SETTING: Trustwide: University Hospitals Bristol and Weston Foundation Trust, North Bristol NHS Trust

FOR STAFF: Clinical staff caring for patients positive for COVID-19

PATIENTS: Adult patients with COVID-19 or high clinical suspicion of COVID-19

Principles and key points

- Patients with COVID-19 are at high thrombotic risk. Assess all medical patients to identify the risk of VTE and bleeding: **As soon as possible after admission to hospital or by the time of the first consultant review.**
- If using pharmacological VTE prophylaxis for medical patients, start it as soon as possible and within 14 hours of admission. There is evidence to support survival advantage in patients who received thromboprophylaxis.
- The disease is characterised by significantly elevated inflammatory markers including D-dimers. A raised D-dimer is associated with higher mortality.
- Bleeding risk is low in the majority of COVID-19 patients.
- For paediatric patients please contact a Paediatric Haematology Consultant to discuss treatment strategies.
- In pregnancy discuss with a clinician experienced in maternal medicine and use multidisciplinary working to provide care, including the application of this guidance.

Recommendations

**Thromboprophylaxis**

**On admission:**

1. Perform and record an appropriate VTE risk assessment (including patients admitted to Emergency Department or Ambulatory Care).
2. Patients established on therapeutic anticoagulation on admission:
   - Patients who are clinically stable should remain on their pre-existing anticoagulant if platelet count remains >50 x 10^9/L.
   - Patients who are clinically unstable consider switching to treatment dose [Low Molecular Weight Heparin (LMWH)]/ Unfractionated Heparin (UFH)
3. Prescribe/administer pharmacological thromboprophylaxis according to Trust VTE guidelines. Enoxaparin is the treatment of choice for inpatient thromboprophylaxis at the BRI and NBT and Tinzaparin at Weston.
Thromboprophylaxis regimes standard of care:

If pharmacological thromboprophylaxis is contraindicated by platelet count or bleeding, consider mechanical methods (e.g. intermittent pneumatic compression) alone.

a) **Patients that are not requiring advanced respiratory support:**

Thromboprophylaxis using standard dosing should be given to all patients with platelets over 50x10⁹/L as per Trust guidelines unless contraindicated e.g. active bleeding, invasive procedure planned within 12h (longer for fondaparinux depending on procedure), prescribed and taking therapeutic anticoagulation, fibrinogen <1.0g/L. Abnormal PT/PTT alone is NOT a contraindication to prophylactic anticoagulation.

b) **Patients on advanced respiratory support (defined as any ventilatory support via an endotracheal or tracheostomy tube, or extracorporeal respiratory support)**

Consider enhanced thromboprophylaxis only in those patients with a particularly high risk of VTE (eg previous VTE within the last 3 months or previous VTE on anticoagulation, or underlying active malignancy). In this group consider using a platelet threshold of > 25x10⁹/L unless there are other contraindications (refer to MHRA CAS alert)²². Otherwise use standard dose thromboprophylaxis.

For enhanced dosing please see Appendix 2

For confirmed diagnosis of VTE, therapeutic anticoagulation can be given if platelet count > 50 x10⁹/L. In the absence of a confirmed diagnosis, a patient can be commenced on treatment dose if there is a strong suspicion of clot(s), but this should be reviewed when diagnostics have confirmed or ruled out an episode of VTE.

Therapeutic anticoagulation is not indicated in general ward or critically ill patients with COVID-19 unless there is a standard clinical indication ²².

**Ongoing management of inpatients**

- Reassess all medical, surgical and trauma patients for risk of VTE and bleeding at the point of consultant review or if their clinical condition changes.
- Pulmonary emboli are seen more frequently in COVID-19 patients than the normal population. D-dimers are unhelpful in evaluating this.
- On step down from advanced respiratory support, patients may revert to standard VTE thromboprophylaxis.

