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Calcium-Free Predilution for Circuit Preservation During CRRT Without Routine Anticoagulation: A Single-Center ICU Pilot Study

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Short Report

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Abstract

Background
Maintaining circuit patency during continuous renal replacement therapy (CRRT) without heparin or regional citrate anticoagulation (RCA) remains challenging in critically ill adults with bleeding risk or when formal anticoagulation protocols cannot be operationalized. We evaluated a calcium-free predilution strategy for CRRT without dedicated circuit anticoagulation in a real-world intensive care unit.

Methods
We performed a retrospective single-center observational pilot study of 14 critically ill adults treated with continuous venovenous hemodiafiltration using calcium-free predilution without routine heparin or RCA. Total CRRT-hours, treatment duration, clotting events, and serial acid-base and ionized calcium data were abstracted. The primary descriptive circuit-performance analysis prespecified treatments lasting at least 16 hours.

Results
The cohort accumulated 525 CRRT-hours. Twelve treatments lasted at least 16 hours, with a median CRRT duration of 36 hours (IQR 25–57). Three clotting events occurred, corresponding to 0.57 clotting events per 100 CRRT-hours, and 11 of 14 treatments (78.6%) were completed without documented filter clotting. Baseline metabolic derangement was substantial, but serial ionized calcium and acid-base abnormalities were clinically manageable with selective supplementation, and no treatment was discontinued because of uncontrolled hypocalcemia or metabolic toxicity.

Conclusion
CRRT using calcium-free predilution was feasible in this small high-risk ICU cohort and achieved acceptable circuit performance despite the absence of formal circuit anticoagulation. This approach should be viewed as a rescue strategy when standard anticoagulation cannot be used or operationalized, not as a replacement for RCA.

Introduction

Continuous renal replacement therapy (CRRT) remains a core supportive modality for critically ill patients with acute kidney injury, severe metabolic derangements, or clinically significant fluid overload, particularly when hemodynamic instability makes intermittent therapy less suitable [1,10]. Premature circuit clotting is one of the most common practical barriers to effective CRRT delivery because it interrupts therapy, reduces delivered dose, increases blood loss, and adds nursing workload and cost [2–4].

Regional citrate anticoagulation is currently the preferred anticoagulation strategy for CRRT when local expertise and monitoring are available, and randomized and meta-analytic data show longer filter life with RCA than with systemic heparin [1–3]. At the same time, RCA is not a zero-burden intervention. It requires protocolized calcium management, biochemical surveillance, and trained staff; in real-world ICU implementation, changes in anticoagulation strategy can also affect resource use and workflow [3,6,8]. Importantly, more recent literature challenges the idea that shock or liver dysfunction are absolute contraindications to RCA, so these states should be described as higher-risk settings requiring careful monitoring rather than blanket exclusions [5,6,12].

For some ICU patients, however, the practical bedside problem is not whether RCA is theoretically superior, but what to do when no formal circuit anticoagulation is being used. In that setting, two non-pharmacologic concepts are biologically attractive. First, predilution reduces hemoconcentration at the membrane and may lessen clotting propensity [4]. Second, calcium-free CRRT fluids reduce ionized calcium availability within the extracorporeal circuit, a mechanism already familiar from RCA-based protocols [4,7,8]. Published work on calcium-free versus calcium-containing solutions

has largely been embedded within RCA protocols rather than anticoagulation-free ICU practice, leaving a gap for real-world data on calcium-free predilution without citrate [7,8].

We therefore examined our single-center ICU experience CRRT without dedicated circuit anticoagulation using calcium-free predilution in critically ill adults. Our objective was to describe feasibility, circuit performance, and physiological tolerance, with particular emphasis on total CRRT-hours, clotting events standardized per 100 CRRT-hours, treatment completion without clotting, and serial acid-base and ionized calcium trajectories.

