



# Letter to the Editor: Venous Thromboembolism in COVID-19: Are Women Different?

Aanchal Kapoor<sup>1</sup>

<sup>1</sup>Department of Critical Care, Respiratory Institute, Cleveland Clinic, Cleveland, OH, United States

Ind J Car Dis Wom 2022;7:7–8.

Address for correspondence Aanchal Kapoor, MD, Department of Critical Care, Respiratory Institute, Cleveland Clinic, Cleveland Clinic | 9500 Euclid Ave. | Cleveland, OH 44195, United States (e-mail: Kapoora@ccf.org).

I read with interest the article<sup>1</sup> about therapeutic anticoagulation in patients with coronavirus disease 2019 (COVID-19) and considerations in women. I applaud the authors for performing rigorous review to address this important clinical concern in COVID-19. High prevalence of venous thromboembolism (VTE) was observed in 22.7% of patients in intensive care units.<sup>2</sup> Observational studies and initial autopsy series showed high rates of both venous and arterial thrombosis as well as prominent pulmonary microvascular thrombosis. Patients with COVID-19 were reported to have 6% more risk to develop VTE as compared to non-COVID-19 patients.<sup>3</sup> In addition, COVID-19-associated coagulopathy was recognized as a marker of disease severity and poor prognosis.

Contrasting results have been reported about the preferred anticoagulation therapy in patients with COVID-19 infection. As evident in the given article,<sup>1</sup> the recommendations by various societies and guidelines kept on changing as the evidence emerged. Elevated D-dimer levels were reported as predictive for breakthrough thrombosis<sup>4</sup> despite standard deep vein thrombosis prophylaxis. Some institutions started risk-stratifying patients for VTE based on the D-dimer cutoff points and started intermediate-dose prophylaxis in critically ill patients with COVID-19.<sup>5</sup> Follow-up studies have confirmed significant coagulopathy associated with severe COVID-19, characterized by marked elevation of fibrinogen, von Willebrand factor, and platelet and profound endothelial activation, but did not confirm predictive value for D-dimer as marker of thrombotic risk. Multicenter randomized trial refuted the benefit of intermediate-dose prophylaxis in changing outcomes in terms of incidence of VTE, treatment with extracorporeal membrane oxygenation, or 30-day mortality.<sup>6</sup>

Later retrospective studies suggested mortality benefit of therapeutic anticoagulation for critically ill patients, particularly those requiring mechanical ventilation.<sup>7</sup> In a randomized controlled trial, therapeutic anticoagulation resulted in improved gas exchange, decreased D-dimer, and higher prevalence of liberation from mechanical ventilation.<sup>8</sup> The two recent international, adaptive, multiplatform, randomized, controlled trials studied the effectiveness and safety of use of therapeutic-dose heparin or low-molecular-weight heparin in this patient population.<sup>9,10</sup> The main findings were that therapeutic-dose heparin or low-molecular-weight heparin reduced mortality among patients with moderate infection but not among those with severe infection. A possible explanation for this difference could be that when infection reaches its severe state, the damage surpasses the reversibility by anticoagulation.

The article methodically outlines the higher predilection of VTE in male population attributing to variant involvement of angiotensin converting enzyme-2. The current National Institutes of Health guidelines recommend prophylactic-dose anticoagulation for pregnant hospitalized patients. Because pregnant females were not included in most clinical trials, there is insufficient evidence either for or against therapeutic anticoagulation.

Trials to evaluate platelet inhibition, therapeutic interventions targeting the endothelium, and platelet activation as well as outpatient anticoagulation strategies are ongoing.

## Conflict of Interest

None declared.

DOI <https://doi.org/10.1055/s-0042-1746420>.  
ISSN 2455-7854.

© 2022. Women in Cardiology and Related Sciences. All rights reserved.

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

## References

- 1 Chhabra ST, Goyal P. Venous thromboembolism in COVID-19: are women different? *Indian J Cardiovasc Dis Women WINCARS* 2020;5(03):200–208
- 2 Nopp S, Moik F, Jilma B, Pabinger I, Ay C. Risk of venous thromboembolism in patients with COVID-19: a systematic review and meta-analysis. *Res Pract Thromb Haemost* 2020;4(07):1178–1191
- 3 Tufano A, Rendina D, Abate V, et al. Venous thromboembolism in covid-19 compared to non-covid-19 cohorts: a systematic review with meta-analysis. *J Clin Med* 2021;10(21):4925. Doi: 10.3390/jcm10214925
- 4 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395(10229):1054–1062
- 5 Choi JJ, Wehmeyer GT, Li HA, et al. D-dimer cut-off points and risk of venous thromboembolism in adult hospitalized patients with COVID-19. *Thromb Res* 2020;196(August):318–321
- 6 Sadeghipour P, Talasaz AH, Rashidi F, et al; INSPIRATION Investigators. 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(16):1620–1630
- 7 Paranjpe I, Fuster V, Lala A, et al. Association of treatment dose anticoagulation with in-hospital survival among hospitalized patients with COVID-19. *J Am Coll Cardiol* 2020;76(01):122–124
- 8 Lemos ACB, do Espírito Santo DA, Salvetti MC, et al. Therapeutic versus prophylactic anticoagulation for severe COVID-19: a randomized phase II clinical trial (HESACOVID). *Thromb Res* 2020;196(January):359–366
- 9 Lawler PR, Goligher EC, Berger JS, et al; ATTACC Investigators ACTIV-4a Investigators REMAP-CAP Investigators. Therapeutic anticoagulation with heparin in noncritically ill patients with Covid-19. *N Engl J Med* 2021;385(09):790–802
- 10 Goligher EC, Bradbury CA, McVerry BJ, et al; REMAP-CAP Investigators ACTIV-4a Investigators ATTACC Investigators. Therapeutic anticoagulation with heparin in critically ill patients with Covid-19. *N Engl J Med* 2021;385(09):777–789