Prevention of Venous Thromboembolism (VTE) and Anticoagulation in patients with Symptomatic COVID-19

May 2020.

Summary of advice:

- Use existing trust guidelines for prophylaxis for VTE. Consider increased dose for intermediate risk, using the doses outlined below.
- Use existing trust guidelines for treatment of diagnosed VTE. In the case of clinical suspicion of VTE without confirmation, use treatment dose LMWH. Consider twice daily dosing following risk assessment (including bleeding risk).

Introduction:

- Patients with severe COVID-19 infection and signs of coagulation activation (including d-dimers >6 times the upper limit of normal (>3.0) have an increased risk of mortality (lower in those receiving LMWH prophylaxis)\(^1\).
- There are concerns that patients with COVID-19 are at high risk of VTE\(^2,3\); it has been reported that 25-30% of COVID-19 critical care patients are diagnosed with VTE events despite usual thromboprophylaxis.
- The following guidance contains pragmatic recommendations for VTE prophylaxis and therapeutic anticoagulation for patients admitted with suspected COVID-19 infection – including at discharge.
- It must be noted that currently there is no evidence that giving higher doses of LMWH reduces risk of VTE and improves outcomes – care should be taken to assess patients’ bleeding risk where considering intermediate dose LMWH (see below).

Recommendations:

- **VTE Risk Assessment**: Undertake for each patient when admitted, documenting thrombosis and bleeding risk factors.

- **Standard dose prophylactic LMWH**: commence in all patients admitted with suspected COVID-19 infection. Use Antiembolic Stockings (AES) if LMWH contraindicated. See Discharge below for further information.

- **Intermediate dose prophylactic LMWH**: can be considered in patients in critical care who may benefit less from standard dose prophylaxis (eg those with Sepsis Induced Coagulopathy &/or high d-dimers or those requiring vasopressors). Once started on twice daily LMWH, continue until discharge (from hospital) unless bleeding concerns/clinically appropriate to reduce
  - Reduce to Standard Dose prophylactic LMWH when medically fit for discharge. See discharge below.

- **Therapeutic LMWH**:
  - Patients in whom there is concern regarding an acute VTE event/who have been diagnosed with an acute VTE event (investigate accordingly wherever feasible).
  - Patients admitted on warfarin anticoagulation – switch to therapeutic dose LMWH (see table below).
  - Patients in whom there is a new indication for anticoagulation (eg. AF)
  - Patients admitted on DOAC for previous VTE – switch to therapeutic dose LMWH; AF patients can continue DOAC if considered appropriate.
• **Discharge (from hospital):**  
  o Therapeutic anticoagulation: if on LMWH, switch to oral anticoagulation; unless contraindicated, choose a DOAC rather than warfarin (any concerns discuss with haematology)  
  o **Prophylaxis of VTE** – consider discharge with prophylactic anticoagulation* if considered at high risk of VTE  
    ▪ eg. past history VTE, strong family history VTE, cancer, active inflammatory disease (eg inflammatory bowel disease or arthritis), significantly reduced mobility, obesity.

NOTES

• For Pregnancy, see separate Guidance.

• For patients already prescribed medicines which increase bleeding risk (e.g. dual anti-platelet therapy), consider these before prescribing and seek specialist advice, where appropriate.

• **Thrombocytopenia.**  
  o Platelets <30 – stop LMWH and use Antiembolic stockings/IPC as appropriate  
  o Platelets 30-50 – Can give prophylactic or intermediate prophylactic dose LMWH unless bleeding concerns-do not give full therapeutic dose (discuss with haematology if concern)  
  o Platelets >50 – give LMWH as per clinical situation – no requirement to dose reduce unless bleeding concerns.

  NB if new fall in platelet count whilst on LMWH – consider Heparin Induced Thrombocytopenia; discuss with haematology.

• **Coagulopathy.**  
  o Prolonged PT and APTT of up to 5 seconds is relatively common in Covid-19 infection; continue with LMWH unless bleeding concerns. If significant coagulopathy discuss with haematology

• *Thromboprophylaxis at Discharge (from hospital):*  
  o Rivaroxaban 10mg once daily OR Dalteparin 5000units once daily for 30 days (reduced to 2500units, where appropriate – see below) after discharge only if considered at high risk VTE and no bleeding concerns.  
  o Please provide 30 day supply at discharge. If providing Dalteparin, please teach patient or carer to self-administer wherever feasible.

