Reviewer's report

Title: How age and sex affect the erythrocyte sedimentation rate and C-reactive protein in early rheumatoid arthritis.

Version: 2
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Reviewer: Robert Shmerling

Reviewer's report:

Reviewer number: 1
Referee's comments to the author(s)

This study attempts to determine the impact of age, gender and BMI on the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) in early rheumatoid arthritis. The findings are of interest but such studies are challenging to perform well given all of the potential confounders. Indeed, this study has a number of limitations, listed below.

I have previously reviewed this paper - the authors have made a number of revisions that have improved the manuscript. However, a number of major limitations remain.

Major compulsory revisions:

1. The lack of information about medications, especially corticosteroids – the authors state that their “aim here was not to provide an exhaustive list of all possible confounders” – fair enough, but the potential impact of NSAIDs, corticosteroids and other medications is too big to discount. It is good that this is now mentioned as a limitation but it is also a flaw that might invalidate the findings. This should be given more discussion.

2. Details about how the diagnosis of RA was established are missing – the authors refer to 2 studies, one of which is in press. The one in press should be omitted and, in addition to stating that the diagnosis was established clinically, the readers should be informed whether or not the clinical diagnosis was established by a certified rheumatologist. This is particularly important given the low disease activity and low rates of positive RF and anti-CCP: while this could be due to early disease it could also be due to non-disease.

3. In the result section, the authors state: “At inclusion, patients had active disease as characterized by a DAS28 score > 2.6” – as I read this, the authors continue to conflate lack of remission with active disease – yes, a DAS > 2.6 is an indication of non-remission; but it does not mean they had high disease activity. By virtue of the clinical data presented, these patients had LOW disease activity, so stating that they had active disease is not as accurate as it could be.

4. The authors state that the study subjects’ relatively low female proportion and
older age is typical of a Dutch early RA study – that may be, but it limits the
generalizability of the findings. Similarly, the relatively low disease activity scores
of these presumably untreated and “active” patients may be due to early
presentation but again, this could limit generalizability – other populations with
more active disease at presentation could have had different results. These
concerns are still not addressed in the discussion of limitations – stating that the
findings are not surprising is not enough.

Minor Essential Revisions: None
Discretionary Revisions: None

Level of interest: An article whose findings are important to those with closely
related research interests

Quality of written English: Needs some language corrections before being
published

Statistical review: Yes, but I do not feel adequately qualified to assess the
statistics.

Declaration of competing interests:
I declare that I have no competing interests.