Thromboprophylaxis and anticoagulation in COVID-19 patients in ICU

BACKGROUND

COVID-19 patients are considered to be at high risk of venous thromboembolism (VTE) as the disease appears to create a prothrombotic, inflammatory state.\(^1\) Increasing evidence is emerging of thrombotic related morbidity and mortality amongst critical care patients. This document outlines management of patients within 2 distinct work streams in ICU – thromboprophylaxis and those receiving renal replacement therapy.

D-DIMER

D-Dimer has been identified as a prognostic indicator. D-Dimer is not a specific marker of VTE but, certainly in non COVID patients, the higher the D-Dimer the more likely its elevation represents a thromboembolic process.

Baseline D-Dimer is to be measured in positive COVID patients who are deemed to be ICU candidates soon after admission and monitored three times a week in critically ill patients.

ENHANCED THROMBOPROPHYLAXIS

All COVID patients in ICU should be considered for “enhanced thromboprophylaxis”. This will be in addition to existing therapies e.g. pneumatic calf compression. This is tailored to platelet count and creatinine clearance.

Dosing and platelet count

<table>
<thead>
<tr>
<th>Platelets</th>
<th>Less than 50 kg</th>
<th>Platelets 30 - 50</th>
<th>Platelets &gt; 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>No thromboprophylaxis</td>
<td>Enoxaparin 20mg x 1 day</td>
<td>Enoxaparin 20mg x 2 day</td>
</tr>
<tr>
<td>100</td>
<td>No thromboprophylaxis</td>
<td>Enoxaparin 40mg x 1 day</td>
<td>Enoxaparin 40mg x 2 day</td>
</tr>
<tr>
<td>150</td>
<td>No thromboprophylaxis</td>
<td>Enoxaparin 40mg x 2 day</td>
<td>Enoxaparin 80mg x 2 day</td>
</tr>
<tr>
<td>More than 150</td>
<td>No thromboprophylaxis</td>
<td>Enoxaparin 60mg x 2 day</td>
<td>Enoxaparin 120mg x 2 day</td>
</tr>
</tbody>
</table>

Dosing and creatinine clearance

When creatinine clearance falls below 30ml/min, the above doses should be reduced by 50%

Dosing in patients with disordered baseline clotting studies

Abnormalities in coagulation screening measures, including a prolonged activated partial-thromboplastin time ratio (aPTTr), have been reported in patients with Covid-19. A prolonged aPTTr may indicate a clotting-factor deficiency or the presence of an inhibitor of coagulation.\(^2\) In these circumstances, individual risk assessment regarding enhanced thromboprophylaxis is required.
Pulmonary thromboembolism (PTE)

If there are specific signs of a PTE, then a CTPA should be considered. If this is not possible, a clinical judgement will have to be made to decide whether full intensity treatment dose anticoagulation should be started.

ASSESSMENT OF BLEEDING RISK

The document recognises that the doses considered above are unlicensed in thromboprophylaxis and patients should be monitored for adverse events. Dose reduction/treatment avoidance should be considered in the following circumstances:

- Active bleeding
- Acute bacterial endocarditis
- Major trauma
- Haemophilia and other haemorrhagic disorders
- Peptic ulcer disease
- Recent cerebral haemorrhage
- Recent surgery (notably to eye or nervous system)
- Severe hypertension

ESCALATION AND DE-ESCALATION

Escalation

Enhanced thromboprophylaxis should be considered at the earliest opportunity. For ward based patients, this would include those with rapid clinical deterioration or those receiving CPAP.

De-escalation

This higher thromboprophylactic LMWH dose should continue on transfer from ICU to ward and until the patient’s condition and mobility have improved. Standard dose thromboprophylaxis can be restarted at this point. Safety of anticoagulation should be reviewed regularly and dose adjusted, guided by bleeding symptoms, platelet count and renal function.

RENALE REPLACEMENT THERAPY

Continuous renal replacement therapy

Regional and national experience in COVID 19 has demonstrated increased frequency of clotting within renal replacement therapy (RRT) circuits.
Patients requiring continuous RRT will be fully anticoagulated with either unfractionated heparin infusion or 0.5mg/kg enoxaparin TWICE DAILY at 6am and 6pm. This may be combined with regional citrate anticoagulation.

If unfractionated heparin is being used, APTT should be used in first instance for monitoring aiming for a ratio 2-2.5.

Anti Xa levels should be considered if the recommended APTT ratio is not being achieved despite dose escalation to >25 units/kg/hr or baseline APTT is >1.5, making it difficult to monitor. Targets for Anti Xa are:

- Twice daily enoxaparin treatment dose - Anti Xa level 0.5-1 unit/ml (check 4 hours post dose at 48 hours).
- Unfractionated Heparin – Anti Xa 0.3-0.7 units/ml

**Intermittent haemodialysis**

Patients should be fully anti-coagulated with 0.5mg/kg enoxaparin TWICE DAILY at 6am and 6pm.

Additional unfractionated heparin will be given during dialysis guided by the renal nurses.

**REFERENCES**