

24-h Post-Dilution Veno-Venous Hemo-Diafiltration (post-CVVHDF) Regional Citrate Anticoagulation (RCA) Protocol

I. 24-hour post-CVVHDF-RCA Protocol: Introduction

Citrate acts as an anticoagulation agent by complexing calcium (Ca) thereby lowering the plasma ionized calcium (iCa) level. Multiple clotting cascade reactions cannot progress if the plasma iCa is <0.4 mM. A high, fixed citrate flow to blood flow ratio in the post-CVVHDF-RCA protocol ensures <0.4 mM iCa and strong anticoagulant activity from the point where the citrate infusion enters the intake (arterial) limb of the blood circuit (**Figure 1.**) until the point where the Ca solution is infused.

About 25-60% of the free $[\text{citrate}]^{3-}$ and $[\text{citrate-Ca}]^{-}$ complex ions are cleared on the high flux and high efficiency HF1400 filter using a commercial Ca-free, bicarbonate-based sterile fluid at an effluent flow which is about 20-50% of the blood flow and is selected based on the patient's weight to prescribe 25-30 ml/kg/h clearance. As significant amount of citrate reaches the patient with the circuit return (venous) blood, therefore patients with severe impairment of systemic citrate clearance (<6 L/hour) require other settings (**See section V.**)

Simultaneous circuit blood pre-citrate infusion and post-filter but before-postdilution infusion glucose values may be measured with a glucometer to estimate glucose dialysance and hence citrate- and Ca-clearance.

Since citrate removal on the dialyzer is achieved with Ca-free dialysate and replacement fluid, the anticoagulation due to the low circuit iCa is maintained despite citrate removal and is only reversed when Ca is infused into the circuit venous limb blood just before it is returned to the patient. The circuit Ca loss and hence the Ca infusion rate is derived using the patient's serum albumin level and the estimated plasma clearance of Ca on the dialyzer. A commercial optical sensor may display the post-filter blood Hct and O_2 saturation values.

