

Prevention of Venous Thrombosis in COVID-19 +ve[‡] adults (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)

Recommendation

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

Venous Thrombosis Prophylaxis

(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 any 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, taken at 4 hours after the start of the infusion, will inform the infusion rate +/- bolus for the 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 during RRT
 - Samples for antiXa monitoring must be taken whilst UFH infusion is running at rate required 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^{##}.

Note – the above UFH regimen, specific to intermittent RRT, should **NOT** be used if a patient has a systemic venous thrombosis – for this, see page 2 **Systemic Venous Thrombosis Treatment**.

[¶] If using tinzaparin, and RRT lasts < 8 hours, standard dose 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.

Systemic Venous Thrombosis Treatment

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
 - Give an IV bolus of 5000 units[#] UFH and commence IV UFH infusion at 1200 units/hr
 - Measure antiXa:
 - 4 hours after start of UFH infusion
 - 4 hours after every change in infusion rate
 - Daily, when no change in infusion rate
 - Infusion rate is adjusted as per table 1.
 - **Bolus doses of heparin are not required to start RRT if the patient is established on the above UFH infusion.**

- 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 may suggest the patient has heparin resistance and subsequent anticoagulation management should be discussed with haematology.

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 $\leq 50 \times 10^9/l$
- 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 thrombocytopenia – see details in page 2, below
- 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 $\geq 230/120$)
- Liver failure and INR>2

Complex Administration Issues

If the above administration protocols cannot be easily followed e.g. if the UFH infusion has to be repeatedly stopped for theatre, please liaise promptly with consultant haematologist for advice, to avoid over- and under- anticoagulation

Heparin Induced Thrombocytopenia

If platelet count falls by more than 50% baseline, or there are any other indications to suggest the development of Heparin Induced Thrombocytopenia (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 > 100 s	> 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 continuous RRT is being used.