**Management of diagnosed VTE in association with COVID-19**

- Clinically stable patients should be managed according to standard treatment protocols, use of DOACs is appropriate in this patient group. Consider the possibility of potential interactions with concomitant medicines and particularly any clinical trial medicines.
- Patients who are clinically unstable should be managed with treatment doses of LMWH/UFH. AntiXa monitoring is not routinely required.
- Given the long half-life of fondaparinux, careful assessment of the risks and benefits is needed prior to starting in this patient group.
- Patients who develop evidence of VTE whilst on therapeutic anticoagulation should be discussed with Haematology.
Review of thrombosis prevention/ thromboprophylaxis on discharge

There is evidence that the thrombotic risk from COVID-19 persists post hospital discharge. There is a lack of evidence for which patients are at specific risk, and what the best treatment and treatment duration should be. Randomised controlled trials are planned to address these clinical questions. **It is recommended that any patient who is admitted to hospital with COVID-19 should be considered for post-discharge thromboprophylaxis (excluding patients who would normally be on anticoagulation who should be transitioned onto their normal anticoagulant if modifications were made during their admission).**

Consider the following patients to be at high risk of VTE post discharge:

1. Patients who were admitted to high dependency unit or ICU for management of COVID-19 at any stage of their admission or who needed advanced respiratory support.
2. Patients who were managed for symptomatic COVID-19 who have additional risk factors: e.g. previous VTE (not on long term anticoagulation), patients with active cancer, patients expected to have ongoing significantly reduced mobility, pregnant or within six weeks postpartum, prolonged admission (>3 days) for COVID-19, or a surgical procedure whilst an inpatient. **NB: The majority of patients will not need thromboprophylaxis on discharge.**

**Choice of agent and duration:**

Pregnancy or breastfeeding women prescribe at least 10 days of prophylactic LMWH (longer if indicated by existing local guidance).

Other patients could be managed with LMWH or an oral agent e.g. rivaroxaban 10mg PO OD or apixaban 2.5mg PO BD (‘off label’) (check renal function prior to prescribing). Duration will relate to risk factors e.g. reduced mobility relative to their normal state 7-14 days is suggested. **NB: The full course of anticoagulation will usually be supplied by the acute Trust at discharge and the date of discontinuation added to the discharge letter.**

**Choice of injectable anticoagulant in special groups:**

All heparins, including enoxaparin, used in the UK are derived from porcine intestine, so may be deemed unacceptable for some patients from certain religious groups and/or vegetarians/vegans. After appropriate counselling patients may accept porcine derived products if it is felt to be ‘lifesaving’ and there is no suitable alternative. Some religious leaders have suggested that because heparins are injected and not ingested and there are multiple manufacturing steps in production of the final product this may mean that they are acceptable to some.

Fondaparinux is a potential alternative to LMWH/UFH. However there are some issues that need to be considered when counselling patients especially when using in elderly and/or clinical unstable patients:

• Fondaparinux is renally excreted but has a much longer half-life compared to the low molecular weight heparins (fondaparinux t_{1/2} =17-22 hrs and maybe longer in the elderly, enoxaparin t_{1/2} =4-7hrs).
• There is no reversal agent for fondaparinux. Although enoxaparin has no specific reversal agent it is partially reversed with protamine and has a shorter t_{1/2})
• There is less experience with longer term fondaparinux use.
• There is no guidance on intermediate dose equivalent or prophylactic weight adjusted dosing.
Appendix 1:

Managing bleeding risk - transfusion support:

a) Management of clinically relevant non-major bleeding or high bleeding risk invasive procedure:
   i. Aim for platelets >50 x10^9/L (usually one adult therapeutic dose of platelets)
   ii. Aim for fibrinogen >1.5 g/L (usually two 5 unit pools of cryoprecipitate).

b) Major haemorrhage is very rare in COVID-19 and less common than VTE. If it occurs maintain:
   i. Platelets >75 x10^9/L,
   ii. Fibrinogen >1.5 -2.0 g/L (cryoprecipitate)
   iii. PT/APTT <1.5 x normal (FFP).

c) Non-bleeding patients who do not need an invasive procedure should not be transfused blood products to correct clotting parameters.

d) In DIC, avoid PCC, rVIIa, and tranexamic acid (increased thrombotic risk).
Appendix 2:

a) Enhanced Low Molecular Weight Heparin (LMWH) or Unfractionated Heparin (UFH) Prophylactic dosing NBT and UHB:

Enhanced LMWH or UFH dosing for severe COVID-19 patients on advanced respiratory support (defined as any ventilatory support via an endotracheal or tracheostomy tube or extracorporeal respiratory support) ¹

¹ The doses in the table and text below are ‘off-label’.

