DOI: 10.53469/jcmp.2025.07(04).52

Current Status in Management of Blood Phosphorus During Continuous Renal Replacement Therapy

Xiaohan Xiu, Xuemei Chen*

Department of Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400042, China
Correspondence Author, 1557451771@qq.com

Abstract: ***Continuous renal replacement therapy (CRRT) is a significant blood purification technique for acute kidney injury in critically ill patients. Blood phosphorus is an important component of human energy metabolism, cellular signal transduction, and acid-base balance, and maintaining normal blood phosphorus levels is crucial for the maintenance of bodily functions. During CRRT, due to the continuous clearance of phosphates, patients are prone to hypophosphatemia, which can lead to severe consequences such as muscle weakness, respiratory failure, and arrhythmias. Inappropriate phosphorus supplementation may lead to hyperphosphatemia, which is associated with poor prognosis. Therefore, effectively monitoring and managing blood phosphorus levels during CRRT has become an important clinical challenge. This study reviews the effect of CRRT on blood phosphorus metabolism and the mechanism, the dangers of abnormal blood phosphorus during CRRT, the current status of blood phosphorus management during CRRT, and the influencing factors.***

Keywords: Continuous renal replacement therapy, Blood phosphorus, Hypophosphatemia, Hyperphosphatemia, Management**.**

1. Introduction

Continuous Renal Replacement Therapy (CRRT) is a blood purification technique widely used in clinical settings for acute kidney injury in critically ill patients. Compared to traditional intermittent hemodialysis, CRRT can more steadily remove metabolic waste, maintain electrolyte balance, and is suitable for hemodynamically unstable patients. Blood phosphorus is a crucial component of human energy metabolism, cell signaling, and acid-base balance, with normal blood phosphorus levels being essential for maintaining bodily functions. During CRRT, due to the continuous clearance of phosphate, patients are prone to hypophosphatemia, which can lead to severe consequences such as muscle weakness, respiratory failure, and arrhythmias. However, inappropriate phosphorus supplementation may increase the risk of hyperphosphatemia, which is associated with poor prognosis. Therefore, how to effectively monitor and manage blood phosphorus levels during CRRT treatment has become a significant clinical challenge.

2. Distribution and Function of Phosphorus Under Physiological Conditions

Phosphorus is an essential element in the human body, participating in various life activities through both organic and inorganic forms. It serves as a crucial component of adenosine triphosphate (ATP), deoxyribonucleic acid (DNA), ribonucleic acid (RNA), cyclic adenosine monophosphate, and glycerophospholipids, playing vital roles in energy metabolism, maintenance and transmission of genetic information, intracellular signal transduction, and preservation of biological membrane structural integrity [1]. Phosphorylation modification represents an important protein modification mechanism within cells, capable of altering protein activity, stability, localization, and other properties, thereby participating in the regulation of cellular life activities and functions [1]. Inorganic phosphates contribute to buffer systems, exerting significant physiological homeostatic effects in acid-base balance regulation [2-5]. Phosphorus is present in all tissues, with 85% deposited in bones, 14% in soft tissues, and a small fraction in extracellular fluid. In extracellular fluid, 85% of phosphorus exists in inorganic forms (as free ions or bound to cations such as calcium and magnesium). Human blood phosphorus levels are typically maintained at 0.8-1.45 mmol/L (2.5-4.5 mg/dL), exhibiting diurnal variation with the lowest concentrations in the morning and highest in the evening [6, 7].

3. Mechanisms and Hazards of Phosphorus Metabolism Disorders in Critically Ill Patients

Critically ill patients often develop phosphorus metabolism disorders due to factors such as inflammatory storms, tissue hypoperfusion, nutritional and metabolic disturbances, and organ dysfunction, leading to abnormal blood phosphorus levels (hypophosphatemia or hyperphosphatemia). This can cause severe damage to multiple organ systems and adversely affect prognosis.

