

Figure S1. Flow diagrams of included patients

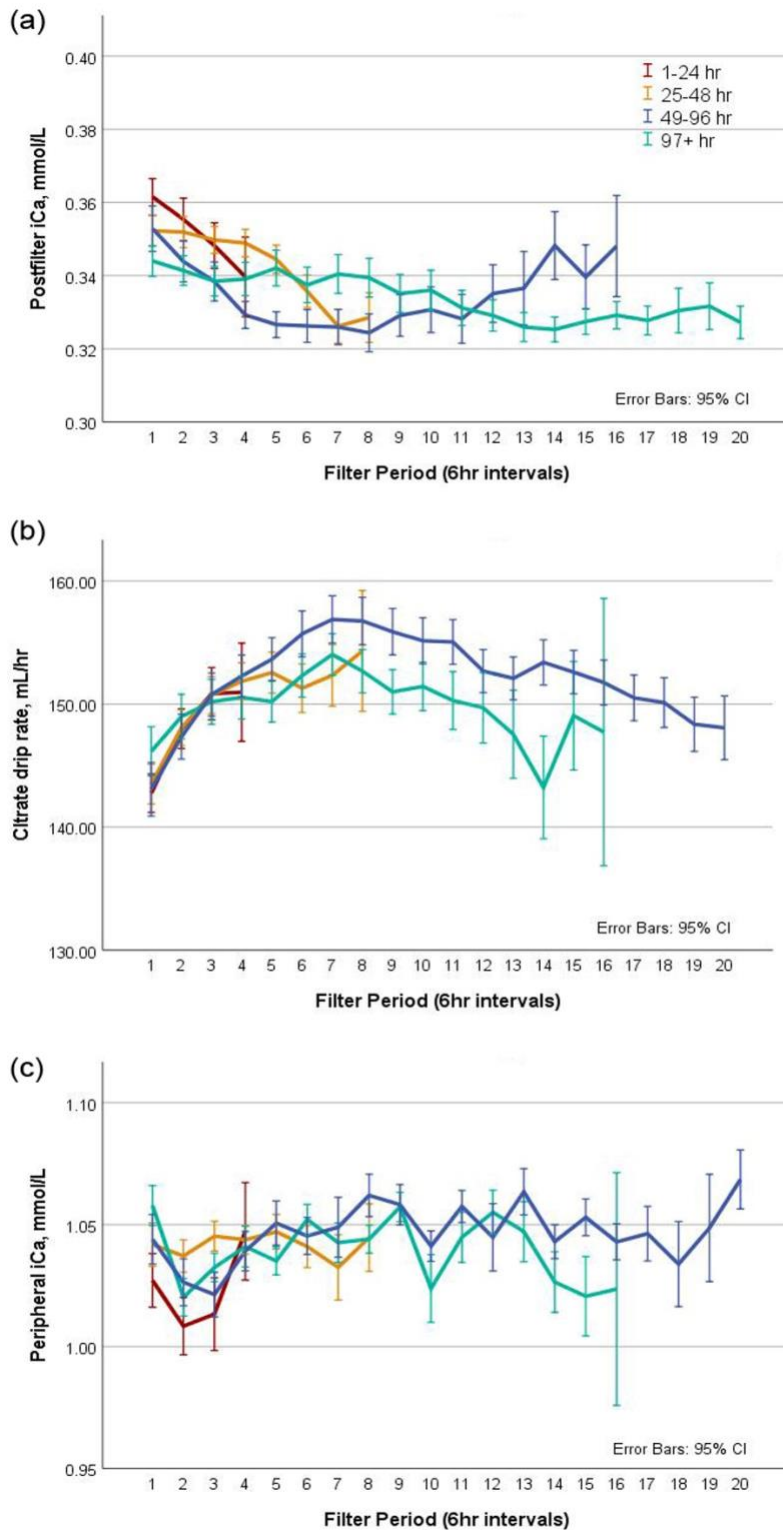


Figure S2. Comparisons of postfilter ionized calcium(a), citrate flow rate(b) and peripheral ionized calcium levels(c) according to filter life group: brown, filter life ≤ 24 hr; yellow, $24 < \text{filter life} \leq 48$ hr; green, $48 < \text{filter life} \leq 96$ hr; blue, filter life > 96

