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.

Response to the Letter to the Editor: Consideration Needed for Early Anticoagulation Following Intravenous tPA in Patients with COVID-19

We thank Dr. Angelo Jimenez and his colleagues for their letter to the editor regarding our report of a multicenter series of patients with coronavirus disease 2019 (COVID-19) who received intravenous (IV) tissue plasminogen activator (tPA) for suspected acute ischemic stroke. Their letter emphasizes the important contribution of a hypercoagulable state in patients with COVID-19.

Dr. Jimenez and his colleagues report 4 patients with large-vessel occlusions in the setting of COVID who received thrombolysis with IV tPA with transient improvement and subsequent recurrence of their presenting neurologic deficits. This observation is worrisome, but is also difficult to interpret without additional information. The initial improvement in NIH stroke scale score following IV tPA may have resulted from recanalization, but may also be explained by blood pressure fluctuations or improved collateral blood flow. Interim imaging demonstrating blood vessel patency alongside clinical improvement would provide additional support for the hypothesis that the noted change in examination was truly a result of recanalization. As large-vessel occlusions are often more successfully treated with mechanical thrombectomy than with IV thrombolytics, it would also be important to know whether the patients underwent thrombectomy and if not, whether there were contraindications that prevented this intervention. Finally, the authors offer no information regarding additional workup and etiology of the strokes. In many patients with COVID-19, strokes are thought to be cardioembolic, meeting criteria for embolic stroke of undetermined source.[1] However, if the strokes described here were due to atherothrombotic occlusions, re-occlusion and stuttering may have been part of the natural history.

We appreciate the authors' suggestion that patients with COVID-19 may be at high risk of re-occlusion following IV tPA given its short half-life, and that earlier anticoagulation could be warranted. However, the fibrinolytic effects of IV tPA are varied and unpredictable, with some patients demonstrating prolonged hypofibrinogenemia in spite of the drug's short half-life.[2] The use of early anticoagulation following intravenous thrombolysis is unstudied, and any theoretical benefit must be weighed against the potentially devastating consequence of intracerebral hemorrhage.

There are no specific studies demonstrating a benefit of anticoagulation for prevention or treatment of acute ischemic stroke in patients with COVID-19. However, several studies have demonstrated a benefit of therapeutic anticoagulation over prophylactic anticoagulation in hospitalized patients in reducing thrombotic events,[3] leading many centers to adopt a protocol of therapeutic anticoagulation for all symptomatic hospitalized COVID-19 patients with acceptable bleeding risk. One major limitation of these studies is that they are limited to hospitalized patients. As our study demonstrates, even ambulatory patients with mild viral symptoms may be at risk for stroke,[4] and further studies are needed to understand the utility of anticoagulation for primary or secondary stroke prevention in this population.

We are in agreement that the understanding of the interplay between COVID-19, hypercoagulability, thrombolysis, and anticoagulation is in its infancy. We look forward to further research on this subject.

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