Reviewer’s report

Title: Cortical and trabecular bone are equally affected in rats with renal failure and secondary hyperparathyroidism

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Reviewer: Ferruh Artunc

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Bajwa, Sanchez et al. report the results of a study evaluating the effect of high phosphorus diet on bone and mineral metabolism in a 5/6 nephrectomy model of chronic kidney disease in rats. Currently, high plasma phosphate levels are seen as a driving force of chronic kidney disease-mineral bone disorder (CKD-MBD) which includes metabolic changes appearing during CKD e.g. SHPT and bone disorder. Thus, lowering plasma phosphate levels is a main goal in the therapy of CKD-MBD. However, the interactions between the main players in CKD-MBD and their sequence of action is yet not fully clear.

In three different treatment groups it is shown, that high phosphorus diet in 5/6 nephrectomized rats leads to changes in bone microstructure and increased levels of PTH and FGF23.

The strengths of this study are the different perspectives under which the bone is studied: radiological methods, histological examinations and humoral parameters. Overall the manuscript is well-written and logically organized.

I suggest to address the following points before publication:

1) A major point of criticism is that the authors don’t report the number of performed individual experiments (n) at any place in the text or the illustrations. Without reporting the number of individual experiments a publication wouldn’t be possible. In case of small n maybe it would be better to show data as scatter graphs or box plots instead of bar graphs.

2) Figure 1A shows a point of taking blood on day twelve after starting nephrectomy. Results from these values were never mentioned neither in the text nor in the figures. If these samples exist, please show the measured values since they may contribute to the understanding of the sequence of observed changes.

3) Please show weight gain and length gain as relative values (fig. 1B).

4) Legend to figure 1: * Significant at p<.05 versus Nx-Phos and control animals. ^Significant at p<.05 versus Nx-Phos and Nx-Control animals.

5) Please reorder the parts of figures 4-6 according to the order in the text.
6) Figure 7 C uses a symbol (#) not described in the legend.

7) Please report r, r2 and p in the legend or figure at figure 7.

8) The last sentence of the discussion should end with the word rats instead of mice.

9) Use the term used in the text for the group-headings in table 1 and 2.

10) Please show representative bone sections and micro-CT scans.

11) Could something be said about the extent of movement of the individual animals? It is conceivable that reduced muscle action as it is to be expected in CKD with developing uremia may lead to changes in bone structure (e.g. Hart NH et al., Mechanical basis of bone strength: influence of bone material, bone structure and muscle action. J Musculoskelet Neuronal Interact., 2017).

12) The hyperphosphatemia model is somehow artificial since CKD patients would not be advised to increase phosphorus load. Please discuss the expected effects of low phosphate diet/phosphate binder as main therapeutic instruments used in CKD-MBD as shown in the paper of Bohnert BN et al. (Impact of phosphorus restriction and vitamin D-substitution on secondary hyperparathyroidism in a proteinuric mouse model. Kidney Blood Press Res., 2015).

13) What’s the explanation for the great difference (more than doubling) between day 19 and day 26 in creatinine values of the control group?

14) It would be interesting to see 25 and 1,25 Vitamin D concentrations.

**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

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Acceptable

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