Methods

Study design and setting

This was a retrospective, single-center observational pilot study conducted in an adult intensive care unit at a tertiary care center. The study evaluated consecutive critically ill adult patients who underwent continuous renal replacement therapy (CRRT) using calcium-free predilution between October 2025 and March 2026.

Eligibility criteria

Adult patients aged 18 years or older were eligible if they underwent CRRT using a calcium-free predilution solution without routine heparin or RCA for circuit anticoagulation. Patients were included in the full safety and feasibility cohort regardless of treatment duration. A prespecified primary descriptive circuit-performance analysis was performed for treatments lasting at least 16 hours, to reduce distortion from very early discontinuation caused by perimortem instability rather than circuit behavior. Patients receiving protocolized systemic heparin or RCA for circuit patency were excluded. Concomitant antithrombotic medications prescribed for non-CRRT indications were recorded but did not constitute the CRRT anticoagulation strategy.

CRRT protocol

All patients received continuous venovenous hemodiafiltration (CVVHDF). Vascular access was obtained via a double-lumen central venous catheter based on clinical feasibility. Blood flow rate was maintained between 100 and 150 mL/min. Predilution replacement fluid was administered at 300–600 mL/h, dialysate flow at 1200–1600 mL/h, and postdilution replacement flow at 0–900 mL/h. Net ultrafiltration was individualized according to the patient's hemodynamic status. The prescribed CRRT dose targeted 20–25 mL/kg/h [1].

A calcium-free solution (Prism0cal) was used for predilution, while a standard bicarbonate-based calcium-containing solution was used as dialysate. No routine anticoagulation with heparin or regional citrate was administered for circuit patency.

Biochemical monitoring and supportive therapy

Serial arterial blood gas and laboratory measurements were obtained during CRRT, including pH, bicarbonate, lactate, potassium, and ionized calcium. Intravenous calcium supplementation and systemic bicarbonate administration were provided at the discretion of the treating clinician based on biochemical abnormalities and bedside assessment.

Post-filter ionized calcium measurements were not available; therefore, the analysis focused on systemic physiological tolerance rather than direct assessment of circuit-level anticoagulation intensity.

Definitions

CRRT-hours were defined as the sum of patient-level total CRRT treatment hours across the cohort. A clotting event was defined as documented filter or circuit loss attributed to clotting in the clinical record. A treatment course without clotting was defined as a CRRT course without documented clot-related circuit loss. Filter lifespan was conceptually

defined as time from circuit start to elective termination or circuit failure; however, exact circuit-level filter lifespan was considered not reliably estimable from the currently uploaded abstraction because replacement-circuit start-stop times were not individually recorded. The main study endpoints were feasibility of treatment delivery, circuit performance, and metabolic safety.

Statistical analysis

Given the pilot design and small sample size, no formal hypothesis testing was performed. Continuous variables were summarized as median (interquartile range [IQR]) or range, as appropriate, and categorical variables as counts and percentages.

Circuit performance was described using total CRRT-hours, clotting events, clotting events per 100 CRRT-hours, and the proportion of treatments completed without documented clotting.

Ethics

The study protocol was approved by the Institutional Ethics Committee of a tertiary care hospital (approval number: 15.04.2026/08). Owing to the retrospective observational design and use of de-identified data, the requirement for informed consent was waived.

Results

Cohort characteristics

Fourteen critically ill adult patients were included in the full safety and feasibility cohort. The median age was 75 years (interquartile range [IQR] 71–81), and 10 patients (71.4%) were male. The cohort was clinically heterogeneous and predominantly comprised patients with post–cardiac arrest syndrome, septic shock or pneumosepsis, and malignancy-associated multiorgan dysfunction.

