COVID-19 DOCUMENT

Coagulopathy in COVID-19: Recommendations for Laboratory Testing and Thromboprophylaxis

CATEGORY:	Guideline
CLASSIFICATION:	Clinical
PURPOSE	This document outlines the guidelines for thromboprophylaxis and laboratory testing of COVID-19 patients at University Hospital Birmingham NHS trust
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Distribution: • **Essential Reading for:** • **Information for:**	 All healthcare professionals providing patient-facing care Wards Managers, Senior Nurses, Divisional Directors of Nursing, Divisional Directors

Thromboprophylaxis Recommendations

Background

Thrombosis is a recognised complication of acute infectious / inflammatory disorders as a result of both immobility through illness and changes in vascular biology and haemostasis promoting thrombosis. Both venous and arterial thrombosis are a common complication of COVID-19 infection.

The pathology of thrombosis in COVID is a combination of traditional thromboembolism and in situ microthrombosis. Thrombotic events may contribute to a poorer outcome in such individuals. It is possible that LMWH has disease modifying properties in patients not requiring invasive ventilation, with current trials suggesting a small reduction in the need for organ support when given at therapeutic doses to non ICU patients although this does slightly increase major bleeding.

When treating COVID-19 patients, early VTE risk factor identification and thromboprophylaxis is essential, as well as high vigilance and prompt treatment of all VTE complications (such as pulmonary embolus).

This revision of the guideline incorporates some of the NICE guidance after critical appraisal of the emerging evidence base. This guidance should be used for all Adult (non-pregnant) patients at UHBFT.

Summary

1. Venous Thrombo-Embolism (VTE) is a recognised complication of COVID-19 infection.
2. The use of at least prophylactic LMWH in all patients admitted to hospital with COVID 19 coagulopathy is recommended unless contraindicated.
3. Escalation to therapeutic LMWH anticoagulation is an option for patients not requiring invasive ventilation on ICU.

Thromboprophylaxis Flowchart

1. Risk assess all patients in the usual manner
    - Thrombotic risk for COVID-19 patients is usually high regardless of mobility – but multiple risks may change the management strategy with consideration of continuing prophylactic Enoxaparin post discharge for up to seven days (eg history of VTE, significant ongoing reduced mobility, obesity, multiple co-morbidities)
    - Assess bleeding risk against usual criteria (accepting that lower platelet counts are tolerated)

ADDITIONAL THROMBOTIC RISKS

- Mobility reduced for ≥ 3 days
- Active Cancer
- Previous VTE disease
- Dehydration
- Metabolic / endocrine pathologies
- Known thrombophilia

BLEEDING RISK / EXCLUSIONS

- Any contraindication to LMWH*
- Evidence of active bleeding including from lungs/respiratory tract or gastrointestinal tract
- Platelet count <30 x10^9/L
- Recent stroke in preceding 4 weeks

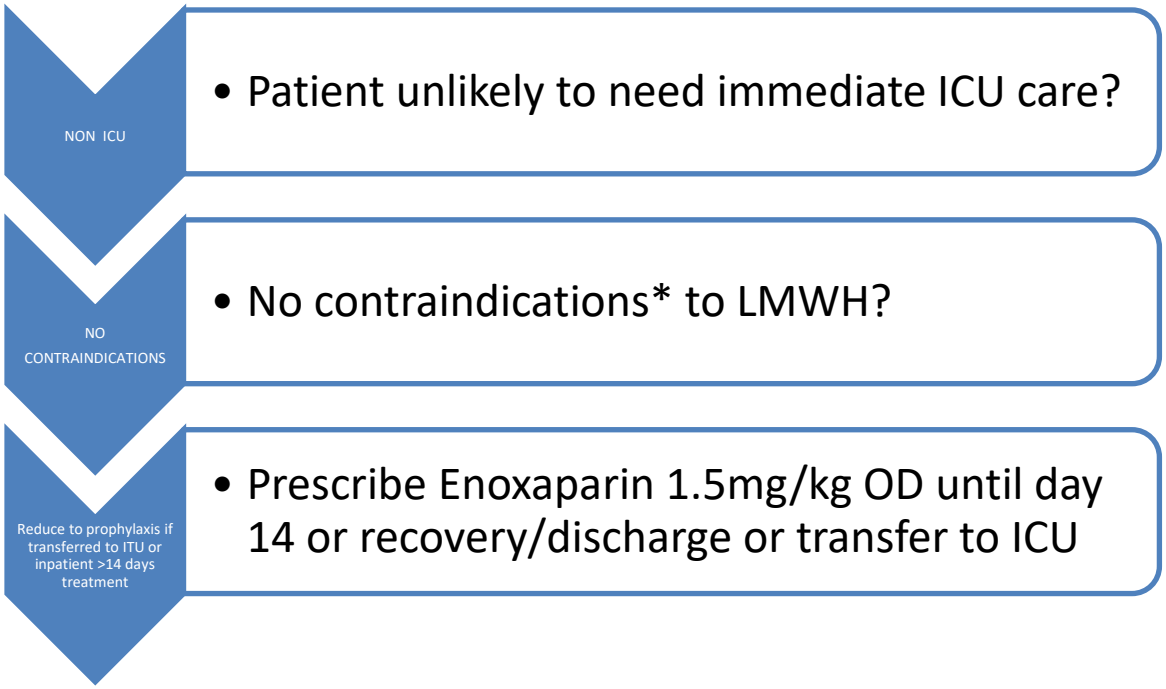
*Conditions include: acute bacterial endocarditis, epidural anaesthesia, haemophilia or other significant haemorrhagic disorders, peptic ulcer, recent cerebral haemorrhage, recent surgery to eye, recent surgery to nervous system, spinal anaesthesia, history of heparin-induced thrombocytopenia, acute major head trauma.

