

Original Article

Continuous blood purification technology for treatment of critically ill patients with chronic renal failure

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Abstract: Objective: To evaluate the effect of continuous blood purification (CBP) on the treatment outcomes in critically ill patients with chronic renal failure (CRF). Methods: This single-center retrospective cohort study included 184 critically ill patients with CRF. According to treatment regimen, patients were allocated into a control group (n = 89; receiving conventional therapy) and an observation group (n = 95; receiving CBP plus conventional therapy). According to patient prognosis, they were categorized into a renal function recovery group (n = 62) and a non-recovery group (n = 122). Treatment outcomes were compared between the two groups, and factors influencing prognosis were analyzed. Results: After treatment, compared with the control group, the observation group showed significant improvements in heart rate (HR), respiratory rate (RR), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), N-terminal pro-brain natriuretic peptide (NT-proBNP), blood urea nitrogen (BUN), serum creatinine (Scr), uric acid (UA), tumor necrosis factor- α (TNF- α), C-reactive protein (CRP), interleukin-6 (IL-6), partial pressure of oxygen (PO₂), bicarbonate (HCO₃⁻), partial pressure of carbon dioxide (PCO₂), and quality of life scores (all $P < 0.05$). No significant difference in complication rates was observed between the two groups ($P > 0.05$). Multivariate logistic regression analysis identified hypertension, low albumin (ALB), low total protein (TP), elevated Scr, and high BUN as independent risk factors for poor renal function recovery, with Scr showing the strongest correlation. Conclusion: CBP may serve as an adjunctive therapy in critically ill patients with CRF, particularly in those with elevated BUN and inflammatory markers. However, its potential association with nutritional risks should be carefully considered.

Keywords: Continuous blood purification technology, severe cases complicated with chronic renal failure, treatment

Introduction

Continuous renal replacement therapy (CRRT) has gradually evolved from intermittent hemodialysis. It is designed for prolonged replacement of impaired renal function and is typically performed as a 24-hour extracorporeal blood purification treatment. By applying the principles of convection and diffusion, CRRT facilitates slow and continuous removal of excess fluid and solutes, offering superior hemodynamic stability. Chronic kidney disease (CKD) affects over 850 million people globally, accounting for approximately 10% of the population [1, 2]. It has become a major chronic disease that poses a serious threat to human health, ranking after cancer, cardiovascular diseases, and diabetes. The prevalence of CKD

is higher in women, yet men face a greater risk of progression to end-stage renal disease (ESRD) [3]. The burden of CKD among adolescents and young adults is also on the rise [4]. CKD is a widespread health issue, affecting about 9.1% of the global population and 12-15% of individuals in upper-middle-income countries. Approximately 2% of CKD patients progress to ESRD, leading to significantly declined quality of life, increased mortality risk, and substantial economic burden [5]. CKD is often asymptomatic or presents with only mild clinical manifestations in its early stages. Currently, public understanding of CKD remains insufficient, and many patients are diagnosed when kidney function is severely impaired, thereby missing the opportunity for optimal early treatment. Chronic renal failure (CRF), also termed

as chronic renal insufficiency, is characterized by chronic progressive damage to the renal parenchyma, accompanied by severe loss of functional nephrons. This results in irreversible destruction of renal parenchyma, significant renal atrophy, and progressive loss of essential renal functions. Clinically, CRF is manifested by retention of metabolic waste products and disturbances in water, electrolytes and acid-base balance. Its core pathological feature is renal interstitial fibrosis, which represents the common final pathway for the progression of various types of CKD toward renal failure [6, 7]. However, the current understanding of the pathological mechanisms underlying CRF remains incomplete, particularly regarding CKD progression caused by common etiologies such as hypertension and diabetes mellitus [8].

Hemodialysis utilizes a semipermeable membrane to enable solute and fluid exchange between blood and dialysate via diffusion and convection, enabling the removal of metabolic waste products (e.g., urea nitrogen), uremic toxins, and excess fluid from circulation. This process partially substitutes for renal excretory function and contributes to the maintenance of water, electrolyte, and acid-base homeostasis [9, 10]. Although hemodialysis cannot completely eliminate all uremic toxins (e.g., certain middle-molecular-weight substances), it effectively prevents the systemic accumulation of metabolic waste [11]. In recent years, hemodialysis techniques have undergone continuous refinement and clinical expansion, contributing to significantly improved survival time in patients with CRF.

For patients with CRF receiving maintenance hemodialysis, clinical management should not only focus on prolonging survival and reducing mortality but also emphasize the preservation of psychological well-being and social functioning, thereby further improving quality of life [12].

