

Anticoagulation-Free Continuous Renal Replacement Therapy Using Calcium-Free Predilution: A Single-Center Pilot Study

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Research Article

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Abstract

Aim

Continuous renal replacement therapy (CRRT) usually requires systemic or regional anticoagulation to maintain circuit patency. However, in real-world intensive care settings, the use of heparin or regional citrate anticoagulation (RCA) may be limited by bleeding risk, severe coagulopathy, and technical or organizational constraints. In addition, in patients with shock and elevated lactate levels, citrate metabolism may be impaired, potentially leading to metabolic complications. In such circumstances, simplified strategies to preserve filter lifespan without formal anticoagulation are needed.

Study Design

This single-center observational study included ten critically ill adult patients who underwent CRRT using a calcium-free predilution solution (Prism0cal) without routine systemic heparin or RCA. The strategy aimed to reduce hemoconcentration and ionized calcium availability within the extracorporeal circuit to preserve filter function. CRRT parameters, treatment duration, filter performance, and reasons for discontinuation were recorded. Serial monitoring of ionized calcium, acid–base status, and metabolic parameters was performed, and systemic calcium and bicarbonate replacement was administered when clinically indicated.

Results

CRRT was successfully initiated in all patients under challenging clinical and organizational conditions. In patients with treatment durations ≥ 16 hours, filters were maintained without anticoagulation-related complications. Interruptions of therapy were primarily related to patient deterioration or technical factors rather than metabolic instability. Ionized calcium levels remained within a manageable range during treatment, although systemic calcium supplementation was required in selected cases. Acid–base parameters generally stabilized during CRRT with supportive bicarbonate therapy when necessary.

Conclusion

Anticoagulation-free CRRT using calcium-free predilution was feasible and physiologically tolerable in critically ill patients when conventional anticoagulation strategies could not be applied. With acceptable circuit performance and manageable metabolic effects, this pragmatic approach may represent a viable alternative in selected high-risk patients and real-world intensive care settings.

Introduction

Continuous renal replacement therapy (CRRT) is a cornerstone of supportive care in critically ill patients with acute kidney injury, severe metabolic derangements, or fluid overload. Maintaining extracorporeal circuit patency remains a major challenge during CRRT, and systemic anticoagulation with heparin or

regional citrate anticoagulation (RCA) is commonly employed to prolong filter lifespan [1, 2]. However, the application of these strategies is often limited in real-world intensive care practice.

Systemic heparinization may be contraindicated in patients with active bleeding, thrombocytopenia, coagulopathy, or recent surgical interventions [3, 5]. Although RCA is considered an effective alternative, it requires preserved citrate metabolism, careful monitoring, and dedicated protocols. In patients with shock, or elevated lactate levels, citrate clearance may be impaired, increasing the risk of metabolic complications such as citrate accumulation, hypocalcemia, and acid–base disturbances [2, 6, 7]. In addition, the complexity of RCA protocols and organizational constraints may limit their routine use in resource-restricted or high-acuity intensive care units.

In this context, simplified anticoagulation-free approaches to CRRT have gained interest. Predilution strategies reduce hemoconcentration within the extracorporeal circuit and may contribute to filter preservation [5]. The use of calcium-free predilution solutions further decreases ionized calcium availability within the circuit [4], potentially mitigating clot formation without the need for formal anticoagulation. This approach represents a pragmatic balance between circuit protection and physiological safety in settings where ideal anticoagulation strategies cannot be consistently implemented.

Accepting that calcium-free predilution may lead to systemic electrolyte and acid–base disturbances, close biochemical monitoring and targeted systemic calcium and bicarbonate supplementation become integral components of this strategy. Rather than eliminating metabolic risk, this approach aims to transform it into a predictable and manageable aspect of CRRT care.

The present study describes our single-center experience with anticoagulation-free CRRT using calcium-free predilution in critically ill patients managed under technical and organizational constraints. We aimed to evaluate the feasibility, circuit performance, and physiological tolerance of this simplified approach in a real-world intensive care setting.

Methods

Study Design

This study was designed as a single-center, observational case series conducted in an adult intensive care unit. The aim was to describe the application of anticoagulation-free continuous renal replacement therapy (CRRT) using a calcium-free predilution solution. No intervention, randomization, or control group was applied.