Critically ill patients often develop hypophosphatemia due to gastrointestinal issues preventing normal food intake or malabsorption, reduced phosphorus intake via the gastrointestinal tract, and insufficient intravenous phosphorus supplementation. When patients resume eating after prolonged starvation, particularly when consuming high-carbohydrate diets, refeeding syndrome occurs. This stimulates excessive insulin secretion, promotes increased cellular uptake and utilization of phosphorus, and enhances phosphorus transfer into cells, leading to decreased serum phosphorus levels. Critically ill patients frequently present with acid-base balance disorders that affect intracellular and extracellular phosphorus shifts. The use of loop diuretics or elevated levels of certain hormones such as PTH (parathyroid hormone) increases phosphorus excretion, further contributing to hypophosphatemia. Additionally, the administration of certain antibiotics, glucocorticoids, β-adrenergic agonists, or insulin-based glucose-lowering therapies may disrupt phosphorus metabolism or excretion, also leading to hypophosphatemia. Hypophosphatemia is relatively common in clinical practice, occurring in

approximately 5% of hospitalized patients, with incidence rates as high as 20% to 80% in critically ill populations [8].

Severe hypophosphatemia and persistent hypophosphatemia lead to respiratory muscle weakness, myocardial depression, arrhythmias, and increased infection risk due to immune suppression, which are closely associated with multiple organ failure in critically ill patients, prolonging mechanical ventilation duration and increasing mortality [9-14]. Wang et al. further confirmed that hypophosphatemia is an independent risk factor for 28-day mortality in ICU patients, with patients having serum phosphate levels below 0.8 mmol/L exhibiting significantly higher mortality than those with normal phosphate levels [9]. In patients with sepsis complicated by acute kidney injury (AKI), low serum phosphate levels were independently associated with 90-day mortality [15], indicating that hypophosphatemia not only affects short-term prognosis but is also linked to long-term outcomes. The study by Wang Hongxin et al. further demonstrated that hypophosphatemia is associated with prolonged ICU stays and higher mortality in critically ill patients [16]. Early and timely phosphate supplementation helps improve patient outcomes. It has been reported that phosphate supplementation can reduce the incidence of arrhythmias in sepsis patients [10], enhance diaphragmatic contractility [17], shorten mechanical ventilation duration in critically ill patients [18], and increase renal function recovery rates in AKI patients [19], thereby improving organ function and survival rates [10, 18, 20]. Therefore, regular monitoring of serum phosphate levels and prompt implementation of appropriate interventions are crucial for critically ill patients.

However, critically ill patients often present with inflammatory storms, acidosis, and renal insufficiency. The release of intracellular phosphorus into the extracellular space and impaired renal phosphate excretion can lead to hyperphosphatemia, while inappropriate phosphate supplementation further increases the risk of developing hyperphosphatemia. Jung et al. found in their study on AKI patients that hyperphosphatemia was significantly correlated with APACHE II and SOFA scores, suggesting that elevated serum phosphorus levels may serve as a biomarker for disease severity in critically ill patients. Persistent and severe hyperphosphatemia can result in hypocalcemia, secondary hyperparathyroidism, and ectopic calcification in blood vessels and soft tissues, thereby increasing the risks of coronary artery calcification, cardiovascular events, renal function deterioration, and mortality [15, 21-28].

4. Blood Phosphorus Management During CRRT Therapy

4.1 Abnormal Blood Phosphorus Levels and Associated Risks During CRRT Treatment

4.1.1 The Impact of CRRT Therapy on Blood Phosphorus Levels

CRRT can continuously and slowly remove metabolic waste and excess fluid from the body, and has now become the most common vital organ replacement therapy in the Intensive Care Unit (ICU) [29]. It is widely used to treat various clinical conditions, including sepsis, acute liver failure (ALF), acute respiratory distress syndrome (ARDS), and cardiogenic shock [27,28,30,31]. However, due to the prolonged continuous solute removal, while improving patient outcomes, CRRT can also induce a series of metabolic disturbances. Phosphate is a small-molecule substance that easily passes through the filter membrane and can be cleared by CRRT. Given the extended duration of CRRT treatment, with continuous solute removal for 24 hours or more per day, hypophosphatemia frequently occurs [32].

