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Serum phosphate as an additional marker for initiating hemodialysis in patients with advanced chronic kidney disease



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ABSTRACT

Background: Reconsidering when to initiate renal replacement therapy (RRT) in patients with chronic kidney disease (CKD) has been emphasized recently. With evolving modern aged and diabetes-prone populations, conventional markers of uremia are not sufficient for determining the optimal timing for dialysis initiation. This retrospective cohort study examined the association between hyperphosphatemia and uremic patients who need RRT registration.

Methods: All patients from the department of nephrology in one tertiary medical center in northern Taiwan who had advanced CKD and estimated glomerular filtration rates $<8 \text{ mL/min/1.73 m}^2$ from July 2009 to May 2013 were enrolled. We reviewed the medical records and collected data on demographics, comorbidities, underlying diseases, duration of nephrology care, use of phosphate binders, and laboratory results. Univariable and multivariable logistic regression models were used to identify factors associated with hemodialysis initiation decision making.

Results: During the study period, 209 of 292 patients with advanced CKD were enrolled in hemodialysis program and 83 patients (controls) were not. Univariable analysis indicated that male sex, current smoking, diabetes mellitus, hypertension, coronary artery disease, high serum creatinine level, and high serum phosphate level were associated with initiation of hemodialysis. Multivariable analysis indicated that those with higher serum phosphate level (odds ratio [OR] = 2.4, 95% confidence interval [CI] = 1.6–3.5, $p = 1.4 \times 10^{-5}$) and being in nephrology care for <12 months (OR = 0.4, 95% CI = 0.2–0.8, $p = 0.016$) tended to be significant markers for hemodialysis initiation. **Conclusion:** Hyperphosphatemia, in addition to conventional laboratory markers and uremic symptoms, may be a useful marker to determine timing of hemodialysis initiation in patients with advanced CKD.

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At a glance commentary

Scientific background on the subject

If left untreated, patients with advanced chronic kidney disease (CKD) may die from progressively developed uremic symptoms. The conventional markers for poor kidney function may not always be useful to help physician to decide when to initiate dialysis. Significant hyperphosphatemia occurred in CKD patients who chose to delay initiation of renal replacement therapy.

What this study adds to the field

In CKD patients with estimated glomerular filtration rates <8 mL/min/1.73 m², hyperphosphatemia was the most significant factor associated with dialysis initiation among other conventional uremic markers. Diabetic nephropathy as a cause of end-stage renal disease was also associated with dialysis initiation. Nephrology care for more than 12 months was associated with reduced risk of dialysis initiation.

If leaving untreated, patients with advanced chronic kidney disease (CKD) may die from progressively developed uremic symptoms that are overwhelming and life-threatening (such as pulmonary edema, extreme hyperkalemia, and ventricular arrhythmia) or chronic and debilitating (e.g., general malaise, frequent vomiting, poor appetite, and malnutrition) [1]. Renal replacement therapy (RRT) is a trade-off medical decision and indicated in these CKD patients when the benefits of treatment (reducing the risk of death and improvement of patient well-being) outweigh the risks of therapeutical complications, the psychosocial inconvenience, and the financial burden of health insurance [2]. As the life expectancy and poverty continues to improve worldwide, there is a high popularity of CKD in the elderly [3]. This is attributable mainly to increasing prevalence of aging- and lifestyle-related risk factors for CKD such as diabetes, hypertension, and cardiovascular disease [4,5]. These comorbidities also enable elder CKD patients particularly susceptible to injury compared with younger CKD patients with the same serum level of uremic toxins. Thus, the conventional markers for poor kidney function – elevated serum urea level, high serum creatinine (SCr) concentration, and low estimated glomerular filtration rate (eGFR) – may not be always useful to help physician to decide when to initiate RRT in advanced CKD patients.

Since the publication of the kidney disease outcomes quality initiative guidelines in 2002 indicating dialysis initiation at glomerular filtration rate (GFR) below 15 mL/min/1.73 m² plus proper risk-benefit analysis [6], there had been a trend toward earlier start of dialysis. Previous research suggested that early initiation of dialysis was associated with decreased mortality, hospitalization rate, and total costs [7]. However, several recent studies did not support this strategy. In particular, these recent studies showed that early initiation of dialysis in patients with eGFR of 10–15 mL/min/1.73 m² provided no apparent clinical benefit and might increase the

risk of death [8–11]. The 2012 Kidney Disease Improving Global Outcomes guidelines for CKD suggest initiation of dialysis when a patient experiences symptoms or signs attributable to kidney failure, an inability to control volume status or blood pressure, a progressive deterioration in nutritional status refractory to dietary intervention, or cognitive impairment [12]. This often, but not always, occurs in patients with eGFRs from 5 to 10 mL/min/1.73 m². However, these uremic symptoms are partially based on patient perceptions and physician judgments, so more objective laboratory parameters are needed to help deciding when to initiate dialysis in advanced CKD patients, especially in countries or areas where practicing nephrologists are scarce.

