



Venous Thromboprophylaxis in ICU patients with COVID-19

Introduction

Most ICU patients are at risk of developing venous thromboembolism (VTE). Emerging data suggest that there is an increased prevalence of thromboembolic events in COVID-19 especially in patients with more severe disease.

Incidence

The incidence of VTE in COVID-19 infection is not well established. COVID-19 infection is associated with severe inflammation, platelet dysfunction, DIC, hypoxaemia and immobility that may all predispose to the development of thromboembolic complications. Abnormalities in coagulation appear to be common and are associated with poorer outcomes. In a study of 183 patients with COVID-19 pneumonia, Tang et al observed prolonged PT and APTT as well as higher D-Dimers in non-survivors compared with survivors.

In a retrospective study, the incidence of VTE in 81 patients admitted to an ICU in Wuhan, China with severe COVID-19 infections was 25%. DVT correlated with disease severity and DIC with the strongest correlation with D-dimer. D-dimer of $> 1.5\mu\text{g/ml}$ had a sensitivity of 85% and a specificity of 89% to predict DVT.

In another study of 184 patients with severe COVID-19 from three academic medical centres in The Netherlands, the authors reported an incidence of 27% patients with confirmed VTE despite most patients receiving standard doses of thromboprophylaxis. Age and coagulopathy (PT > 3 s and APTT > 5 s) were independent predictors of a thrombotic event.

Diagnosis of PE

Given the apparent increased incidence of VTE in COVID-19, clinicians should suspect VTE if sudden worsening of hypoxaemia or tachycardia occurs or if clinical signs suggestive of DVT develop.

Diagnosing VTE may be more complex in patients with COVID-19 due to the clinical state of the patient, making movement to the radiology department difficult i.e ventilator-dependent with high oxygen requirements.

Ultrasound of the lower limbs may be used as point-of-care testing. Similarly, echocardiography with signs of increasing right ventricular dilatation may be suggestive of pulmonary embolism

Risk assessment and anticoagulant dosing

In a retrospective analysis by Tang et al involving 449 patients with severe COVID-19, only 22% received prophylactic LMWH heparin for 7 days or longer. D-dimer and PT correlated with mortality. Survival was higher in patients receiving prophylactic dose of LMWH who had D-Dimers > 3 mcg/ml or Sepsis-Induced Coagulopathy (SIC) score ≥ 4 .

All critically ill patients should receive prophylactic anticoagulation with LMWH (suggested over unfractionated heparin to reduce contact) unless risk of bleeding is judged higher than thrombosis. Local guidelines and dosing as in ICU management protocol 2019 may be used.

When to initiate therapeutic anticoagulation has not been fully elucidated due to a lack of high quality data on safety and efficacy. There is currently no evidence that increasing the dose of LMWH thromboprophylaxis improves clinical outcomes or reduces the risk of VTE.

It may be reasonable to consider higher doses of LMWH in high risk patients i.e. D-dimer levels (>1.5mcg/ml). This decision should be considered on a case-to-case basis considering both the risk of thrombosis and bleeding

Possible approach to LMWH dosing

	CrCL > 30ml/min	CrCL < 30ml/min
Standard Risk Patient ¹	S/C Enoxaparin 40mg q24h	UFH 5000U q8H or q12H
High Risk Patient ² D dimer >1.5mcg/ml	S/C Enoxaparin 40mg q12H (weight <100kg) ³	No clear data on choice or dose

¹Higher dose to be considered in obese patients as per local guidelines

²To be considered on a case to case basis considering both risk of thrombosis and bleeding

³In patients > 100kg, higher doses may be required⁸

Other considerations:

In patients where anticoagulation is contraindicated, use mechanical thromboprophylaxis e.g. intermittent pneumatic compressor (IPC).

Prophylactic doses of anticoagulant may be considered with platelets of >30, 000 and therapeutic anticoagulant may be considered with platelets >50000.

Minor prolongations of PT and APTT (up to 5 seconds) are common in COVID-19 and are not absolute contraindications to thromboprophylaxis.

Consider extended anticoagulation with LMWH or DOAC up to 45 days after discharge in high risk patients with reduced mobility and at low risk of bleeding.

Disclaimer: The evidence on the use of anticoagulation in patients with COVID-19 is not well established as this is an evolving disease. It remains the responsibility of the readers to keep abreast on new developments.

References:

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