4.1.1.1 Incidence and Hazards of Hypophosphatemia in CRRT

The incidence of hypophosphatemia during CRRT treatment is high, with the RENAL study showing that approximately 54-65% of patients develop hypophosphatemia during CRRT [33]. Female patients, those with longer CRRT treatment durations, and those with lower pre-treatment serum phosphate levels are at higher risk of hypophosphatemia (OR=2.484, 1.054, 0.469) and are more prone to severe hypophosphatemia [34]. Even intravenous phosphate supplementation or the use of phosphate-containing CRRT solutions during CRRT cannot completely prevent hypophosphatemia. Crowley et al. found that when using phosphate-free replacement fluid Prismasol and phosphate-containing replacement fluid Phoxillum (1 mmol/L), the incidence rates of CRRT-associated hypophosphatemia were 24.9% and 6.2%, respectively [35]. Moreover, persistent hypophosphatemia during CRRT reduces the chances of successful extubation in mechanically ventilated patients, leading to longer hospital stays and higher mortality rates [8, 12, 36].

4.1.1.2 CRRT Hyperphosphatemia Hazards

Critically ill patients often experience inflammatory storms leading to cellular damage, AKI, or multiple organ dysfunction syndrome. The release of intracellular phosphorus or impaired phosphorus excretion results in hyperphosphatemia, necessitating higher doses of CRRT to remove excess phosphorus. Insufficient CRRT treatment doses or incorrect phosphorus supplementation further increase the risk of hyperphosphatemia. Crowley et al. found that using phosphorus-containing replacement fluid Phoxillum (1 mmol/L) could reduce CRRT-induced hypophosphatemia and decrease intravenous phosphorus supplementation, but the incidence of hyperphosphatemia was higher (37% vs. 27.7%) [35]. Hyperphosphatemia is associated with poor prognosis in critically ill patients. Thongprayoon et al. discovered in a study of critically ill patients with AKI undergoing CRRT that hyperphosphatemia (serum phosphorus ≥4.6 mg/dL) before and during CRRT was significantly associated with higher 90-day mortality (OR 1.62 and 2.22, respectively) [15]. Zhou et al. also observed in a study of critically ill children receiving CRRT that hyperphosphatemia (serum phosphorus >7.4 mg/dL) before and during CRRT was linked to increased 90-day mortality risk (OR 3.74 and 7.34, respectively) [37]. Jung et al. similarly found in a study of AKI patients undergoing CRRT that elevated serum phosphorus levels before CRRT, 24 hours after CRRT, and an increase in serum phosphorus levels 24 hours post-CRRT compared to pre-treatment levels were associated with higher 28-day and 90-day mortality risks [21].

Therefore, how to effectively monitor and manage blood phosphorus levels during CRRT treatment has become an important topic in clinical research.

4.2 Current Status of Blood Phosphorus Management During CRRT Therapy

4.2.1 Prevention and Treatment Strategies for Hypophosphatemia in CRRT

The high incidence of hypophosphatemia in critically ill patients and its association with adverse outcomes have garnered widespread attention. ESPEN (2023) recommends that critically ill patients should undergo blood phosphorus testing at least once daily during the first week of ICU admission. For patients with refeeding hypophosphatemia (<0.65 mmol/L or a loss >0.16 mmol/L), blood phosphorus should be rechecked 2-3 times daily and supplemented as needed. However, no specific phosphorus supplementation protocol was provided [38]. Due to the continuous and prolonged clearance of water and solutes during CRRT, which significantly impacts acid-base balance and electrolytes, disturbances in blood phosphorus levels frequently occur. There is currently no consensus on blood phosphorus management protocols during CRRT. Current preventive and therapeutic measures for CRRT-induced hypophosphatemia include oral phosphorus supplementation, intravenous phosphorus supplementation, or phosphorus-containing CRRT solutions.

Clinically, hypophosphatemia can be corrected by oral administration of sodium phosphate or potassium phosphate. Oral phosphorus is primarily absorbed in the small intestine through passive absorption via the paracellular pathway along a concentration gradient and active transport via the transcellular pathway mediated by the sodium-dependent phosphate cotransporter 2b (NaPi2b) [39]. However, oral phosphorus supplementation has a slow onset of action and often causes gastrointestinal adverse reactions such as nausea, vomiting, bloating, abdominal pain, and diarrhea, resulting in poor patient tolerance. Critically ill patients frequently present with gastrointestinal dysfunction or intestinal obstruction requiring fasting, making it difficult to correct hypophosphatemia through oral phosphorus supplementation.