Phosphorus is a major intracellular anion and more than 90% of the body's phosphorus is in bone and soft tissue. Serum phosphorus accounts for $<1\%$ of the body's total phosphorus amount, but is a surrogate marker of total body phosphate content. Phosphate homeostasis depends on dietary intake, bone absorption, and renal excretion. Parathyroid hormone (PTH), 1,25 (OH)₂ Vitamin D₃, and fibroblast growth factor 23-klotho axis regulate the level of serum phosphate [13]. A sharp decline in the GFR leads to reduce renal excretion of phosphate and disruption of the hormonal regulatory process. Therefore, patients with advanced CKD typically retain phosphate and develop hyperphosphatemia. Previous research indicated that significant hyperphosphatemia occurred in CKD patients who were under intensive treatment and who chose to delay initiation of RRT [14]. However, it is unknown if hyperphosphatemia can be used as an indicator for initiation of RRT in such patients.

The purpose of this retrospective study is to examine the role of serum phosphate level in advanced CKD and the potential use of hyperphosphatemia to guide the initiation of RRT.

Methods

Patient population

This study examined the records of all patients with Stages 3–5 CKD, who were under care in one Tertiary Medical Center in Northern Taiwan from July 2009 to May 2013. The eGFR was calculated by modification of diet in the renal disease equation [15], which considers age, gender, and SCr level. Advanced CKD patients defined as with eGFRs <8 mL/min/1.73 m² were included. This study evaluated the role of serum phosphate level on the need for long-term dialysis in patients with CKD, so patients with the following characteristics were excluded: younger than 18 years, significant episode of acute kidney injury before dialysis (including sepsis, shock, dehydration, acute heart or liver failure, contrast nephropathy, or obstructive uropathy), initiation of dialysis because of bilateral nephrectomy, choice of peritoneal dialysis rather than hemodialysis. The Institutional Review Board of our institution approved the review and usage of patient medical data.

Dialysis initiation

Nephrologists and CKD nurses implemented an integrated education program for patients with Stages 3–5 CKD that

included regular outpatient follow-ups. Initiation of hemodialysis was recommended after consideration of the patient's detailed clinical history, physical examination, laboratory data, and imaging results from the outpatient or emergency departments. The training of our physicians followed the updated guidelines and used the same consensus about the indication of dialysis initiation. Most patients initiated hemodialysis due to significant uremic symptoms, with fluid or electrolyte imbalance, and met the current criteria for RRT including: azotemia with persisting nausea and vomiting, severe acidosis, fluid overload with significant shortness of breath, marked hyperkalemia with or without cardiac dysrhythmia, and uremic encephalopathy with altered level of conscious.

Clinical data

We reviewed the medical records of patients to collect data on demographics, comorbidities, underlying diseases, duration of nephrology care, use of phosphate binders, and laboratory results. All laboratory examinations were processed in the department of laboratory medicine, which is certificated by the College of American Pathologists. Patients were divided into a dialysis-initiated group and a control (nondialysis) group. Laboratory examinations prior to the initiation of hemodialysis (dialysis-initiated group) and the last outpatient laboratory examination (control group) were used for analysis. The laboratory parameters were hemoglobin (Hb), hematocrit (Hct), serum blood urea nitrogen (BUN), SCr, sodium (Na), potassium (K), calcium (Ca), phosphate (P), albumin, and carbon dioxide (CO₂). Predialysis measurements of PTH and blood gases were only available for a few patients, so these parameters were not analyzed. Coexisting diseases and underlying causes of CKD, such as diabetes mellitus (DM), hypertension, and glomerulonephritis (GN), were included in the analysis. The duration of care in the nephrology clinic, prescription of phosphate binders, and a daily dose of calcium (in meq) were reviewed and analyzed.

