Reviewer's report

Title: Changes in bone marrow lesions in response to weight loss in obese knee osteoarthritis patients: A prospective cohort study

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Reviewer: Daichi Hayashi

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Review comments for BMC Musculoskeletal Disorders 4278849507772953

Overall comment: The study aimed to investigate the changes in bone marrow lesions (BMLs) after a 16-week weight loss program in obese persons with knee OA, and relate changes in BML to the effect of weight loss. Authors did not find significant association between improvement in BML scores and weight loss, and concluded BMLs do not respond to a rapidly decreased body weight. There is a crucial oversight in the methodology which could be the cause for not finding a significant association between weight loss and BML improvement.

Major compulsory revisions

- In the abstract, please state the total number of subjects included in the study.
- Despite a rather extensive list of references, authors missed an important paper which described the association between BMLs and malalignment of the knee (Hayashi D, et al. Osteoarthritis and Cartilage: 2012;20(11):1227-33. Since obesity and mechanical load are closely related, and so are the malalignment and mechanical load in the more loaded compartment, authors should include the issue of malalignment in the discussion of the present study. Authors did include measurement of knee mechanical axis, and thus the aforementioned paper should be cited and discussed its relevance to the finding of this study.
- In the same line of thinking, authors should analyze the relationship between weight loss and BML changes in a compartment-specific manner. Although authors do state that they read radiographs 'for each knee compartment' but they did not clearly say whether this means medial/lateral compartments, or patellofemoral/tibiofemoral compartments. Authors did the whole-knee analysis without treating medial and lateral compartments separately. This may be the principal reason why they did not find any significant association. I would be interested to see if: (i) stratifying the cohort according to varus/valgus/neutral alignment, and (ii) perform analysis in the medial and lateral compartments, separately. In doing so, authors should also consider adding 'medial compartment in varus knees' and 'lateral compartment in valgus knees' to form 'more loaded compartment', which can then be compared to neutrally loaded knees (neutral alignment). In 'less loaded compartment', I would not expect to see any effects of weight loss anyway, since that compartment is not mechanically under stress from the first place. For details of compartment based
analysis, please refer to Hayashi et al's paper.

- My major concern is that authors used coronal STIR and T1w, as well as sagittal T2w/PDw sequences for BML assessment. Were T2w/PDw sequences fat-saturated? If so, it is OK, but if not, it is not an adequate methodology. Using only coronal STIR for BLOKS assessment does not seem to be feasible, since BLOKS subregions are defined using sagittal slice (as well as coronal).

- Although authors read cartilage, osteophytes and meniscus using BLOKS, it is not entirely clear how they integrated those reading into their analysis. Yes, those readings are presented in Table 1, but what about their significance in the main analysis (i.e. association between weight loss and BML improvement?) Please discuss.

- Weight loss of 10% of BMI or above is an arbitrary cut-off point set by the authors. What if different cut-off points are used? Also, what if weight loss is assessed as a continuous variable without a cut-off point? Would they make any difference to the findings? Please explore.

Minor revisions

- The first paragraph (first 5 lines of Background) is too general, and is not necessarily directly relevant to this study. Authors should delete this paragraph, and start the manuscript with the second paragraph, which is about obesity. This study is all about obesity and BMLs, NOT knee osteoarthritis in general.

- Figure 1 is very hard to read, because of the font used and a lack of proper formatting. Please revise this figure so that it is visually more appealing.

- In Figure 1, authors mention 'medial tibiofemoral compartment'. However, in the Methods section, authors did not explain how they performed compartment-specific analysis. They did not mention the term 'medial' or 'lateral'. On the other hand, they did mention 'patellofemoral' compartment and 'tibiofemoral' compartment. Please clarify in the Methods section if medial/lateral compartments were assessed separately.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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.