During CRRT therapy, intravenous phosphorus supplementation is commonly used to prevent or treat CRRT-related hypophosphatemia. However, due to the complexity of human phosphate kinetics, serum phosphorus concentration depends on the balance between phosphorus production in the blood and its excretion from extracellular fluid or redistribution within body compartments. Critically ill patients often experience transcellular redistribution of phosphate, meaning serum phosphorus levels do not fully reflect total body phosphorus stores. The rapid clearance of phosphorus by CRRT may exacerbate this shift, making it difficult to accurately assess phosphorus removal during CRRT or maintain stable serum phosphorus levels through this method. Yang et al. found in a study of AKI patients receiving CRRT that even with daily serum phosphorus monitoring and corresponding intravenous phosphorus supplementation, this approach failed to prevent hypophosphatemia during CRRT [12].

Multiple research findings indicate that using phosphorus-containing replacement solutions can significantly reduce the incidence of hypophosphatemia during CRRT [6, 35, 40-44] and shorten its duration [43, 45], without affecting other electrolyte levels [46]. However, there is currently a lack of standardized phosphorus supplementation protocols for phosphorus-containing replacement solutions, with varying concentrations used across different regions. In the United States, CRRT solutions contain a phosphate concentration of 1.0 mmol/L (3.1 mg/dL), while in Europe, the concentration is 1.2 mmol/L (3.7 mg/dL) [47]. A study by Song et al. explored the effects of different phosphorus concentrations in replacement solutions, demonstrating that a 2.0 mmol/L phosphorus solution effectively corrects hypophosphatemia, whereas a 3.0 mmol/L solution, while rapidly increasing serum phosphorus levels, may elevate the risk of hyperphosphatemia [45]. Crowley et al. found that using a 1 mmol/L phosphorus-containing replacement solution (Phoxillum) effectively reduced the incidence of hypophosphatemia (6.2% vs. 24.9%), but also significantly increased the occurrence of hyperphosphatemia (37% vs. 27.7%) [35]. Therefore, the concentration and dosage of phosphorus-containing replacement solutions should be adjusted based on individual patient conditions to achieve optimal serum phosphorus control.

4.3 Factors Influencing Blood Phosphorus Management During CRRT

Different CRRT treatment modalities exhibit variations in phosphate clearance efficiency. Saunders et al. pointed out that the three main modes of CRRT — continuous veno-venous hemofiltration (CVVH), continuous veno-venous hemodialysis (CVVHD), and continuous veno-venous hemodiafiltration (CVVHDF) — differ in their phosphate clearance capacity, with CVVHDF demonstrating the highest phosphate loss rate [48]. Therefore, distinct phosphate supplementation protocols should be formulated for different CRRT modalities to prevent the occurrence of hypophosphatemia or hyperphosphatemia.

The anticoagulation method is also a significant factor affecting blood phosphorus metabolism during CRRT. Research by Zhang et al. found that in patients with liver failure, a CRRT protocol using citrate anticoagulation was safer than the traditional heparin anticoagulation protocol and could reduce the occurrence of calcium metabolism disorders, thereby decreasing the incidence of blood phosphorus abnormalities through calcium-phosphorus metabolism [49]. This suggests that optimizing anticoagulation strategies may be an effective approach to reducing blood phosphorus abnormalities in CRRT patients.

Studies have found that patients receiving nutritional support with enteral nutrition formulas are more prone to severe hypophosphatemia during CRRT treatment [50], which may be related to refeeding syndrome in this patient population. After prolonged fasting, critically ill patients restarting dietary intake experience elevated blood glucose and insulin concentrations along with increased metabolic activity, leading to intracellular phosphate shifts and subsequent hypophosphatemia [51]. Therefore, greater attention should

be paid to the selection of nutritional methods, nutrient composition, and the timing of enteral nutrition initiation in critically ill patients.