Table 1. Baseline characteristics and key CRRT performance metrics

Variable	Value
Patients, n	14
Age, median (IQR), years	75 (71–81)
Male sex, n (%)	10 (71.4)
Post–cardiac arrest syndrome, n (%)	7 (50.0)
Sepsis or pneumosepsis, n (%)	6 (42.9)
Total CRRT-hours	525
Treatments lasting ≥16 h, n (%)	12 (85.7)
Median CRRT duration (≥16 h), h (IQR)	36 (25–57)
Overall median CRRT duration, h (IQR)	29 (22–45)
Clotting events, n	3
Clotting events per 100 CRRT-hours	0.57
Treatments without documented clotting, n (%)	11 (78.6)
Total circuit interruptions (filter loss), n	5
Baseline pH, median (IQR)	7.16 (7.07–7.26)
Baseline bicarbonate, mmol/L, median (IQR)	14.5 (13.0–17.0)
Baseline lactate, mmol/L, median (IQR)	7.9 (3.9–13.5)
Baseline ionized calcium, mmol/L, median (IQR)	1.10 (1.02–1.15)
Total filters used	Not reliably estimable
Median filter lifespan	Not reliably estimable

CRRT indicates continuous renal replacement therapy; IQR, interquartile range. The circuit-performance analysis included treatments lasting ≥16 hours. Circuit interruptions include both clotting-related events and catheter-related technical issues. Exact filter utilization and circuit-level filter lifespan could not be determined due to the lack of consistent circuit-level timestamps.

CRRT was most commonly initiated for metabolic acidosis with anuria, although selected patients were treated for severe dysnatremia or refractory hypercalcemia. Two patients were receiving low-molecular-weight heparin in combination with antiplatelet therapy for non-CRRT cardiac indications at treatment initiation; however, no patient received anticoagulation specifically for the purpose of maintaining extracorporeal circuit patency.

Circuit performance

Across the full cohort, a total of 525 CRRT-hours were delivered. Twelve of 14 treatments lasted ≥16 hours and were included in the prespecified circuit-performance analysis; in this subset, the median CRRT duration was 36 hours (interquartile range [IQR] 25–57; range 17–96).

Across the full cohort, three clotting events were documented, corresponding to 0.57 clotting events per 100 CRRT-hours. Eleven of 14 treatments (78.6%) were completed without documented filter clotting. A total of five circuit

interruption events were recorded in four patients. Of these, three were attributed to circuit clotting, while two episodes in a single patient were related to catheter dysfunction requiring revision and were not classified as clotting-related circuit failure. In many cases, CRRT termination was driven by death, refractory shock, or achievement of treatment goals rather than circuit failure, potentially limiting the observed incidence of clotting events.

Metabolic and acid-base observations

Metabolic derangement at CRRT initiation was substantial. Baseline median pH was 7.16 (interquartile range [IQR] 7.07–7.26), bicarbonate 14.5 mmol/L (IQR 13.0–17.0), and lactate 7.9 mmol/L (IQR 3.9–13.5). Baseline median systemic ionized calcium was 1.10 mmol/L (IQR 1.02–1.15), with higher values observed in patients treated for hypercalcemia.

Serial ionized calcium and acid–base measurements demonstrated biochemical variability during CRRT; however, no treatment was discontinued due to uncontrolled hypocalcemia or refractory acid–base disturbances. The lowest recorded ionized calcium level was 0.75 mmol/L during prolonged treatment, and metabolic abnormalities were managed with selective calcium and bicarbonate supplementation according to clinical need.

Filter lifespan and treatment-density metrics

The available data allowed reliable assessment of total CRRT-hours, clotting-event rate, and treatment-level clotting outcomes. However, exact filter utilization per patient and median filter lifespan could not be determined, as circuit-level start and stop timestamps for each filter were not consistently available.

Accordingly, circuit performance was described using treatment-level and time-standardized metrics rather than filter lifespan analysis.

