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# In Reply: May Cooler Heads Prevail During a Pandemic: Stroke in COVID-19 Patients or COVID-19 in Stroke Patients?

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# May "Anticipation" Prevails during a Pandemic: Stroke in COVID-19 Patients is a Reality!

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- Conception or design of the work: AS, PJ
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It is with interest and surprise that we read the correspondence entitled: “May Cooler Heads Prevail During a Pandemic: Stroke in COVID-19 Patients or COVID-19 in Stroke Patients?”

Millions have been infected with COVID-19, and hundreds of thousands have died since December 2019. The current pandemic has shocked the world at all levels. With any pandemic progressing at such a rapid pace, the healthcare system has to rely on three elements to confine and limit fatalities until a sufficiently high level of scientific evidence has been compiled. The three elements are: (1) Previous epidemiological data (if available),[1-8] (2) sharing current unusual trends, (3) and reacting promptly to implement a change.

One aspect of this COVID-19 pandemic is the increased incidence of thrombotic events in the body in general and cerebrovascular in particular,[9-27] with unusual cases of previously healthy young individuals presenting with ischemic strokes.[28-35] While the authors mention that there is currently no high level prospective data showing an increase in stroke rates in younger patients (and we agree that this would be difficult to obtain), there is plenty of literature describing this finding.[28-35] So the authors agree that COVID-19 causes a prothrombotic state, but why is COVID-19 a bystander or incidental finding when the stroke is the initial presentation in young patients with no risk factors?

The authors say, “*The findings presented remain anecdotal and lack the methodological and statistical rigor to claim that COVID-19 infection increases stroke risk in the youth*”. The authors are right, at the early phase of the pandemic and when unsual trends were observed there was a paucity of evidence; however, Oxley et al. just described the five enounters without drawing any conclusions and they stated “*The association between large-vessel stroke and Covid-19 in young patients requires further investigation*”. Currently, there is more than anecdotal evidence linking COVID-19 to stroke. The incidence of stroke in COVID-19 hospitalized patients ranges from 0.9-2%,[33,36-38] increasing to 5.7% in severe disease.[36] COVID-19 has been reported to be an independent predictor of stroke (OR, 3.9; 95% CI, 1.7–8.9; P0.001),[39] and compared to influenza, it has a 7.5-fold higher rate of ischemic stroke.[38] Second, several recent publications reported a similar experience to Oxley et al. in terms of stroke occurrence in the young.[28-35] Two extensive multicenter studies reviewing large vessel occlusion in COVID-19 that are under review have observed that among a group of patients undergoing a mechanical thrombectomy 19% were under 50 years,[33] and 34% under 55 (12 centers from the USA and Europe). Refuting such observations early on during the pandemic before completely understanding the full manifesations of COVID-19 should be reconsidered by the authors. Along the same line of

thoughts, children were perceived to be spared from COVID-19 severe manifestations.[40,41] However, later the Centers for Disease Control and Prevention based on small published observations,[42-45] issued a national health advisory to report on cases meeting the criteria for multisystem inflammatory syndrome.[46] Results of such efforts identified 186 patients with multisystem inflammatory syndrome in children and adolescents with COVID-19 disease.[20] The moratlity rate was 2%, 80% receiving intensive care, 40% presenting with Kawasaki disease–like features, and 8% developing Coronary artery disease. Usually 5% of children with Kawasaki's disease present with cardiovascular shock, while in the setting of COVID-19 it was 50% (10-folds higher).

The authors attributed stroke in the setting of COVID-19 to a single factor, a prothrombotic state induced by systemic inflammation,[47] however, they did not consider additional factors such as embolic events in the background of myocarditis and arrhythmia, thrombotic microangiopathy, coagulopathy and thrombocytopenia, and direct viral invasion (CNS endothelium and cardiomyocytes).[9-20] Additionally, ACE2 viral-mediated downregulation in the CNS inhibits the neuroprotective effects of ANG-II (anti-inflammatory via its binding to the Mas receptor and vasodilator effect) and tips the balance for ANG-I (a potent vasoconstrictor) thereby increasing stroke severity.[48-57]

It is the responsibility of healthcare professionals to promptly report any noteworthy trends and being vocal in the media to reach the largest audience to spread awareness. Small case series with uncommon trends would alarm the healthcare system to be more vigilant when exposed to such presentations and alert the public to the seriousness of this disease. Whether the media coverage helped with awareness and encouraged people with stroke symptoms to present early to the hospital or resulted in just fear and anxiety among the young is yet to be determined. If the price to pay in spreading stroke awareness in the COVID-19 positive younger population is fear and anxiety in some people, maybe it is not so bad after all. Maybe the young will start taking this pandemic more seriously. Such an approach is similar to an attitude in general surgery, where they operate on 25% of negative appendectomies to avoid missing true positives.[58-62] In our case, it is not as serious because spreading awareness is not even a surgical intervention! Finally, doesn't the public know that there is a higher mortality rate with COVID-19, even among the youth? If so, which would cause more fear and anxiety, stroke or death?

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