The use of carotid ultrasonography in the assessment of subclinical atherosclerosis and the paradoxical effect of corticosteroids on atherosclerosis in patients with rheumatoid arthritis.

Comment on the review article by Avalos et al.

Sirs,
We have read with great interest the superb review article by Avalos et al. titled “Atherosclerosis in rheumatoid arthritis (RA) and systemic lupus erythematosus”. With respect to the presence of subclinical atherosclerosis in patients with RA, we would like to emphasize a few points that may be of potential interest for the readers of the journal.

Although classic (traditional) cardiovascular (CV) risk factors along with the presence of chronic systemic inflammation and a specific genetic background (e.g. carriage of HLA-DRB1*04- shared epitope alleles) have been proposed to account for the increase risk of accelerated atherosclerosis and CV events observed in patients with RA, we also found subclinical atherosclerosis, established by carotid ultrasonography, and defined as an increase of carotid intima-media thickness (IMT) and increased incidence of carotid plaques, in a series of RA patients with long-standing disease without classic CV risk factors or clinically evident CV disease compared to matched controls.

Moreover, we did not observe a significant correlation between the mean cumulative dose of prednisone and the presence of subclinical atherosclerotic determined by an increased carotid IMT (3) or by the presence of endothelial dysfunction in patients with RA (4). Likewise, we did not find a significant correlation between the left ventricular diastolic dysfunction observed in patients with RA and the cumulative prednisone dose (5). Taken together, these observations further support the claim of a paradoxical effect of corticosteroids against the progression of atherosclerosis in patients with RA due to the antiinflammatory effect mediated by these drugs.

Finally, we have recently observed that carotid IMT is also a good predictor of CV events in patients with RA. We found that after a 5-year follow-up, the value of carotid IMT may predict the risk of CV events (6). Carotid IMT was greater in RA patients who, over the extended follow-up, experienced CV events compared with the remaining RA patients who did not have CV complications. Also, carotid IMT categorized in quartiles was strongly associated with CV events over the 5-year-follow-up period; none of the patients with carotid IMT less than 0.77 mm had CV events, while 6 of the 10 patients with carotid IMT greater than 0.91 mm experienced CV events (6). Furthermore, carotid IMT yielded a high predictive power for the development of CV events over the 5-year follow-up period. In this regard, the area under the ROC curve was 0.93 for a model that only included carotid IMT and 0.90 for carotid plaque (6). These data highlight the potential use of carotid ultrasonography to establish the risk of CV events in patients with RA.

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References

Reply
Sirs,
We thank Dr. Gonzalez-Gay and colleagues for their interest in our review. They comment on the association between atherosclerosis and the ‘shared epitope’ of HLA-DRB1 that is associated with rheumatoid arthritis, particularly more severe disease. The specific mechanisms, inflammatory or immunological, which are responsible for this association with atherosclerosis will be of great interest.

Cardiovascular risk may indeed be increased in RA without the existence of clinical cardiovascular disease or traditional cardiovascular risk factors, but it is likely that atherosclerosis is accelerated by the coexistence of both traditional cardiovascular risk factors and non-traditional risk factors such as RA (1, 2).

The relationship between corticosteroids and atherosclerosis in rheumatic diseases is likely to be complex, depending on dose and duration of therapy, underlying disease severity and its response to corticosteroids, and individual variability. As Gonzalez-Gay et al. discuss, several studies have found no association between corticosteroid treatment and atherosclerosis in RA, and indeed, the QUEST-RA study suggested that steroids decrease risk in some patients (3).

The relationship between surrogate markers of the severity of atherosclerosis such as carotid IMT and coronary calcium and hard cardiovascular outcomes is of interest, and clearly an area that will require additional studies with adequate sample sizes to allow for statistical adjustment for covariates known to affect cardiovascular risk.

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References