

# Clinical guide for the prevention, detection and management of thromboembolic disease in patients with COVID-19

## Background

- Several studies have demonstrated coagulation changes in patients with COVID-19, especially in those with severe disease, and this is associated with a worse prognosis.
- Emerging data, alongside recent clinical experience, have suggested a high prevalence of venous thromboembolism (VTE) in patients with COVID-19.
- Disseminated intravascular coagulation (DIC) is a late disease event in COVID-19 infection, is associated with multiple organ failure and should be treated as per standard guidance.
- This document provides guidance on the prevention, diagnosis and management of VTE in patients with COVID-19 who are seen in hospital.
- The effectiveness of most interventions in the context of COVID-19 is currently uncertain. This guide is informed by emerging information about COVID-19 management as well as best available evidence from non-COVID-19 patients. It will be updated when further evidence is available.
- COVID-19 related clinical trials are important to the rapid development of an evidence base for this new disease and should be supported. The list of prioritised trials for COVID-19 is available on the [National Institute for Health Research website](#).

## Prevention

### Emergency department (ED) and ambulatory care

- Inflammatory parameters typically have increased levels in COVID-19 patients and these patients may also have reduced mobility, putting them at risk of VTE.
- Thromboprophylaxis should be considered in ambulatory COVID-19 patients and they should have a clinical risk assessment according to local protocols.
- D-dimer level (range or rate of increase) cannot be used to predict VTE risk.
- A baseline chest X-ray (CXR) should be undertaken in patients with respiratory symptoms associated with COVID-19 infection. If a pulmonary embolism is suspected as part of the clinical picture, a CT pulmonary angiogram (CTPA) should be considered. This decision should not be based on a D-dimer.

## Ward based care

Ward based care (level 1) is defined as those patients who do not require mechanical organ support.

- A VTE risk assessment should be completed for all patients admitted to hospital as per local hospital policy and national guidance.
- Standard prophylactic dose low molecular weight heparin (LMWH) is recommended for COVID-19 patients requiring ward-based care.
- Patients already on anticoagulation with a vitamin K antagonist or direct oral anticoagulant (DOAC) can either continue with current anticoagulation or switch to LMWH.
- Thromboprophylaxis should be continued for the length of inpatient stay.
- D-dimer levels alone should not be used to guide LMWH dosing.
- Patients with additional risk factors for VTE (for example, active inflammatory disease, malignancy, comorbidities including haemoglobinopathies, past or current history of VTE) may require a higher dose of thromboprophylaxis.

## High dependency unit (HDU) and critical care

HDU and critical care includes level 2 and level 3 care and is defined as those patients requiring one or more organ support.

- A VTE risk assessment should be completed for all patients admitted to HDU/critical care.
- According to the Department of Health and Social Care VTE risk assessment tool, all patients admitted to critical care are considered at high risk of VTE.
- Higher doses of LMWH are suggested as patients with severe COVID-19 appear to have an increased incidence of VTE. These should be balanced with the individual patient's bleeding risk. An intermediate dose of LMWH – increasing prophylactic dosing to twice daily or a larger dose once daily – should be considered.
- Dosing should take into consideration weight, renal function, platelet count and coagulation screen.
- These parameters require regular monitoring throughout the patient's admission.

## Acute kidney injury requiring renal replacement therapy (RRT) may occur with severe COVID-19

- A prothrombotic state has been observed in COVID-19 patients.
- Clot formation within filter circuits, even with regional anticoagulation, is a frequent problem.
- Treatment dose low molecular weight heparin may be required in addition to regional anticoagulation for these patients to increase the life of the circuit.
- LMWH is preferred to unfractionated heparin due to ease of use and more reliable pharmacokinetics.
- Patients who recover sufficient renal function not to require further renal support must receive intermediate dose LMWH, adjusted to their renal function.
- Regular monitoring of the full blood count, coagulation screen, creatinine clearance and estimated glomerular filtration rate (eGFR) is advised to guide dosing.

- Anti-Xa measurements can be undertaken if there is concern about renal function, weight and platelets/coagulation.
- Anti-Xa levels may be preferable in sites using unfractionated heparin, as APTT ratios are affected by increased factor VIII and fibrinogen levels.
- Routine Anti-Xa measurements are not required for thromboprophylaxis or treatment.
- For patients stepped down from level 2/3 care to level 1 care who are on an intermediate dose prophylaxis, consider reducing to standard thromboprophylactic LMWH.

### Thromboprophylaxis on discharge from hospital of COVID-19 patients

- There is currently no specific evidence on the use of thromboprophylaxis following discharge from hospital following COVID-19 infection.
- Extended thromboprophylaxis may be considered on discharge in those patients who are high risk, including those with a critical care admission and reduced pre-admission mobility. 14 to 28 days of thromboprophylaxis with LMWH may be considered in such patients.

