Prevention and Treatment of Venous Thrombosis in COVID-19 +ve‡ adult inpatients (pregnant and non-pregnant) undergoing renal replacement therapy (RRT) on Critical Care Wards‡‡

‡ COVID-19 +ve = clinical features of COVID-19 infection and/or PCR positive for COVID-19

‡‡Includes COVID-19 +ve inpatients receiving RRT in Critical Care wards (High Dependency or Intensive Care) for Acute Kidney Injury (AKI) or Chronic Kidney Disease (CKD)

- There is significant anecdotal evidence that patients who are COVID-19 +ve are at increased risk of thrombosis, both in RRT circuit lines and systemically
- Usual anticoagulation measures during RRT, including citrate and/or boluses of LMWH, may be ineffective in this patient population
- A continuous infusion of UFH, instead of citrate and/or LMWH, may be more effective
- AntiXa measurements are required to monitor the effectiveness of unfractionated heparin (UFH) in COVID-19 +ve patients (APTTr is unreliable, likely due to the very high FVIII levels in these patients)

Recommendation

Patients who are COVID-19 +ve, and require RRT in Critical Care, should be considered for continuous IV infusions of Unfractionated Heparin (UFH)

(Some critical care areas may wish to use tinzaparin boluses during RRT, rather than switch to UFH, as per RRT protocols written pre-COVID-19 - see link) ¶

- Start the UFH IV infusion at the same time as the episode of RRT commences.
- Give an IV bolus of 5000 units# UFH and commence IV UFH infusion at 1200 units/hr *[recommended preparation: heparin sodium 20ml vial of 1000 units/ml (total concentration: 20,000 units/20ml)]*
- Measure antiXa 4 hours after start of infusion (request 'antiXa UFH' on Trakcare stating time sample taken). During RRT, target antiXa is 0.3-0.7 - refer to Table 1 overleaf for recommended dose adjustments.
- If UFH infusion rate requires adjustment during RRT, an antiXa level should be measured 4 hours after the change in infusion rate.
- APTTr monitoring should not be used at <u>any</u> time
- Do NOT give additional thromboprophylaxis with UFH or LMWH whilst this regimen is being used
- ***Specific to Continuous RRT***
  - The antiXa level must be requested urgently as this will inform dose change for ongoing RRT
  - Patients can receive regional citrate within the filter alongside systemic UFH
- ***Specific to Intermittent RRT***
  - If RRT is planned to last ≤6 hours, the antiXa level will inform the infusion rate +/- bolus for next episode of RRT.Once RRT is complete, switch UFH infusion rate to 500 units/hr and continue until next episode of RRT *(off label)*
  - AntiXa monitoring is only required to guide UFH infusion rate <u>during</u> RRT
  - Samples for antiXa monitoring <u>must</u> be taken whilst UFH infusion is running at rate for RRT
  - After the initial RRT session, subsequent boluses of UFH, prior to each RRT, should be 4000 units. If the antiXa measured during the last episode of RRT was <0.4, the bolus dose of UFH can be increased, up to a maximum of 7000 units.

¶ If using tinzaparin, and RRT lasts <8 hours, standard thromboprophylaxis should be given during the remaining 16 hours e.g. enoxaparin 20mg 6-8 hours after episode of RRT ends.

Omit bolus if patient has received prophylactic dose LMWH/UFH in the last 4 hours.

Use Table 1 to calculate change in dose of UFH for ongoing/next RRT episode

Table 1. Recommended UFH dose changes based on AntiXa levels

Modified from Normogram from University of Wisconsin, USA (available here)

AntiXa level (IU/ml)	Infusion rate change	Other recommendations
<0.1	Increase by 400 units/hr	Consider bolus 2000 Units
0.1-0.19	Increase by 200 units/hr	-
0.2-0.29	Increase by 100 units/hr	-
0.3-0.7	No change	-
0.71-0.8	Decrease by 100 units/hr	Discontinue infusion for 30 minutes
0.81-1.7	Decrease by 200 units/hr	Discontinue infusion for 1 hour
>1.7	Decrease by 300 units/hr	Discontinue infusion for 1 hour

Contraindications against use of UFH

- Platelet count ≤ 50 $x10^9$/l
- Receiving anticoagulation for another reason
- Patient considered to be at high bleeding risk e.g. recent intracranial haemorrhage, untreated inherited/acquired bleeding disorders
- Trauma with high bleeding risk
- Active bleeding
- Heparin induced thrombocytopaenia – see details in page 2
- Acute stroke (use IPC if immobile & contact stroke team for guidance)
- Within 6 hours of procedures e.g. surgery, lumbar puncture
- Acute bacterial endocarditis
- Persistent hypertension (BP ≥230/120)
- Liver failure and INR>2

Heparin Induced Thrombocytopaenia

If platelet count falls by more than 50% baseline, or there are any other indications to suggest the development of Heparin Induced Thrombocytopaenia (HIT), calculate HIT score (using this link) and discuss urgently with consultant haematologist.

