Post-transplantation hypophosphatemia is associated with renal graft survival

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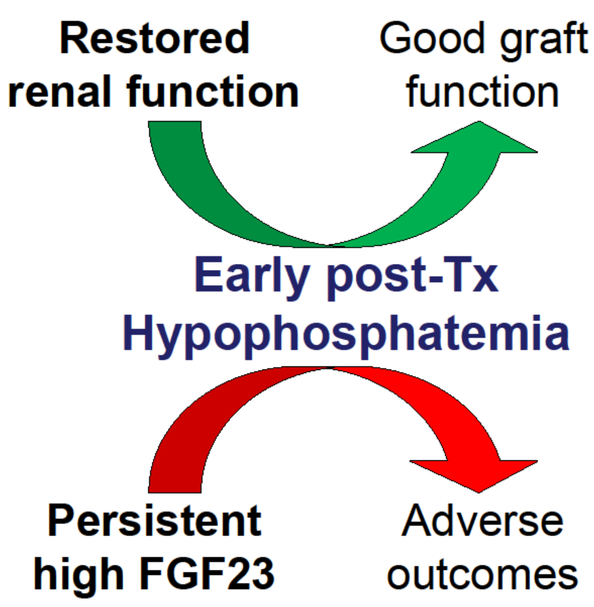
Introduction

- Hypophosphatemia is common after kidney transplantation (Tx)
- Post-Tx hypophosphatemia is considered the consequence of residually high levels of fibroblast growth factor 23 (FGF23) and parathyroid hormone (PTH) early after Tx, in the context of a transplanted kidney able to excrete large amounts of phosphate
- The development of post-Tx hypophosphatemia may be either *beneficial*, since it represents good kidney function, or *deleterious,* since it represents long-term recipient exposure to high levels of FGF23 and PTH.

Figure 1. Hypothesis: Restored renal function vs FGF23



Aim

To investigate whether post-Tx hypophosphatemia is associated with the risk of 1) graft failure or 2) (cardiovascular) mortality

Methods

- In a cohort of renal transplant recipients (n=957), the lowest serum phosphate during the first year after transplantation was recorded.
- Post-Tx hypophosphatemia was categorized as
  - severe <0.5 mmol/L
  - mild 0.5-0.7 mmol/L
  - absent >0.7 mmol/L
- Associations between hypophosphatemia and graft failure or mortality were analyzed in multivariable Cox regression model.

Results

Table 1. baseline characteristics

	All patients (n=957)	Hypophosphatemia category: Absent (n=136)	Mild (n=375)	Severe (n=446)
Lowest post-Tx, phosphate mmol/L	0.52 [0.41-0.63]	0.79 [0.73-0.88]	0.58 [0.54-0.64]***	0.40 [0.34-0.46]***
Age, y	49 [39-59]	49 [36-58]	50 [40-58]	49 [39-59]
Gender, n (%) male	557 (58%)	64 (47%)	221 (59%)	272 (61%)**
Living donor (%)	24	21	17*	29
eGFR mL/min/1.73m²	52 [39-66]	41 [26-53]	49 [38-60]***	58 [46-70]***
Time to lowest phosphate, days	33 [21-51]	35 [15-68]	35 [22-53]	32 [21-48]

