Continuous Renal Replacement Therapy on Fresenius MultiFiltrate® - ICU - Full Clinical Guideline - Burton only

Reference no.: CG-ICU/2020/041

1. Introduction

The following document provides a reference guide for users of the Fresenius MultiFiltrate® continuous renal replacement therapy (CRRT) system with citrate, heparin or epoprostenol anticoagulation. Citrate is the default mode of anticoagulation on the critical care unit at the Queens Hospital Burton.

2. Aim and Purpose

The aim of this guide is to be a quick reference to users; both nurses and doctors in day to day aspects of using the CRRT as well as in special patients population, It also provide guidance on the most recent evidence of the size and site of vascular access required.

3. Definitions, Keywords

CRRT	Continuous renal replacement therapy
CVVHD	Continuous venovenous haemodiafiltration
Vas Cath	Vascular access Catheter

4. Main body of Guidelines

1. Locking the Vascath to Prevent Clotting

If the vascath is not used for more than 1 hour it should be locked with Heparin.
i. Flush vascath with 10 ml of 0.9% Sodium Chloride.
ii. The volume required for each lumen is indicated on the hub or clips of the catheter. Using a 2.5 ml syringe draw up the exact volume of Heparin 1000 u/ml for each lumen and inject slowly over 5-10 seconds.
iii. Label line as "Contains Heparin". Keep the label well clear of the Luer connectors as the label glue is difficult to remove and may become contaminated.
iv. Prior to initiation of CRRT the Heparin should be aspirated and discarded, and catheter flow assessed with a 20ml syringe.

2. Preparing the Machine for use with Citrate

- Switch on the machine and wait for the functional test to be completed.
- Select Ci-Ca anticoagulation.
- Select a new treatment.
- Choose CVVHD.
- Check all the starting conditions have been fulfilled:
  - Citrate solution concentration – 136 mmol/L (4%)
  - Citrate volume 1000ml

- Calcium solution concentration – 100 mmol/L
- Calcium volume 500ml
- Calcium free HF solution used (Ci-Ca® Dialysate K4).

• Confirm conditions are fulfilled.
• Follow the step-by-step guide to prime the machine.

3. Technique, Setup and Overview

• Standard therapy with the Fresenius multiFiltrate® is continuous venovenous haemodialysis (CVVHD) with citrate anticoagulation (Ci-Ca® CVVHD).
• The citrate dose is determined by the **circuit** ionised calcium ($iCa2^+$); the calcium dose is determined by the **systemic** (or patient) $iCa2^+$.
• **An overview for running Ci-Ca® CVVHD is:**

i. Select the dialysis solution. If using Ci-Ca® CVVHD, the default will be Ci-Ca® Dialysate K4. (Ci-Ca® Dialysate K2 is available when enhanced clearance of potassium is required).
ii. Select the starting dialysis flow rate and blood flow rate according to ideal body weight, using either the 'default' or 'enhanced' tables (section 5).
iii. Sample **systemic** $iCa2^+$ **within the hour prior to commencement of CRRT**, to determine whether pre-treatment with calcium is necessary and to determine the starting calcium chloride dose (section 6).
iv. Begin CVVHD and check the **circuit** $iCa2^+$ **5 minutes later**. This is used to adjust the citrate dose (section 8).
v. Systemic and circuit $iCa2^+$ are then checked **every 6 hours** and the doses of calcium chloride and citrate are adjusted respectively (sections 6 and 7 respectively). (The only exception to this is where the systemic $iCa2^+$ is very low (<1.0mmol/L), mandating re-sampling of systemic $iCa2^+$ 2 hours later, instead of 6 hours later).
vi. Perform **ABGs 2-4 hourly** to monitor pH, K_+, $iCa2^+$, and acid base status. Adjustments in blood flow or dialysis flow may be made for acidosis/ alkalosis (section 10).
vii. Calculate the T:I ratio with the **morning bloods**. Laboratory total calcium (T) and arterial ionised calcium (I) are taken simultaneously (identified by an asterisk on the critical care chart) and a calculated ratio of >2.25 is suggestive of citrate accumulation (section 10).