Kanduri et al. found that COVID-19 patients with AKI had a higher incidence of moderate and severe hyperphosphatemia (≥7-10 mg/dL and >10 mg/dL) during RRT compared to non-COVID-19 AKI patients (86% vs. 60%, 50% vs. 18%). Elevated blood phosphorus levels were associated with higher lactate dehydrogenase (LDH), and increased LDH levels reflected a hyperinflammatory state, suggesting that the cytokine storm in COVID-19 patients leads to cellular damage and increased intracellular phosphorus release, which may contribute to the higher incidence of hyperphosphatemia. The study also found that hyperphosphatemia was associated with shorter RRT duration, as COVID-19 patients with AKI were more prone to filter clotting/occlusion during RRT, leading to reduced filter lifespan and shorter RRT runtime. Additionally, reduced phosphorus clearance efficiency during RRT was another important factor contributing to hyperphosphatemia [52]. Female patients and those with lower pre-RRT blood phosphorus levels were more susceptible to hypophosphatemia [34]. Therefore, in managing blood phosphorus levels during CRRT, it is necessary to consider different populations and disease factors, particularly establishing individualized management strategies for conditions with high inflammation / hypercoagulability similar to COVID-19, female patients, and those with lower pre-CRRT blood phosphorus levels.

Critically ill patients often present with fluid overload and metabolic acidosis, leading to intracellular phosphorus shifting extracellularly and elevating serum phosphorus levels. During CRRT treatment, as acidosis is gradually corrected, phosphorus re-enters the cells. The efficiency of phosphorus clearance by CRRT may be influenced by factors such as CRRT dose, phosphorus concentration in the replacement fluid, and pre-CRRT serum phosphorus levels. Leypoldt et al. developed a steady-state phosphate balance model to assess the impact of CRRT dose on serum phosphate concentrations when using phosphate-free and phosphate-containing RRT solutions. This model aims to individualize CRRT treatment dose and RRT phosphate concentration to maintain serum phosphorus within the desired range during therapy. However, to simplify calculations, the model neglects the transcellular shift of phosphate between intracellular and extracellular fluids during CRRT and assumes constant initial phosphate generation and clearance rates that remain unchanged throughout treatment. In reality, these parameters are dynamic and unstable during CRRT, indicating the need for further optimization of this model [53]. With advancements in science and technology, artificial intelligence (AI) and machine learning are increasingly applied in medicine [54, 55]. By integrating dynamic monitoring and large-scale medical data analysis, predictive models can be developed to achieve precise assessment and real-time adjustment of serum phosphorus levels, enabling personalized phosphorus management strategies. The quality of medical data is crucial for model performance, requiring authenticity, reliability, and completeness. However, medical data are often incomplete, inconsistent, or subject to interference, potentially compromising model accuracy and reliability. Current AI systems rely on historical data for training, but their reasoning capabilities remain inferior to human physicians when dealing with complex factors such as rare diseases, multiple comorbidities, or patient psychological states. Additionally, low patient trust in AI hinders effective dynamic dialogue for comprehensive medical history extraction, increasing the risk of misdiagnosis [56, 57].

4.4 Inadequacies in Blood Phosphorus Management During CRRT

Currently, there is no unified standard for blood phosphorus management during CRRT, with significant variations in phosphorus supplementation protocols adopted across different regions and institutions, and no systematic clinical guidelines have been established. The individualized management model remains underdeveloped, as existing blood phosphorus management measures are largely empirical and have yet to achieve precise, personalized intervention strategies. There is insufficient research on long-term outcomes, with current studies primarily focusing on the impact of short-term blood phosphorus fluctuations on disease progression, while the mechanisms underlying the effects of hypophosphatemia on long-term prognosis require further exploration. Additionally, there is limited research on the economic costs and feasibility of CRRT-related blood phosphorus management, and how to balance patient benefits with medical costs in clinical practice remains an issue worthy of attention.

5. Looking Ahead

Future research should focus on the following directions: First, optimizing standardized protocols for blood phosphorus management during CRRT by conducting multicenter randomized controlled trials to further validate the clinical efficacy of different phosphorus supplementation regimens and establish standardized phosphorus management strategies. Second, strengthening research on individualized blood phosphorus management by integrating dynamic monitoring technologies, big data analytics, and AI predictive models to develop more precise phosphorus regulation approaches for personalized interventions. Third, evaluating the long-term prognostic impact of hypophosphatemia, further exploring its role in prognostic assessment for critically ill patients, and clarifying its relationship with multi-system dysfunction and survival rates. Fourth, investigating novel phosphorus supplementation strategies by optimizing the formulations and administration methods of phosphorus supplements to enhance safety and efficacy. Fifth, assessing the economic feasibility of blood phosphorus management to optimize the cost-effectiveness of CRRT phosphorus management while ensuring patient benefits and improving the utilization efficiency of medical resources.