2. If patient is already on full oral anticoagulation, maintain this during admission. Consider switching to therapeutic LMWH if needed, especially if invasive procedures anticipated.

3. If no strict contraindications give VTE prophylaxis according to the table beneath:

Prophylactic Enoxaparin dosing for patients with COVID		
Body weight	Creatinine clearance	Enoxaparin dose
50-110 kg	>30 ml/min	40 mg once daily
<50 kg weight **or** creatinine clearance: <30 ml/min*		20 mg once daily
Patients >110 kg		40 mg twice daily
*Note: eGFR can be used for patients with normal body muscle mass		

4. For patients admitted to the ward, not requiring invasive respiratory support, CONSIDER escalating to a therapeutic dose of Enoxaparin



Contraindications/exclusions for therapeutic LMWH in non ICU patients with COVID:

- known bleeding within the last 30 days requiring emergency department presentation or hospitalisation
- known history of an inherited or active acquired bleeding disorder
- known history of heparin induced thrombocytopenia
- recent ischaemic stroke
- Platelet count < 50x 10^9/L
- Haemoglobin < 80 g/L
- Severe renal impairment (eGFR <30 mL/min)
- Severe liver disease
- Pregnancy (excluded from trial)
  - Patient on antiplatelet therapy

5. For immobile patients on ITU with contraindications to LMWH, consider Intermittent Pneumatic Compression (flotrons®)

Coagulation Screening Recommendations

Summary

There is currently insufficient evidence that D dimer should be used to modify LMWH dosing. The D dimer is usually raised in patients with COVID and therefore is not a reliable way of identifying COVID patients with acute venous thrombosis. DIC is rarely seen other than in end stage disease.

Recommendations[1-5]:

1. Full coagulation screening in COVID19 infected inpatients can be done on admission and then repeated if admitted to critical care; however this is not mandatory as there is limited clinical utility. Routine repeat coagulation screens are NOT recommended
    - FBC
    - PT (INR) and APTT
    - Fibrinogen
    - D dimer

2. Prophylactic LMWH (adjusted for weight and renal function – see above) should be given to all patients with COVID19 unless there is a clear contraindication, active bleeding, a platelet count <30 x 10^9/L or fibrinogen <0.5 g/L
    - A prolonged INR or APTT is not in itself a contraindication to LMWH
    - For immobile patients on ITU with contraindications to LMWH, consider IPC (flotrons)

3. Do not give plasma products or platelets based on abnormal coagulation tests unless there is active bleeding

Appendix B: Evidence for thromboprophylaxis

Use of intermediate dose LMWH (eg. 1mg/kg Enoxaparin INSPIRATION trial) in patients on ICU has not been shown to give better outcomes than standard prophylaxis. While further trials are awaited (eg. REMAP-CAP sub-study) UHB will revert to standard prophylactic doses of Enoxaparin for patients on ICU

In an open-label, adaptive, multiplatform, controlled trial, patients who were hospitalised with Covid-19 and who were not critically ill (which was defined as an absence of critical care–level organ support at enrollment) were randomised to receive pragmatically defined regimens of either therapeutic-dose anticoagulation with heparin or usual-care pharmacologic thromboprophylaxis. The primary outcome was organ support–free days. Therapeutic LMWH for 14 days in non ICU patients increased survival to discharge without organ support by 4%. The risk of major bleeding increased by 1%. This was a combined analysis of ATTACC, ACTIV-4a, and REMAP-CAP Clinical Trials. The number of patients recruited represented a minority of those screened and issues remain about the safety and transferability of the benefit/risk to a more unselected population of hospital patients who now have access to newer disease modifying drugs. There was also variance in the doses of LMWH used in the control arm of the study. NICE guidance suggests 'consider' the use of therapeutic LMWH in non ICU patients admitted with COVID

Current published evidence suggests a relatively low rate of post discharge VTE (Roberts et al, 2020) so UHB have not adopted a blanket policy of giving 7 days of LMWH to all patients admitted with COVID as some admissions may be short in patients who maintain reasonable mobility and without other risk factors for thrombosis. However patients must be assessed individually and LMWH prescribed post discharge if they have a higher risk of thrombosis (eg past history of VTE, ongoing significant immobility, significant obesity and other co-morbid conditions)

References

- Effect of Intermediate-Dose vs Standard-Dose Prophylactic Anticoagulation on Thrombotic Events, Extracorporeal Membrane Oxygenation Treatment, or Mortality Among Patients With COVID-19 Admitted to the Intensive Care Unit. The INSPIRATION Randomized Clinical Trial. JAMA. 2021;325:1620-1630
- Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19. The ATTACC, ACTIV-4a, and REMAP-CAP Investigators. N Engl J Med 2021; 385:790-802
- COVID-19 rapid guideline: managing COVID-19. NICE guideline NG191 updated 2/9/21

www.nice.org.uk/guidance/ng191https://www.nice.org.uk/guidance/ng191/resources/covid19-rapid-guideline-managing-covid19-pdf-51035553326

- Roberts et al. Postdischarge venous thromboembolism following hospital admission with COVID-19. Blood 2020;136: 1347-1350. doi:10.1182/blood.2020008086