Materials and methods

Study population

This retrospective study enrolled 184 critically ill patients with CRF admitted to the First People's Hospital of Linping District between January 2022 and June 2024. According to treatment method, patients were allocated into

a control group (n = 89) receiving conventional therapy and an observation group (n = 95) receiving continuous blood purification (CBP) in addition to conventional therapy. According to clinical outcomes, patients were further categorized into a renal function recovery group (n = 62) and a non-recovery group (n = 122) to identify factors associated with prognosis in critically ill patients with CRF.

Renal function recovery was defined using a stratified approach according to baseline dialysis status. For patients who were dialysis-dependent before the onset of critical illness, recovery was defined as successful liberation from kidney replacement therapy (KRT) for at least 30 consecutive days [13, 14]. For patients not receiving dialysis at baseline, recovery was defined as improvement in estimated glomerular filtration rate (eGFR) from < 15 to > 15 mL/min/1.73 m², from 15-30 to > 30 mL/min/1.73 m², or from 30-50 to > 50 mL/min/1.73 m² at 6-month follow-up [13].

Inclusion criteria: (1) Diagnosis of CRF corresponding to CKD stages 4-5 (eGFR < 30 mL/min/1.73 m²) with admission due to critical complications arising from the primary disease (e.g., severe infection, metabolic disorders, hemodynamic instability, and multiple organ dysfunction); (2) Age > 19 years; and (3) Adequate ability to understand and communicate. Exclusion criteria: (1) Severe mental illness; (2) Comorbid conditions such as stroke, malignant tumor, or heart failure; (3) History of neurodegenerative diseases (e.g., dementia, Parkinson's disease) or severe diabetic neuropathy; and (4) Long-term substance abuse.

This study was approved by the Ethics Committee of the First People's Hospital of Linping District. Due to the retrospective design, the requirement for informed consent was waived by the Ethics Committee.

Treatment methods

(1) Conventional treatment. Patients in the control group received conventional therapy, including monitoring of vital signs (e.g., body temperature, heart rate, and blood pressure) and routine supportive care. Basic medical treatment was administered based on the patient's primary disease.

(2) Continuous blood purification (CBP) protocol. Patients in the observation group received CBP in addition to conventional treatment. Continuous veno-venous hemofiltration or venovenous slow continuous ultrafiltration was selected according to clinical indication. A PRISMA bedside hemofiltration machine and compatible CBP consumables were used. The hemofilter (ME102, Gambro) was replaced daily. Bicarbonate-based replacement solution was administered in pre-dilution mode, with a flow rate maintained at 1,000-3,000 mL/h. Hemofiltration replacement fluid was either commercially prepared (Guangdong Huayuan Changfu Pharmaceutical Co., Ltd.) or automatically diluted using a Jinbao blood purification machine. Blood flow velocity was maintained at 128.5 ± 12.3 mL/min (range: 111-132 mL/min). Treatment duration and frequency were individualized based on the patient's degree of hypercatabolism. The total treatment duration ranged from 9 to 71 hours.

(3) Nursing and monitoring measures. Psychological intervention: Due to chronic nature of their underlying disease, patients often experienced negative emotions that could adversely affect treatment adherence. Nursing staff communicated with patients regularly, explaining the function, principles, and adverse reactions of CBP. Patient awareness and compliance were enhanced through structured education and reinforcement of positive treatment outcomes. Monitoring during treatment: vital signs, including respiratory rate, heart rate, and blood pressure, were continuously monitored. Any abnormal conditions were reported to the doctor promptly for timely intervention. Arteriovenous pressure and the flow rate and color of CBP replacement fluid were observed, and infusion parameters were adjusted accordingly. Vascular access management: A double-lumen central venous catheter was used due to its safety, long indwelling time, and adequate blood flow capacity. After intubation, close observation was performed to prevent compression, kinking, or displacement. Arteriovenous pressure and catheter patency were routinely assessed. In cases of abnormal pressure elevation, timely corrective measures were taken. The puncture site and local tissues were observed for bleeding, redness, or signs of infection. Dressings were changed regularly under strict aseptic conditions. The vascular catheter was maintained in a clean and dry

state and replaced promptly if contaminated. For unconscious patients, enhanced fixation was applied to prevent catheter dislodgment. Fluid balance intervention: Relevant parameters were individualized based on the patient's condition and cardiac function to ensure adequate filtration while preventing complications such as pulmonary edema, heart failure, and hypotension. Hemodynamics were continuously monitored to ensure hourly fluid balance and circulatory stability. Electrolyte and acid-base balance were adjusted dynamically according to clinical changes. Outcome assessment: The 36-Item Short Form Health Survey (SF-36) was used to assess quality of life of patients before and after intervention. Higher scores indicated better quality of life.