References

[1] Lin YH. Revisiting the Clinical Classification, Grading, and Staging of Respiratory Failure [J]. Medical Theory and Practice, 2011, 24(20): 2430-2434.

[2] Heung, M. Mueller BA. Prevention of hypophosphatemia during continuous renal replacement therapy—An overlooked problem [J]. Semin Dial, 2018, 31: 213-218.

[3] Song YH, Seo EH, Yoo YS, et al. Phosphate supplementation for hypophosphatemia during continuous renal replacement therapy in adults [J], Renal Failure, 2019, 41(1), pp. 72–79.
[4] Tandukar S, Palevsky PM. Continuous renal replacement therapy: who, when, why, and how [J]. Chest, 2019, 155(3): 626-638.
[5] Lin WT, Zhang X, Yang M, et al. Research Progress on Hypophosphatemia Associated with Continuous Renal Replacement Therapy [J]. Chinese Blood Purification, 2021, 20(03): 193-196.
[6] Broman M, Carlsson O, Friberg H, et al. Phosphate-containing dialysis solution prevents hypophosphatemia during continuous renal replacement therapy [J]. Acta Anaesthesiologica Scandinavica, 2011, 55: 39-45.
[7] Cho A, Lee YK, Park HC. Impact of electrolyte-rich dialysate during continuous renal replacement therapy on serum phosphate and potassium in ICU patients [J]. PLoS ONE 2020, 15(9): e0238867.
[8] Sin JCK, King L, Ballard E, et al. Hypophosphatemia and Outcomes in ICU: A Systematic Review and Meta-Analysis [J]. J Intensive Care Med. 2021, 36(9):1025-1035.
[9] Demirjian S, Teo BW, Guzman JA, et al. Hypophosphatemia during continuous hemodialysis is associated with prolonged respiratory failure in patients with acute kidney injury [J]. Nephrol Dial Transplant, 2011, 26(11):3508-14.
[10] Schwartz A, Brotfain E, Koyfman L, et al. Association between Hypophosphatemia and Cardiac Arrhythmias in the Early Stage of Sepsis: Could Phosphorus Replacement Treatment Reduce the Incidence of Arrhythmias? [J]. Electrolyte Blood Press, 2014, 12(1): 19-25.
[11] Shor R, Halabe A, Rishver S, et al. Severe hypophosphatemia in sepsis as a mortality predictor [J]. Ann Clin Lab Sci, 2006, 36: 67-72.
[12] Yang Y, Zhang P, Cui Y, et al. Hypophosphatemia during continuous veno-venous hemofiltration is associated with mortality in critically ill patients with acute kidney injury [J]. Crit Care. 2013, 19;17(5):R205.
[13] Hendrix RJ, Hastings MC, Samarin M, et al. Predictors of Hypophosphatemia and Outcomes during Continuous Renal Replacement Therapy [J]. Blood Purif. 2020, 49(6):700-707.
[14] Lim C, Tan HK, Kaushik M. Hypophosphatemia in critically ill patients with acute kidney injury treated with hemodialysis is associated with adverse events [J]. Clin Kidney J. 2017, 10(3):341-347.
[15] Thongprayoon C, Radhakrishnan Y, Cheungpasitporn W, et al. Association of Serum Phosphate Derangement With Mortality in Patients on Continuous Renal Replacement Therapy [J]. Can J Kidney Health Dis, 2022, 9:20543581221114697.
[16] Wang HX, Wang YL, Lu XY, et al. Analysis of Blood Phosphorus Level Changes in Critically Ill Patients During Continuous Renal Replacement Therapy[J]. Modern Practical Medicine,2023,35(10):1372-1374.
