Carotid ultrasound (CU) intima media thickness (IMT) and lipid profile were measured. A dyslipidaemic profile and higher IMT were observed in the early RA cohort compared with healthy individuals, both of which improved after a year of methotrexate and prednisolone treatment. The relationship between inflammation and lipid profile is complex with recent studies providing comparative data on the impact of effective RA treatments.[3]

The authors therefore strongly recommend CU as a simple, cost-effective and widely accessible tool for CV assessment. While we agree fully with the need for low-cost screening tools, in particular CU, cardiac magnetic resonance imaging (CMR) is unique in providing highly reproducible and sensitive assessments of not only vascular stiffness, but also cardiac function, ischaemia and importantly, myocardial tissue characterisation. This allows a more detailed approach to phenotype the pathophysiological processes of CVD in immune-mediated inflammatory diseases (IMIDs) and how these inter-relate over time. The value of such comprehensive assessment is essential in furthering understanding of disease mechanisms and treatment effects. While CMR may not be available equally across all settings, this cannot be a reason to discourage its use—on the contrary, wider access to this important imaging modality needs to be urged and supported.

We agree that coronary computed tomography angiography (CCTA) is instructive in providing assessment of coronary artery atherosclerotic pathology, with more emergent measures offering the opportunity of further risk stratification beyond structural and anatomical assessment of lesions.[4]

We would also highlight that interaction between rheumatologists and cardiologists and cardiac radiologists is not a limitation and multidisciplinary clinics and meetings are well established in rheumatology practice with integrated 'cardiorheumatology' practice being increasingly adopted.[5] A perceived lack of such practices in a local setting cannot be a reason not to employ the optimal tools for assessment.

Finally, International and national guidelines recommend CCTA and CMR in risk stratification, deeming these to be cost-effective.[6] This underscores the importance of delivering well-designed trials in IMIDs to inform future use of non-invasive imaging. In an era of precision medicine, we would strongly argue for the evaluation of sensitive and robust imaging methods to inform research studies and future clinical practice.

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