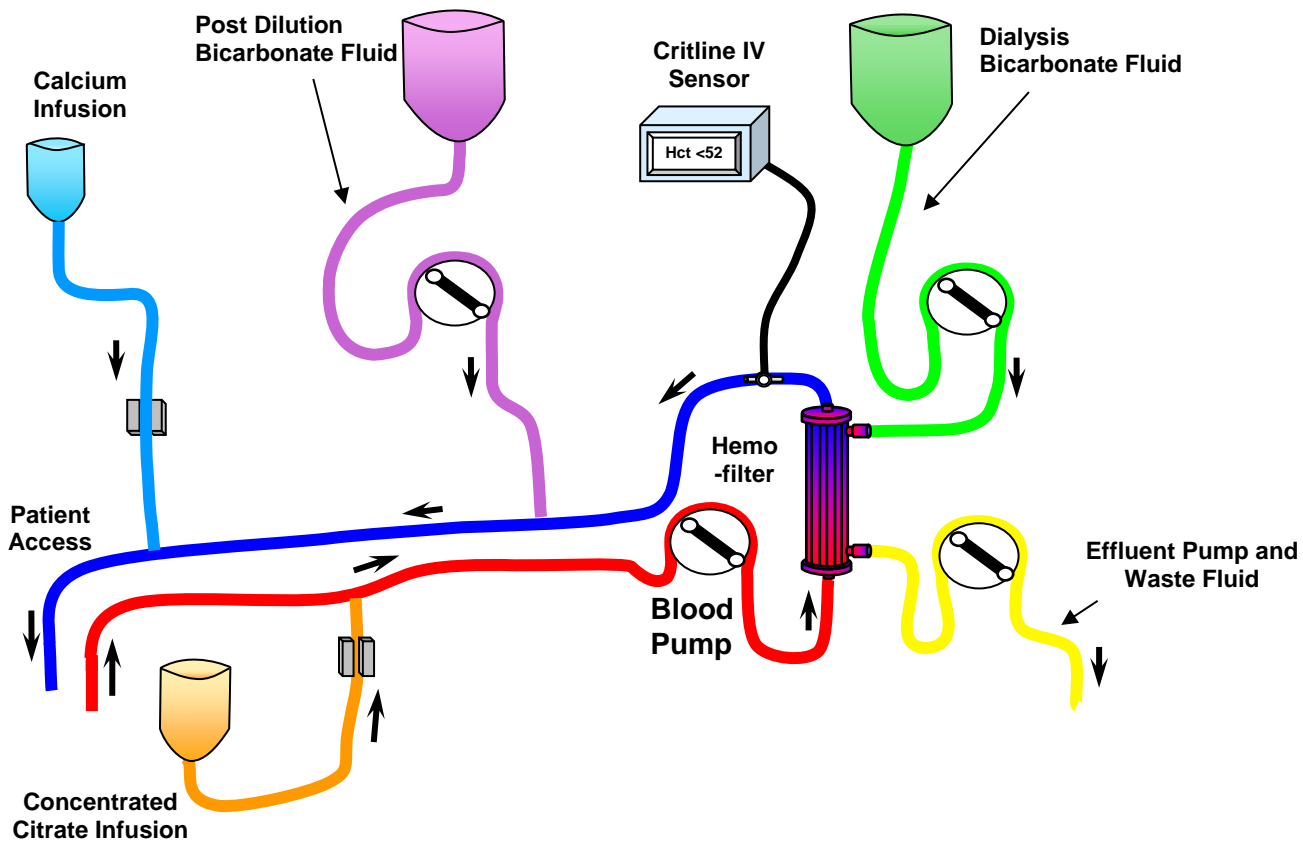


Figure 1. Prismaflex post-CVVHDF System with Calcium Infusion Pump

After the citrate infusion, the circuit total Ca is normal but the iCa is low because of the high citrate level. After the Ca-free post-CVVHDF blood purification step total Ca, citrate and iCa levels are all lower. The Ca-infusion restores total Ca to normal for adequate systemic blood clotting after citrate metabolism in the patient. Infusing Ca on the venous limb of the blood circuit prevents Ca dosing errors due to access recirculation.

II. CVVHDF RCA: Table 1. FIXED CRRT Settings Selected Based on the Patient's Current Weight:

Settings Weight	Blood Flow QB ml/min	ACDA Citrate Flow ml/hour	Dialysate Flow QD mL/hour	Post-Dilution Flow QRF mL/hour
<=50 kg	100	250	500	500
51-60 kg	100	250	650	650
61-70 kg	100	250	800	800
71-80 kg	100	250	950	950
81-90 kg	150	300*	1050	1050
91-100 kg	150	300*	1200	1200
101-110 kg	150	300*	1350	1350
111-120 kg	150	300*	1500	1500
121-130 kg	150	300*	1650	1650
131-140 kg	150	300*	1800	1800
>=141 kg	150	300*	1950	1950

1. Initial settings based on patient weight from Table 1. Smaller patients <=80 kg will be treated with a lower QB to keep single pass citrate extraction > 25%. *The physician may order ACDA flow rates up to 375 ml/hour very rarely if circuit iCa < 0.3 mM is desired.

2. Adjust the settings for QD and QRF based on systemic hemoglobin changes during CVVHDF:

The post-filter Hct <= 52% upper limit (the highest circuit Hct) may be continuously displayed by an optical sensor after the post-dilution+net UF filtration step. The nurse is to call the nephrology fellow if the post-Hct > 52% to reduce the post-dilution flow and increase the dialysate flow to achieve a post-filter Hct <=52.

3. The total hourly net ultrafiltration (UF) is calculated by the nurse: Any net UF value as dictated by the patient's needs can be set by the ICU nurse hourly. If the postfilter Hct is >= 52% (unlikely to happen unless the systemic Hb >= 12 g/dL and large net UF goals are prescribed) the physician will have to decrease the QRF flow while increasing the QD flow to keep the sum of QD+QRF unchanged.

