Conflicts of interest

All authors have no conflicts of interest to declare.

References

[1] Kim Y, Yoo KD, Kim HJ, et al. Association of serum mineral parameters with mortality in hemodialysis patients: data from the Korean end-stage renal disease registry. *Kidney Res Clin Pract* 37:266-276, 2018

[2] Wakasugi M, Kazama JJ, Wada A, Hamano T, Masakane I, Narita I. Functional impairment attenuates the association between high serum phosphate and mortality in dialysis patients: a nationwide cohort study. *Nephrol Dial Transplant* 2018 Aug 13. doi: 10.1093/ndt/gfy253. [Epub ahead of print]

[3] Sakaguchi Y, Fujii N, Shoji T, et al; Committee of Renal Data Registry of the Japanese Society for Dialysis Therapy. Magnesium modifies the cardiovascular mortality risk associated with hyperphosphatemia in patients undergoing hemodialysis: a cohort study. *PLoS One* 9:e116273, 2014

[4] Lee S, Ryu JH, Kim SJ, Ryu DR, Kang DH, Choi KB. The relationship between magnesium and endothelial function in end-stage renal disease patients on hemodialysis. *Yonsei Med J* 57:1446-1453, 2016

[5] Sakaguchi Y, Hamano T, Isaka Y. Effects of magnesium on the phosphate toxicity in chronic kidney disease: time for intervention studies. *Nutrients* 9:112, 2017

The authors' reply

Kidney Res Clin Pract 37:421-422, 2018
pISSN: 2211-9132 • eISSN: 2211-9140
https://doi.org/10.23876/j.krcp.18.0136

Yunmi Kim[1], Kook-Hwan Oh[2]

[1]*Department of Internal Medicine, Dongguk University College of Medicine, Gyeongju, Korea*
[2]*Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea*

We appreciate the interest of Dr. Wakasugi and Dr. Sakaguchi in our recent publication about the association of serum mineral parameters with mortality in hemodialysis patients, an analysis of the data from the nationwide Korean Society of Nephrology (KSN) End-Stage Renal Disease (ESRD) Registry. As they have commented, our results have some discrepancy with other studies on the association between serum phosphorus level and mortality, including one from Japanese Renal Data Registry data [1], in that hyperphosphatemia was not significantly associated with increased mortality. Although limited, data from one study showed results similar to ours. In a Portuguese observational cohort study, patients with hyperphosphatemia did not show difference in mortality (hazard ratio [HR], 1.00; 95% confidence interval [CI], 0.74–1.35), whereas patients with hypophosphatemia showed increased mortality (HR, 1.29; 95% CI, 1.07–1.55) [2].

We speculated several explanations for our results. Favorable nutritional status may have attenuated the hazardous effect of hyperphosphatemia. In our *post-hoc* analysis of the KSN ESRD Registry data, increased risk of mortality in the high phosphorus group was exhibited only if combined with concurrent low serum albumin level, suggesting that the nutritional status attenuated the harmful effect of high phosphorus level (Table 1). Nutritional indices other than serum albumin could provide further information. However, we were unable to examine the relevance of normalized protein nitrogen appearance (nPNA) in the relationship between phosphorus

Received November 12, 2018; **Accepted** November 12, 2018

Correspondence: Kook-Hwan Oh
Department of Internal Medicine, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea. E-mail: khoh@snu.ac.kr
ORCID: https://orcid.org/0000-0001-9525-2179

Table 1. All-cause mortality by serum phosphorus and albumin categories

Phosphorus (mg/dL)	Albumin (g/dL)	Number	Adjusted HR* (95% CI)	*P* value
< 3.5	< 3.8	2,021	2.255 (1.935–2.628)	< 0.001
	≥ 3.8	1,640	1.243 (1.022–1.512)	0.030
3.5–5.5	< 3.8	3,994	1.665 (1.454–1.907)	<0.001
	≥ 3.8	7,281	Reference	
> 5.5	< 3.8	1,562	1.744 (1.456–2.089)	< 0.001
	≥ 3.8	4,935	1.012 (0.861–1.189)	0.888

CI, confidence interval; HR, hazard ratio.

*Adjusted for age, sex, dialysis vintage, etiology of renal failure, history of cardiovascular diseases, body mass index, hemoglobin, single-pool Kt/V, corrected calcium, and intact parathyroid hormone.

and mortality, because data on nPNA were missing in many subjects.

Second, we performed analysis based on one-time measurement of phosphorus at baseline. Serum phosphorus is known to have a wide diurnal variation. The Kidney Disease Improving Global Outcomes Guidelines recommends that therapeutic choice of phosphate-lowering treatment be based on repeated measures of serum phosphorus level. The increased mortality risk of high phosphorus was accentuated in a time-dependent model compared to the baseline model [1,3].

Third, Koreans tend to ingest phosphorus less from milk products and more from legumes and vegetables compared with the United States population [4,5]. Differences in food sources of phosphorus intake may partly account for the non-significant risk of hyperphosphatemia.

As was suggested, performance status and magnesium can also affect the outcome of hyperphosphatemic patients, information on which is not available in the current KSN ESRD Registry.

Further research to investigate possible confounding factors is needed using analysis of repeated measurement of phosphorus level or more comprehensive analysis including diet and nutritional variables.

Conflicts of interest

All authors have no conflicts of interest to declare.

References

[1] Taniguchi M, Fukagawa M, Fujii N, et al; Committee of Renal Data Registry of the Japanese Society for Dialysis Therapy. Serum phosphate and calcium should be primarily and consistently controlled in prevalent hemodialysis patients. *Ther Apher Dial* 17:221-228, 2013

[2] Garagarza C, Valente A, Caetano C, Oliveira T, Ponce P, Silva AP. Hypophosphatemia: nutritional status, body composition, and mortality in hemodialysis patients. *Int Urol Nephrol* 49:1243-1250, 2017

[3] Liu CT, Lin YC, Lin YC, et al. Roles of serum calcium, phosphorus, PTH and ALP on mortality in peritoneal dialysis patients: a nationwide, population-based longitudinal study using TWRDS 2005-2012. *Sci Rep* 7:33, 2017

[4] Choi MK, Kim HS, Lee WY, Lee H, Ze KR, Park JD. Comparative evaluation of dietary intakes of calcium, phosphorus, iron, and zinc in rural, coastal, and urban district. *J Korean Soc Food Sci Nutr* 34:659-666, 2005

[5] McClure ST, Chang AR, Selvin E, Rebholz CM, Appel LJ. Dietary sources of phosphorus among adults in the United States: results from NHANES 2001-2014. *Nutrients* 9:95, 2017