### Suggested approach to thromboprophylaxis in patients with COVID-19

Setting	Recommendation
ED/ambulatory care – patient to be discharged	Standard thromboprophylaxis dose LMWH (appropriate for weight/renal function – as per local policy) may be considered depending on risk assessment (RA).
Ward based (level 1 care)	Standard thromboprophylaxis dose LMWH (appropriate for weight/renal function – as per local policy); consider increased dose for patients who have two or more non-COVID-19 VTE risk factors.
High dependency/critical care (level 2/3 care)	Intermediate dose LMWH (appropriate for weight/renal function – as per local policy). Once daily or twice daily dosing.
Renal replacement therapy (RRT)	If there are concerns regarding filters clotting frequently consider treatment dose LMWH or UFH as per hospital policy.
Step down to ward from intensive care unit/HDU	Consider standard thromboprophylaxis dose LMWH (appropriate for weight/renal function – as per local policy).
Discharge from hospital	Thromboprophylaxis may be relevant: RA.

## Diagnosis of VTEs

- Early data suggest a high incidence of VTE (deep vein thrombosis (DVT)/pulmonary embolism (PE)) in patients with COVID-19.
- Imaging studies may be difficult to perform because of illness severity and infection control measures.
- **Clinical suspicion of DVT:** doppler ultrasound is recommended as normal.
- **Sudden deterioration and increasing oxygen requirement:** PE should be considered. Confirmation should be made, if possible, by CTPA.
- If a CTPA is indicated but not possible for medical reasons, please discuss with radiology/nuclear medicine if a scintigraphic perfusion or V/Q lung scan can be performed.
- Where clinical suspicion is high and confirmatory imaging is not possible, therapeutic anticoagulation should be considered, with close assessment of bleeding risk and confirmation of diagnosis when feasible.
- Echocardiography is recognised as a useful modality in the diagnosis of pulmonary embolism. However, it appears this may be of limited utility in the diagnosis of PE in COVID-19 given the frequent right ventricular (RV) dysfunction that is seen as part of the underlying condition in severe cases. However, when RV dysfunction is severe, the diagnosis of PE is important to consider.
- A perfusion-only single photon emission computerised tomography (SPECT) associated with low-dose CT of the chest, omitting the ventilation component, could be a safe option while preserving the diagnostic quality of the scan and avoiding unnecessary risk related to aerosolisation and possible viral spread.
- Perfusion-only SPECT low-dose CT is appropriate in all patients with suspicion of acute pulmonary embolism, including also patients with dyspnoea of equivocal nature, PE – and/or COVID-19 pneumonia-related. The low-dose CT component increases the diagnostic accuracy of the test, as perfusion defects can be correlated with parenchymal abnormalities on the CT found in COVID-19 infection.
- In pregnant women, for radiation dose reduction, a perfusion-only SPECT without CT remains a diagnostic option. However, in certain cases, if the pregnant woman has associated risk factors (such as cardiovascular disease, asthma, etc) and falls in the clinical vulnerable group for COVID-19 infection, a perfusion-only SPECT with low-dose CT may be still considered.
- Lung perfusion scan using [99mTc]-MAA is a safe procedure and should be considered if CTPA is contraindicated. Furthermore, SPECT-CT perfusion imaging may emerge as a significant imaging modality for the management of patients with COVID-19 illness.

## Treatment of VTEs

### Confirmed VTE

- Patients with confirmed VTE should commence treatment dose LMWH, dosed appropriately for weight and renal function.
- Treatment should be for a minimum duration of three months. Longer durations may be required based on clinical assessment.
- DOACs can be considered if patients are sufficiently well to take oral medication or may be switched to a DOAC as their condition improves, if no invasive procedures are anticipated and they are not on interacting medications.

### Role of thrombolysis

- Patients with intermediate and high-risk confirmed PE and signs of haemodynamic instability may be suitable for intravenous thrombolysis. There is limited experience of the role of this in patients with COVID-19.
- If using systemic thrombolysis, a 50% dose reduction can be considered based on standard systemic doses and repeated, if necessary, for patients *in extremis* or who have a large clot burden as per standard thrombolysis protocols.
- Catheter directed thrombolysis, if available, may be utilised.

### Discharge and follow up

- Patients with confirmed DVT should be followed up according to local protocol.
- Patients with confirmed PE may be considered for multidisciplinary follow up, based on initial clinical findings and investigations. Those patients with intermediate and high-risk PE may require a repeat echocardiogram and lung function tests.

### Other considerations

There is currently no proven role for antiplatelet agents in the prevention or treatment of COVID-19 related thromboembolic disease.

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