Observation indices

(1) Primary outcomes. Primary outcomes were assessed before treatment and at 24 hours after treatment, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C); albumin (ALB), total protein (TP), N-terminal pro-brain natriuretic peptide (NT-proBNP), blood urea nitrogen (BUN), serum creatinine (Scr), uric acid (UA), sodium (Na^+), potassium (K^+), tumor necrosis factor- α (TNF- α), C-reactive protein (CRP), interleukin-6 (IL-6), partial pressure of oxygen (PaO_2), bicarbonate (HCO_3^-), and partial pressure of carbon dioxide (PaCO_2).

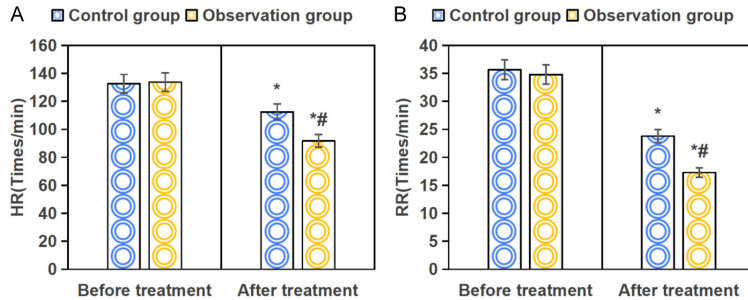
(2) Secondary outcomes. Secondary outcomes included heart rate (HR), and respiratory rate (RR) that were recorded before treatment and 24 hours after treatment. The 36-Item Short Form Health Survey (SF-36) [15] was used to assess quality of life, with higher scores indicating better quality of life. In addition, the incidence of treatment-related complications, including hypotension, bleeding, and extracorporeal circuit clotting, was recorded in both groups.

Statistical analysis

SPSS 22.0 was used for statistical analysis. Continuous variables were expressed as mean $\pm$ standard deviation (SD) and compared using the student's t-test. Categorical variables were expressed as numbers and percentages (n, %) and compared using χ^2 tests.

Table 1. Comparison of baseline characteristics between the control and observation groups

Indicator		Control group (n = 89)	Observation group (n = 95)	t/ χ^2	P
Sex	Male	59	60	0.587	0.763
	Female	32	33		
Age (Years)		62.68±7.29	63.92±7.72	0.846	0.562
Hypertension		40	43	0.678	0.831
Diabetes		9	10	0.524	0.677
Chronic renal insufficiency		11	12	0.853	0.735

**Figure 1.** Comparison of vital signs between the two groups before and after treatment. A. Heart rate (HR); B. Respiratory rate (RR). Notes: * $P < 0.05$, compared with before treatment, # $P < 0.05$, compared with the control group.

Comparison of vital signs between the two groups before and after treatment

As shown in **Figure 1**, there were no significant differences in HR or RR between the two groups before treatment ($P > 0.05$). After treatment, both HR and RR decreased significantly in both groups ($P < 0.05$), with significantly lower post-treatment values in the observation group than the control group ($P < 0.05$).

Stepwise logistic regression analysis was used for variable selection. Independent variables with a significance level of $P < 0.05$ for entry were included in the model to identify independent predictors of the dependent outcome and to reduce multicollinearity, thereby constructing an optimal regression model. The discriminative ability of the logistic regression model was evaluated using the Hosmer-Lemeshow goodness-of-fit test ($P > 0.05$ indicating good fit) and the area under the receiver operating characteristic curve (AUC-ROC). A P -value < 0.05 was considered statistically significant.

Results

Comparison of general information

Table 1 presents the baseline characteristics of the control group and the observation group. A total of 184 patients were enrolled, including 89 in the control group and 95 in the observation group. There were no significant differences between the two groups in terms of sex, age, or comorbidities, including hypertension, diabetes mellitus, and chronic renal insufficiency ($P > 0.05$), indicating good baseline comparability.

Comparison of blood lipid profiles between the two groups before and after treatment

As shown in **Figure 2**, there were no significant differences in baseline lipid profiles between the two groups ($P > 0.05$). After treatment, TC, TG, and LDL-C levels were significantly reduced in both groups ($P < 0.05$), with more pronounced reduction observed in the observation group ($P < 0.05$). In contrast, HDL-C levels were significantly increased, with a greater increase in the observation group ($P < 0.05$).