Study Population

All adult patients (≥ 18 years) who underwent CRRT using a calcium-free predilution solution during the study period were retrospectively screened.

Inclusion Criteria

Patients were included if they met all of the following criteria:

CRRT performed without routine systemic heparin or regional citrate anticoagulation

Use of a calcium-free solution for predilution

Availability of baseline clinical data and at least one set of arterial blood gas measurements during CRRT

CRRT duration ≥ 16 hours for inclusion in the primary analysis

Patients with CRRT duration < 16 hours were included only in descriptive analyses and excluded from the primary evaluation of circuit performance.

Exclusion Criteria

Patients were excluded from the primary analysis if they met any of the following criteria:

Planned use of systemic heparin or regional citrate anticoagulation

Use of calcium-containing predilution solutions

Incomplete documentation of CRRT settings and biochemical monitoring preventing meaningful data interpretation

Data Collection

For each included patient, the following data were recorded:

Demographic characteristics (age, sex)

Primary diagnosis and indication for CRRT

CRRT settings (blood flow rate, predilution rate, dialysate flow rate, ultrafiltration rate)

Type of solutions used

Duration of CRRT and reason for discontinuation

Filter changes and documented technical reasons

Serial laboratory measurements including arterial blood gases, ionized calcium, acid–base parameters, lactate levels, and routine biochemical data when available

Ethics Approval

The study protocol was reviewed and approved by the local Institutional Ethics Committee (approval number:). Given the retrospective observational design and the use of anonymized patient data, the requirement for informed consent was waived.

CRRT Modality and Settings

All patients were treated with continuous venovenous hemodiafiltration (CVVHDF). Vascular access was obtained using a double-lumen central venous catheter, preferentially placed in the femoral vein according to clinical feasibility.

CRRT was initiated using the following standardized settings:

Blood flow rate: 150 mL/min

Predilution flow rate: 300 mL/h

Dialysate flow rate: 1200 mL/h

Post-dilution replacement fluid: not used

Ultrafiltration rate: individualized according to clinical indication, generally ranging between 0 and 100 mL/h

The prescribed CRRT dose was targeted between 20–25 mL/kg/h in all patients [1, 8].

CRRT Solutions

A calcium-free solution (Prism0cal®) was used exclusively for predilution in all patients. A standard bicarbonate-based dialysate solution containing calcium was used as dialysate. No calcium-containing replacement fluids were used in the predilution or post-dilution phases.

This configuration was selected to allow calcium depletion within the extracorporeal circuit while maintaining systemic calcium delivery through the dialysate and, when necessary, intravenous supplementation.

Anticoagulation Strategy

No systemic heparin or regional citrate anticoagulation was routinely used during CRRT. Anticoagulation decisions were standardized for the study protocol and were not modified unless required for non-CRRT-related indications. The calcium-free predilution strategy was intentionally selected to reduce intrafilter ionized calcium availability and hemoconcentration as a pragmatic alternative to formal anticoagulation.

Systemic Calcium and Bicarbonate Supplementation

Systemic calcium supplementation was administered intravenously when ionized calcium levels decreased below clinically acceptable thresholds. Bicarbonate supplementation was provided at the discretion of the attending physician in cases of persistent metabolic acidosis despite CRRT.

No predefined infusion protocol was used; supplementation was individualized based on laboratory values and clinical assessment.

Statistical Analysis

Given the exploratory nature of this single-center observational case series and the limited sample size, statistical analysis was primarily descriptive. No formal hypothesis testing was planned.

Continuous variables were summarized as median and interquartile range (IQR) or mean $\pm$ standard deviation, depending on data distribution. Categorical variables were presented as counts and percentages.

Given the limited sample size and heterogeneous treatment durations, longitudinal trends were reported descriptively without graphical aggregation.

Results

Patient Characteristics

A total of 10 critically ill adult patients who underwent anticoagulation-free CRRT using calcium-free predilution were included in the study. Of these, 7 patients with CRRT duration $\geq$ 16 hours were included in the primary descriptive analysis, while 3 patients with shorter treatment duration were included in safety and feasibility assessments only.