<table>
<thead>
<tr>
<th>Weight</th>
<th>CrCl ≥15ml/min Enoxaparin</th>
<th>CrCl&lt;15ml/min Unfractionated Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 50kg</td>
<td>Enoxaparin 20mg SC BD</td>
<td>Heparin 2,500 Units SC BD</td>
</tr>
<tr>
<td>50-100kg</td>
<td>Enoxaparin 40mg SC BD</td>
<td>Heparin 5,000 Units SC BD</td>
</tr>
<tr>
<td>&gt;100kg</td>
<td>Enoxaparin 60mg SC BD</td>
<td>Heparin 5,000 Units SC TDS</td>
</tr>
</tbody>
</table>

b) Enhanced Low Molecular Weight Heparin (LMWH) or Unfractionated Heparin (UFH) Prophylactic dosing Weston General Hospital:

Enhanced LMWH or UFH dosing for severe COVID-19 / Patients on advanced respiratory support (defined as any ventilatory support via an endotracheal or tracheostomy tube, or extracorporeal respiratory support) ¹

<table>
<thead>
<tr>
<th>Weight</th>
<th>CrCl ≥15ml/min Tinzaparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 50kg</td>
<td>Tinzaparin 2,500 units SC BD</td>
</tr>
<tr>
<td>50-90kg</td>
<td>Tinzaparin 3,500 units SC BD</td>
</tr>
<tr>
<td>91-120kg</td>
<td>Tinzaparin 4,500 units SC BD</td>
</tr>
<tr>
<td>&gt;120kg</td>
<td>May benefit from 50 units/kg up to a maximum of 9000 units SC BD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>CrCl &lt;15ml/min Unfractionated Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 50kg</td>
<td>Heparin 2,500 units SC BD</td>
</tr>
<tr>
<td>50-100kg</td>
<td>Heparin 5,000 units SC BD</td>
</tr>
<tr>
<td>&gt;100kg</td>
<td>Heparin 5000 units SC TDS</td>
</tr>
</tbody>
</table>

If patient is on haemodialysis or ultrafiltration with a creatinine clearance of <30 ml/min consider using anti-factor Xa measurement to assess the therapeutic effect of LMWH. Using a Creatinine clearance calculator (https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation) is advised in preference to eGFR at extremes of body weight:
APPENDIX 3: References

4. The DIC score is of prognostic value in COVID-19 pneumonia. BSH Haemostasis and thrombosis Task Force 18.3.20.
22. MHRA CAS alert 23-Dec-2020 Therapeutic Anticoagulation (Heparin) in the management of severe COVID-19 patients CAS-ViewAlert (mhra.gov.uk)
## APPENDIX 4: Authors

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| RELATED DOCUMENTS AND PAGES | VTE risk assessment  
Intranet VTE hub: http://sharepoint/QICA/Pages/Sites/VTE/VTEMain.aspx  
COVID-19 related clinical guidance  
https://link.nbt.nhs.uk/Interact/Pages/Section/Default.aspx?Section=5240  
BNSSG Formulary Covid related prescribing guidance: remedy pathway (bnssgccg.nhs.uk) |
| --- | --- |
| AUTHORISING BODY | Approval: CRG; Silver Command; circulated to Trust Thrombosis Committee members  
APMOC committee |
| SAFETY | Based upon emerging evidence and international expert opinion  
Adapted from original document developed jointly with UHB (Drs Bradbury & Clarke) |
| QUERIES AND CONTACT | VTE lead for clinical area  
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