<table>
<thead>
<tr>
<th>Standard dose Dalteparin Thromboprophylaxis</th>
<th>eGFR ≥20 ml/min/1.73m²</th>
<th>eGFR &lt;20 ml/min/1.73m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45kg</td>
<td>2500units once daily</td>
<td>2500units once daily</td>
</tr>
<tr>
<td>45-99kg</td>
<td>5000units once daily</td>
<td></td>
</tr>
<tr>
<td>100-149kg</td>
<td>7500units once daily</td>
<td></td>
</tr>
<tr>
<td>Greater than 150kg</td>
<td>5000units twice daily</td>
<td></td>
</tr>
</tbody>
</table>

**Intermediate dose Dalteparin Thromboprophylaxis (patients who are on/ have been on critical care)**

<table>
<thead>
<tr>
<th>Weight</th>
<th>eGFR ≥20 ml/min/1.73m²</th>
<th>eGFR &lt;20 ml/min/1.73m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45kg</td>
<td>2500units twice daily</td>
<td>2500units once daily*</td>
</tr>
<tr>
<td>45-99kg</td>
<td>5000units twice daily</td>
<td>2500units twice daily*</td>
</tr>
<tr>
<td>100-149kg</td>
<td>7500units twice daily</td>
<td>2500units twice daily*</td>
</tr>
<tr>
<td>Greater than 150kg</td>
<td>10,000units twice daily</td>
<td></td>
</tr>
</tbody>
</table>

*Peak anti-Xa levels should be measured on day 3 of LMWH to ensure therapeutic anticoagulation. Samples should be taken 3-4 hours after administration. Intermediate dose levels should be below 1.0 for once daily dosing and below 0.5 for twice daily dosing.
### Therapeutic dose Dalteparin

<table>
<thead>
<tr>
<th>Weight</th>
<th>Cr Cl &gt;= 30mL/min</th>
<th>Cr Cl 20-30mL/min*</th>
<th>Twice daily dosing in CrCl &gt;30mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45kg</td>
<td>7,500units once daily</td>
<td>7500units once daily*</td>
<td>5000units am, 2500units pm</td>
</tr>
<tr>
<td>45-56</td>
<td>10,000units once daily</td>
<td>10,000units once daily*</td>
<td>7500units am, 5000units pm</td>
</tr>
<tr>
<td>57-68</td>
<td>12,500units once daily</td>
<td>10,000units once daily*</td>
<td>7,500units twice daily</td>
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<tr>
<td>69-82</td>
<td>15,000units once daily</td>
<td>12,500units once daily*</td>
<td>5000units am, 2500units pm</td>
</tr>
<tr>
<td>83-100</td>
<td>18,000units once daily</td>
<td>15,000units once daily*</td>
<td>10,000units am, 7500units pm</td>
</tr>
<tr>
<td>101-115</td>
<td>10,000units twice daily*</td>
<td>18,000units once daily*</td>
<td>10,000units twice daily*</td>
</tr>
<tr>
<td>116-140</td>
<td>12,500units twice daily*</td>
<td>10,000units twice daily*</td>
<td>12,500units twice daily*</td>
</tr>
<tr>
<td>&gt;140kg</td>
<td>15,000units twice daily*</td>
<td>12,500units twice daily*</td>
<td>15,000units twice daily*</td>
</tr>
</tbody>
</table>

*Peak anti-Xa levels should be measured on day 3 of LMWH to ensure therapeutic anticoagulation. Samples should be taken 3–4 hours after administration. Therapeutic levels are between 1.0 and 2.0 for once daily dosing and between 0.5 and 1.0 for twice daily dosing.

Twice daily dosing of Dalteparin 100units/kg bd may be preferred in critical care and patients who may require procedures/ those at higher risk of bleeding.

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4. Alex Spyropoulos et al. Modified IMPROVE VTE risk score and elevated d-dimer identify a high venous thromboembolism risk in acutely ill medical population for extended thromboprophylaxis. TH Open 2020:4:e59-e65

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