Table 2. Patient-level CRRT characteristics and outcomes

ID	Sex	Age, years	Primary ICU diagnosis	CRRT indication	Duration, h	Circuit interruptions, n	Clotting-related	CRRT termination
P01	M	32	Intracerebral hemorrhage, post–cardiac arrest syndrome, MODS	Metabolic acidosis + anuria	43	0	No	Goals achieved
P02	F	75	Metastatic cervical cancer, post–cardiac arrest syndrome, MODS	Metabolic acidosis + anuria	24	0	No	Death
P03	M	60	Lung cancer, hypercalcemia, post–cardiac arrest syndrome, MODS	Metabolic acidosis + anuria + hypercalcemia	29	1	Yes	Refractory shock / technical
P04	M	91	Pneumonia/ARDS, septic shock	Metabolic acidosis + anuria	9	2	No	Death
P05	M	95	Ischemic stroke, post–cardiac arrest syndrome, MODS	Metabolic acidosis + anuria	28	0	No	Death
P06	F	56	Post–cardiac arrest hypoxic encephalopathy	Hypervolemic hypernatremia	67	0	No	Goals achieved
P07	M	72	Systemic malignancy, chemotherapy, MODS	Metabolic acidosis + anuria + hypervolemic hyponatremia	19	1	Yes	Refractory shock / technical
P08	M	89	Inferior myocardial infarction, post–cardiac arrest syndrome	Metabolic acidosis + anuria	17	0	No	Death
P09	M	74	Acute coronary syndrome, ventricular fibrillation, post–cardiac arrest syndrome	Metabolic acidosis + anuria	7	0	No	Death
P10	F	76	Ischemic stroke, pneumosepsis, septic shock	Uremic symptoms + volume overload + anuria	25	0	No	Death
P11	M	83	Pneumosepsis, septic shock	Metabolic acidosis + anuria	96	0	No	Goals achieved
P12	M	74	Metastatic gastric cancer, pneumosepsis, hypercalcemia	Hyponatremia + refractory hypercalcemia	47	0	No	Goals achieved

P13	M	79	Ischemic stroke, pneumosepsis, septic shock	Metabolic acidosis + anuria	71	0	No	Goals achieved
P14	F	70	Pneumonia, septic shock	Metabolic acidosis + anuria	43	1	Yes	Death

Circuit interruptions reflect recorded episodes of circuit loss and should not be interpreted as the total number of filters used. Some interruptions were related to catheter dysfunction rather than clotting, and exact filter utilization could not be determined due to the lack of circuit-level timestamps.

Table 3. Safety and protocol-related observations

Event	Value	Comment
Clotting-related circuit loss	3 patients	P03, P07, P14
Catheter-related circuit interruption	1 patient (2 episodes)	P04
Lowest ionized calcium, mmol/L	0.75	During prolonged treatment
CRRT discontinuation due to hypocalcemia	0	None documented
CRRT discontinuation due to acid–base disturbances	0	None documented
Median filter lifespan	Not available	Not determined due to lack of circuit-level timestamps
Filters per patient	Not available	Not determined due to lack of replacement-circuit records

Discussion

In this single-center ICU pilot study, CRRT without dedicated circuit anticoagulation using calcium-free predilution was feasible and enabled delivery of 525 CRRT-hours in a highly unstable cohort. The most clinically relevant performance signal was not treatment duration alone, but the combination of standardized clotting burden and treatment completion: only three clotting events occurred across the cohort, corresponding to 0.57 events per 100 CRRT-hours, and 78.6% of treatments were completed without documented clotting.

In the context of a rescue strategy applied without protocolized heparin or regional citrate anticoagulation, these findings suggest that acceptable circuit performance can be achieved under real-world ICU conditions.

These findings should not be interpreted as evidence that calcium-free predilution is equivalent or superior to regional citrate anticoagulation (RCA). Current guidelines and randomized studies consistently support RCA as the preferred anticoagulation strategy for CRRT when feasible, with longer filter lifespan and improved circuit patency compared with systemic heparin or no anticoagulation in selected high-risk populations [1–3,5].