[17] Aubier M, Murciano D, Lecocguic Y, et al. Effect of hypophosphatemia on diaphragmatic contractility in patients with acute respiratory failure [J]. N Engl J, 1985;313:420e4.
[18] Miller CJ, Doepker BA, Springer AN, et al. Impact of Serum Phosphate in Mechanically Ventilated Patients With Severe Sepsis and Septic Shock [J]. J Intensive Care Med. 2020, 35(5):485-493.
[19] Schiffl H, Lang SM. Severe acute hypophosphatemia during renal replace-ment therapy adversely affects outcome of critically ill patients with acute kidney injury [J]. Int Urol Nephrol 2013, 45:191e7.
[20] Zazzo JF, Troché G, Ruel P, et al. High incidence of hypophosphatemia in surgical intensive care patients: Efficacy ofphosphorus therapy on myocardial function [J]. Intensive Care Medicine, 1995, 21(10): 826-31.
[21] Jung SY, Kwon J, Park S, et al. Phosphate is a potential biomarker of disease severity and predicts adverse outcomes in acute kidney injury patients undergoing continuous renal replacement therapy [J]. PLoS One. 2018, 13(2):e0191290.
[22] Chang AR, Anderson C. Dietary Phosphorus Intake and the Kidney [J]. Annu Rev Nutr, 2017, 37: 321-46.
[23] Villa-bellosta R, Ravera S, Sorribas V, et al. The Na+-Pi cotransporter PiT-2 (SLC20A2) is expressed in the apical membrane of rat renal proximal tubules and regulated by dietary Pi [J]. Am J Physiol Renal Physiol, 2009, 296(4): F691-9.
[24] García MA, Varsavsky M, Cortés BM, et al. Phosphate disorders and clinical management of hypophosphatemia and hyperphosphatemia [J]. Endocrinol Diabetes Nutr (Engl Ed). 2020, 67(3): 205-215.
[25] Vervloet MG, Van Ballegooijen AJ. Prevention and treatment of hyperphosphatemia in chronic kidney disease [J]. Kidney Int. 2018, 93(5):1060-1072.
[26] Wang H, Zhang L, Liao W, et al. Hyperphosphatemia rather than hypophosphatemia indicates a poor prognosis in patients with sepsis [J]. Clin Biochem. 2021, 91:9-15.
[27] Wei S, Li Y, Zhang C, Guo X, et al. Prognostic value of serum phosphate levels in sepsis: a systematic review and meta-analysis [J]. PeerJ. 2023, 11:e16241.
[28] Zheng WH, Yao Y, Zhou H, et al. Hyperphosphatemia and Outcomes in Critically Ill Patients: A Systematic Review and Meta-Analysis [J]. Front Med (Lausanne). 2022, 9:870637.
[29] Brain M, Winson E, Roodenburg O, et al. Non anti-coagulant factors associated with filter life in continuous renal replacement therapy (CRRT): a systematic review and meta-analysis [J]. BMC nephrology, 2017, 18: 1-27.
[30] Ankawi G, Neri M, Zhang J, et al. Extracorporeal techniques for the treatment of critically ill patients with sepsis beyond conventional blood purification therapy: the promises and the pitfalls [J]. Crit Care, 2018, 22(1):262.
[31] Wendon J, Cordoba J, Dhawan A, et al. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure [J]. J Hepatol, 2017, 66(5): 1047-81.
[32] Rastogi A, Bhatt N, Rossetti S, et al. Management of hyperphosphatemia in end-stage renal disease: a new paradigm [J]. Journal of Renal Nutrition, 2021, 31(1): 21-34.

