Reviewer’s report

Title: Plasminogen activator inhibitor-1 concentrations and bone mineral density in postmenopausal women with type 2 diabetes mellitus

Version: 1 Date: 16 Dec 2015

Reviewer: Rachel Crowley

Reviewer's report:

The authors have performed the extra analysis requested and have made a number of changes as suggested.

However the extra analysis does raise questions about the conclusions made.

Again, what is of interest here is propensity to fracture and bone quality in these patients. In the absence of fracture data or qualitative measurements of bone, BMD is the measurement of interest. Therefore the finding that there is no association between BMD and PAI-1 after adjustment for age and BMI is highly relevant (line 181, and Table 2).

Both in the abstract and the conclusion there are statements that PAI-1 influence on bone density is mediated through metabolic factors, but this study has not demonstrated how PAI-1 is associated with BMD so a re-write should reflect that it is a study of association only.

It appears from the data that metabolic factors such as insulin and BMI influence PAI-1, and that these factors also influence BMD, and that PAI-1 may purely be a marker of metabolic status.

It may be an alignment issue in the Supplementary Tables when converted to PDF but it appears that hip BMD changed from a positive to a negative correlation after the PAI-1 model was
adjusted, and that insulin correlation was negative in model VI. Supplementary Tables 2 & 3 are confusing to the message of the study.

In line 223 of the discussion there is a statement that suggests PAI-1 is lower in those with lower BMI and lower insulin - but insulin was not lower in the lower BMD patient groups. The study may not have been powered to detect this, and the discussion should reflect this - as a stand-alone statement it doesn't make sense to tie the bone effects to insulin if there was no difference in insulin levels between the groups.

Overall I think the conclusions should reflect that PAI-1 appears to be a marker of metabolic status that correlates with measures of bone density and turnover; whether it is itself an agent that affects bone would need to be investigated in a further study.

Corrections:
line 75 hospitalized
Suppl Table 1: Spellings Risk Hypertension Sulfonylurea

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
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