Comparison of ALB and TP levels between the two groups before and after treatment

As demonstrated in **Figure 3**, there were no significant differences in baseline ALB or TP levels between the two groups ($P > 0.05$). After treatment, both ALB and TP levels decreased significantly in the two groups ($P < 0.05$), and the decrease was more pronounced in the observation group ($P < 0.05$).

Comparison of cardiac and renal function indicators between the two groups before and after treatment

At baseline, there were no significant differences in cardiac and renal function indicators

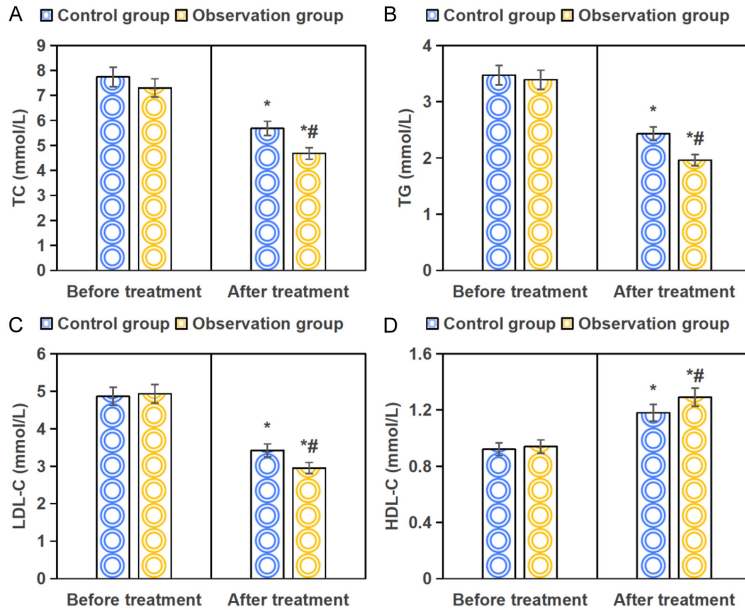


Figure 2. Comparison of lipid parameters between the two groups before and after treatment. A. Total cholesterol (TC); B. Triglycerides (TG); C. Low-density lipoprotein cholesterol (LDL-C); D. High-density lipoprotein cholesterol (HDL-C). Note: * $P < 0.05$, compared with before treatment; # $P < 0.05$, compared with the control group.

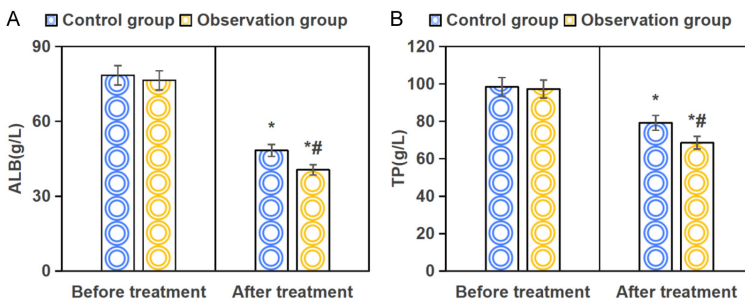


Figure 3. Comparison of albumin (ALB) and total protein (TP) levels between the two groups before and after treatment. A. ALB; B. TP. Notes: * $P < 0.05$, compared with before treatment; # $P < 0.05$, compared with the control group.

between the two groups ($P > 0.05$). After treatment, NT-proBNP, BUN, Scr, and UA decreased significantly in both groups ($P < 0.05$), with a more pronounced decrease observed in the observation group ($P < 0.05$; **Figure 4**).

Comparison of electrolyte levels between the two groups before and after treatment

Before treatment, there were no significant differences in electrolyte parameters between the two groups ($P > 0.05$). After treatment, both sodium (Na^+) and potassium (K^+) levels

increased significantly in both groups ($P < 0.05$), and the increase was more pronounced in the observation group ($P < 0.05$; **Figure 5**).

Comparison of inflammatory markers between the two groups before and after treatment

Before treatment, there were no significant differences in inflammatory markers between the two groups ($P > 0.05$). After treatment, TNF- α , CRP, and IL-6 levels decreased significantly in both groups ($P < 0.05$), with more pronounced decrease observed in the observation group ($P < 0.05$; **Figure 6**).

Comparison of arterial blood gas parameters between the two groups before and after treatment

As shown in **Figure 7**, there were no significant differences in blood gas parameters between the two groups before treatment ($P > 0.05$). After treatment, pO_2 and HCO_3^- significantly increased in both groups ($P < 0.05$), with a more significant increase observed in the observation group ($P < 0.05$). In contrast, pCO_2 significantly decreased in both groups ($P < 0.05$), with a more

significant decrease observed in the observation group ($P < 0.05$).