[33] Bellomo R, Cass A, Cole L, et al. Intensity of continuous renal-replacement therapy in critically ill patients [J]. N Engl J Med, 2009, 361(17): 1627-1638.
[34] Song YY, Sun YH, Huang DC, et al. A Retrospective Study on the Occurrence and Prognosis of Hypophosphatemia in Critically Ill Patients During CRRT[J]. Chinese Critical Care Medicine Electronic Journal,2024,10(2):164-172.
[35] Crowley KE, DeGrado JR, Charytan DM. Serum glucose and phosphorus concentrations during continuous renal replacement therapy using commercial replacement solutions with or without phosphorus [J]. Hemodial Int. 2020, 24(3):330-334.
[36] Serpa NA, Naorungroj T, Gallagher M, et al. Impact of Intensity of Continuous Renal Replacement Therapy on Duration of Ventilation in Critically Ill Patients: A Secondary Analysis of the RENAL Trial [J]. Blood Purif. 2023, 52(11-12):888-897.
[37] Zhou X, He J, Zhu D, et al. Relationship between serum phosphate and mortality in critically ill children receiving continuous renal replacement therapy [J]. Front Pediatr. 2023, 11:1129156.
[38] Singer P, Blaser AR, Berger MM, et al. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit [J]. Clin Nutr. 2023, 42(9): 1671-1689.
[39] Yee J, Rosenbaum D, Jacobs JW, et al. Small Intestinal Phosphate Absorption: Novel Therapeutic Implications [J]. Am J Nephrol. 2021, 52(7):522-530.
[40] Manghat P, Sodi R, Swaminathan R. Phosphate homeostasis and disorders [J]. Ann Clin Biochem, 2014, 51(Pt 6): 631-56.
[41] Thompson Bastin ML, Adams PM, Nerusu S, et al. Association of Phosphate Containing Solutions with Incident Hypophosphatemia in Critically Ill Patients Requiring Continuous Renal Replacement Therapy [J]. Blood Purif, 2022, 51(2): 122-9.
[42] Chua HR, Schneider AG, Baldwin I, et al. Phoxilium vs Hemosol-B0 for continuous renal replacement therapy in acute kidney injury [J]. Journal of Critical Care, 2013, 28(5): 884.e7-.e14.
[43] Godaly G, Carlsson O, Broman M. Phoxilium® reduces hypophosphataemia and magnesium supplementation during continuous renal replacement therapy [J]. Clinical Kidney Journal, 2016, 9(2): 205-10.
[44] Morabito S, Pistolesi V, Tritapepe L, et al. Continuous venovenous hemodiafiltration with a low citrate dose regional anticoagulation protocol and a phosphate - containing solution: effects on acid-base status and phosphate supplementation needs [J]. BMC Nephrol, 2013, 14: 232.
[45] Song YH, Seo EH, Yoo YS, et al. Phosphate supplementation for hypophosphatemia during continuous renal replacement therapy in adults [J]. Renal Failure, 2019, 41(1): 72-9.
[46] Hu MC, ShiizakI K, Kuro-o M, et al. Fibroblast growth factor 23 and Klotho: physiology and pathophysiology of an endocrine network of mineral metabolism [J]. Annu Rev Physiol, 2013, 75: 503-33.
[47] Christov M, Jüppner H. Phosphate homeostasis disorders [J]. Best Pract Res Clin Endocrinol Metab, 2018, 32(5): 685-706.
[48] Saunders H, Rehan A, Hashmi MF, et al. Continuous Renal Replacement Therapy [M]. Treasure Island (FL): StatPearls, 2025.
[49] Zhang W, Bai M, Yu Y, et al. Safety and efficacy of regional citrate anticoagulation for continuous renal replacement therapy in liver failure patients: a systematic review and meta-analysis [J]. Critical Care, 2019, 23: 1-11.
[50] Preiser J C, Arabi Y M, Berger M M, et al. A guide to enteral nutrition in intensive care units: 10 expert tips for the daily practice [J]. Crit Care, 2021, 25(1):424.
[51] Reber E, Friedli N, Vasiloglou MF, et al. Management of Refeeding Syndrome in Medical Inpatients [J]. J Clin Med, 2019, 8(12).
[52] Kanduri SR, Ramanand A, Varghese V, et al. Refractoriness of Hyperkalemia and Hyperphosphatemia in Dialysis-Dependent AKI Associated with COVID-19 [J]. Kidney360. 2022, 3(8):1317-1322.
[53] Leypoldt JK, Echeverri J, Harenski K, et al. Predictions of Serum Phosphate Concentration during Continuous Renal Replacement Therapy Using a Steady-State Mass Balance Model [J]. Blood Purif. 2024, 53(1):40-48.
[54] Yang ZY, Zhu XY, Yu JY, et al. Applications and Prospects of Artificial Intelligence in Interventional Medicine[J]. Journal of Interventional Radiology, 2025, 34(04):441-444.
[55] Qi C, Wang Y. Applications of Artificial Intelligence in Diagnostic Pathology[J/OL]. Journal of Diagnostic Pathology, 1-9[2025-04-07].
[56] Wu T. Generative Artificial Intelligence Technology Empowers the Risks and Regulations of Smart Healthcare Construction[J]. Medicine and Society, 2025, 38(03):9-16.
[57] Nong P, Platt J. Patients' Trust in Health Systems to Use Artificial Intelligence [J]. JAMA Netw Open. 2025, 8(2):e2460628.