III. CVVHDF RCA: Determining the Initial rate of the 136 mM CaCl₂ in 0.9% saline infusion:

The main purpose of the Ca-infusion is to replace the Ca lost on the dialyzer. This loss is the product of the plasma Ca-clearance times the goal serum total Ca level. The patient's serum albumin level determines the target plasma total Ca level needed to keep the plasma iCa around 1.05-1.25 mmol/L with systemic citrate clearance estimated at about 15 L/hour and systemic citrate level estimated in the 0.7-1.4 mM range. The systemic albumin should be checked once every 24 hours. The nephrologist may adjust the Ca-infusion rate

based on daily albumin levels. The extra glucose delivered with the ACDA is offset by CRRT effluent glucose losses with the glucose-free dialysate- and replacement fluids resulting in an about neutral glucose balance.

1. Table 2.: Initial 136 mM CaCl₂-infusion (mL/h) for GOAL Systemic iCa 1.15 mM:

Albumin Effluent	0.0-0.7 g/dL	0.8-1.2 g/dL	1.3-1.7 g/dL	1.8-2.2 g/dL	2.3-2.7 g/dL	2.8-3.2 g/dL	3.3-3.7 g/dL	3.8-4.2 g/dL	4.3-4.7 g/dL	4.8-5.2 g/dL
<=1400 m/h	16	17	17	18	19	19	20	20	21	21
1401-1700	20	20	21	22	23	23	24	25	25	26
1701-2000	23	24	25	26	27	28	28	29	30	31
2001-2300	26	27	28	30	31	32	32	33	34	35
2301-2600	32	33	34	35	37	38	39	40	41	42
2601-2900	35	37	38	39	41	42	43	44	45	46
2901-3200	38	40	42	43	44	46	47	48	50	51
3201-3500	42	43	45	47	48	50	51	53	54	55
3501-3800	45	47	48	50	52	54	55	57	58	60
3801-4100	48	50	52	54	56	57	59	61	63	64
4101-4400	51	53	55	57	59	61	63	65	67	68
4401-4700	54	56	58	60	63	65	67	69	71	73

The effluent flow is = ACDA+ QD+QRF+NetUF. Use NetUF=100 to calculate the effluent flow. For patients with expected good to fair citrate metabolism the initial Ca infusion rate is prescribed by the nephrology team based on the effluent flow row and the last measured systemic serum albumin column using Table 2. For such patients use CRRT fluids with at least 25 mEq/L bicarbonate level.

2. Increasing the Table 2. initial Ca-infusion rate up 13% for GOAL Systemic iCa 1.3 mM:

To target a higher systemic iCa of 1.3 mM (at the ICU team's discretion) simply multiply by 1.13 the initial Ca-infusion rate derived from **Table 2.** (required as **Table 2.** is designed for goal systemic iCa 1.15 mM).

3. Increasing the initial Ca-infusion rate up 30%with expected poor systemic citrate clearance 6L/hour:

Some patients may have moderate impairment of systemic citrate metabolism (usually lactate >4 but < 10, with or without laboratory and clinical findings of impaired liver function but no evidence of shock liver (see below). For these patients take the Ca-infusion rate determined in Step 1 and/or 2 and multiply by 1.3 to get their initial Ca infusion rate. Also use CRRT fluids with at least 30 mEq/L bicarbonate level.

