

## **Reviewer #1**

In this review article, the authors describe the relationship between vascular calcification and bone and mineral metabolism in patients with kidney transplantation. They also report on the adverse effects of immunosuppressive agents. This paper is clinically interesting, but there are some points that need to be addressed. Minor comments: There are various spelling mistakes that should be corrected. For example: 1. On page 6 (line 6), hyphosphatemia → hypophosphatemia 2. On page 7 (line18), of of → of 3. On page 8 (line 21), factures → factors 4. On page 11 (line 17), is the word “biphosphonates” correct? (bisphosphonates?) 5. On page 11 (line 23), is “calcification deposition” correct?

[Thank you for your praising remarks and for your suggestions. The manuscript has been revised carefully and all spelling mistakes have been corrected](#)

## **Reviewer #2**

The authors reported the vascular calcification, bone and mineral metabolism after kidney transplantation. This manuscript is well written and important, because the authors clearly describe that mineral and bone disorders persist after kidney transplantation, and that alterations of mineral and bone metabolism contribute to vascular calcification progression and poor cardiovascular outcome.

[Thank you for your praising remarks](#)

However, some concerns are raised. I hope to revise the concerns adequately.

(1) The authors estimated vascular calcification using coronary artery calcium score. Although this is adequate method, it is not enough to estimate vascular calcification after kidney transplantation because of the scarce data. Ankle

brachial index and pulse wave velocity are known to be available for estimating the levels of arteriosclerosis including vascular calcification. Therefore, the authors may refer the manuscripts of ankle brachial index and pulse wave velocity to estimate vascular calcification.

Thank you for your suggestion. In our opinion ABI and PWV are only a very indirect measures of vascular calcification. In fact, an abnormal ABI is mainly dependent upon development of obstructive peripheral arterial disease; it is only when the ABI is abnormal high (typically  $> 1.3-1.4$ ) that one is justified to think of vascular calcification as the underlying disease causing it.

An increased PWV could be the consequence of degradation of myocytes and accumulation of collagen fibers in the vessel wall, not simply the accumulation of calcium in the vessel wall layers.

Finally, these 2 methodologies do not give a quantitative measure of vascular calcification and are therefore unable to show a quantitative change over time of the burden of vascular calcification.

With these caveats in mind, we added a new section at the end of the paper prior to the conclusions

(2) The contents in Table 1 are well written in the manuscript (page 10, 2nd paragraph to page 12, 1<sup>st</sup> paragraph). Therefore, the authors should delete Table 1.

Typically review articles benefit from some graphical and tabulated information that makes the reading and reviewing of the data in the article easier, and we would propose keeping the Table. However, if the Editor and the Reviewer feel

strongly in this direction, we will be happy to remove it in a second review.