Baseline demographic and clinical characteristics are summarized in Table 1.

Table 1. Baseline Demographic and Clinical Characteristics

Overall cohort: n = 10

Age, years	median 76 (IQR ~60–91)
Male sex, n (%)	8 (80%)
Female sex, n (%)	2 (20%)

Primary diagnosis, n (%)

Post-resuscitation syndrome (<i>Post-resuscitation syndrome defined according to Negovsky's post-cardiac arrest disease concept</i>)	4 (40%)
Hypoxic encephalopathy	1 (10%)
Septic shock	2 (20%)
Cardiogenic shock	1 (10%)
Malignancy-related multiple organ failure	1 (10%)
Intracranial hemorrhage / brain death	1 (10%)

CRRT indication, n (%)

Metabolic acidosis + anuria	9 (90%)
Hypervolemic hypernatremia	1 (10%)

CRRT characteristics

CRRT duration, hours	median ~24 (IQR ~16–57)
CRRT ≥16 hours	7 (70%)
CRRT <16 hours	3 (30%)

Filter performance

Filter change required	2 (20%)
CRRT discontinued due to filter clotting / technical failure	2 (20%)
Single filter throughout treatment without issues	6 (60%)

Systemic supplementation

Systemic calcium supplementation	6 (60%)
Systemic bicarbonate supplementation	4 (40%)

The median age of the cohort was advanced, and the majority of patients were male. The most common underlying clinical conditions were post-resuscitation syndrome [9], septic shock, and cardiogenic shock. CRRT was initiated primarily for severe metabolic acidosis and anuria, except for one patient in whom hypervolemic hyponatremia was the primary indication.

At CRRT initiation, most patients exhibited severe metabolic derangements, including marked acidemia and elevated lactate levels, consistent with high illness severity. Coagulation abnormalities and thrombocytopenia were frequently observed. Conventional anticoagulation strategies were not routinely used in any patient.

CRRT was discontinued due to achievement of treatment goals, patient deterioration or death, or technical reasons, depending on the individual clinical course.

Circuit Performance and Reasons for CRRT Discontinuation

Among the overall cohort (n = 10), CRRT was discontinued for predefined clinical or technical reasons. In two patients (20%), CRRT was terminated due to filter clotting and/or technical failure, precluding further continuation of therapy. In two additional patients (20%), filter replacement was required due to technical causes; in one patient, circuit function was restored following catheter replacement, while in another patient, filter replacement was necessitated by air entry into the drainage line, after which CRRT was successfully continued.

In two patients (20%), CRRT was discontinued after achievement of predefined treatment goals, namely correction of hypervolemic hyponatremia in one patient and completion of donor management in another. In the remaining six patients (60%), CRRT was terminated due to refractory shock and subsequent death, reflecting the severity of the underlying critical illness rather than circuit-related limitations.

Overall, six patients (60%) completed CRRT uneventfully using a single filter throughout the treatment period, while filter replacement was required in two patients (20%) and CRRT could not be continued in two patients (20%) due to filter-related technical failure.

Median CRRT durations reported in critically ill post–cardiac arrest and refractory shock populations often range between 24 and 48 hours, largely reflecting early mortality rather than circuit failure, which is consistent with the treatment durations observed in our cohort [10].

Ionized Calcium Trends

Serial measurements of ionized calcium demonstrated a manageable and predictable profile during CRRT. Mild decreases in ionized calcium were observed in several patients during treatment, particularly

in the early hours. Systemic calcium supplementation was administered in 6 patients (60%) based on laboratory values and clinical judgment.

Despite the absence of regional citrate anticoagulation, no episodes of clinically significant or refractory hypocalcemia were observed. Ionized calcium levels were clinically manageable with selective supplementation.

Acid–Base Parameters

At CRRT initiation, most patients exhibited severe metabolic acidosis, reflected by low arterial pH and bicarbonate levels. During CRRT, gradual stabilization of acid–base parameters was observed in patients with treatment durations ≥ 16 hours.

Systemic bicarbonate supplementation was required in 4 patients (40%), primarily during the early phase of CRRT. In patients with sufficient treatment duration and follow-up, arterial pH and bicarbonate levels showed an overall trend toward stabilization or partial correction over time.