4. CRRT Dialysate Solutions

There are three dialysate fluids which are stored in separate locations on the ICU:

i. Ci-Ca® Dialysate K4, to be used **only** with Ci-Ca® CVVHD. This is the appropriate starting dialysate fluid for patients with hyperkalaemia.
ii. Ci-Ca® Dialysate K2, to be used **only** with Ci-Ca® CVVHD. This dialysate is appropriate where enhanced clearance of potassium is required, or when Ci-Ca® Dialysate K4 has failed to clear potassium adequately. Our stock levels of this fluid are low as it is infrequently used, so more will have to be ordered urgently from pharmacy if the clinical need for this fluid arises. It is stored in a separate location to Ci-Ca® Dialysate K4.

iii. MultiBic® Dialysate, to be used **only** when using non-citrate anticoagulation. It is stored in a separate location to Ci-Ca® Dialysate K4. Unlike Ci-Ca® dialysate, MultiBic® dialysate contains calcium. If non-citrate anti-coagulation (heparin or Epoprostenol) is used with Ci-Ca® dialysate, the patient's calcium levels will rapidly plummet, causing life threatening complications. The setup of MultiBic® is described in detail later on in this guidance.

Ci-Ca® Dialysate K4 and K2 is presented in one bag separated into two. The two compartments must be mixed before the fluid is used and the date and time of mixing recorded on the bag. Once mixed, it must be used within 12 hours.

5. Selecting the Starting Dialysis Flow Rate and Blood Flow Rate

- The ratio of dialysis flow rate: blood flow rate is determined by ideal body weight and should be numerically "20:11" at the start of CVVHD. It can then be adjusted according to the acid base balance of the patient (see section 9).
- The **default** blood and dialysis flow rates are:

'Default' Blood and Dialysis Flow Rates

Ideal Body Weight	<60kg	60 – 90kg	>90kg
Dialysis Flow Rate	1600 mL/h	2000 mL/h	2400 mL/h
Blood Flow Rate	80 mL/min	100 mL/min	120 mL/min
Citrate Dose	4.0 mmol/L	4.0 mmol/L	4.0 mmol/L
Calcium Dose	See Table 3, Section 6		

Table 1: 'Default' blood and dialysis flow rates

- The dialysate flow rate can be increased (**enhanced flow**) in the following circumstances, to the levels illustrated in table 2:

i. Severe metabolic acidosis (with pH <7.2 and BE < -10mmol/L).
ii. Hyperkalaemia (Potassium ≥ 6.5mmol/L).
iii. Inadequate clearance in response to default dialysis flow rate.
iv. Poisoning (e.g. ethylene glycol).

'Enhanced' Blood and Dialysis Flow Rates

Ideal Body Weight	<60kg	60 – 90kg	>90kg
Dialysis Flow Rate	2000 mL/h	2600 mL/h	3200 mL/h
Blood Flow Rate	100 mL/min	130 mL/min	160 mL/min
Citrate Dose	4.0 mmol/L	4.0 mmol/L	4.0 mmol/L
Calcium Dose	See Table 3, Section 6		

Table 2: 'Enhanced' blood and dialysis flow rates.

- A daily assessment of the blood and dialysis flow is required to ensure appropriate and efficient use of the consumables. It is rare that enhanced flows are required for more than 24 hours, hence the need to assess this daily.

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6. Management of Serum Calcium

- The target systemic (**measured from the arterial line**) ionised calcium (iCa^{2+}) = 1.12-1.20mmol/L.
- Check arterial iCa^{2+} within the hour before commencing treatment.
- If iCa^{2+} ≤1.11mmol/L, pre-treat with calcium chloride 10mls in 50mls 0.9% sodium chloride, administered over 30 minutes via a central line. CRRT can commence before this infusion has finished.
- Use the table below to then set the starting calcium chloride dose and to determine when to re-check the iCa^{2+}.

Pre-Treatment Requirement and Starting Doses of Calcium Chloride

Systemic iCa2+ (mmol/L)	< 1.00	1.00 - 1.11	1.12 - 1.20	1.21 - 1.45	> 1.45
Pre-treatment with calcium Chloride	Yes	Yes	No	No	No
Starting dose Calcium Chloride (mmol/L)	2.0	1.9	1.7	1.5	1.4
Check first systemic iCa_{2+} and review calcium dose after	2 hours	6 hours	6 hours	6 hours	6 hours

Table 3: Starting doses of calcium chloride.