IV. Adjust the Ca-infusion rate +/-10-20% using systemic iCa levels every 6 hours:

An arterial line or central venous line blood gas iCa and glucose will be checked at t=0 (just before CRRT start), and after start at 2, 4, 6 hours and then every 6 hours during the post-CVVHDF-RCA procedure. At the same time, CRRT circuit immediate post-filter iCa and glucose will also be checked every 12 hours by blood gas and charted on the CRRT flow sheet together with the postfilter optical Hct from the Crit-Line IV device. The systemic blood iCa at CVVHDF start is NOT used to adjust the initial Ca-infusion rate. It is expected that the systemic iCa will usually be near GOAL +/-0.1 mM with the initial Ca infusion rate. Some patients may sequester Ca in their tissues (for instance with acute pancreatitis or rhabdomyolysis) or conversely may release Ca from their bones (for instance with hypercalcemia of malignancy). Systemic citrate accumulation >2.5 mM is also possible in severe shock/liver failure. Such patients may require significant adjustments to their initial Ca infusion rate based on systemic iCa levels as in **Table 3 (Standard iCa Goal 1.15 mM) OR Table 4 (High iCa Goal 1.3 mM)**. For patients who require systemic total Ca levels > 12 mg/dL with albumin <=5.2 g/dL to keep their iCa >= 1.15 mM the physician should change to the SHOCK CVVHDF settings as in **Section V**.

Table 3: 136 mM CaCl₂ Infusion Rate Change Based on Systemic iCa Every 6 hours: GOAL 1.15 mM

	The patient's ionized calcium level checked every 6 hours				
	Less than <0.95 mmol/L	0.95 – 1.04 mmol/L	1.05 - 1.25 mmol/L	1.26 – 1.4 mmol/L	More than >1.4 mmol/L
Current Ca-infusion Flow Rate mL/h	Increase Rate +20%; notify ICU and Nephro fellows	Increase Rate +10%	No Change	Reduce Rate -10%	Reduce Rate -20%; notify ICU and Nephro fellows
<=15	+2 ml/h	+1 ml/h	No change	-1 ml/h	-2 ml/h
16-25	+4 ml/h	+2 ml/h	No change	-2 ml/h	-4 ml/h
26-35	+6 ml/h	+3 ml/h	No change	-3 ml/h	-6 ml/h
36-45	+8 ml/h	+4 ml/h	No change	-4 ml/h	-8 ml/h
46-55	+10 ml/h	+5 ml/h	No change	-5 ml/h	-10 ml/h
56-65	+12 ml/h	+6 ml/h	No change	-6 ml/h	-12 ml/h
66-75	+14 ml/h	+7 ml/h	No change	-7 ml/h	-14 ml/h
76-85	+16 ml/h	+8 ml/h	No change	-8 ml/h	-16 ml/h
86-95	+18 ml/h	+9 ml/h	No change	-9 ml/h	-18 ml/h
96-105	+20 ml/h	+10 ml/h	No change	-10 ml/h	-20 ml/h

Table 4: 136 mM CaCl₂ Infusion Rate Change Based on Systemic iCa Every 6 hours: GOAL 1.3 mM

	The patient's ionized calcium level checked every 6 hours				
	Less than <1.1 mmol/L	1.1 – 1.19 mmol/L	1.2 - 1.4 mmol/L	1.41 – 1.55 mmol/L	More than >1.55 mmol/L
Current Ca-infusion Flow Rate mL/h	Increase Rate +20%; notify ICU and Nephro fellows	Increase Rate +10%	No Change	Reduce Rate -10%	Reduce Rate -20%; notify ICU and Nephro fellows
<=15	+2 ml/h	+1 ml/h	No change	-1 ml/h	-2 ml/h
16-25	+4 ml/h	+2 ml/h	No change	-2 ml/h	-4 ml/h
26-35	+6 ml/h	+3 ml/h	No change	-3 ml/h	-6 ml/h
36-45	+8 ml/h	+4 ml/h	No change	-4 ml/h	-8 ml/h
46-55	+10 ml/h	+5 ml/h	No change	-5 ml/h	-10 ml/h
56-65	+12 ml/h	+6 ml/h	No change	-6 ml/h	-12 ml/h
66-75	+14 ml/h	+7 ml/h	No change	-7 ml/h	-14 ml/h
76-85	+16 ml/h	+8 ml/h	No change	-8 ml/h	-16 ml/h
86-95	+18 ml/h	+9 ml/h	No change	-9 ml/h	-18 ml/h
96-105	+20 ml/h	+10 ml/h	No change	-10 ml/h	-20 ml/h

V. CVVHDF RCA for severe SHOCK patients with expected ZERO systemic citrate metabolism:

These patients will often have systemic lactate > 10 mM, require FFP and or dextrose drips, and/or develop systemic total Ca/ionized Ca ratio > 2.5 (mM/mM) on CVVHDF settings according to **Sections II and III**.

