Reviewer's report

Title: Association between metabolic syndrome and bone fractures: a meta-analysis of observational studies

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Reviewer: Claudia Gagnon

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Sun K et al. conducted a meta-analysis of observational studies (both cross-sectional and prospective cohort studies) on the association between metabolic syndrome (MetS) and fractures. They found that there was no association between MetS and fractures in both the cross-sectional and prospective cohort studies. There was however a significant heterogeneity among the prospective cohort studies (n=3).

Results from published observational studies on the topic have been inconsistent. The main reason for the discordant results is the fact that MetS is a heterogeneous syndrome that requires the presence of at least 3/5 criteria for its diagnosis (NCEP-ATPIII criteria). Predominance of different components of the MetS in the various studies may contribute to the discrepant results. The relationship between each of the components of the MetS and bone is extremely complex. One of the components may have a positive effect on bone while another component may have a deleterious effect. Moreover, the confounders that were adjusted for in the studies were highly variable and may further contribute to the discordant results. I am thus unsure that looking at the MetS as a whole is the best way to assess clinically whether this syndrome impact on fracture risk. I think that it would be more useful to know which components of the MetS are associated with an increased or a reduced risk of fracture.

Discretionary revisions

1. The authors correctly acknowledge in their discussion (p.13, first para) that evaluating the association between individual components of MetS and fractures would be more appropriate. I think that this meta-analysis would contribute greatly to the current knowledge if it could evaluate, in some way, the impact of the components of MetS on fracture risk. Would it be possible to do a meta-analysis of the association between each of the components of MetS and bone fractures in the same studies (n=8)?

2. To help the reader better assess the validity of the studies, it would be interesting to add somewhere (perhaps in Table 1) the following information for each study: RR (or OR) and their 95% CI, factors that were adjusted for in the analyses, the number of fractures observed and finally, the duration of follow-up for the prospective cohort studies.

3. In the discussion, lines 5-6 from the bottom: another cause of heterogeneity
among cohort studies is the duration of follow-up. The Rancho Bernardo Study, that found an increased risk of fractures in people with the MetS, had a very short follow-up of about 2 years while the other two studies (Tromso and MINOS), that found a reduced risk of fractures in people with the MetS, had a longer follow-up of 6 and 10 years, respectively. More details on the 3 cohort studies could be provided. For instance, the Tromso study used non-fasting samples for glucose and triglycerides, they also used BMI in the definition instead of waist circumference and the fractures were not limited to non-trauma fractures.

4. Subgroup analyses were only done for cross-sectional studies (Table 2). Did the addition of the 3 cohort studies change the results?

Minor essential revisions

1. Results p.11, 2nd para: MINOS study did not report cross-sectional data. Did you want to mention the Rancho Bernardo study instead?

2. The paper is generally well written although I found some mistakes throughout the text. I would suggest that the paper be reviewed by the authors before publication.

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: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.