Figure 2. Pie chart of phosphate categories

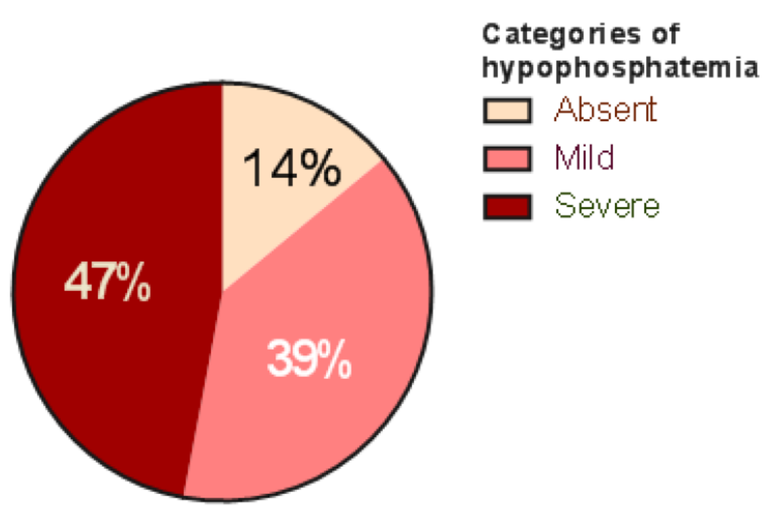


Figure 3. Plot of days between Tx and lowest serum phosphate measurement

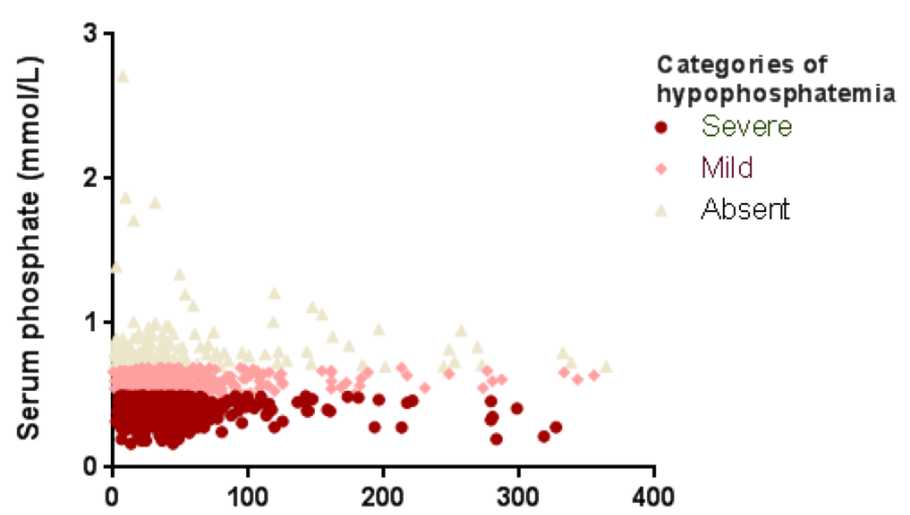


Table 2. Multivariate COX-regression model of hypophosphatemia on graft failure

	Absent	Mild	Severe	Continuous
Model 1	Ref	0.54 [0.36-0.79]**	0.44 [0.30-0.65]***	0.41 [0.29-0.59]***
Model 2	Ref	0.49 [0.30-0.80]**	0.58 [0.36-0.94]***	0.54 [0.34-0.85]**
Model 3a	Ref	0.41 [0.24-0.72]**	0.41 [0.22-0.73]**	0.30 [0.16-0.52]***

Table 3. COX-regression of hypophosphatemia on mortality and cardiovascular mortality

	Absent	Mild	Severe	Continuous
Model 3b	Ref	1.20 [0.67-2.15]	1.23 [0.69-2.22]	1.16 [0.78-1.72]
Model 3b	Ref	0.29 [0.13-0.67]**	0.25 [0.11-0.58]**	0.30 [0.14-0.63]**

Model 1: adjusted for recipient age and gender
Model 2: model 1 + eGFR at time of lowest phosphate and log proteinuria
Model 3a: model 2 + adjusted for cold ischemia time, total mismatches, dialysis vintage, acute rejection, delayed graft function, CNI use, donor age and donor gender
Model 3b: model 2 + adjusted for smoking status, pre- or post-transplant diabetes mellitus, and CV history
* P<0.05; ** P<0.01; *** P<0.001

Conclusion

Patients with post-Tx hypophosphatemia are at lower risk of graft failure and CV mortality. Post-Tx hypophosphatemia reflecs a good graft function, independent of eGFR.

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