Reviewer's report

Title: Determinants of vertebral endplate changes: a magnetic resonance imaging study in middle-aged male workers

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Reviewer: Charlotte Leboeuf-Yde

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General
This is an interesting article on a hot topic. I think it could benefit from some changes, though.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Abstract. It would be helpful if all variables used in the analyses were listed in the methods section. Otherwise the reader cannot judge the value of the final results of the multivariate analyses.

2. You need to be more careful with your references. Perhaps you should check that you have quoted everything correctly. I had some of your references at hand and I do not always agree with you on your interpretation of their contents.

Specifically:
- Background, 1st para: Ref.1 Modic 1988 (Imaging of degenerative disk disease...) does not contain original data and should therefore not be used as a reference of "facts". Ref. 2 is the one you should refer to, when using Modic as the source. Also de Roos (ref 3) is OK. Adding a narrative text as reference gives the reader the false impression that there is multiple underlying evidence.

- In the Background, 2nd para you discuss risk factors. In your last sentence, I suggest that you place the relevant references after each statement, for the sentence to read: "In addition to age (19,20), weight (19) and male gender (19) have been shown to be associated with Modic changes." In other words, your ref. 1 should not be included because it is not a study of risk factors. In ref. 19, I found positive associations with age, males and weight. Ref. 20, which is the only of your three suggested references that can identify risk, as it had prospective data, did in fact fail to detect any factors associated with new Modic changes (notably age and physical work load did not turn out positive) but you had only 23 such subjects, so that might be an explanation and also, new Modic changes might be relevant at an earlier stage only. According to the cross-sectional data though, there was a postitive association with age but not with physical workload. Therefore, you should not speak about "increased risk" but merely of association, and definitly not "associations with an increasing risk".
- Background, third para, second sentence. You say that you choose to study the L5-S1 level because a previous study (ref 21) had shown the association between Modic changes and pain to be "so prominent at the L5-S1 level". According to the text in that article, in which number of episodes, VAS for pain last week and past 3 months were reported for L5-S1 and for all lumber levels, the odds ratios were not higher for L5-S1. However, as far as I remember, in most studies on the prevalence of Modic changes, these are most COMMON in the lowest disc, so perhaps that is what you should write instead?

2b. And if you concentrate on L5-S1, why then do the analyses at all levels? Or...if you believe that L5-S1 is so important, why not analyze L5-S1 separately and those above as one group? All this overlapping of individuals seems a pity.

3. Materials and methods, image analysis. A very good description of this aspect, the only things I did not find was a statement as to whether the radiologists were blind also to the study subjects' clinical picture. There was no intra-examienr reliability study for the disc degeneration study, I take it? Is there a reference on how easy it is to do this reliably?

4. I have a serious problem with the division of Modic I and II into separate groups. If you consider II to be the continuation of I, they should be analyzed together. When, in the bivariate analysis you find that BMI and waist circumference are linked with type II but not the two combined, this might be a function of age (type II comes after type I, i.e. for many a function of age). This can be seen to be true in your multivariate analysis where BMI is significantly associated with both Modic II and Modic both types. When you state in your report that you found nothing for the Modic Is, this gives the reader a feeling that there is nothing interesting there, but it might simply be that they were too few for significant findings to occur. If you want to conduct your analyses in this way (and you should decide that but then at least tell us why you do it), and if you then want to account for the type Is, you must tell us if the estimates were similar to those found for type II, but that the low number prevented significance.

5. Statistical analysis. You tell us what the reference group is in your modic analyses but you do not say anything about this in relation to the disc degeneration group.

6. In a previous study, to which you refer (14), it was noted that people without degenerative disc findings on MRI resembled people with degenerative disc findings but WITHOUT Modic changes on a number of variables but that disc degeneration COMBINED with Modic changes did produce a large number of statistically significant associations. Therefore, I think that your study would benefit from another approach: 1. People without severe disc degeneration and without Modic changes should should make up one subgroup, 2. people with severe disc degeneration and without Modic changes should make up another subgroup, and 3. people with both severe disc degeneration and Modic changes should make up the third group. As it is now, you cannot really compare your two
groups, those with Modic changes and those with severe disc degeneration, because they contain overlapping individuals. I suspect that you will augment your odds ratios, if you do it the other way round, as suggested.