Comparison of quality-of-life scores between the two groups before and after treatment

As shown in **Figure 8**, there were no significant differences in quality-of-life scores between the two groups before treatment ($P > 0.05$). After treatment, all SF-36 domain scores—including mental health, emotional role, social function, physical function, physical role, bodily pain, vitality, and general health in both groups

Influence of CBP on patients with severe CRF

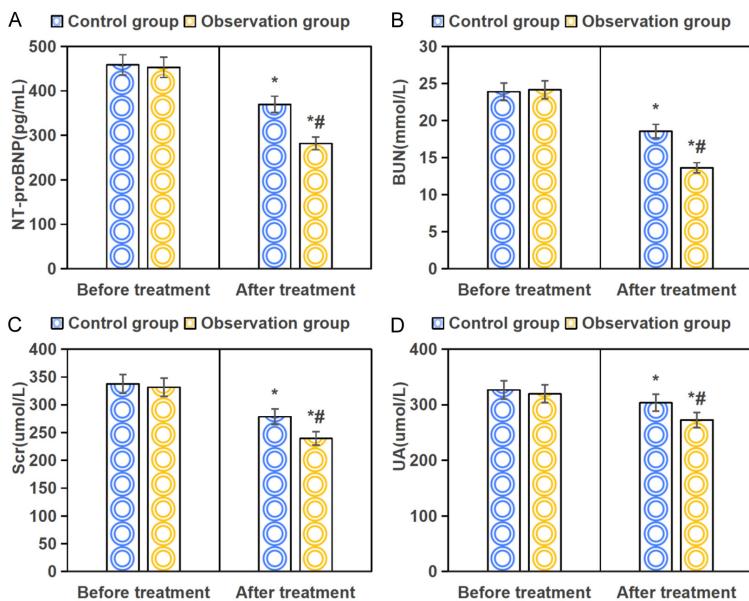


Figure 4. Comparison of cardiac and renal function parameters between the two groups before and after treatment. A. N-terminal pro-brain natriuretic peptide (NT-proBNP); B. Blood urea nitrogen (BUN); C. Serum creatinine (Scr); D. uric acid (UA). Notes: * $P < 0.05$, compared with before treatment; # $P < 0.05$, compared with the control group.

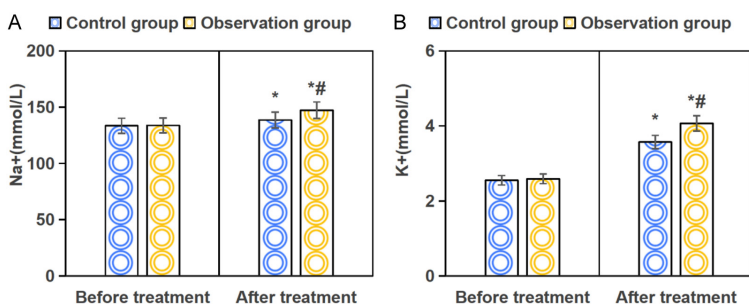


Figure 5. Comparison of electrolyte levels between the two groups before and after treatment. A. Sodium (Na⁺); B. Potassium (K⁺). Notes: * $P < 0.05$, compared with before treatment; # $P < 0.05$, compared with the control group.

were significantly increased ($P < 0.05$), with more pronounced improvements observed in the observation group ($P < 0.05$).

Comparison of complications between the two groups of patients

Table 2 shows the comparison of complications between the two groups of patients. No significant differences were observed between the two groups in the incidence of hypotension,

bleeding, or extracorporeal circuit coagulation ($P > 0.05$).

Analysis of prognostic factors in critically ill patients with CRF

Table 3 presents the univariate analysis of factors associated with renal function recovery, and **Table 4** shows the multivariate logistic regression analysis.

In the multivariate model, candidate variables included age, sex, hypertension, diabetes mellitus, chronic renal insufficiency, ALB, TP, Scr, and BUN. Among these, age and sex were included as forced adjustment variables to control for potential confounding, while other variables were selected using a forward stepwise logistic regression method (entry criterion $P < 0.05$, removal criterion $P > 0.10$).

Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test, which yielded a χ^2 value of 6.84 with 8 degrees of freedom ($P = 0.55$), indicating good agreement between predicted and observed outcomes. Model discrimination was evaluated using the AUC, which was 0.82 (95% CI: 0.76-0.88), demonstrating good discriminative performance.

