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Original Article

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 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 m^2, 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 m^2 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 m^2 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 m^2. 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 D_3, 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 m^2 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