In addition, recent ICU implementation studies suggest that RCA can be applied safely in experienced centers, including patients traditionally considered at higher risk [6,12]. Accordingly, the present study should be interpreted within a

narrower clinical context—as a pragmatic rescue strategy in situations where protocolized anticoagulation is not used or cannot be implemented at the bedside.

The physiological rationale of this approach is plausible. Predilution reduces hemoconcentration at the membrane, a recognized contributor to circuit clotting [4]. In addition, the use of calcium-free predilution may decrease ionized calcium availability within the extracorporeal circuit, partially mimicking one component of the anticoagulant effect observed in citrate-based protocols [4,7,8].

However, unlike regional citrate anticoagulation, this strategy does not provide controlled citrate delivery or allow for targeted post-filter calcium monitoring. Accordingly, any potential reduction in clotting propensity is likely mediated by a combination of dilutional and calcium-related effects and requires ongoing systemic biochemical monitoring.

The metabolic findings are clinically important, as they help define the safety profile of this approach. Patients initiated CRRT with marked acid–base derangement, and serial measurements demonstrated fluctuations in ionized calcium and bicarbonate levels during therapy. These alterations frequently required targeted supplementation and close biochemical monitoring.

Rather than indicating metabolic neutrality, the findings suggest that this strategy is associated with a manageable metabolic burden under standard ICU monitoring conditions.

The clinical relevance of this study lies in its reflection of real-world ICU practice. In many settings, implementation of full regional citrate anticoagulation (RCA) protocols may be limited by staffing constraints, training requirements, local experience, and the need for intensive biochemical monitoring, even in centers where RCA is recognized as the preferred standard [6,8].

In this context, calcium-free predilution represents a pragmatic rescue strategy for situations in which protocolized anticoagulation is not used or cannot be implemented at the bedside.

This study has several limitations. It is a small, single-center, retrospective, and uncontrolled analysis, and the study population is clinically heterogeneous. Two patients had very short treatment durations, and early death may have influenced circuit-patency assessment by limiting observation time.

In addition, there was no direct comparator group using systemic heparin or regional citrate anticoagulation, no adjudicated bleeding outcomes, no delivered-dose analysis, no post-filter ionized calcium monitoring, and no circuit-level timestamps to support formal filter-survival analysis. A minority of patients also received concomitant systemic antithrombotic therapy for non-CRRT indications.

These limitations restrict the generalizability of the findings and should be considered when interpreting the results.

Larger prospective studies are needed to evaluate this approach in comparison with both standard no-anticoagulation practice and regional citrate anticoagulation in clearly defined high-risk ICU populations. Future investigations should incorporate circuit-level timestamps, delivered dose, bleeding outcomes, calcium balance, and resource utilization to provide a more comprehensive assessment of efficacy and safety.

Such studies are essential to determine the role of calcium-free predilution beyond a single-center pilot experience and to define its place within contemporary CRRT anticoagulation strategies.

Conclusion

Continuous renal replacement therapy using calcium-free predilution was feasible in this small cohort of critically ill adults and achieved acceptable circuit performance despite the absence of protocolized heparin or citrate anticoagulation.

These findings suggest that calcium-free predilution may serve as a monitored ICU rescue strategy in situations where standard circuit anticoagulation is not used or cannot be implemented. This approach should not be considered a replacement for regional citrate anticoagulation, and prospective comparative studies with circuit-level time-to-failure data are required.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Institutional Ethics Committee of a tertiary care hospital (approval number: 15.04.2026/08). Owing to the retrospective observational design and use of de-identified data, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

The de-identified participant-level dataset is not publicly available due to the small size of the cohort and the potential risk of patient identification. De-identified data may be available from the corresponding author upon reasonable request and subject to institutional and ethical approval.

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Declaration of competing interest

The authors declare no competing interests.

Author contributions

Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review and editing: C.C.

Preprint disclosure

An earlier version of this work was posted as a preprint on Research Square. The submitted version reflects an expanded dataset and substantial revision.

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