After adjustment for age and sex, hypertension (OR = 4.922, 95% CI: 1.372-7.328), low ALB (OR = 2.281, 95% CI: 1.061-4.321), low TP (OR = 2.538, 95% CI: 1.068-4.375), high Scr (OR = 2.791, 95% CI: 1.256-4.728), and high BUN (OR = 1.601, 95% CI: 1.209-2.033) were identified as independent risk factors for poor renal function recovery. In contrast, age, sex, diabetes, and chronic renal insufficiency were not statistically significant in the final model (age: $P = 0.34$; sex: $P = 0.48$;

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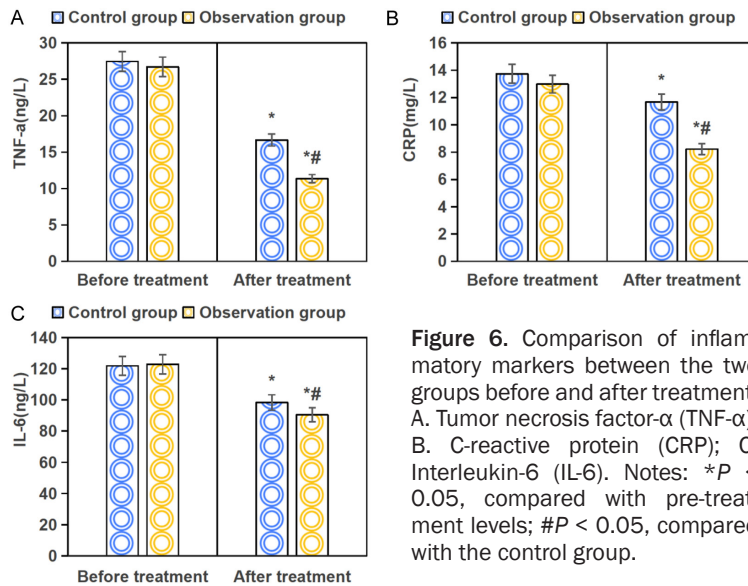


Figure 6. Comparison of inflammatory markers between the two groups before and after treatment. A. Tumor necrosis factor- α (TNF- α); B. C-reactive protein (CRP); C. Interleukin-6 (IL-6). Notes: * $P < 0.05$, compared with pre-treatment levels; # $P < 0.05$, compared with the control group.

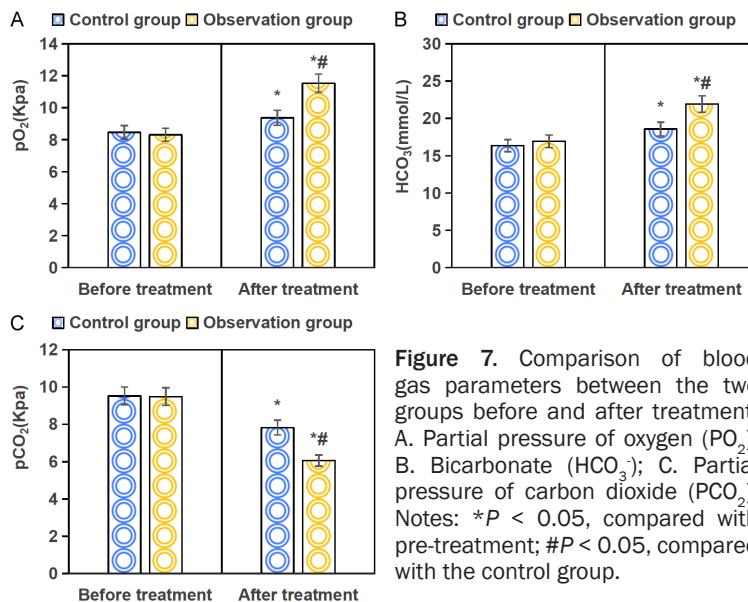


Figure 7. Comparison of blood gas parameters between the two groups before and after treatment. A. Partial pressure of oxygen (PO₂); B. Bicarbonate (HCO₃⁻); C. Partial pressure of carbon dioxide (PCO₂). Notes: * $P < 0.05$, compared with pre-treatment; # $P < 0.05$, compared with the control group.

diabetes: $P = 0.62$; chronic renal insufficiency: $P = 0.51$).

Discussion

The present study showed that patients in the observation group receiving CBP combined with conventional therapy exhibited significant improvements in HR, RR, lipid profiles, cardiac and renal function parameters, inflammatory markers, arterial blood gas parameters, and health-related quality of life compared with the control group. Moreover, no significant difference was observed in the incidence of treat-

ment-related complications between the two groups.