7. In your result section you seem to forget that AGE was positively associated with Modic changes and degeneration and also in the discussion.

8. Discussion, 1st para. "To the authors' knowledge, no population-based study has previously focused on the determinants of modic changes". You have one such study in your list of references, number 14, Per Kjær.

9. In the Discussion, second para, last sentence, you introduce for the first time the fact that you found most Modic changes at the levels of the two lowest discs. However, you have forgotten to tell us about that in the Result section, as far as I can see. In fact, you seem to have forgotten to add references to some of your tables and figures, throughout the text.

10. Discussion, third para: Why mention waist circumference, when it vanished in the MVA analyses?

11. Discussion p.10 at the bottom of the page. You speak about smoking and degeneration and Modic changes and talk about a trend between smoking and Modic changes but not with disc degeneration and use a Finnish twin study (ref 5) to support these findings. However, you need to read that report again. They did not deal with Modic changes, as far as I remember and what did they conclude on smoking again? There were two such studies, in the first study they found something which they refuted in number two, if I remember it correctly.

12. I do not quite understand your interpretation of your own data on p.11, last para. You say that the determinants of Modic changes and severe disc degneration differ espacially at L5-S1 level. Looking at Table 4 with the MVA analyses, I note that age is positively associated with both Modic and degeneration, regardless if you report results for all levels or only at L5-S1. BMI is related to Modic regardless all levels of L5-S1 but not with severe disc degeneration, regardless where in the spine. Only vibration exposure comes out significant at L5-S1 only (for discs) but not for all level discs vs. not for all levels or L5-S1 in Modic changes.

13. In the discussion section, last para before conclusions, you say that the determinants of Modic type I and II are different. You did not study this aspect, so this text should be removed. I have discussed this aspect before in this text.

14. References. I believe that the "et al" procedure is inadmissible in this journal. All authors should be listed, is my experience.

15. Check if you have referred to all tables and figures in the text. I could not find a reference to Table 1 and I could only find Fig. 1.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of
a term, which the author can be trusted to correct)

1. The title would benefit if the subject of disc degeneration was included. For example "Determinants of vertebral endplate changes and disc degeneration..."

2. Method. This comment comes too late, but how did you succeed in squeezing your study subjects into your à priori (don't forget the accent on the "a") alcohol consumption groups? They do not include all possibilities. For example, nobody was supposed to drink alcohol once a month or 4-11 times a month, nor was it possible to drink alcohol 5-6 times a week.

3. Results. I suggest that you start your result section by a brief demographic description of your study sample including differences/no differences between the two study groups. You should not only describe your Modic findings but also your disc findings in this initial text.

4. Determinant of Modic changes, p.8, 4th line. You write that the odds ratios "ranged from 1.42 to 1.48" but they did not range as there were only two values. In other words: "They were 1.42 and 1.48, respectively."

5. Discussion, second para. You find a larger prevalence of Modic changes (56%) than that in a previous Danish study (22%). You suggest that this can be explained by a gender difference. Why? In the Danish study there was no significant overrepresentation of males with Modic changes. However, in the Danish study, all study subjects were 40 yrs. In yours, you had a more older subjects and a considerably larger number of people with Modic II, which is consistent with them being older. Is that not a better explanation?

6. You then proceed to discuss age (as I suggest above). However, your three references (1,19, 20) are suspect. Ref. 1 is a narrative text, and in ref 19 age was found to be linked with Modic changes but in ref. 20 age was not linked with new cases of Modic but only with present Modic changes...

7. When you, in the discussion, p.12, second para, talk about the limitations of your study and the temporal relationship, I think that it is worth emphasising again that AGE is a true predictor for both disc degeneration and Modic changes.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

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.