Subclinical Vasculitis as a Potential Mechanism to Explain the Heightened Cardiovascular Risk in Rheumatoid Arthritis

Zahi A. Fayad, PhD; Jeffrey D. Greenberg, MD, MPH; Jan Bucerius, MD, PhD

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From the Translational and Molecular Imaging Institute, Mount Sinai School of Medicine, New York, NY (Z.A.F.); Department of Radiology, Mount Sinai School of Medicine, New York, NY (Z.A.F.); Department of Cardiology, Zena and Michael A. Weiner Cardiovascular Institute and Marie-Josée and Henry R. Kravis Cardiovascular Health Center, Mount Sinai School of Medicine, New York, New York, NY (Z.A.F.); Division of Rheumatology, New York University Hospital for Joint Diseases, New York, NY (J.D.G.); Department of Nuclear Medicine, Maastricht University Medical Center, Maastricht, the Netherlands (J.B.); Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Center, Maastricht, the Netherlands (J.B.); Department of Nuclear Medicine, University Hospital RWTH Aachen, Aachen, Germany (J.B.).

Correspondence to Zahi A. Fayad, PhD, Translational and Molecular Imaging Institute, Mount Sinai School of Medicine, 1 Gustave L. Levy Pl, PO Box 1234, New York, NY 10029. E-mail zahi.fayad@gmail.com


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In the context of the current study by Mäki-Petäjä and colleagues, represents 1 further step for establishing vascular FDG-PET in routine clinical care. It is not only that this highly renowned group from Cambridge provided first insights into the vascular changes in patients experiencing rheumatoid arthritis (RA) and the effect of anti-tumor necrosis factor α (TNF-α) therapy on inflammation in the vasculature in those patients, they mainly, once again, provided a well-designed, prospective, vascular-tailored study about vascular PET imaging covering a new topic of noninvasive evaluation of vascular inflammation. The importance of performing those well-designed clinical trials cannot be overemphasized, because they are clearly needed to flatten the way of PET to enter into routine clinical care in patients with vascular disease. Furthermore, they provided a broad spectrum of FDG-uptake parameters such as the standardized uptake value, the target to background ratio, and the most diseased segment. Based on these analyses, they were able to show that patients with RA have an increased aortic FDG uptake even in comparison with patients with stable cardiovascular disease (CVD). Furthermore, they provided data indicating that TNF-α therapy is likely able to reduce aortic inflammation in those patients. In general, this study emphasizes the importance of FDG-PET imaging not only for identifying patients at risk for vascular inflammation and, consequently, for CVD, but also for serving as an end point for treatment evaluation.

It is also important to emphasize the background population of this study. Although it is now well recognized that inflammation plays an important role in plaque vulnerability in the general population, the role of RA-related inflammation, and perhaps, more importantly, autoimmunity, as a driver of heightened CVD risk in the RA population remains incompletely understood. In fact, the interpretation of the study results by the authors as “subclinical vasculitis” is particularly intriguing to the rheumatology community, given the established role of autoantibodies and autoimmunity in a subset of vasculitides. From a clinical perspective, aortic vasculitis has previously been described in the RA population by Gravallese et al in an autopsy-based case series, linked to coronary arteritis and myocardial infarction in a subset of RA-related aortitis cases. Thus, it is plausible that aortic vasculitis may be linked to a more generalized vasculitis that includes the coronary arteries and could contribute to the heightened CVD risk observed in the RA population.

The study by Mäki-Petäjä and colleagues is an important contribution to the rheumatology community for another
reason. Although it has been observed in multiple studies that anti-TNF biologics reduce the risk of incident CVD events in RA patients, the underlying mechanism(s) have been widely debated.26 The current study adds diminution of localized vascular inflammation to the growing list of potential mechanisms by which anti-TNF biologics may reduce CVD risk. One important limitation of this study is that it is not clear whether other immunomodulator biological drug classes, or even methotrexate, can reduce vascular inflammation in a comparable manner. For RA-related outcomes, including joint counts, patient-reported outcomes, and achievement of clinical remission, there is a growing literature that nonbiological RA drugs such as methotrexate, in particular, prescribed as combination therapy, can frequently achieve clinical outcomes comparable to targeted biological therapies, including anti-TNF drugs.27

The work by Maki-Petäjä and colleagues raises a number of additional intriguing questions. An important question is whether or not the extent of aortic vascular inflammation detected by PET can actually predict clinical CVD events in the RA population. Moreover, if vascular inflammation by PET does indeed predict incident CVD events, are there surrogate biomarkers that can be applied to clinical practice more easily and in a more cost-effective manner? Specifically, what is the relationship between circulating inflammatory biomarkers and vascular inflammation? And finally, to what extent can short-term changes in such biomarkers predict changes in vascular inflammation and CVD risk? In many respects, this study raises several interesting questions that need to be answered in the future, and yet it can be viewed as a landmark study that pushes forward our understanding of a potential mechanism underlying the heightened CVD risk in the RA population.

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Disclosures

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