- Subsequent systemic iCa^{2+} is sampled **every 6 hours** and the calcium chloride dose adjusted in accordance with Figure 1.
- If the iCa^{2+} result is <1.00, take the next serum iCa^{2+} **in 2 hours**, not 6 hours.
- If the systemic iCa2+ rises to the point where the protocol indicates that you turn off the calcium, you must change to non- citrate anticoagulation and MultiBic® dialysis fluid; **under no circumstances should you run the citrate without the calcium running concurrently**.
- Alternatively assess whether or not CVVHD is required. Discuss with a senior doctor.

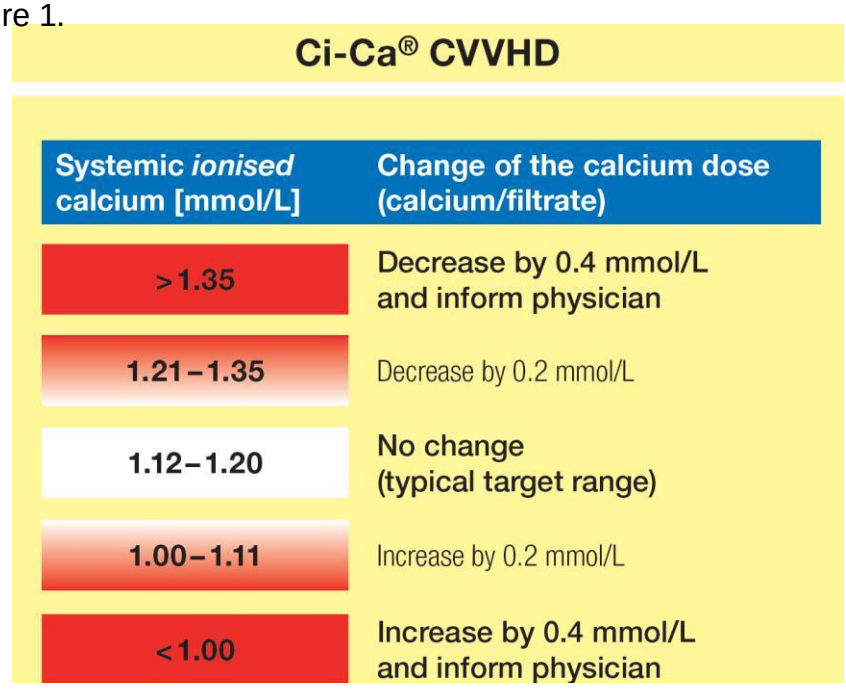


Figure 1: Dose adjustment for calcium chloride based on systemic iCa^{2+}

• NB All samples for systemic iCa^{2+} should be taken from the patient's arterial line. In exceptional circumstances the red "arterial" sampling port on the filter circuit can be used, except if the vascath lines have been switched.

7. Management of Citrate Anticoagulation

• Anticoagulation of the CRRT circuit is directed by the **post filter** iCa^{2+}.
• This is measured by drawing blood from the blue sampling port on the filter circuit (not from the patient).
• The optimum range is between 0.25 – 0.34 mmol/L.
• The first sample is taken **5 minutes** after commencement of CRRT and once every **6 hours** thereafter, and the dose of citrate adjusted as indicated in Figure 2.