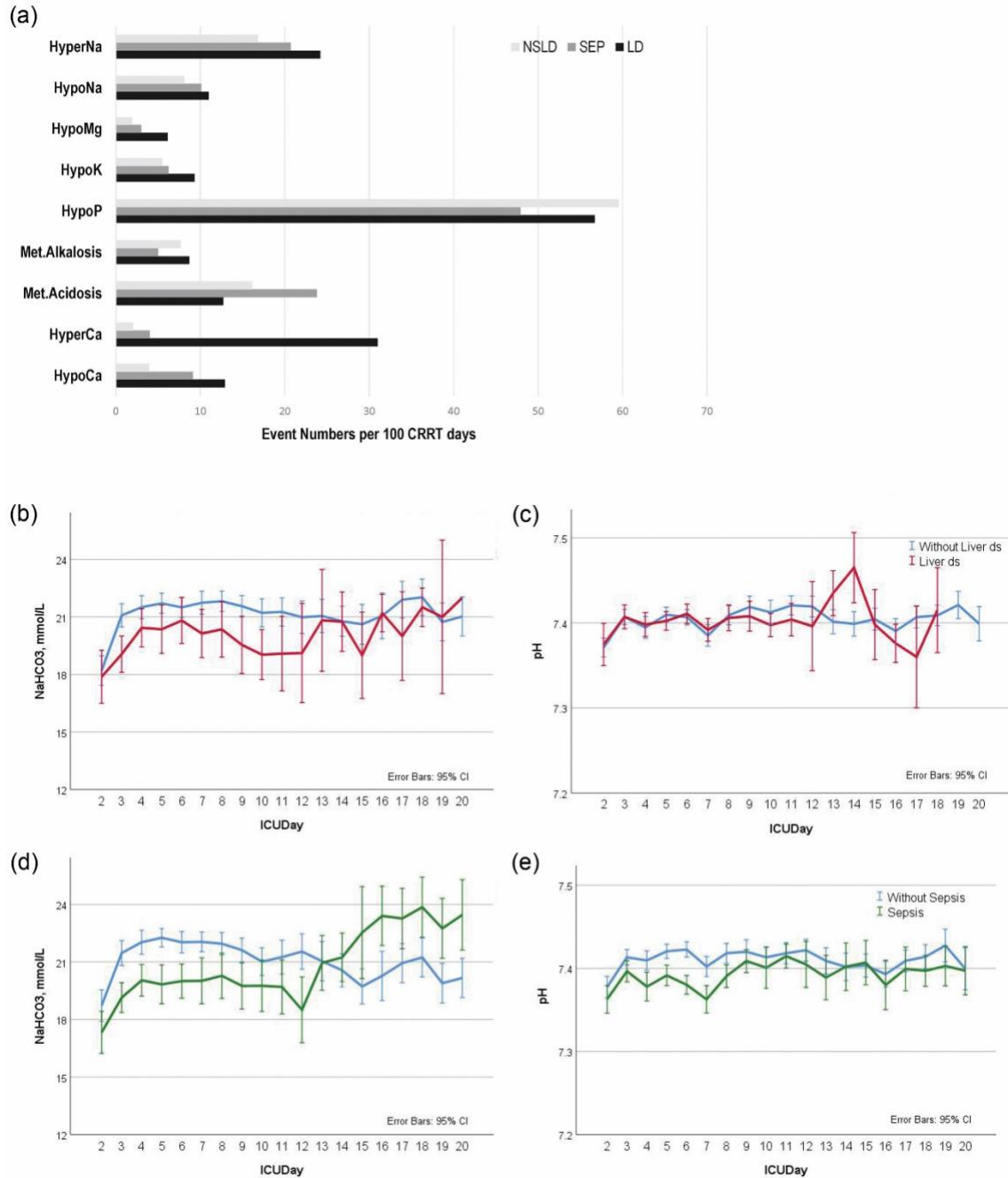


Figure S3. Metabolic complications of RCA with calcium containing solutions (a) Incidence of metabolic complications among the patients with liver disease (LD, black bar), sepsis without liver disease (SEP, gray bar), and without liver disease or sepsis (NSLD, light gray bar) (b) Changes of NaHCO₃ and (c) pH level in patients with liver disease (d) Changes of NaHCO₃ and (e) pH in patients with sepsis; Red line in (b) and (c), patients with liver disease; Blue line in (b) and (c), patients without liver disease; Green line in (d) and (e), patients with sepsis; Blue line in (d) and (e), patients without sepsis

