Practice | Five things to know about ...

Antithrombotic agents in patients with COVID-19

Faizan Khan MSc, Tobias Tritschler MD MSc, Ryan Zarychanski MD MSc

■ Cite as: *CMAJ* 2022 May 24;194:E704. doi: 10.1503/cmaj.220189

Coagulopathy and thrombosis are associated with poor outcomes in patients hospitalized with COVID-19

COVID-19 is associated with hypercoagulability and endothelial injury, which contribute to an increased risk of macro- and microvessel thrombosis, disease progression and death.¹

2 Antithrombotic agents are not recommended for thromboprophylaxis in outpatients with mild COVID-19

In a randomized controlled trial terminated early owing to lower than expected event rates, neither acetylsalicylic acid (ASA) nor apixaban (at prophylactic or therapeutic doses) reduced rates of major adverse cardiovascular or pulmonary events, compared with placebo, in outpatients with mild COVID-19.^{2,3}

Therapeutic-dose heparin improves survival without organ support in noncritically ill hospitalized patients

Therapeutic-dose low-molecular-weight or unfractionated heparin is recommended for noncritically ill patients in hospital with COVID-19 who are not at high risk of bleeding.³ In a large trial, therapeutic-dose heparin, compared with usual-care thromboprophylaxis, increased the probability of survival to discharge without organ support (80% v. 76%, number needed to treat = 25) and the risk of major bleeding (1.9% v. 0.9%, number needed to harm = 100).⁴

Thromboprophylaxis with standard-dose heparin is recommended in critically ill patients

In critically ill patients with COVID-19 who require organ support, neither therapeutic nor intermediate doses of heparin confer clinical benefit over usual-care thromboprophylaxis but are associated with known risks of bleeding.^{3,5}

Acetylsalicylic acid does not improve outcomes in unselected hospitalized patients

The use of ASA to prevent death or the need for organ support in unselected patients in hospital with COVID-19 is not recommended.^{3,6}

References

- Leentjens J, Van Haaps TF, Wessels PF, et al. COVID-19-associated coagulopathy and antithrombotic agents — lessons after 1 year. Lancet Haematol 2021;8:e524-33.
- Connors JM, Brooks MM, Sciurba FC, et al.; ACTIV-4B Investigators. Effect of antithrombotic therapy on clinical outcomes in outpatients with clinically stable symptomatic COVID-19: the ACTIV-4B randomized clinical trial. JAMA 2021;326:1703-12.
- 3. Antithrombotic therapy in patients with COVID-19. Bethesda (MD): National Institutes of Health; updated 2022 Feb. 24. Available: www.covid19treatmentguidelines.nih.gov/therapies/antithrombotic-therapy/ (accessed 2022 Mar. 16).

- ATTACC Investigators; ACTIV-4a Investigators; REMAP-CAP Investigators; Lawler PR, Goligher EC, Berger JS, et al. Therapeutic anticoagulation with heparin in noncritically ill patients with COVID-19. N Engl J Med 2021;385:790-802.
- REMAP-CAP Investigators; ACTIV-4a Investigators; ATTACC Investigators; Goligher EC, Bradbury CA, McVerry BJ, et al. Therapeutic anticoagulation with heparin in critically ill patients with COVID-19. N Engl J Med 2021;385:777-89.
- RECOVERY Collaborative Group. Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet* 2022;399:143-51.

Competing interests: Ryan Zarychanski reports receiving operating grants from the Canadian Institutes for Health Research, National Institutes of Health, Ontario Fast Grants, Thistledown Foundation, Research Manitoba, CancerCare Manitoba Foundation, Victoria General Hospital Foundation and the Manitoba Medical Services Foundation, and research operating support as the recipient of the Lyonel G Israels Research Chair in Hematology. No other competing interests were declared.

This article has been peer reviewed.

Affiliations: School of Epidemiology and Public Health (Khan), University of Ottawa; Clinical Epidemiology Program (Khan), Ottawa Hospital Research Institute, Ottawa, Ont.; Department of General Internal Medicine (Tritschler), Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; Department of Internal Medicine (Zarychanski), Max Rady Faculty of Health Sciences, University of Manitoba; CancerCare Manitoba (Zarychanski), Winnipeg, Man.

Content licence: This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY-NC-ND 4.0) licence, which permits use, distribution and reproduction in any medium, provided that the original publication is properly cited, the use is noncommercial (i.e., research or educational use), and no modifications or adaptations are made. See: https://creativecommons.org/licenses/by-nc-nd/4.0/

Correspondence to: Faizan Khan, fkhan039@uottawa.ca

CMAJ invites submissions to "Five things to know about ..." Submit manuscripts online at http://mc. manuscriptcentral.com/cmaj