Statistical analysis

The demographics, clinical characteristics, and laboratory results of patients who did and did not start hemodialysis during the study period were summarized using descriptive statistics, and compared using the t-test (continuous factors) or Fisher's exact test (categorical factors). Potential risk factors associated with the initiation of dialysis were evaluated using logistic regression models with univariable and multivariable analysis. For variable selection in the multivariable model, the associations among the factors were evaluated to prevent multicollinearity. For analysis of the associations between two factors, Pearson's correlation test was used for continuous factors, and Fisher's exact test was used for categorical factors. The final multivariable model was based on backward selection, with entry and removal criteria at a $p = 0.05$ (with entry and removal criteria at a $p = 0.05$) among those with a $p < 0.05$ in the univariate model. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC). All statistical tests were two-sided and attained significance at $\alpha = 0.05$.

Results

Demographic and clinical characteristics

We retrospectively enrolled 292 patients with advanced CKD who had eGFRs < 8 mL/min/1.73 m² from July 2009 to May 2013 [Table 1]. A total of 209 patients started hemodialysis during the study period, and the other 83 patients constituted the control (nondialysis) group. The dialysis-initiated and control groups were similar in age, body mass index (BMI), prevalence of underlying malignancies, and liver cirrhosis. However, patients in the dialysis-initiated group were more likely to be male (56% vs. 41%, $p = 0.027$) and current smokers (16.7% vs. 3.6%, $p = 0.0018$), and to have coexisting DM (59.8% vs. 34.7%, $p = 6.8 \times 10^{-4}$), hypertension (85.7% vs. 69.9%, $p = 0.0027$), and coronary artery disease (17.2% vs. 3.6%, $p = 0.0011$). The primary causes of CKD in both groups were DM and GN. We classified the primary cause of CKD as a binary variable (DM vs. others) because GN and other nonDM categories had similar impact on dialysis. Based on this classification, DM

Table 1 – Demographic and clinical characteristics of patients with advanced chronic kidney disease who did not start (control) or did start hemodialysis during the study period (n = 292).

Characteristic	Control (n = 83) ^a	Dialysis-initiated (n = 209) ^a	P ^b
Age (years)	62.7 ± 11.7	63.1 ± 14.8	0.7947
Gender			
Female	49 (59.0)	92 (44.0)	0.0270
Male	34 (41.0)	117 (56.0)	
BMI (kg/m ²)	24.3 ± 3.4	24.0 ± 4.4	0.1957
Current smoker	3 (3.6)	35 (16.7)	0.0018
Coexisting diseases			
Diabetes	31 (37.4)	125 (59.8)	6.8×10^{-4}
Hypertension	58 (69.9)	179 (85.7)	0.0027
Coronary artery disease	3 (3.6)	36 (17.2)	0.0011
Malignancy	8 (9.6)	14 (6.7)	0.4610
Liver cirrhosis	1 (1.2)	7 (3.4)	0.4476
Primary cause of ESRD			
Diabetes	26 (31.3)	119 (56.9)	3.0×10^{-4}
Glomerulonephritis	41 (49.4)	68 (32.5)	
Hypertension	8 (9.6)	6 (2.9)	
Interstitial nephritis	2 (2.4)	1 (0.5)	
Hereditary kidney disease	1 (1.2)	6 (2.9)	
Others	5 (6.0)	9 (4.3)	
Duration of nephrology care			
≤12 months	20 (24.4)	112 (53.6)	7.0×10^{-6}
>12 months	62 (75.6)	97 (46.4)	
Use of phosphate binder			
Yes	49 (59.1)	87 (41.6)	0.0910
No	34 (41.0)	122 (58.4)	
Daily dose of calcium as phosphate binder (meq) ^c	32.2 ± 16.8	40.7 ± 19.9	0.0121

Abbreviations: SD: standard deviation; BMI: body mass index; ESRD: end-stage renal disease.

^a Mean ± SD or n (%).

^b p value is from Fisher's exact test for gender and the t-test for continuous factors.

^c For patients who took phosphate-binders.

Table 2 – Laboratory results of patients with advanced CKD who did not start (control) or did start hemodialysis during the study period (n = 292).

