Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Anticoagulation, Statins and "Arterial Thrombotic Sequalae after Covid-19: Mind the Gap"

To the Editor:

The findings of thrombosis as the initial presenting event in patients with history of COVID-19 has baffled investigators since the beginning of the pandemic.[1] Borreli et al. describe in their paper, "Arterial Thrombotic Sequalae after Covid-19: Mind the Gap" three cases of arterial thrombotic complications after a completely resolved COVID-19 infection. Of note, COVID-19 was diagnosed in one patient with antibodies and the other patients were noted to have COVID-19 based on clinical symptoms diagnosed prior. Their study raises the issue of persistent endothelial dysfunction in patients with a history of COVID-19 and the role of this dysfunction in acute limb ischemia.[2]

We understand that anticoagulation is important in reducing mortality in hospitalized patients with COVID-19.[3,4] Unfractioned heparin appears to be the inpatient anticoagulant of choice given its well-known efficacy as well as its suppressive effect on the cytokine-mediated inflammatory process that results in endothelial dysfunction caused by COVID-19.[3,4] Furthermore the high incidence of kidney dysfunction and low levels of anti-thrombin in severe COVID-19 infection make low-molecular weight heparin a suboptimal choice.[5] Postoperative anticoagulation after treatment of acute limb ischemia is necessary given the persistent underlying hypercoagulable state. Unfractionated heparin is typically resumed shortly after initial intervention to prevent proximal or distal propagation of the residual thrombus to maintain collateral vessel patency.[6] Less is known regarding optimal postoperative outpatient anticoagulation.

While pursuing an understanding of the benefits of anticoagulation in COVID-19 patients, additional consideration must be made for statin therapy. Statins are involved in endothelial stabilization, and it is well-known that COVID-19 has been described as a disease of endothelial dysfunction. Similar to recommending statin therapy for patients with peripheral artery disease (PAD) to reduce major adverse limb events[7], it is important to explore further the role of statin in patients with COVID-19, potentially in preventing thrombotic complications. Studies have shown that statins:

- Are associated with decreased mortality in hospitalized patients with COVID-19 based on a propensity-matched retrospective study of 2,626 patients.[8]
- May reduce infectivity of COVID-19 by decreasing the cholesterol in plasma membranes thus minimizing invasion since viruses bind receptors concentrated in the lipid membranes. [9,10,11]
- May reduce inflammation by lowering IL-6 levels.[11]

INSPIRE/INSPIRATION-statin (INSPIRE-S) randomized control trials are underway exploring the role of anticoagulation and statin therapy in critically ill patients with COVID-19.[12] Meanwhile, we encourage research on the role of statin therapy in decreasing COVID-related limb threatening events as well.

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REFERENCES

1. Ilonzo N, Rao A, Berger K, et al. Acute thrombotic events as initial presentation of patients with COVID-19 infection. J Vasc Surg Cases Innov Tech 2020;6:381–3.
2. Borrelli MP, Buora A, Scrivere P, et al. Arterial Thrombotic Sequalae After Covid-19: Mind the Gap. Ann Vasc Surg 2021:S0890–5096 00356-3.
3. Rico Mesa JS, Rosas D, Ahmadian Tehrani A, et al. The role of anticoagulation in COVID-19-induced hypercoagulability. Current cardiology reports 2020;22:53.
4. Kamel AM, Sobhy M, Magdy N, et al. Anticoagulation outcomes in hospitalized Covid-19 patients: a systematic review and meta-analysis of case-control and cohort studies. Reviews in medical virology 2020:e2180.
5. Barrett CD, Moore HB, Yaffe MB, et al. ISTH interim guidance on recognition and management of coagulopathy

in COVID-19: A comment. Journal of thrombosis and haemostasis: JTH 2020;18:2060–3.
6. Bellosta R, Luzzani L, Natalini G, et al. Acute limb ischemia in patients with COVID-19 pneumonia. Journal of vascular surgery 2020;72:1864–72.
7. Sucharitkul PPJ, Jones KL, Scott DJA, et al. Lipid optimisation in lower extremity peripheral arterial disease. Ann Vasc Surg 2021:S0890–5096 00364-2.
8. Gupta A, Madhavan MV, Poterucha TJ, et al. Association between antecedent statin use and decreased mortality in hospitalized patients with COVID-19. Nat Commun 2021;12:1325.
9. Sanchis Gomar F, Perez Quilis C, Favaloro EJ, et al. Statins and other drugs: Facing COVID-19 as a vascular disease. Pharmacol Res 2020;159:105033. doi:10.1016/j.phrs.2020.105033.
10. Barkas F, Milionis H, Anastasiou G, et al. Statins and PCSK9 inhibitors: what is their role in coronavirus disease 2019? Med Hypotheses 2021;146:110452.
11. Pawlos A, Niedzielski M, Gorzelak Pabis P, et al. COVID-19: Direct and Indirect Mechanisms of Statins. Int J Mol Sci 2021;22:4177 Published 2021 Apr 17. doi:10.3390/ijms22084177.
12. Bikdeli B, Talasaz AH, Rashidi F, et al. Intermediate versus standard-dose prophylactic anticoagulation and statin therapy versus placebo in critically-ill patients with COVID-19: rationale and design of the INSPIRATION/INSPIRATION-S studies. Thromb Res 2020;196:382–94. doi:10.1016/j.thromres.2020.09.027.