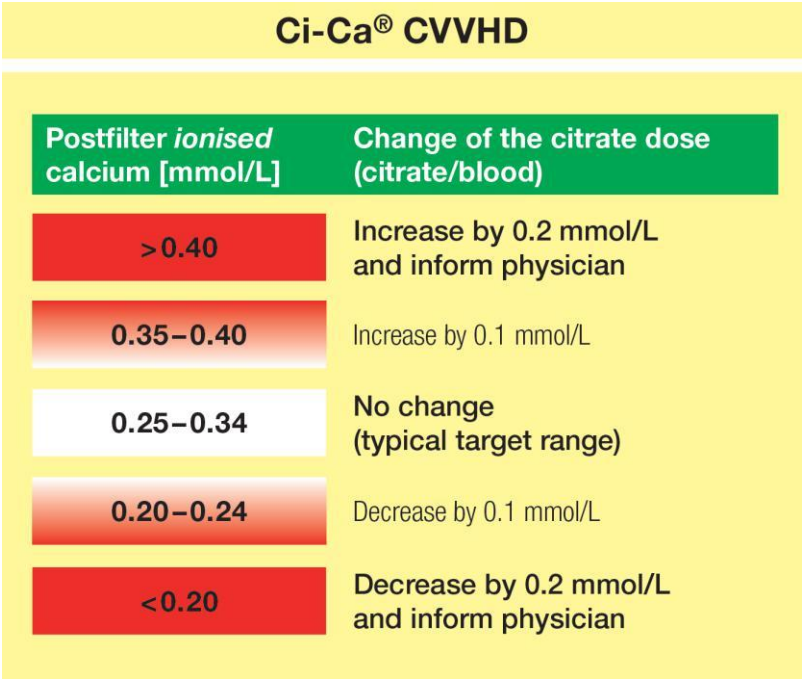


Figure 2: Dose adjustment for citrate based on circuit iCa^{2+}

8. Management of Potassium, Magnesium and Phosphate

• Check Potassium, Magnesium and Phosphate daily and replace if low as per unit protocol.
• Potassium is controlled by dialysate flow. Use the 'enhanced' blood and dialysate flow if serum $K^+ \geq 6.5$ mmol/L. If this does not bring down the potassium, consider switching the dialysate fluid to Ci-Ca K2. Supplement by central infusion if K^+ is ≤ 4.4.
• Magnesium forms complexes with citrate which can be dialysed out. Ci-Ca K4 dialysate contains 0.75 mmol/L of Mg^{2+}, which should help maintain serum levels. If needed, supplement Mg^{2+} in accordance with the unit protocol.
• Ci-Ca K4 dialysate contains 1.25mmol/l of phosphate which should help maintain levels. If needed, supplement phosphate in accordance with the unit protocol.

9. Acid Base Balance

Principles:
• Over 50% of the calcium-citrate complexes formed inside the circuit is dialysed out.
• The rest are re-infused into the patient together with some unbound citrate. Citrate is metabolised to bicarbonate (which is an oxygen dependent process), mainly in the liver but also in muscle, and the citrate-bound calcium is released as free ionised calcium.

a. Metabolic Alkalosis (pH > 7.45 with BE > 5 mmol/L)

Potential causes:

i. The patient's underlying condition.

ii. Incorrect setting of dialysate and blood flow rates - dialysate rate too low relative to the blood flow rate, giving an excess supply of citrate to the patient.

iii. Deliberate increase of citrate rate in order to target a lower than standard post-filter iCa^{2+} range.

iv. Impaired clearance of calcium-citrate complexes (associated with a rise in systemic iCa^{2+}).

Overall dose ≈ Dialysate flow	Blood flow
1600 mL/h	80 mL/min
2000 mL/h	100 mL/min
2200 mL/h	110 mL/min
2600 mL/h	130 mL/min
3000 mL/h	150 mL/min
3200 mL/h	160 mL/min
3600 mL/h	180 mL/min

Table 4: Standard blood and flow rates

Actions:

- Treat the underlying medical condition.
- Check the dialysate and blood flow rates (see Table 4).
- If clearance is adequate (serum urea <10 mmol/L), reduce blood flow rate by 20 to 30%* and keep **dialysate** dialysate rate constant (minimum blood flow= 80ml/min).
- If clearance is inadequate (serum urea >10 mmol/L), increase dialysate flow rate by 20 to 30%* and keep blood flow rate constant.

*A 20% change in blood or dialysate flow will manifest as approximately a 4mmol/L change in the acid/base status but will take some hours to develop.

b. Metabolic Acidosis (pH <7.35 with BE < -5 mmol/L)

Potential causes:

i. The patient's underlying condition.

ii. CRRT has not been going long enough to correct the renal failure-induced metabolic acidosis.

iii. Incorrect setting of dialysate and blood flow rates - dialysate rate too high relative to the blood flow rate, so insufficient citrate reaching the patient.

iv. Citrate accumulation – if accompanied by T:I calcium ratio >2.25.