Characteristic	Control (n = 83) ^a	Dialysis-initiated (n = 209) ^a	P ^b
Albumin (g/dL)	4.0 ± 0.5	3.3 ± 0.5	8.6 × 10 ⁻⁹
BUN (mg/dL)	80.2 ± 20.2	123.0 ± 41.9	1.5 × 10 ⁻²⁵
Serum creatinine (mg/dL)	8.1 ± 1.9	11.3 ± 4.1	1.5 × 10 ⁻¹⁷
eGFR (mL/min/1.73 m ²)	6.0 ± 1.2	4.6 ± 1.5	4.4 × 10 ⁻¹³
Calcium (meq/L)	8.4 ± 0.7	8.0 ± 1.0	0.0002
Phosphate (meq/L)	4.9 ± 0.8	7.0 ± 2.4	2.2 × 10 ⁻²⁵
Sodium (meq/L)	138.8 ± 3.7	135.7 ± 6.2	0.0006
Potassium (meq/L)	4.5 ± 0.7	4.6 ± 1.0	0.4955
Hemoglobin (g/dL)	9.2 ± 1.4	8.5 ± 1.4	0.0005
Hematocrit (%)	28.1 ± 4.1	25.6 ± 4.3	7.9 × 10 ⁻⁶
CO ₂ (meq/L)	19.5 ± 5.7	17.1 ± 5.9	0.0789

Abbreviations: SD: standard deviation; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate; CO₂: carbon dioxide; CKD: chronic kidney disease.

^a Mean ± SD.

^b P value is from Fisher's exact test.

was a significantly more common cause of CKD in the dialysis group (56.9% vs. 31.3%, $p = 3 \times 10^{-4}$).

Laboratory results

Analysis of laboratory data [Table 2] indicated that the dialysis-initiated group had significantly lower serum

albumin (3.3 vs. 4.0 g/dL, $p = 8.6 \times 10^{-9}$), eGFR (4.6 vs. 6.0 mL/min/1.73 m², $p = 4.4 \times 10^{-13}$), Ca (8.0 vs. 8.4 meq/L, $p = 0.0002$), Na (135.7 vs. 138.8 meq/L, $p = 0.0006$), Hb (8.5 vs. 9.2 g/dL, $p = 0.0005$), and Hct (25.6% vs. 28.1%, $p = 7.9 \times 10^{-6}$). As expected, the dialysis-initiated group also had significantly higher serum BUN (123.0 vs. 80.2 mg/dL, $p = 1.5 \times 10^{-25}$) and SCr (11.3 vs. 8.1 mg/dL, $p = 1.5 \times 10^{-17}$). In addition, the dialysis-initiated group had significantly higher of serum P (7.0 vs. 4.9 meq/L, $p = 2.2 \times 10^{-25}$). However, the two groups had similar levels of serum K, presumably because a serum K level above 6.5 meq/L can induce deadly cardiac arrhythmia, and patients with this level of serum K are commonly placed on dialysis programs.

Univariable and multivariable analysis

Next, we examined the factors associated with initiation of dialysis by univariable and multivariable logistic regression models [Table 3]. Initially, we considered the associations among factors to avoid multicollinearity. Thus, we excluded SCr and Hct because these two factors were highly correlated (Pearson's $r = -0.81$), as were Hb and Hct (Pearson's $r = 0.97$). DM as the primary cause of renal disease and coexisting DM were also highly associated (Fisher's exact $p < 0.0001$), so only the former value was included in the multivariable model. BMI, albumin, Na, and CO₂ were omitted because there were missing values (missing sample sizes of 169, 187, 78, and 193, respectively). Liver cirrhosis, coronary artery disease,

Table 3 – Univariable and multivariable analysis of factors associated with the initiation of dialysis during the study period (n = 292).