Table S1. UCSD CRRT electrolyte protocol

UCSD CRRT electrolyte protocol
Add to Primasate according to K and Mg values Potassium chloride to increase the concentration in 1 mEq/L to 4 mEq/L Magnesium sulfate 50 % to increase concentration of Mg in 1 to 2 mEq/L
Check Mg / K / P every 6 hours and replace as necessary. (For use in critical care areas only).
Magnesium (Mg) If serum Mg < 1 mg/dL, give 2 grams IV over 2 hour x 3 doses (6 grams total). Recheck serum magnesium 1 hr after infusion.
Potassium (K) (For central access only). If serum K <3 mEq/L call MD, then give KCl 20 meq over 1 hr x 4 doses. Maximum total rate not to exceed 20 mEq/hr. Recheck serum K 1 hr after last dose.
Phosphate (P) If serum P < 1 mg/dL, give 10 mEq sodium phosphate over 1.5 hrs x 4 doses. Use sodium phosphate 10 mEq/50mL D5W IVPB. Recheck serum phosphate 1 hour after last infusion. If serum P <3 mg/dL, give sodium phosphate 10 meq/50 ml x 2 doses. If serum P <2.5 mg/dL, give sodium phosphate 10 meq/50 ml x 3 doses. If serum P <2 mg/dL, give sodium phosphate 10 meq/50 ml x 4 doses.

Table S2. Cutoff values of electrolyte used in metabolic complication measurement

(a)	Low	Target	High
pH	<7.30	7.35~7.45	≥7.50
NaHCO ₃ , mmol/L	<22.0	22.0~30.0	≥30
Ionized calcium, mmol/L	<0.85	0.85~1.05	
Total calcium, mg/dL		8.5~10.6	≥10.6
Sodium, mmol/L	<136	136~145	≥145
Potassium, mmol/L	<3.5	3.5~5.1	≥5.1
Magnesium, mg/dL	<1.6	1.6~2.4	≥2.4
Phosphate, mg/dL	<2.7	2.7~4.5	≥4.5

(b)	Mild	Moderate	Severe
Hypocalcemia, mmol/L	-	0.80 ≤ iCa < 0.85	< 0.80
Hypercalcemia, mg/dL	10.6 ≤ Total Ca < 14	12 ≤ Total Ca < 14	≥ 14
Metabolic acidosis, pH	7.25 ≤ pH < 7.30	7.20 ≤ pH < 7.25	< 7.20
Metabolic alkalosis, pH	7.50 ≤ pH < 7.55	7.55 ≤ pH < 7.60	≥ 7.60
Hypophosphatemia, mg/dL	2.0 ≤ P < 2.7	1.0 ≤ P < 2.0	< 1.0
Hypokalemia, mmol/L	3.0 ≤ K < 3.5	2.5 ≤ K < 3.0	< 2.5
Hypomagnesemia, mg/dL	-	1.0 ≤ Mg < 1.6	< 1.0
Hyponatremia, mmol/L	130 ≤ Na < 136	125 ≤ Na < 130	< 125
Hypernatremia, mmol/L	145 ≤ Na < 152	152 ≤ Na < 160	≥ 160

Abbreviations: iCa, ionized calcium; Total ca, serum total calcium; P, phosphate; K, potassium; Na, sodium. We did not categorize mild hypocalcemia and hypomagnesemia because target values were kept below the lower cut off the normal range in some patients.

Table S3. Acute on chronic liver failure grade at CRRT initiation

Single organ dysfunction score (median, IQR)	
Liver	2(1-3)
Kidney	3(3-3)
Brain	3(1-3)
Coagulation	2.5(1-3)
Circulatory	2.5(2-3)
Respiratory	1(1-1)
Total number failure	3(2-4)
CLIF organ failure score	13(11-15)
ACLF grade (n, %)	
Grade 1	4(12.5)
Grade 2	5(15.6)
Grade 3	23(71.9)

Table S4. Replacement solutions used in the CRRT circuit.

