Author's response to reviews

Title: Low level of physical activity in women with rheumatoid arthritis is associated with cardiovascular risk factors but not with body fat mass - a cross sectional study

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Author's response to reviews: see over
Dear Editor

First of all, we would like to thank the reviewers for their very careful, constructive and pertinent review of this paper allowing us to improve our manuscript quality. In the following lines you’ll find an answer to each of the points raised by the reviewers. We sincerely hope that those modifications will meet your expectations.

Reviewer 1

1. It would be very interesting to have a mechanistic explanation of how exercise might affect risk factors without affecting inflammation or obesity (two of the potential causes of risk factors).

   Yes, this is a very interesting question. We are well-aware of the anti-inflammatory responses of exercise, which is partly mediated by muscle derived interleukin (IL)-6. The explanation for the non-association between total physical activity and inflammation in the present study is probably dependant on the rough variables of inflammation we used, DAS28 and ESR, in a cohort of patients with low disease activity. In only in one of the pre-defined activities, walking, we found an association with DAS28. We have now emphasized the association between walking and disease activity in the discussion.

   We suggest that despite that the total physical activity in the present patients was not high enough to reduce fat mass, it was sufficient to reduce the risk factors for CVD, probably by reducing sub clinical inflammation (see about walking above).

2. One more difference between your study and that of Stavropoulos-Kalinoglou et al. is that they also included male participants. Could that explain some of the discrepancies?

   We don’t think so, but can’t be sure. Males studied earlier have also been reported to be in the overweight range, but of course they may have higher physical activity. For safe we have added information about men in discussion.

3. The energy intake of your patients seems to be very low (<1700kcal/per day). This is almost in the range of calorific restriction/diet. If you calculate total daily energy expenditure from your data (age, height, weight for REE, physical activity from IPAQ scores and thermal effect of feeding from FFQ), you might find that some patients (especially those in the higher activity quartiles) might be in negative energy balance. If this has been happening over a year, these people should be very lean. If not, this could be an indication of misreporting food intake or physical activity. In other studies where energy intake in RA was reported (Stavropoulos-Kalinoglou et al. do as well), it was >2000kcal and closer to the average for the general population. Could this have affected your results?

   The lower mean caloric intake is probably due to underreporting and several studies suggest that the underreporting is increasing with an increasing BMI. However, we have in an earlier study
shown that the reported intake of fatty acids correlated well with that found in subcutaneous fat. That finding supports the correctness of the proportions of the dietary intake components, even if underreporting of total intake has been done. So we don’t think that underreporting affects our results.

Reviewer 2
1. What is the authors’ explanation regarding this high prevalence of obesity?

This is probably due to the RA disease. During the course of the RA disease changes in body composition, with reduced fat free mass occurs. The decline in fat free mass is often associated with increased fat mass, i.e. rheumatoid cachexia and is associated with excess production of inflammatory cytokines, reduced peripheral insulin action.

2. Were the RA patients studied as overweight as the general Swedish population to whom they were compared in terms of physical activity?

They were only compared, the patients and the general population, as to the level of total physical activity. We had no possibility to compare the amount of fat mass, as only an overall mean BMI value are given in the reference for the general population. That was 26.1, slightly higher than in the present patients.

3. Might there be some association between even low-medium disease activity state to obesity despite seemingly adequate calorie expenditure and reasonable calorie uptake?

We can only speculate about this. Probably low-grade inflammation play a role, but that can not explain the obesity in full. We have recently reported that when reducing disease activity in patients getting TNF-blockade, the fat mass increased. Thus, so far some other hitherto unknown factors are involved.

According to your proposal we have added the reference on dyslipidemia in RA but not those dealing with infliximab-treatment.

Best Regards,

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