Reviewer's report

Title: Risk of low bone mineral density in patients with rheumatoid arthritis treated with biologics

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Reviewer: Md Yuzaiful Md Yusof

Reviewer's report:

Comment to the Authors:

The main question asked by the authors was relevant which was to identify the risk factors for osteoporosis in RA patients treated with biological DMARDs. This is important as osteoporosis is still prevalent despite treatment with biologics. Despite some improvement of the manuscript from the initial submission, I have major concerns regarding the statistical analysis and the lack of applicability to clinical practice (findings are not novel).

Major Compulsory Revisions:

1. Why was univariate analysis performed? I do not think this is necessary. The outcome was categorical variable (binary), and logistic regression was sufficient enough to fit a model that could identify predictors of the outcome.

2. More importantly, I have a concern with regards to exclusion of sex in the logistic regression analysis. In principle, the authors had one outcome and tried to identify a list of independent risk factors for it rather than had one outcome and one exposure, thus needed to adjust for confounding factors. It seems to me that the authors are treating the statistical software as a black box rather than imputing the clinically meaningful predictors into the model. Correlation does not equate to dependency and it is still unclear why sex is excluded – as this variable still satisfies the assumption for a logistic regression analysis.

3. In the multivariable analysis, advanced age, history of past thoracic or lumbar vertebral fracture, lower BMI, longer disease duration and higher Steinbrocker classification were significant factors for BMD <70% of YAM. The first 3 are not new findings and in fact, have already been incorporated into FRAX and ORIS tools for fracture prediction. The last 2 may be important however the authors did not emphasise the importance of these factors and certainly higher Steinbrocker classification was not even discussed in the Discussion.

4. Why was femoral neck BMD selected to diagnose osteoporosis but a history of vertebrae fracture was chosen as an independent variable? In addition, the confidence interval was very wide (1.9-16.4) and no explanation was given for this.

5. In Table 3, what did the p=0.67 represent? There were 4 categories or level of comparisons involved and was the multiple testing corrected?
6. It would have been more novel if the logistic regression analysis was carried out after stratifying the therapy to anti-TNF vs non-anti-TNF groups.

Minor revision:

1. In Method section line 13, this should be changed to predicting risk factors associated with a BMD #70% rather than #70%.

2. The subtitles: “Influence of methylprednisolone therapy on osteoporosis” and “Influence of disease activity on osteoporosis” – Influence should be changed to association. This is a cross-sectional study, hence only association can be deduced but not the “Cause or Effect.”

3. For a complex statistical analysis, I think other software such as STATA or SPSS should be used.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interest