Variables	
No. filter hour 28,671	
Pre-filter Replacement flow rate, ml/hr	483.1±35.1
Pre-filter Replacement solutions [‡]	
0.9% saline	39.1%
0.45% saline	48.4%
Sterile water +150mEq/L of NaHCO ₃	1.5%
0.45% saline + 75mEq/L of NaHCO ₃	0.5%
Not described	10.4%
Post-filter fluid for deaeration chamber flow rate, mL/hr	196.4±34.9
Post-filter solutions for deaeration chamber [‡]	
0.9% saline	46.2%
0.45% saline	39.7%
0.45% saline + 75mEq/L of NaHCO ₃	10.5%
Sterile water +150mEq/L of NaHCO ₃	3.3%
Not described	0.4%
Intravenous substitution flow rate, ml/hr	622.2±167.6
Intravenous substitution solutions [‡]	
0.9% saline	48.4%
Prismasol	41.6%
Individualized NaHCO ₃ based solution*	7.3%
0.45% saline	0.4%
Not described	2.3%

‡ % application of solution was calculated per 28,671 filter hours, *includes sterile water+150mEq/L of NaHCO₃, sterile water+75mEq/L of NaHCO₃, half saline+ 75 mEq/L of NaHCO₃

Table S5. Filter changing reasons according to the filter life group in patients with liver disease or sepsis

(a) LD	Filter Life Group				Total
	1 ≤ 24h	2 25-48h	3 49-96h	4 >96h	
Total number of filters	45	31	16	12	104
Not recorded, n	22(48.9%)	11(35.5%)	7(43.8%)	0	40(38.5%)
Recorded, n	23(51.1%)	20(64.5%)	9(56.3%)	12(100%)	64(61.5%)
Reason to change filters among the recorded					
Unrelated to therapy, n(%)	9(39.1)	6(30.0)	5(55.6)	4(33.3)	24(37.5)
Time, n(%)	0(0)	0(0)	0(0)	8(66.7)	8(12.5)
Access, n(%)	1(4.3)	0(0)	0(0)	0(0)	1(1.6)
Clotting, n(%)	11(47.9)	10(50.0)	4(44.4)	0(0)	25(39.1)
Low efficacy, n(%)	2(8.7)	4(20.0)	0(0)	0(0)	6(9.3)

(b) SEP	Filter Life Group				(n=99) Total
	1 (n=49) ≤ 24h	2 (n=27) 25-48h	3 (n=7) 49-96h	4 (n=16) >96h	
Not recorded, n	19(38.8%)	13(48.1%)	1(14.3%)	0	33(33.3%)
Recorded, n	30(61.2%)	14(51.9%)	6(85.7%)	16(100%)	66(66.7%)
Reason to change filters among the recorded					
Unrelated to therapy, n(%)	18(60.0)	7(50.0)	3(50.0)	3(18.8)	31(47.0)
Time, n(%)	0(0)	0(0)	0(0)	9(56.3)	9(13.6)
Access, n(%)	3(10.0)	1(7.1)	1(16.7)	2(12.5)	7(10.6)
Clotting, n(%)	8(26.7)	5(35.8)	1(16.7)	1(6.3)	15(22.7)
Low efficacy, n(%)	1(3.3)	1(7.1)	1(16.7)	1(6.3)	4(6.0)

Abbreviations: LD, filters with liver disease; SEP, filters with sepsis in the absence of liver disease

Table S6. Comparisons of new onset metabolic complications among different disease groups in patients with RCA-CRRT