Actions:

- Treat the underlying medical condition.
- Check the blood and dialysate flow rates (see Table 4).
- Allow more time for RRT to correct the acidosis.

- Increase clearance rate by switching to the 'enhanced' blood and dialysis flow rates (Section 6) or in accordance with the above table. The maximal rates are 200ml/min and 4000ml/h respectively.
- Increase blood flow rate by 20 to 30%* and keep dialysate rate constant (minimum blood flow= 80ml/min).
- For management of citrate accumulation, see section 11.
- Consider giving 8.4% sodium bicarbonate.

*A 20% change in blood or dialysate flow will manifest as approximately a 4mmol/L change in the acid/base status but will take some hours to develop.

10. Citrate Accumulation: Detection

Refer to principles in section 9.

Failure to metabolise citrate to bicarbonate is rare, and mostly occurs in the presence of liver dysfunction and/or poor systemic perfusion (producing cellular hypoxia).

- The systemic citrate chelates calcium in the body, leading to a fall in systemic ionised calcium (iCa^{2+}). The response is to increase the delivered calcium dose (as directed in section 7). This results in a high serum total (**uncorrected**) calcium (T), but a low serum ionised calcium (I), or a high T:I ratio (>2.25).

- Acidosis may develop as the breakdown of citrate to bicarbonate ceases and citrate ions produce an anion gap acidosis. As citrate competes with lactate in the Krebs cycle, accumulation is often associated with increasing lactatemia.
  i. Total to ionized calcium ratio (T: I ratio) > 2.25.
  ii. Marked drop in systemic ionised calcium. (Be suspicious if the calcium dose has risen to >2.0mmol/L).
  iii. Elevated total calcium > 3mmol/L.
  iv. Metabolic acidosis (but consider other causes).

The elevated T:I ratio is the parameter which best correlates with raised citrate levels. This is calculated daily using the morning bloods; the laboratory sample (for total calcium) and the arterial sample (for ionised calcium) **are taken simultaneously by the bedside nurse and the calculation performed by the ICU resident, who enters the result on the daily bloods sheet**. The relevant arterial sample is identified on the critical care chart by an asterisk (entered by the nursing staff), allowing the doctor to identify the ionised calcium for the T: I calculation.

Refer to the duty consultant if citrate accumulation is suspected.

11. Citrate Accumulation: Management

If the signs of citrate accumulation accompany a rapidly increasing lactic acidosis, citrate anticoagulation should cease, and the patient switched to another form of anticoagulation. Continuing to use citrate will just make the acidosis worse.

In the absence of a rapidly worsening lactic acidosis, follow the algorithm in Figure 3, below. ('Clinically relevant citrate accumulation' refers to the 4 signs identified in section 11).

