Reviewer's report

Title: Urinary Phosphorus Excretion per Creatinine Clearance as A Prognostic Marker for Progression of Chronic Kidney Disease: A Retrospective Cohort Study

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Reviewer: Nadine Kaesler

Reviewer's report:

Major Compulsory Revisions

The manuscript by Kawasaki et al. describes the impact of urinary phosphorous load per creatinine clearance on the progression of chronic kidney disease. Having an early marker for phosphate load is of interest, but the authors need to point out the importance of their established marker. Balancing phosphorous on creatinine is a simple method and creatinin clearance it is already considered in established markers, i.e. fractional excretion or tubular reabsorption. Recently, Bech et al reported the impact of fractional excretion on progression of CKD (Bech AP, J Nephrol, 2015) in relation to FGF 23. Here, corresponding FGF23 levels in serum and fractional excretion of phosphate are missing. The source of protein is not included, although it is a direct link to the bioavailability of alimentary phosphorous and its excretion. Phosphorous excretion is dependent on CKD stages (as shown by the authors) but the number of observations in CKD 2 and 3 are low. Data of CKD progression of individuals is missing. Therefore the evidence for U-P/24h-CCr being a valid marker for CKD progression in all CKD stages is low. Using creatinine clearance as marker for nephron number needs to be confirmed. The discussion of the advantage for using U-P/24h-CCr is contradictory.

Abstract:

1) Lines 6-8: How does the ratio of U-P/24h-CCr reflect the phosphate loss for each nephron? A proof that 24h-CCr is a marker for nephron number is missing. Why is it important to normalize to creatinine clearance?

2) Many studies deal with negative outcome of high levels of phosphate in serum. What is the advantage of this established marker than for example phosphate in serum? Can you show a graph that it is an earlier marker than phosphate in serum in these patients by a graph (results section)?

3) Usually FGF23 is one marker which increases early in serum. How is the association of U-P/24-CCr with FGF 23 in serum?

4) What is the key result for the conclusion?

Material & Methods:
5) The source of protein is of importance, for example for association of phosphate with protein rich foods has reduced bioavailability from plant origin. Phosphate intake is not mentioned but excretion is highly dependent on phosphate intake.

6) Table 1: An average BMI of 59.8 is highly obese- is that the correct figure? Please give a more detailed description of CKD patients in the results section.

7) Table 1: 86% of the patients were in CKD stage 5. Were all CKD stages analysed all together? Was there an adjustment for CKD stages?

8) How was the tubular reabsorption calculated? Usually it considers GFR and Creatinine.

Results:
9) Figure 1 a) and b): The impact of showing the regression of both approaches is not clear. Graphs need more detailed descriptions. Are all CKD stages included?

10) Urinary phosphate increase by high protein intake might due to the increased uptake, as it is associated with protein rich foods. Can the authors comment?

Discussion:
11) Why is phosphate in serum only increased in Quartile 4? Is this the reason that U-P/24h-CCr is not associated with serum phosphorous in CKD stage 3?

12) What is the outcome of an association of fractional phosphorous excretion with CKD progression?

The work of Bech 2015 shows no impact on CKD progression by fractional phosphate excretion, which needs to be discussed here.

13) The alternate model which normalises to GFR showed similar results. Why is U-P/CCr preferred to normalisation to GFR?

14) Which information provides U-P/CCr that is described by the established maker, i.e. fractional excretion, TRP and phosphate in serum? As no data of fractional phosphate excretion is provided here, it is difficult to evaluate the better impact of U-P/CCr on CKD progression.

15) Page 14 Line 14-16 The study was performed with U-P/24h-CCr (U-P/CCr in line 14? U-P/Cr in line 16). Suitability of spot urine is speculaive and contradictory to the strength section where the circadian change of phosphate excretion is mentioned. Here in the discussion section it is pointed out as only advantage of using this marker.

Minor Essential Revisions

Material & Methods:
16) Page 9-10 Lines 16-2: There are several typos in one sentence: Primary hyperparathyroidism, evidence for, missing values

17) Page 10, Lines 2 and 5: Missing values of patients are mentioned twice.

Strength & Limitations:
18) Page 15 lines 4-5 First sentence seems to be incomplete
19) Page 15 line 7: Referring to phosphate binder or phosphate restriction studies should not be part of this section and could be moved to the general discussion for importance of phosphate metabolism.
20) Page 15 line 8: Phosphate in serum or urine?

Discretionary Revisions

Abstract/Introduction:
21) A short overview of the different factors influencing the phosphate excretion might be helpful.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.