	All	LD			SEP	NSLD	P	
		G 1	G 2	G3				
Total CRRT days	1,227	178	17	27	134	198	851	
Hypocalcemia	6.0	12.9*	5.9	11.1	14.1	9.1*	3.9	0.004
Moderate	2.7	4.5	0	7.4	4.4	3.0	2.2	
Severe	3.3	8.4	5.9	3.7	9.6	6.1	1.6	
Hypercalcemia	6.7	31.0*	31.6	0	36.6	4.0	2.0	<0.001
Mild	5.0	23.0	31.6	0	26.1	3.0	1.5	
Moderate	0.7	3.2	0	0	4.2	0.5	0.2	
Severe	1.0	4.8	0	0	6.3	0.5	0.2	
Hypophosphatemia	57.1	56.7	57.9	66.7	54.2	47.0	59.5	0.364
Mild	35.4	35.3	47.4	29.6	34.5	30.2	36.7	
Moderate	21.1	20.3	10.5	33.3	19.0	16.3	22.5	
Severe	0.5	1.1	0	3.7	0.7	0.5	0.4	
Metabolic acidosis	16.9	12.7*	15.2	5.2	15.9	23.8	16.1	0.042
Mild	8.1	6.4	7.7	0	7.7	9.9	8.1	
Moderate	3.9	1.7	0	3.7	3.7	5.0	4.0	
Severe	4.9	4.6	7.5	1.5	4.5	8.9	4.0	
Metabolic alkalosis	7.2	8.7	15.6	1.5	0	5.0	7.7	0.685
Mild	5.8	7.5	0	0	0	4.0	6.0	
Moderate	0.7	1.2	7.4	0	0	1.0	0.6	
Severe	0.7	0	8.2	1.5	0	0	1.1	
Hypomagnesemia	2.7	6.4	0	3.7	7.7	3.0	1.9	0.264
Moderate	2.7	6.4	0	3.7	7.7	3.0	1.9	
Severe	0	0	0	0	0	0	0	
Hypokalemia	6.2	9.3	23.1	0	8.8	6.2	5.5	0.317
Mild	5.7	7.6	15.4	0	7.7	6.2	5.1	
Moderate	0.6	1.7	7.7	0	1.1	0	0.4	
Severe	0	0	0	0	0	0	0	
Hyponatremia	8.4	11.4	32.7	6.1	9.3	10.7	7.0	0.649
Mild	7.3	10.0	28.5	6.1	8.1	10.7	5.8	
Moderate	0.5	0.9	0	0	1.2	0	0.5	
Severe	0.6	0.5	4.2	0	0	0	0.7	
Hypernatremia	18.6	24.6	15.8	40.7	22.5	20.3	16.8	0.773
Mild	17.8	23.5	15.8	37.0	21.8	19.3	16.1	
Moderate	0.7	1.1	0	3.7	0.7	1.0	0.6	
Severe	0.1	0	0	0	0	0	0.1	

Abbreviations: RCA, regional citrate anticoagulation; CRRT, continuous renal replacement therapy; LD, cases with liver disease; SEP, cases with sepsis in the absence of liver disease; NSLD, cases without sepsis or liver disease. Foot note: *p<0.05 compared to the NSLD, P-value was calculated based on the Generalized linear mixed effects model.

Table S7. Incidence of citrate accumulation according to patient condition

ACLF grade	Total	LD			SEP	NSLD	P	
		G1	G2	G3				
Number of patients	128	32	4	5	23	29	67	
Calcium Ratio ≥ 2.5 , n(%)	17(13.3)	11(34.4)	1(25.0)	1(20.0)	9(39.1)	2(6.9)	4(6.0)	<0.001
Calcium Ratio ≥ 2.5 and pH <7.3, n(%)	8(6.3)	5(15.6)	0	1(20.0)	4(17.4)	1(3.4)	2(2.9)	0.005
Calcium Ratio ≥ 2.5 and NaHCO ₃ <20 mmol/L, n(%)	5(3.9)	3(9.4)	0	0	3(13.0)	1(3.4)	1(1.5)	0.165

Abbreviations; LD, patients with liver disease; SEP, patients with sepsis in the absence of liver disease; NSLD, patients without sepsis or liver disease

Table S8. Factors associated with ICU mortality

	HR	95% CI	P-value
Age, yr	1.014	0.986-1.043	0.30
Sex (Male)	1.210	0.508-2.883	0.74
Body mass index, kg/m ³	0.986	0.933-1.043	0.64
Sepsis (Yes)	1.393	0.606-3.201	0.20
Liver disease (Yes)	1.495	0.548-4.084	0.83
Citrate accumulation* (Yes)	0.685	0.256-1.828	0.47
SOFA score at CRRT start	1.233	1.072-1.419	0.003

Abbreviations: SOFA, sequential organ failure assessment; CRRT, continuous renal replacement therapy. Foot note:

*Estimation of citrate accumulation, calcium ratio ≥ 2.5