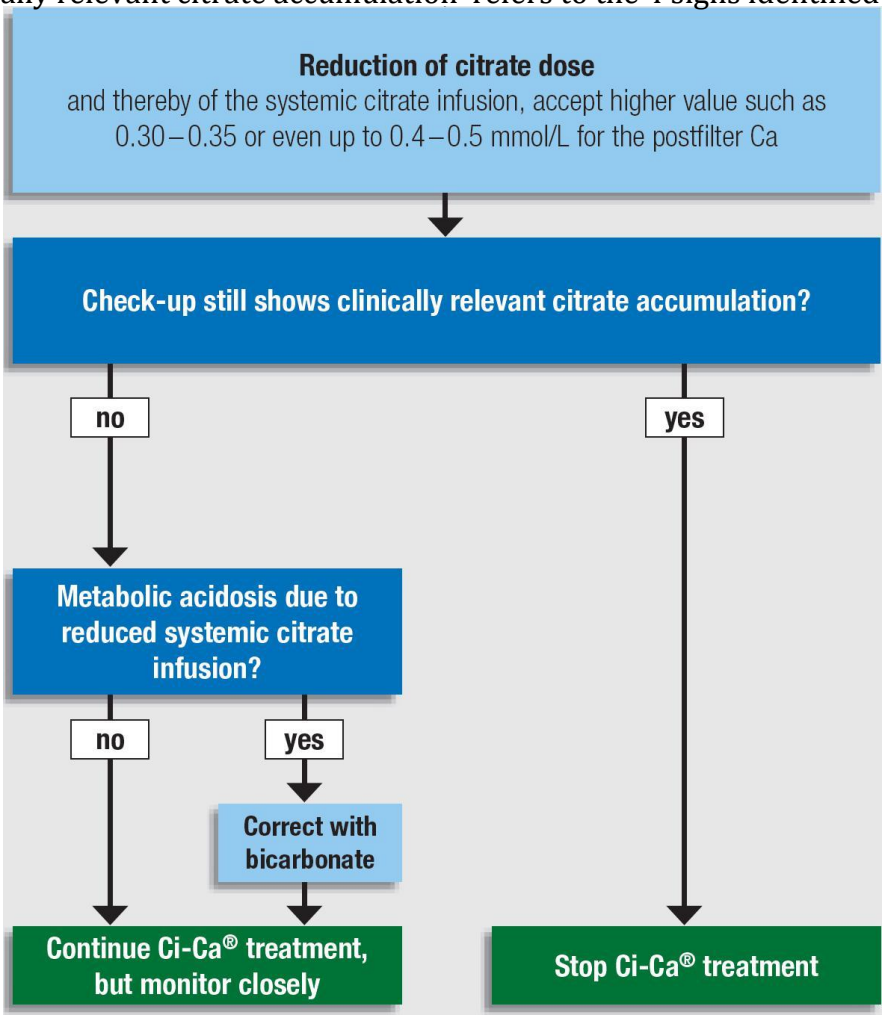


Figure 3: Algorithm for management of citrate accumulation

- Monitor the circuit (post-filter) iCa^{2+} 6 hours after reducing the citrate dose and titrate to achieve the target of 0.35-0.4mmol/L (and up to 0.5mmol/L if needed) as illustrated above. Use the adjusted infusion regime in Figure 4 for guidance of how to set the citrate infusion.
- Monitor the calcium infusion requirement and T:I calcium ratio. These should both decrease if less citrate is accumulating.
- Hypercalcaemia may develop as the citrate is slowly metabolised and the calcium from the citrate-calcium complexes is slowly released. Anticipate hypermagnesemia through the same mechanism.

Postfilter *ionised* calcium [mmol/L]	Change of the citrate dose (citrate/blood)
>0.40	Increase by 0.1 mmol/L
0.35–0.40	No change (typical target range)
0.25–0.34	Decrease by 0.1 mmol/L
0.20–0.24	Decrease by 0.2 mmol/L and inform physician

Figure 4: Adjusted citrate infusion regime for suspected citrate accumulation

- If the circuit clots early or there are no improvements in the signs of citrate accumulation, switch to another mode of anticoagulation.

12. Circuit Life and Restarting Therapy

- Once primed the circuit may be left in re-circulation mode for up to a maximum of 10 hours.
- Once connected to the patient, if the circuit is then disconnected and placed into re-circulation mode (e.g. for CT scan), the circuit must be reconnected within 4 hours.
- If you restart Ci-Ca® CVVHD within 6 hours of interruption, you can set the dialysate/blood flow rates, citrate and calcium doses as they were before disconnection unless the patient's clinical condition has changed. If this is the case, discuss with a senior ICU doctor.
- Ci-Ca® CVVHD circuits can be used for a maximum of 120 hours (**5 days**), rather than the 72 hours recommended by the manufacturer.

13. VTE Prophylaxis

- With citrate anticoagulation VTE prophylaxis is required.
- Unless contraindicated, this should be a mechanical device in addition to LMWH.

14. Documentation

The following will be recorded in the patient record:

- Blood flow
- Dialysate flow
- Venous pressure
- Arterial pressure
- Trans membrane pressure
- Ultrafiltration rate
- Calcium dose
- Citrate dose