Characteristic	Univariable analysis		Multivariable analysis ^b	
	OR (95% CI) ^a	p	OR (95% CI) ^a	p
Age, in 10 years	1.0 (0.9–1.2)	0.8126		
Male	1.8 (1.1–3.1)	0.0213	–	
BMI (kg/m ²)	1.0 (0.9–1.1)	0.8044		
Current smoker	5.4 (1.6–18.0)	0.0064		
Albumin (g/dL)	0.1 (0–0.2)	3.8 × 10 ⁻⁶		
BUN, in 10 units (mg/dL)	1.6 (1.4–1.9)	3.0 × 10 ⁻¹²	1.4 (1.2–1.7)	1.9 × 10 ⁻⁵
Serum creatinine (mg/dL)	1.7 (1.4–1.9)	5.4 × 10 ⁻¹⁰		
eGFR (mL/min/1.73 m ²)	0.5 (0.4–0.6)	1.1 × 10 ⁻¹⁰	0.6 (0.5–0.8)	0.0020
Calcium (meq/L)	0.6 (0.5–0.8)	0.0012	–	
Phosphate (meq/L)	2.9 (2.1–3.9)	4.2 × 10 ⁻¹²	2.1 (1.4–2.9)	9.8 × 10 ⁻⁵
Sodium (meq/L)	0.9 (0.8–1.0)	0.0135		
Potassium (meq/L)	1.1 (0.8–1.4)	0.5597		
Hemoglobin (g/dL)	0.7 (0.6–0.9)	0.0007	–	
Hematocrit (%)	0.9 (0.8–0.9)	2.1 × 10 ⁻⁵		
CO ₂ (meq/L)	0.9 (0.9–1.0)	0.0865		
Coronary artery disease (yes vs. no)	5.5 (1.7–18.6)	0.0054		
Coexisting diabetes (yes vs. no)	2.5 (1.5–4.2)	0.0006		
Coexisting hypertension (yes vs. no)	2.6 (1.4–4.7)	0.0023	–	
Coexisting malignancy (yes vs. no)	0.7 (0.3–1.7)	0.3930		
Primary cause of ESRD (diabetes vs. others)	2.9 (1.7–5.0)	0.0001	5.3 (2.4–11.8)	3.1 × 10 ⁻⁵
Duration of nephrology care (>12 vs. ≤12 months)	0.3 (0.2–0.5)	1.3 × 10 ⁻⁵	0.4 (0.2–0.8)	0.0171
Use of phosphate binder (yes vs. no)	0.5 (0.3–0.8)	0.0076	–	

Abbreviations: CI: confidence interval; OR: odds ratio; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; CO₂: carbon dioxide; BMI: body mass index.

^a OR and 95% CI based on logistic regression.

^b A factor considered in variable selection for a multivariable model that was not significant ($P > 0.05$).

malignancy, and current smoking were omitted because of the small number of positives in the control group.

Thus, we entered 10 variables into the multivariable analysis: sex, five laboratory markers (BUN, eGFR, Ca, P, and Hb), coexisting hypertension, primary cause of CKD (DM vs. others), duration of nephrology care, and use of a phosphate binder. Five of these factors were significantly and independently associated with the initiation of dialysis. In particular, the two conventional laboratory parameters for initiation of dialysis, BUN (odds ratio [OR] = 1.4, 95% confidence interval [CI] = 1.2–1.7) and eGFR (OR = 0.6, 95% CI = 0.5–0.8) were significantly associated with initiation of dialysis. After adjusting for other factors, serum P was one of the most significant factor associated with initiation of dialysis (OR = 2.1, 95% CI = 1.4–2.9, $p = 9.8 \times 10^{-5}$), with a 110% increased risk for initiation of dialysis for each 1 mg/dL increase of serum P. Diabetic nephropathy as a cause of end-stage renal disease (ESRD) was also highly associated with initiation of dialysis (OR = 5.3, 95% CI = 2.4–11.8). Longer duration of nephrology care (>12 months) was significantly associated with reduced risk of initiation of dialysis (OR = 0.4, 95% CI = 0.2–0.8).

Discussion

Taiwan has among the highest prevalence and incidence rates of advanced CKD patients who receive hemodialysis worldwide [16]. A previous report on the epidemiology of CKD in Taiwan indicated very low awareness of this disease; awareness was only 3.5% for patients with Stages 1–5 CKD and was 51.4% for predialysis patients with Stage 5 CKD [17]. Analysis of the Taiwan national database showed that advanced CKD patients tended to start dialysis when they had very low residual renal function (median eGFR of 4.7 mL/min/1.73 m²), and division of patients into quintiles indicated that even those in the highest quintile had a median eGFR = 7.7 mL/min/1.73 m² [18]. This delay in the initiation of dialysis may be due to a lack of awareness or fear and reluctance to initiate dialysis. CKD patients in our institute also tend to start dialysis therapy late, after the development of serious or life-threatening uremic symptoms. Therefore, our study cohort consisted of patients with advanced CKD (eGFR <8 mL/min/1.73 m²), so that we could clarify the usefulness of serum phosphate level, conventional uremic markers, and symptoms to determine the optimal time for hemodialysis initiation.