Multivariate regression analysis identified hypertension, low ALB, low TP, elevated Scr and BUN as independent risk factors for poor renal function recovery, among which Scr demonstrated the strongest predictive value. These findings are consistent with previous studies showing that CBP can continuously and effectively remove inflammatory mediators and metabolic wastes, stabilize hemodynamics, and thereby improve organ function in critically ill patients [16-18].

This study innovatively integrated multidimensional clinical indicators to comprehensively evaluate the therapeutic effects of CBP and, for the first time, established the dominant predictive value of Scr in critically ill patients with CRF. Furthermore, the study design adopted a dual-path analysis based on treatment grouping and prognostic grouping, which not only assessed intervention effects but also explored prognostic factors, enhancing logical rigor.

It is worth noting that the observation group showed more pronounced reductions in ALB and TP levels. This may

be related to treatment-related nutrient loss associated with CBP. Critically ill patients are often in a state of hypercatabolism [19]. CBP, especially high-volume hemofiltration, may results in the unintended removal of amino acids, water-soluble vitamins, and low-molecular-weight proteins while clearing middle- and large-molecular-weight inflammatory mediators [20, 21]. The convective and adsorptive effects of the filter on solutes, as well as potential blood loss during the treatment process, are direct causes of decreased serum protein levels [22]. Therefore, the more significant decrease in protein levels in the observation

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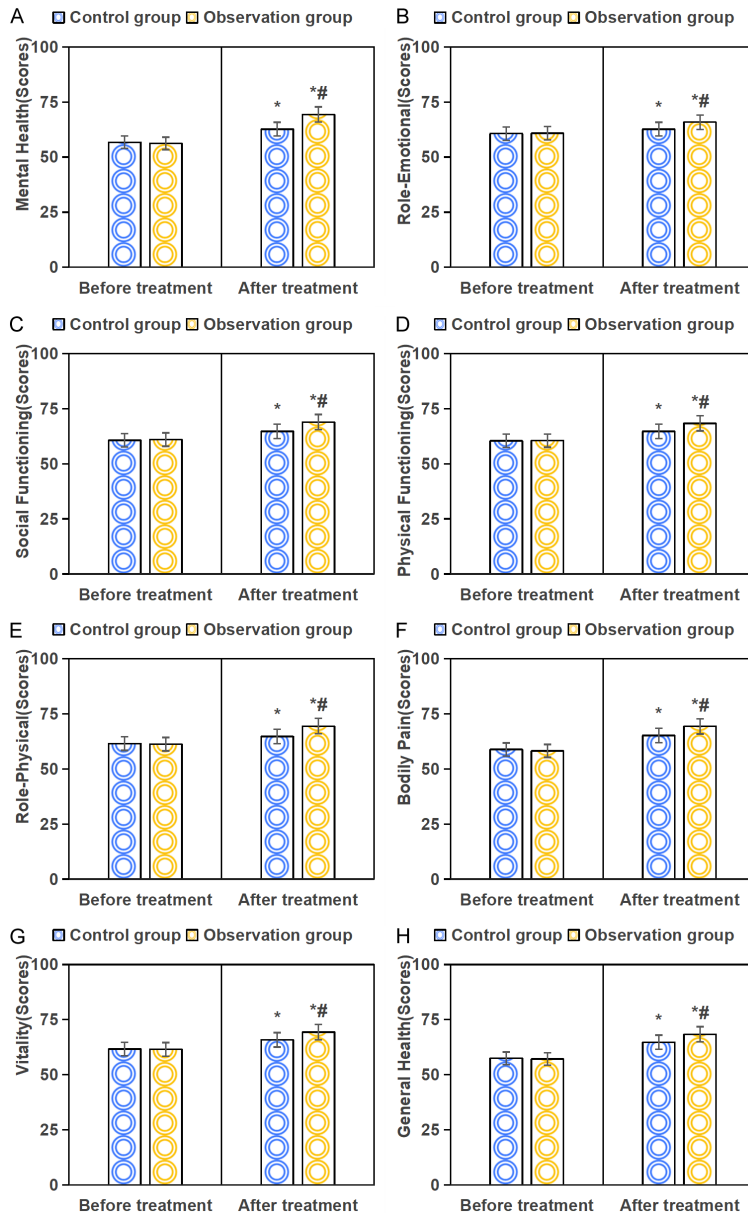


Figure 8. Comparison of quality-of-life scores between the two groups before and after treatment. A. Mental Health; B. Emotional Role; C. Social Function; D. Physical Function; E. Physical Role; F. Bodily Pain; G. Vitality; H. General Health. Notes: * $P < 0.05$, compared with pre-treatment score; # $P < 0.05$, compared with the control group.

group likely reflected, to a large extent, nutrient loss associated with CBP treatment. This finding suggests that when implementing CBP for critically ill patients, nutritional support strategies must be strengthened. Such strategies should not only ensure adequate energy supply but also include precise monitoring and supplementation of proteins and amino acids to maintain nitrogen balance.