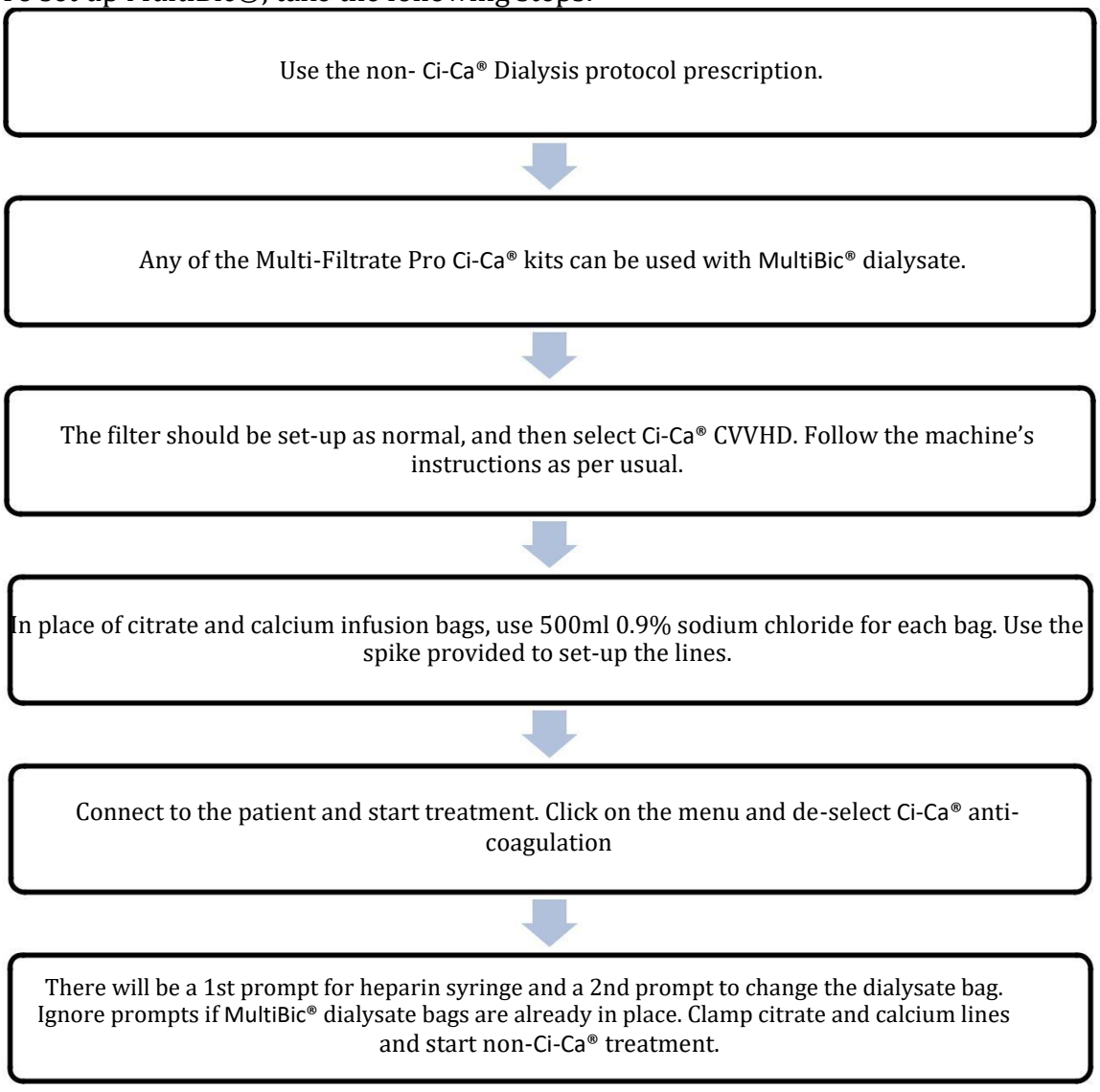
- Filter and systemic iCa^{2+} on the filtration prescription and filtration observation chart.
- The large patient observation chart should **only be used for arterial samples**.
- Fluid balance should be charted every 2 hours.
- T:I ratio on the CRRT prescription Chart.

Citrate and calcium infused into the CRRT circuit should not be added to the fluid chart as this is accounted for within the fluid balance calculated by the machine.

15. Heparin or Epoprostenol Anticoagulation and set up of MultiBic® Dialysis Fluid

- Conversion from citrate to heparin or epoprostenol anticoagulation is a consultant decision and is made off the back of citrate accumulation or other complication of citrate use.
- Heparin or epoprostenol anticoagulation can **only** be used with MultiBic® dialysis fluid. Ci-Ca® dialysis fluid must not be used as it does not contain calcium. As calcium is not infused as part of heparin or epoprostenol treatment, the patient's serum calcium will rapidly fall to life threatening levels.