CRRT Settings Weight	CRRT Circuit Set	Blood Flow QB ml/min	ACDA Citrate Flow ml/hour	Dialysate Flow QD mL/hour	Post-Dilution Flow QRF mL/hour
<70 kg	HF1000	60	150	1500	600
71-140	HF1400	100	250	2500	1000
>141 kg	HF1400	150	300	3750	1500

Table 5: PrismaFlex FIXED settings for severe SHOCK patients according to weight.

These settings ensure > 75% single pass citrate removal on the dialyzer limiting systemic citrate accumulation to <=2.5 mM even in the absence of citrate metabolism. For these patients use CRRT fluids with at least 35 mEq/L bicarbonate level. The patient may also need a systemic D5 infusion at 30-50-80 ml/hr for neutral CRRT glucose balance (a D5 infusion will likely already be present as the D5W part of a vasopressor or isotonic bicarb or N-acetylcysteine infusion).

1. Adjust the settings for QD and QRF based on circuit post-filter Hct during CVVHDF:

The goal post-filter Hct <= 52% (the highest circuit Hct) will be continuously displayed by an optical sensor. If the systemic Hb is >12 and with large net UF goals excessive circuit hemoconcentration >52 Hct may develop after the post-dilution+net UF filtration step. The nurse will call the fellow to increase the QD and decrease the QRF to achieve post-filter Hct <=52% while keeping QD+QRF unchanged.

2. Table 6: Initial rate (ml/hour) of the 136 mM CaCl₂ in 0.9% saline infusion for SHOCK patients:

Weight Albumin	<70 kg: Effluent 2.3 L/hour	71-140 Kg: Effluent 3.8 L/hour	>141 kg: Effluent 5.6 L/hour
0.0-0.7 g/dL	34	56	79
0.8-1.2 g/dL	35	58	82
1.3-1.7 g/dL	36	60	85
1.8-2.2 g/dL	37	62	87
2.3-2.7 g/dL	38	63	90
2.8-3.2 g/dL	39	65	92
3.3-3.7 g/dL	40	67	94
3.8-4.2 g/dL	41	68	97
4.3-4.7 g/dL	42	69	99
4.8-5.2 g/dL	43	71	101

The amount of Ca removed from the circuit blood is impacted by the systemic albumin level and systemic citrate accumulation about 2-2.5 mM at a fixed ACDA+ QD+QRF = effluent flow rate (determined by weight category). Ca-infusion dosing is largely independent of the intake blood Hb level if the systemic Hb < 14 g/dL and the FIXED post-CVVHDF flow settings are selected from **Table 5**. The initial Ca infusion rate is prescribed by the nephrology team based on the weight column and the last measured serum albumin using **Table 6**. To target a higher systemic iCa of 1.3 mM (at the ICU team's discretion) simply multiply by 1.13 the initial Ca-infusion rate derived from

Table 6. (Required as **Table 6**. is designed for goal systemic iCa about 1.15 mM).

3. Adjust the Ca-infusion rate +/-10-20% using systemic iCa levels every 6 hours:

Systemic iCa levels for SHOCK patients should be monitored at t=0 just before CRRT start and after start at 2, 4, 6 hours and then every 6 hours as for other patients discussed under **Section IV**. **Tables 3 OR 4** may be used to adjust the Ca-infusion rate for goal systemic iCa 1.15 or 1.3 mM, respectively.