

EDITORIAL

Implication of new atherosclerotic carotid plaques in the cardiovascular outcome of patients with rheumatoid arthritis

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See related research by Zampeli *et al.*, <http://arthritis-research.com/content/14/2/R44>

Abstract

Early detection of atherosclerosis is of major importance to reduce the increased incidence of cardiovascular (CV) complications observed in patients with rheumatoid arthritis (RA). Prospective studies have shown that an abnormally increased carotid intima-media thickness and the presence of plaques assessed by carotid ultrasound are good markers to predict the development of CV events in these patients. Age, classic CV risk factors, and corticosteroid use are also predictors of new plaque formation in patients with RA. Active treatment of the disease may decrease the inflammatory burden, leading to a reduction in the progression of subclinical atherosclerosis in these patients.

Rheumatoid arthritis (RA) is a disease associated with accelerated atherosclerosis and increased risk of cardiovascular (CV) events. In this issue of *Arthritis Research & Therapy*, Zampeli and colleagues [1] longitudinally assessed the association with new carotid artery plaques in a series of non-diabetic patients with RA. Besides highlighting the expected influence of age and traditional CV risk factors, the authors highlighted the potential influence of corticosteroid use as an independent risk factor for new plaque formation in the follow-up of these patients [1]. This interesting study raises a series of points that deserve to be addressed.

First, the importance of early detection of atherosclerosis in RA before the development of CV complications. In

this regard, the detection of endothelial dysfunction by brachial ultrasonography and the presence of abnormally increased carotid artery intima-media thickness (IMT) and carotid plaques by carotid ultrasound constitute a major breakthrough as they allow the presence of subclinical atherosclerosis in patients with RA to be identified [2]. In this respect, a recent study confirmed a correlation between the presence of endothelial dysfunction (considered an early step in the atherogenesis process) and morphological data showing abnormally increased carotid IMT in RA patients with a disease duration of longer than 7 years [3]. However, carotid ultrasound is technically easier to perform than flow-mediated endothelium-dependent brachial ultrasound and, in the hands of trained professionals, is a technique with low interobserver variability. Furthermore, as observed in low- and intermediate-risk groups of non-rheumatic individuals [4], both carotid IMT and the presence of carotid plaques have proven to be good predictors of CV events in patients with RA [5,6].

Second, in their study, Zampeli and colleagues [1] focused specifically on carotid plaques. With respect to this, carotid plaques constitute the best expression of atherosclerotic disease. Also, technically, it may be easier to detect carotid plaques than to evaluate the carotid IMT.

Third, the study by Zampeli and colleagues confirmed the implication of age and classic CV risk factors as predictors of new plaque formation in RA. In keeping with these observations, age was found to influence the degree of severity of the carotid IMT and the presence of carotid plaques in both patients with RA and matched controls [7]. Nevertheless, Zampeli and colleagues did not disclose any influence of the chronic inflammation as an additional predictor of new plaque formation. This result is somehow unexpected as RA is a chronic inflammatory disease, and, even in quiescent stages of the disease, inflammation is always present. A plausible explanation for that may be the relatively low duration

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between the first (baseline) and the second (follow-up end) ultrasound evaluations (mean of 3.6 years) in this series [1]. With respect to this, on the basis of a study of 631 consecutive patients with RA, del Rincón and colleagues [8] showed that IMT increases per unit of age in proportion to RA duration. In the study by del Rincón and colleagues [8], carotid IMT increased from 0.154 mm/10 years among patients with RA for not more than 7 years to 0.295 mm/10 years among patients with RA for at least 20 years. The duration of the disease was also associated with the presence of carotid plaques in patients with RA [7].

Fourth, Zampeli and colleagues observed an association between corticosteroid use and new plaque formation. In keeping with that, a recent longitudinal study on predictors of progression of carotid atherosclerosis in RA showed that cumulative exposure to prednisone was associated with progression of carotid IMT [9]. In contrast, patients receiving tumor necrosis factor inhibitors at baseline had a lower adjusted rate of progression of carotid IMT in comparison with non-users [9]. Also, in line with our earlier comment on the potential influence of chronic inflammation, the higher swollen joint counts and higher average C-reactive protein levels were both associated with incident or progressive plaque [9]. Therefore, it seems to be evident that active treatment of the disease may be required to reduce the inflammatory burden, leading to a reduction in the progression of sub-clinical atherosclerosis and the risk of CV events in these patients. We cannot exclude that the association of new plaque formation with corticosteroid use, reported by Zampeli and colleagues, may indicate the presence of some kind of confounding factor as the longer intention-to-treat time with higher dose of corticosteroid may indirectly indicate a higher degree of severity probably associated with higher inflammatory burden in some patients.

Finally, we have to keep in mind that RA is a complex disease and that the increased incidence of CV complications in RA may be the result of interactions between genetic influence [10], chronic inflammation [10], and traditional CV risk factors [11]. In conclusion, recent studies reinforce the importance of non-invasive surrogate markers of atherosclerosis, in particular of carotid ultrasound, to predict the CV outcome of patients with RA.

Abbreviations

CV, cardiovascular; IMT, intima-media thickness; RA, rheumatoid arthritis.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MAG-G and CG-J made equal contributions to the conception and design of this editorial. Both authors read and approved the final manuscript.

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