Reviewer’s report

Title: Low bone turnover in premenopausal women with type 2 diabetes mellitus as an early process of diabetes-associated bone alterations: a cross-sectional study

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Reviewer: Guillaume Mabilleau

Reviewer's report:

I read with attention the manuscript entitled "low bone turnover in premenopausal women with type 2 diabetes mellitus as an early process of diabetoporosis: a cross-sectional study". The main goal of this study was to assess whether changes in bone turnover occur early in T2DM by investigating the circulating levels of CTx and P1NP in premenopausal women.

Overall, the manuscript is well written and pleasant to read. The english syntax is ok. However, the idea that bone turnover markers are altered in T2DM premenopausal women in not new and has already been investigated by Christensen and Svendsen (Osteoporosis Int, 1999, 10: 307-311) who reported a reduction in bone resorption an no effects on bone formation. The difference between the current and the published studies should be clearly stated in the introduction.

Major concerns:

- Page 3, line 80: the authors state that diabetoporosis is characterized by "microarchitectural changes" without citing them. Furthermore, lines 88-89 they reported changes in cortical porosity. It should be stated here that changes in cortical porosity is the only significant microarchitectural changes observed in a subset of Afro-American T2DM population and is not often observed in the rest of this subpopulation or Caucasian. As such, I would recommend being more precise when reporting microarchitectural changes and rather state that it is indeed cortical porosity.

- The assessment of bone resorption is made by investigating the circulating levels of CTx. CTx corresponds to a fragment of the triple helix of collagen that sustain some cross-links. However, cross-linking of the collagen matrix is altered and reduced in T2DM and as such, investigation of CTx might be problematic to draw any conclusions in T2DM as lower value may represent same extent of bone resorption but less cross-linking of the collagen matrix. This is one of the reasons why assessment of bone turnover is not massively reported in the literature. This should be discussed in the discussion as a limitation to this study.
- The alcohol consumption and smoking status of the premenopausal women enrolled in the study should be reported, as these two factors are known to lead to osteoporosis.

- Page 9, line 210-212: the authors stated that the low bone turnover lead to higher bone mineralization that is not captured by measuring BMD alone. This statement is erroneous. The lowest the bone turnover, the highest maturation, and hence mineralization, of the bone matrix components. As such, an increase in bone mineralization might be perceived as an increase in BMD although the bone quantity is unchanged. This is one of the hypothesis to explain why BMD is increased in T2DM.

**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.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

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I am able to assess the statistics

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