At the same time, the reduction in serum protein levels may also reflect improvements in systemic inflammatory status. Acute kidney injury and critical illness are often accompanied by systemic inflammatory response syndrome and increased capillary endothelial permeability, leading to substantial translocation of plasma proteins from the intravascular to the interstitial space [23, 24]. Therefore, the decline in serum protein levels may represent a combined effect of nutritional consumption and inflammation-related redistribution rather than a purely deleterious phenomenon. In clinical practice, nutritional support should be strengthened while simultaneously considering the inflammatory milieu to maintain metabolic homeostasis.

This study does have several limitations. First, as a single-center retrospective study, inherent selection bias and unmeasured confounding factors cannot be fully excluded. Second, the relatively limited sample size (only 62 cases in the renal function recovery group) may limit the statistical power and generalizability of the findings. Third, detailed CBP-related parameters, such as replacement fluid volume and anticoagulation strategy, were not systematically recorded, precluding a reliable dose-effect analysis. In addition, the large heterogeneity in treat-

ment duration (9-71 hours) may affect outcomes. Future studies should conduct multicenter, prospective randomized controlled trials, adopt standardized CBP protocols and extend follow-up, incorporate biomarkers to establish accurate predictive models, and explore individualized strategies for adjusting treatment intensity based on dynamic BUN changes.

Influence of CBP on patients with severe CRF

Table 2. Comparison of treatment-related complications between the control and observation groups

Complication	Control group (n = 89)	Observation group (n = 95)	χ^2	P
Hypotension	12 (13.48%)	11 (11.58%)	0.153	0.704
Bleeding	8 (8.99%)	9 (9.47%)	0.011	0.911
Circuit coagulation	5 (5.62%)	6 (6.32%)	0.042	0.840

Table 3. Univariate analysis of factors associated with treatment outcome in critically ill patients with CRF

Indicator		Renal function recovery group (n = 62)	Renal function not recovered group (n = 122)	t/ χ^2	P
Gender	Male	40	79	0.467	0.524
	Female	22	43		
Age (Years)		62.78±8.34	63.78±7.23	0.525	0.482
Hypertension		22	61	7.353	0.021
Diabetes		7	12	0.578	0.646
Chronic renal insufficiency		8	15	0.625	0.522
ALB (g/L)		50.35±6.24	42.67±5.68	6.357	0.025
TP (g/L)		78.21±7.18	65.34±7.43	8.256	0.021
Scr (umol/L)		227.68±15.67	273.75±18.24	6.979	0.039
BUN (mmol/L)		12.46±2.94	17.34±2.18	7.563	0.018

Notes: ALB: Albumin; TP: Total Protein; Scr: Serum Creatinine; BUN: Blood Urea Nitrogen; CRF: Chronic Renal Failure.

Table 4. Multivariate logistic regression analysis of independent risk factors for treatment outcome in critically ill patients with CRF

Indicator	B	SE	Wald	P	OR	95% CI
Hypertension	1.678	0.765	4.122	0.028	4.922	1.372, 7.328
ALB	0.825	1.372	7.867	0.008	2.281	1.061, 4.321
TP	0.931	1.245	8.265	0.008	2.538	1.068, 4.375
Scr	3.524	1.577	7.137	0.005	2.791	1.256, 4.728
BUN	0.471	0.142	11.027	0.001	1.601	1.209, 2.033

Notes: ALB: Albumin; TP: Total Protein; Scr: Serum Creatinine; BUN: Blood Urea Nitrogen; CRF: Chronic Renal Failure.

Conclusion

CBP significantly improves vital signs, metabolic parameters, cardiac and renal function, blood gas status, and quality of life, without increasing the incidence of complications. CBP may serve as an effective adjunctive therapy for critically ill patients with CRF, particularly in those with significantly elevated Scr and inflammatory markers (TNF- α , CRP, IL-6), despite the potential risk of treatment-associated reductions in serum ALB and TP.

Disclosure of conflict of interest

None.

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