

## Thromboprophylaxis in COVID-19

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Patients with COVID-19 can develop a prothrombotic state that may complicate their illness. Specialty organizations and expert groups agree that patients with COVID-19 need anticoagulation, though the exact dosing and duration remains a matter of debate.

The Acute Medicine COVID Workgroup has updated recommendations concerning VTE prophylaxis and anticoagulation choice in patients with COVID-19. Changes have been implemented to coincide with the latest high-quality evidence available.

- In non-ICU level patients with an expected hospital length of stay >72 hours, there is evidence to suggest benefit outweighs risk of treatment dose anticoagulation for VTE prophylaxis.
- In ICU level patients evidence suggests against the use of empiric treatment anticoagulation for VTE prophylaxis outside of a high suspicion of or confirmed VTE.

### Inpatient Management

#### Standard Prophylaxis

D-Dimer < 1.0 mg/L  OR  ICU admission	CrCl ≥ 30 mL/min	BMI < 40 kg/m <sup>2</sup> : enoxaparin 40 mg subcutaneous daily  BMI ≥ 40 kg/m <sup>2</sup> : enoxaparin 40 mg subcutaneous BID
	CrCl < 30 mL/min	BMI < 40 kg/m <sup>2</sup> : heparin 5000 units subcutaneous TID  BMI ≥ 40 kg/m <sup>2</sup> : heparin 7500 units subcutaneous TID

#### Empiric Treatment Dose Anticoagulation

Consider calculating pre-test probability for DVT with IMPROVE VTE score or Wells' score and order US to rule out DVT

Contradictions include: dual antiplatelet therapy, recent stroke (within 3 months), or active bleeding

D-dimer ≥ 1.0 mg/L in non-ICU patients  OR  High suspicion of VTE	CrCl ≥ 30 mL/min	exoxaparin 1mg/kg subcutaneous BID
	CrCl < 30 mL/min	heparin Infusion

#### Literature Review and Evidence

Multiple guidelines including the NIH, WHO, ACC, ISTH, and ASH recommend VTE prophylaxis for hospitalized patients with COVID-19 if not contraindicated. VTE prophylaxis has been shown to reduce the risk of mortality in patients hospitalized with COVID-19.<sup>8,9</sup>

Because of the severity of coagulopathy in critically ill COVID-19 patients and reports of high rates of VTE despite routine prophylaxis, a more aggressive anticoagulation strategy using therapeutic dosages of anticoagulated have been studied. The available evidence to inform the clinical management of COVID-19 associated coagulopathy is continuously evolving.<sup>1,2,3,4,5,6,7</sup>

Several retrospective studies suggested that treatment with high-intensity prophylactic anticoagulation or therapeutic anticoagulation may be associated with lower mortality compared with standard VTE prophylaxis.<sup>9, 10, 14, 15</sup>

Results from the prospective multiplatform adaptive-design trial that include REMAP-CAP, ATTAC, and ACTIV-4a investigators evaluated therapeutic-dose anticoagulation versus standard thromboprophylaxis in hospitalized patients with COVID-19.

- In the noncritically ill patient population, the initial strategy of therapeutic-dose anticoagulation increased the probability of survival to hospital discharge, and reduced use of cardiovascular or respiratory support as compared to standard thromboprophylaxis.<sup>13</sup>
- In the critically ill patient population, the initial strategy of therapeutic-dose anticoagulation did not have an impact on probability of survival to hospital discharge or organ support.<sup>14</sup>



## Discharge VTE Prophylaxis

Based on the MICHELLE trial (Ramacciotti, et. al., 2022 Lancet) we recommend considering post discharge VTE chemoprophylaxis for discharges at high-risk of subsequent VTE when bleeding risk can be minimized

- High-risk may be defined by an elevated IMPROVE VTE score or a high d-dimer with other risk factors
  - IMPROVE VTE score  $\geq 4$ , OR
  - IMPROVE VTE score 2-3 and D-dimer  $> 1 \text{ mg/L (FEU)}$
- Bleeding risk may be defined by an elevated HAS BLED score .