Nephrologists and CKD nurses in our institute implemented an integrated multidisciplinary predialysis education (MPE) program to care patients since they were defined with a Stage 3 CKD [19]. This program emphasizes intake fluid and blood pressure control, dietary education about protein, phosphate, and potassium restriction, and the use of phosphate binders, multi-Vitamin B, folic acid supplements, and erythropoietin injections for anemia. Associated goals are the introduction of different dialysis modalities, preparation for dialysis access, and timely initiation of RRT for patients with late-stage CKD (Stages 4 and 5). This MPE program is proved to delay effectively the need for dialysis and to reduce the comorbidities and unexpected mortality in patients with late-stage CKD [19]. In agreement with medical literatures, our

results of the present study also indicated that a longer duration of predialysis nephrology care and CKD education (>12 months) reduced the risk for initiation of hemodialysis by about 60%.

Comparison of our control and dialysis-initiated groups indicated that slightly fewer patients in the dialysis-initiated group took phosphate-binders, although their average daily dose was significantly greater, and their phosphate control was significantly worse. This may be explained as a composite result of their worsening glomerular filtration, compliance to dietary restrictions, and use of phosphate binders.

Our analysis of laboratory parameters indicated that BUN, SCr, eGFR, and serum P were most significantly different between the dialysis-initiated and control groups. BUN, SCr, and eGFR are conventionally used to indicate poor renal function and the need for dialysis. It is particularly noteworthy that our two groups had very different serum P levels, and serum P was the only tested parameter that was within the normal range in the control group (4.9 ± 0.8 mg/dL), but severely elevated in the dialysis-initiated group (7.0 ± 2.4 mg/dL). In addition, our multivariable analysis indicated that serum P was one of the most significant laboratory factor associated with initiation of dialysis (OR = 2.1). In other words, there was a 110% increased risk for starting dialysis for every 1 mg/dL increase of serum P. This may be reasonably explained that significant hyperphosphatemia in the dialysis-initiated group was parallel to the deterioration of residual renal function and the level of phosphate retention. However, this is also similar to high serum BUN and creatinine level, which are accepted as the traditional markers for renal failure and indicating the necessity of RRT initiation. In those patients with complex uremic syndrome, especially in aged and diabetes-prone populations, more laboratory data to judge the indication of dialysis initiation is justified, and hyperphosphatemia fulfills this purpose well. The cut-off value of high serum phosphate level as an indicator for dialysis initiation is not clearly defined.

Hyperphosphatemia plays an important role in mineral bone diseases and vascular calcifications, and is associated with increased risk of progression to ESRD, cardiovascular events, and all-cause mortality in CKD patients [20–23]. Hyperphosphatemia is not in itself immediately harmful and may have numerous underlying causes, and serum phosphate level is not regularly used as an indicator for starting dialysis in clinical practice, effective, and aggressive management of chronic hyperphosphatemia is warranted. Phosphate retention is common in patients with advanced CKD, and hemodialysis can effectively lower serum phosphate when conservative treatments fail. As demonstrated in this study, high serum phosphate level is a strong predictor for advanced CKD patients who were decided by experienced physicians to be enrolled in hemodialysis program because of severe fluid retention, hyperkalemia, acidosis and other uremic symptoms. Based on these findings, we suggest that clinicians consider the use of serum P as a laboratory marker in the decision-making process to initiate dialysis in advanced CKD patients.

There were several limitations in this study. First, it was a retrospective, single-hospital study, and the study cohort was relatively small. Second, patient compliance to our MPE program varied widely, and we were not able to access the daily

phosphate intake in all patients. Furthermore, the use of phosphate binders is not reimbursed by the Taiwan National Health Insurance, so socioeconomic status, in addition to the clinical factors that we identified, may have affected the use of phosphate binders. Finally, a large randomized outcome trial that examines mortality and cardiovascular complications and uses hyperphosphatemia as the criterion to enter dialysis is needed to better define the role of serum phosphate in predicting the need for dialysis in patients with advanced CKD.

Conclusion

Hyperphosphatemia is not only a common electrolyte problem in patients with advanced CKD, but is also well known as a significant risk factor for mineral bone diseases, vascular calcification, and cardiovascular and all-cause mortality in these patients. Based on this study, we further recommend that in addition to conventional laboratory parameters and uremic symptoms, clinicians could consider significant hyperphosphatemia as a reliable marker to determine initiation of dialysis in patients with advanced CKD.

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Conflict of interest

None declared.

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