Lactate and Metabolic Severity

Baseline lactate levels were elevated in most patients, consistent with shock and global ischemia–reperfusion injury. During CRRT, lactate levels remained variable and were largely influenced by the underlying clinical condition rather than the CRRT protocol itself. No abrupt lactate elevations attributable to the calcium-free predilution strategy were observed.

Safety Observations

No treatment interruptions were attributed to uncontrolled electrolyte disturbances or acid–base derangements. Short-duration CRRT treatments (< 16 hours) were discontinued due to early patient deterioration or death rather than circuit-related metabolic complications.

Discussion

Principal Findings

In this single-center observational case series, anticoagulation-free CRRT using a calcium-free predilution solution was feasible in a cohort of critically ill patients managed under significant clinical and organizational constraints. Despite the absence of systemic heparin or regional citrate anticoagulation, acceptable circuit performance was achieved in the majority of patients. Most treatments were completed using a single filter, and filter-related interruptions occurred in a limited number of cases, primarily due to technical factors.

The relatively short median CRRT duration observed in this cohort reflects the extreme illness severity and high mortality rate of the study population and is consistent with previously reported CRRT durations in post-resuscitation and refractory shock cohorts [10].

Importantly, no CRRT interruptions were attributed to uncontrolled electrolyte or acid–base disturbances related to the calcium-free predilution strategy. Ionized calcium levels were clinically manageable with selective supplementation, and acid–base parameters showed stabilization during treatment in patients with sufficient CRRT duration. These findings suggest that this simplified approach can provide a physiologically tolerable alternative for circuit preservation when standard anticoagulation strategies cannot be applied.

Physiological Tolerance and Safety Considerations

The deliberate use of calcium-free predilution inevitably introduces the need for close monitoring of systemic calcium and acid–base status. In our cohort, systemic calcium supplementation was required in a proportion of patients, and bicarbonate supplementation was administered selectively. These interventions were predictable and manageable and did not lead to treatment discontinuation.

Notably, metabolic trends observed during CRRT appeared to reflect the severity of the underlying critical illness rather than protocol-related complications. The absence of refractory hypocalcemia or uncontrollable acidosis supports the physiological tolerability of this approach when applied with appropriate monitoring and supportive care.

Clinical Applicability in Real-World Intensive Care Settings

This study reflects real-world intensive care practice, where ideal anticoagulation strategies may not always be feasible due to patient-related factors, staffing limitations, or workflow constraints. In such environments, a simplified and reproducible CRRT strategy may be preferable to complex protocols that cannot be consistently implemented.

Calcium-free predilution without formal anticoagulation offers a balance between circuit preservation and physiological safety. While this approach does not eliminate the need for clinical vigilance, it allows CRRT to be delivered in settings where alternative strategies may be impractical or contraindicated.

Limitations

Several limitations must be acknowledged. The study is limited by its small sample size, single-center design, and observational nature. The patient population was heterogeneous, and treatment durations varied, limiting the ability to draw firm conclusions regarding long-term circuit performance or comparative efficacy. Additionally, the absence of a control group precludes direct comparison with citrate- or heparin-based anticoagulation strategies.

Future Directions

Larger prospective studies are needed to further evaluate anticoagulation-free CRRT strategies using calcium-free predilution, particularly in selected high-risk populations. Comparative studies assessing

circuit lifespan, metabolic tolerance, and resource utilization may help define the role of this approach within contemporary CRRT practice.

As a pilot experience, this strategy should be viewed as a complementary option rather than a replacement for established anticoagulation protocols.

Conclusion

Anticoagulation-free CRRT using calcium-free predilution appears to be a feasible and physiologically tolerable strategy in critically ill patients when conventional anticoagulation methods cannot be applied. In this real-world case series, acceptable circuit performance was achieved with a limited need for filter replacement, and metabolic disturbances were predictable and manageable with selective systemic supplementation. While this approach does not aim to replace established anticoagulation protocols, it may serve as a pragmatic alternative in selected high-risk patients and resource- or workflow-limited intensive care settings. Further prospective studies are required to better define its role in contemporary CRRT practice.

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