Standard versus No post-filter ionized calcium monitoring in regional citrate anticoagulation for continuous kidney replacement therapy (NPC trial)

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Introduction

Post-filter ionized calcium (pfCa) in regional citrate anticoagulation (RCA) for continuous kidney replacement therapy (CKRT) was monitored for filter efficacy of citrate by adjusting the citrate dose. However, standard monitoring to maintain this level can cause potentially high citrate dose leading to increased risk of hypocalcemia and metabolic complications.

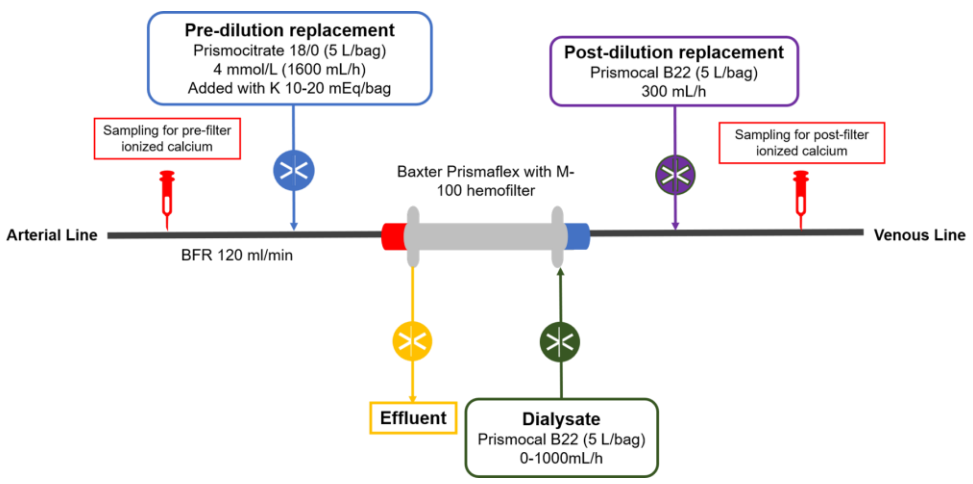
Our objective was to test efficacy and safety of no pfCa monitoring among critically ill patients receiving CKRT with RCA for both filter life span and citrate-related complications.

Methods and Materials

A non-inferiority randomized trial was conducted between January 2021 to October 2021 at King Chulalongkorn Memorial Hospital in Thailand. The trial was registered at clinicaltrial.gov (NCT04792424).

Critically ill patients receiving CKRT with an RCA starting citrate dose of 4 mmol/L were randomized to receive either standard pfCa monitoring, consisting of adjustments to the citrate dose to achieve a pfCa level of 0.25-0.35 mmol/L, or no pfCa monitoring, consisting of blinding the pfCa level and maintaining the initial citrate dose without adjustment. The circuit schematic of the study was shown in **Figure 1**.

Figure 1 Circuit schematic

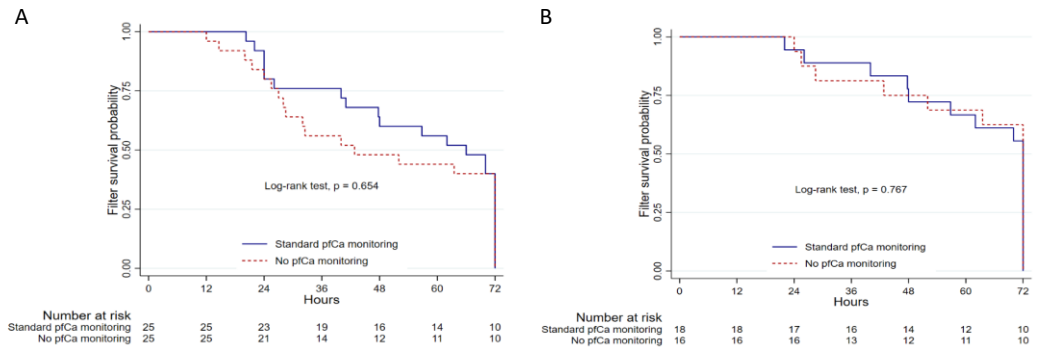


Results

Fifty patients were randomized into either the standard pfCa monitoring group (n=25) or a no pfCa monitoring group (n=25). The filter life span showed no difference between both groups (54±20 hours vs 47±23 hours, absolute difference 7.1 hours [90% CI -3.2, 17.5], p=0.65). Among adjusted filters with account only for the maximum duration of circuit life span at 72 h and circuit clotting, the mean filter life span also not different between groups (61±17 h standard pfCa vs 60 ± 19 h no pfCa monitoring; 90% CI: -9.4, 11.3) **(Figure 2)**.

Results

Figure 2 Kaplan-Meier curves of filter survival at 72 h



(A) time (h) from continuous kidney replacement therapy with regional citrate anticoagulation initiation until any cause of filter replacement (reach the upper limited time at 72 h following manufacturer's recommendation) or filter termination (filter clotting or non-filter clotting) or citrate discontinuation

(B) time (h) from continuous kidney replacement therapy with regional citrate anticoagulation initiation until filter replacement (reach the upper limited time at 72 h following manufacturer's recommendation) or filter clotting

Compared to the no pfCa monitoring group, the standard pfCa monitoring group had a significantly higher citrate dose (4.43±0.32 vs 4 mmol/L, p<0.001) and higher rate of severe hypocalcemia (44% vs 20%, p=0.13). No statistical differences were found in filter clotting, citrate accumulation, citrate overload, and mortality between both groups. **(Table 1)**

Table 1 Secondary outcomes

	Standard pfCa Monitoring (N=25)	No pfCa Monitoring (N=25)	P-value
Circuit Outcomes			
Filter clotting, n (%)	8 (32)	7 (28)	0.76
Average sieving coefficient	0.78 ± 0.05	0.79 ± 0.07	0.55
Citrate Outcomes			
Citrate dose, mmol/L	4.43 ± 0.32	4.00 ± 0.00	<0.001
Post-circuit ionized calcium, mmol/L	0.38 ± 0.03	0.41 ± 0.05	0.006
Systemic ionized calcium, mmol/L	0.95 ± 0.07	0.95 ± 0.07	0.98
Systemic total calcium, mg/dL	7.96 ± 0.59	8.11 ± 0.70	0.43
Calcium Ratio	2.09 ± 0.21	2.13 ± 0.23	0.46
Patient with Calcium Ratio > 2.5, n (%)	3 (12)	4 (16)	1.00 (f)
Complication			
Citrate accumulation, n (%)	1 (4.0)	1 (4.0)	1.00 (f)
Citrate overload, n (%)	9 (36)	7 (28)	0.76 (f)
Severe hypocalcemia, n (%)	11 (44)	5 (20)	0.13 (f)
Clinical Outcomes			
28 d mortality, n (%)	11 (44)	11 (44)	1.00
90 d mortality, n (%)	14 (56)	17 (68)	0.38

Conclusion

Among critically ill patients receiving CKRT with RCA, no pfCa monitoring by maintaining the citrate dose of 4 mmol/L showed no difference in filter life span and citrate-related complication. This suggests that reducing or eliminating pfCa monitoring is safe and feasible.