Prevention of thrombosis in COVID-19 +ve‡ adult inpatients over 16 years of age (pregnant and non-pregnant) undergoing renal replacement therapy (RRT) on Critical Care Wards‡‡

‡Patients are classified as COVID-19 +ve if they have clinical features of COVID-19 infection and/or test 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 low molecular weight heparin (LMWH), may be ineffective in this patient population
- A continuous infusion of unfractionated heparin (UFH), in addition to 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)

- 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/hour *[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' – contact Haematology Labs at UHC on ext 27404 to discuss but need to record 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

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

Specific to continuous RRT (Continuous veno-venous haemodiafiltration **(CVVHDF)**)

- The prophylactic LMWH should be **suspended** whilst on the UFH infusion.
- In addition to the usual Citrate anticoagulation, UFH infusions can be administered where there is a problem with filter clotting if deemed appropriate by the treating consultant. The UFH would be in **addition** to the citrate anticoagulated circuit.
- The anti-Xa level must be requested after 4 hours as this will inform dose change for ongoing RRT.
- For periods where continuous RRT is temporarily suspended (e.g. changing of filters sets or periods of observation off filtration to determine intrinsic renal function), the UFH infusion rate should be reduced to 500 units/ hour until to provide baseline thromboprophylaxis.
- Once continuous RRT is no longer required (i.e. patient's renal function has recovered or they are transitioned to IHD) regular LMWH dosing can be re-established and UFH stopped (refer to Code of Practice for Medicines Governance – section 9b for further guidance on prescribing "off-label" medicines).

Specific to intermittent RRT (Intermittent Haemodialysis **(IHD)**)

- The prophylactic LMWH regimen should be **continued.**
- The UFH infusion will only run for the duration of RRT (usually <6hours).
- The anti-Xa level will be checked at 4 hours or at the end of the period of RRT, whichever is first. This will inform the infusion rate +/- bolus for next episode of RRT.
- AntiXa monitoring is used to guide UFH infusion rate **during** RRT.
- Samples for antiXa monitoring must be taken whilst UFH is running at a rate for RRT.
- After the initial RRT session, subsequent boluses of UFH, prior to each RRT, should be 5000units. 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 7000units.

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/hour	Consider bolus 2000 Units
0.1 - 0.19	Increase by 200 units/hour	-
0.2 - 0.29	Increase by 100 units/hour	-
0.3 - 0.7	No change	-
0.71 - 0.8	Decrease by 100 units/hour	Discontinue infusion for 30 minutes
0.81 - 1.7	Decrease by 200 units/hour	Discontinue infusion for 1 hour
>1.7	Decrease by 300 units/hour	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 below
- Acute stroke (use intermittent pneumatic compression if immobile & contact stroke team for guidance)
- Within 6 hours of procedures e.g. surgery, lumbar puncture
- Acute bacterial endocarditis
- Persistent hypertension (BP ≥230/120mmHg)
- 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.

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 measured using the regimen described above aiming for the same target antiXa 0.3-0.7, and any 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
    - Reduced therapeutic dose subcutaneous dalteparin and an antiXa level measured 4 hours post 3rd dose (aiming for a treatment target antiXa 0.5-1.2) [to arrange an antiXa level for LMWH, contact Haematology Lab at UHC on extension 27404 to discuss].
    - Refer to ADTC 75: Administration Guide Dalteparin (Fragmin®) pre-filled single dose syringes for treatment of Deep Vein thrombosis (DVT) and Pulmonary Embolism (PE) in non-pregnant adult patients > 16 years, for advice on dosing recommendations for patients with renal impairment.

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.

Adapted with kind permissions from NHS Greater Glasgow & Clyde guideline (version 7) 30 October 2020

Bibliography

1. NHS Greater Glasgow & Clyde. 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. Version 7, 30 October 2020. Available from: https://handbook.ggcmedicines.org.uk/guidelines/covid-19-coronavirus/thromboprophylaxis-in-covid-19-patients/ (accessed 15th January 2021).