Reviewer’s report

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

Version: 0 Date: 09 Oct 2015

Reviewer: Rachel Crowley

Reviewer's report:

The authors have measured PAI-1, bone turnover markers and markers of inflammation in a cohort of postmenopausal women with type 2 diabetes mellitus separated into groups of normal BMD, osteopenia and osteoporosis as measured by DXA. The hypothesis was that PAI-1 has a role in bone remodeling in this population

Major Comments:

1 - The hypothesis was that PAI has a role in bone remodeling, therefore the dependent variable in the model should be taken as either BMD or bone turnover markers. It would be more appropriate to model either of these outcomes and include PAI-1 in the variables of interest, rather than see if bone density measurement / markers contribute to variability in PAI-1.

2 - The statement in the discussion that 'These results support the hypothesis that an inflammatory process in overweight and obese women achieves its effect through suppression of bone formation rather than resorption which is consistent with previous studies' should be removed. There is no reference range or normal control data reported to show that bone turnover is suppressed in this group and there is no difference in inflammation markers across the 3 groups. In order to establish why patients with T2DM and normal BMD fracture one would need a qualitative measurement, which was not part of this study.
3 - References in the introduction and discussion to type 1 diabetes should be removed, as they don't add to this particular study.

4 - A comment should be made on the high HbA1cs in this study, as subjects did not achieve ADA targets for either glycaemic control or lipid levels.

5 - Mention is made of glitazones in the discussion but the number of patients on agents such as glitazones, DPPIV inhibitors and SGLT2 inhibitors should be reported clearly. These agents are known to affect bone metabolism.

6 - It should be stated that bone markers were tested in the fasting state.

7 - Suggest remove comment on weight / body composition change, as this is not a longitudinal study.

Minor points

1 - key words should include osteoporosis and osteopenia

2 - add in space in line 65 between cytokine and is, and in line 108 between single and layer.

3 - line 78 should read ...growing evidence of association between PAI and bone metabolism markers...

4 - line 201 osteoporosis line 258 various

**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?**

If not, please specify which controls are required in your comments to the authors.

No
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

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