To set up MultiBic®, take the following steps:



To convert from Ci-Ca® without changing the circuit:

a. When Using Heparin:

- Go to 'Treatment' screen, then 'Syringe Change'.

- Prepare the heparin infusion using the 50mL "Injectomat Spritze 50ml" syringes as neat solution of heparin (1000 units/mL). Use only 25 ml in each syringe to avoid frequently expiring syringes. These syringes are only used with the Fresenius machines and are stored with the CVVHD filters.
- Fit in the carrier and start as per the non-citrate protocol.
- Attach the heparin syringe and manually prime the line.
- Consider an IV loading dose of 5000U unless the patient has a coagulopathy (APTT >50seconds) on commencing CRRT. The integral heparin pump is used to give this bolus.
- Start the infusion according to body weight as follows:

➢ <60kg- 1ml/hour (1000U/hour)
➢ 61-80kg- 1.3ml/hour (1300U/hour)
➢ >80kg- 1.6ml/hour (1600U/hour)

- Follow infusion protocol on the filtration prescription chart.
- Check APTT ratio after **four hours** and review against the table below.
- If APTT is within target range (45-77 sec) then re-check it in **six hours** (instead of four hours) and review.
- If out of range, and after each change, wait **four hours** before the next APTT check and review against the table below.

APTT (seconds)	Infusion Rate Change
>210	Stop infusion for 60 min then REDUCE by 0.5 mL/hour (500 units/hour)
151-210	REDUCE by 0.5 mL/hour (500 units/hour)
121-150	REDUCE by 0.3 mL/hour (300 units/hour)
101-120	REDUCE by 0.2 mL/hour (200 units/hour)
78-100	REDUCE by 0.1 mL/hour (100 units/hour)
45-77	NO CHANGE
36-44	INCREASE by 0.2 mL/hour (200 units/hour)
<36	INCREASE by 0.4 mL/hour (400 units/hour)

Table 5: Decision table for heparin infusion rate according to APTT

b. When Using Epoprostenol:

- A separate syringe pump is required.
- Make up the solution to 10,000ng/ml.
- Attach syringe to the line and prime manually.
- Start the systemic infusion at 4 ng/kg/min when the following steps are complete.

- On the 'Treatment' screen choose 'Deselect Ci-Ca anticoagulation'.
- Confirm decision by selecting 'Yes' on the next screen.
- Confirm all conditions for change are fulfilled.

- All pumps will stop except the blood pump. You will be asked to change the bags-change to MultiBic® dialysis fluid. Once the change is made and accepted, the pumps will recommence.

16. Vascath selection

A) Site: In order of preference as per KDIGO guidelines 2012

1. Right Internal Jugular Vein.
2. Femoral vein.
3. Left Internal Jugular vein.
4. Subclavian vein. (Dominant side)
5. Subclavian vein. (Non-Dominant side)

B) Length:

1. Right Internal Jugular Vein.	15 cm
2. Femoral vein.	25 cm
3. Left Internal Jugular vein.	20 cm
4. Right Subclavian vein.	15-20 cm
5. Left Subclavian vein.	20 cm

C) Diameter:

CVVHD does not require large bore catheters, so 11-13 Fr is preferable over larger catheters.

5. References:

A) KDIGO guidelines; can be found at (accessed 18/11/2019)

https://kdigo.org/guidelines/acute-kidney-injury/

B) Anaesth Crit Care Pain Med 36(2017) 313-319

6. Documentation Controls

Development of Guideline:	Dr Amro Katary Dr Paul Smith Sarah Charlesworth Heather Whiteman
Consultation with:	Based upon the work by Leeds Teaching Hospitals NHS Trust and Guy's and St. Thomas' NHS Foundation Trust and the guideline produced by Plymouth NHS Trust. Thanks to Dr Andy Georgiou for sharing their protocols.
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Review Date:	April 2026
Key Contact:	Dr Amro Katary (Amro.katary@nhs.net)