If a provider chooses to prescribe VTE prophylaxis on discharge we recommend:

- Rivaroxaban (Xarelto) 10 mg daily for 35 days
  - *Copay cards are available in outpatient pharmacy*

## IMPROVE VTE Score and Risk Factors

Risk Factor	IMPROVE VTE Score
Previous VTE	+3
Known thrombophilia	+2
Current lower-limb paralysis	+2
Current cancer	+2
Immobilized $> 7$ days	+1
ICU Stay	+1
Age $> 60$	+1

**References:**

1. Bikdelli, M.V. Madhavan, D. Jimenez, et al. COVID-19 and thrombotic or thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy and Follow-up. Journal Pre-proof Journal of the American College of Cardiology
2. F.A. Klok, M.J.H.A. Kruip, N.J.M. van der Meer, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thrombosis Research (2020), <https://doi.org/10.1016/j.thromres.2020.04.013>
3. Flumignan R, et al. Prophylactic anticoagulants for people hospitalized with COVID-19. Cochrane Systematic Review. Oct 2020.
4. Leonard-Lorant, X. Delabranche, F. Severac, et al. Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-Dimer levels. Pre-proof Radiology
5. N. Tang, D. Li, S. Wang, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J ThrombHaemost2020.
6. N. Tang, H. Bai, X. Chen, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. Pre-proof. doi:10.1111/JTH.14817
7. Ostrowski S, et al. Consecutive thrombelastography clot strength profiles in patients with severe sepsis and their association with 28-day mortality: a prospective study. Journal of critical care. 2013.
8. Paranjpe, V. Fuster, A. Lala, et al. Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19, Journal of the American College of Cardiology (2020), doi: <https://doi.org/10.1016/j.jacc.2020.05.001>
9. Nadkarni, G. Lala, A. Bagiella, E, et al. Anticoagulation, Bleeding, Mortality, and Pathology in Hospitalized Patients With COVID-19. J Am Coll Cardiol. 2020 Oct 20;76(16):1815-1826.
10. Aberbe, L. Risco, C. Ayis, S. The association between treatment with heparin and survival in patients with COVID-19. J Thomb Thrombolysis. 2020;50 (2):289-301
11. Daughety, M. Morgan, A. Forst, E, et al. COVID-19 associated coagulopathy: Thrombosis, hemorrhage and mortality rates with an escalated-dose thromboprophylaxis strategy. Thromb Res. 2020 Oct 25;196:483-485.
12. Sadeghipour P, et al. 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.
13. The ATTACC, ACTIV-4a, and REMAP-CAP Investigators. Therapeutic anticoagulation with heparin in noncritically ill patients with Covid-19. NEJM. 2021;385(9).
14. The REMAP-CAP, ACTIVE-4a, and ATTACC Investigators. Therapeutic anticoagulation with heparin in critically ill patients with Covid-19. NEJM. 2021;385(9):777-789.
15. Ramacciotti, et. al., Rivaroxaban versus no anticoagulation for post-discharge thromboprophylaxis after hospitalisation for COVID-19 (MICHELLE): an open-label, multicentre, randomised, controlled trial . 2022. The Lancet

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**Revision History**

This document is active and further recommendations are forthcoming. It will be updated as additions develop.

Revision	Description of Changes	Approvals	Date
1.0	Initial Document	Clinical Leadership Council	4/8/2021
2.0	Updated d-dimer reference range	Acute Medicine Clinical Practice Council	09/02/2021
3.0	Changed dosing options	Acute Medicine Clinical Practice Council	9/10/2021
4.0	Added discharge prophylaxis recommendation based on MICHELLE trial	Acute Medicine Clinical Practice Council	01/12/2022
5.0	Added IMPROVE VTE score criteria	Acute Medicine Clinical Practice Council	02/12/2022