Protocol for patients on RRT who experience circuit thrombosis despite the use of systemic UFH

- Take sample to measure antithrombin activity when patient on ≤ 500 units/hr UFH
  (test available Mon-Sun 8am-10pm)
  - If antithrombin <50 iu/l, consider changing systemic anticoagulation to argatroban*
  - If antithrombin >50 iu/l, increase UFH bolus dose to 7000 units and hourly infusion to 2000 units/hr. If circuit thrombosis occurs during next cycle of RRT despite this increase in UFH regimen, consider changing systemic anticoagulation to argatroban*

Use of argatroban in COVID+ve patients during RRT, without HIT

- There is some evidence that argatroban may be an effective alternative to UFH in COVID +ve patients.
- Argatroban monitoring is usually via APTTr. The APTTr is unreliable at measuring UFH levels in COVID+ve patients due to high FVIII levels. Argatroban monitoring should be less affected by high FVIII levels. However, there is minimal experience in this area.
- Evidence suggests that APTTr 1.5-3.0 correlates with argatroban levels of 0.5-2.2 ng/ml.

- Given the lack of experience in this area and to minimise the risk of bleeding and thrombosis, it is recommended that APTTr and argatroban levels should be measured to guide dosing.
- Until further evidence is obtained, the APTTr should be considered in favour of the argatroban level when adjusting infusion rates of argatroban.
- When RRT session is complete, patients should return to an UFH infusion, at a rate of 500 units/hr

Table 2 Dosing and monitoring of Argatroban

IV bolus - None **Initial Rate of infusion - 1 microgram/kg per min** **Use a 1mg/ml solution** **Measure APTTr and argatroban concentration 2 hours after start of infusion**			
APTTr and APTT	**Argatroban ng/ml**	**Infusion rate change**	**Next APTTr**
APTTr < 1.5, regardless of APTT	<0.5	Increase by 0.5 micrograms/kg/min	2 hours
APTTr 1.5 - 3.0 and APTT ≤ 100 secs	0.5-2.2	No change	2 hours*
APTTr >3.0 or APTT > 100s	>2.2	Stop infusion until the aPTTr is 1.5 - 3.0; Resume at half of the previous infusion rate	2 hours

*After 2 consecutive APTTr +/- argatroban levels within target range, no further monitoring required.
During subsequent RRT sessions, the argatroban infusion rate should be set at that which previously provided a therapeutic APTTr +/- argatroban level.
For Continuous RRT, once 2 consecutive APTTr +/- argatroban levels are within target range, APTTr and argatroban levels should be checked daily whilst CRRVF continues.

Systemic Venous Thrombosis

If a patient develops a systemic venous thrombosis during their inpatient stay it is important to establish if the thrombosis occurred prior to, or during, the patient being adequately anticoagulated with UFH. If **prior to,** then use the following anticoagulation regimens:

- Renal impairment (CrCl <30ml/min) **with** ongoing RRT
    - **The regimen of IV UFH used to treat systemic venous thrombosis is identical to that used to prevent circuit thrombosis during RRT.** Therefore IV UFH and antiXa measurements should follow the regimen described above, aiming for a target antiXa 0.3-0.7, and adjustments in infusion rates made as per Table 1.
- The first antiXa measurement should be 4 hours after the start of the UFH infusion with measurements taken 4 hours after every change in infusion rate. When no change in infusion rate is required, antiXa should be measured daily.Renal impairment (CrCl <30ml/min) but **no longer** on RRT
    - Therapeutic dose SC dalteparin and an antiXa level measured 4 hours post 3rd dose (aiming for target antiXa 0.5-1.2 [request 'AntiXa LMWH' on Trakcare]) as per GGC guideline.

If a systemic venous thrombosis occurs once a patient is established on UFH for prevention of circuit thrombosis during RRT, this suggests the patient may have problems with heparin resistance and subsequent anticoagulation management should be discussed with haematology.

NHS Greater Glasgow and Clyde

COVID-19 APPROVED GUIDANCE

OFFICIAL SENSITIVE

Note: This guidance has been fast-tracked for approval for use within NHSGGC

Covid-19 Thrombosis Prevention Critical Care and High Dependency RRT Pts

This guidance is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guidance, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following guidance, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The version of this document on the Clinical Guideline Directory is the only version that is maintained.
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