

In Reply: Dismantling the Apocalypse Narrative: The Myth of the COVID-19 Stroke

To the Editor:

We read the authors' response to our letter with surprise and amusement.^{1,2} Their lengthy, 1500-word, 60-reference manuscript is actually quite hard to read and follow at times.² Multiple arguments are being presented throughout the text, though none of which directly relevant to the issue at hand, namely, whether "young and middle-aged people, barely sick with COVID-19, are dying of strokes."³ That, in our opinion, is the myth.

That said, we agree with the authors that some other COVID-19-related claims are generally more factual, less debatable. Those are not myths. Here are some examples:

- (1) COVID-19 is a highly contagious disease.
- (2) It has led to a pandemic of historic proportions.
- (3) It has a low, yet significant mortality rate in the elderly and those with underlying medical comorbidities.
- (4) Given its high contagiousness and rapid spread, the threat to public health, specifically the risk of overwhelming the health-care system, is real.
- (5) Coagulation disorders and thromboembolic events are relatively common in critically ill patients with severe COVID-19, which can lead to arterial and venous strokes.

We are very much familiar with the studies the authors cite and absolutely concur with them that the pathophysiology of COVID-19 is still poorly understood, and that "we don't have a full grasp on its manifestations yet." However, we disagree with the authors' claim that thrombosis and microangiopathy in the lungs is a unique feature of COVID-19.² In fact, autopsy studies have shown that thrombi in the pulmonary vasculature are an almost universal finding in patients with the acute respiratory distress syndrome.⁴ Moreover, aside from the lung, other major organs were not found to be directly affected by SARS-CoV-2, including the brain.⁵⁻⁸ To date, there is still no evidence that COVID-19 is associated with higher rates of coagulopathy compared with sepsis from other sources.^{9,10} Interestingly, in a recent large-scale study from a renowned academic institution in the authors' own city, Philadelphia, the vast majority of COVID-19 patients who suffered a stroke had conventional cardiovascular risk factors, and traditional stroke mechanisms were the rule.¹¹

We are glad to see the authors backtracking on their previous claims that young people with mild COVID-19 and otherwise no cardiovascular risk factors are at serious risk of stroke.² Their present statement – "The data presented represents patients without regard for non-specific terminology, such as severe or mild. In fact, the publications simply point out that COVID-19

puts patients at risk of stroke." – is actually quite reassuring. Of course, that has not been their official position in the multitude of media interviews they have been generously giving (roughly 2 interviews per patient reported) or their multiple publications recycling the same small case series.^{3,12-17} Moreover, as of today, the authors' own webpage still states the following: "Young patients with no risk factors for stroke may have an increased risk if they have contracted COVID-19, whether or not they are showing symptoms of the disease ... Young people, who may not know they have the coronavirus, are developing clots that cause major stroke."¹² Thus, for the sake of consistency, we invite the authors to edit the contents of their webpage to more accurately reflect their current position.

In a pandemic of such serious proportions, what is a moral and ethical imperative for us, physicians, is to exert self-control and refrain from making radical, assertive public statements, when those are based merely on loose science and anecdotal data. It goes without saying that statements of that sort have the potential of exacerbating anxiety and stoking fear in an already terrified, highly vulnerable population. By virtue of the same, it is a moral and ethical imperative for journalists to refrain from irresponsibly publicizing such claims. The title of the Washington Post article referenced below is probably the best textbook illustration of harmful sensationalism.³ Instead of feeding into the collective anxiety, the onus is on us, physicians, to remain a soothing voice of reason in such difficult times. While it serves to remain vigilant and to generate hypotheses in the face of unusual observations, one should always strive to confirm such hypotheses using sound scientific methodology before indiscriminately sounding the alarm. Our actions have real consequences in the real world.

For instance, the secondary implications and indirect human and economic tolls of the COVID-19 pandemic were recently well documented. A nationwide study showed that up to a third of excess deaths in 2020 were not directly caused by COVID-19 infections.¹⁸ Global disruption of health-care resources for other prevalent diseases, including hypertension, diabetes, cancer, and cardiovascular emergencies have occurred during the pandemic.^{19,20} Specifically, stroke care has been seriously impacted, including limitations in multidisciplinary care, delays in time-sensitive thrombolytic therapy, and reduced availability of diagnostic services and stroke unit beds.²¹ Moreover, increased rates of anxiety, depression, and suicidal ideation have all been reported, potentially leading to increased rates of suicide.²²⁻²⁴ The dangerous effects of extended lockdowns and school closures, especially the increasing rates of child abuse, are also coming to light.^{25,26} From an economic standpoint, financial depression in the US is estimated to reach \$16 trillion, while gross domestic product reduction across the globe is expected to reach 5.2%.^{27,28} During the pandemic, over 40 million people in the US lost their jobs, resulting in the highest rate and largest over-the-month

TABLE. Point-by-Point Response to Authors' Query

Query	Response
1	See text.
2	<p>We did not accuse the authors of claiming their patients were younger than 50 yr. Rather, the first published and widely publicized paper claiming an association between mild COVID-19 and stroke, one that the authors themselves have endorsed and have heavily relied upon in their study, had used 50 yr as cutoff age for young patients.³⁴ By using a slightly higher cutoff age of 55 yr, the authors seem to engage in convenient cherry picking, with the intent to push through their message. While they have every right to do so, we also reserve the right, while critically reviewing their data, to apply the same age cutoff that had been adopted in the previous publication.</p> <p>We do not generally contest that, across the board, the risk of stroke is increased in the setting of critical illness due to severe COVID-19. This has, in fact, been suggested by "multiple publications from many different geographies." However, as the authors know, the vast majority of those studies had failed to adjust for disease severity, thereby lumping together mild and severe COVID-19 cases. In contrast to critically ill patients with COVID-19, there is no evidence that young and healthy patients with mild COVID-19 are at increased risk of stroke.</p>
3	<p>(a) Twelve patients were older than 50 yr. (b) Eight had cardiovascular risk factors. Overall, 12 (out of 14) had either (a) or (b). No confusion here.</p>
4	See answer to query #2 above.
5	<p>We are glad to hear directly from the authors that their patients had undergone "standard complete" stroke workups. However, the authors failed to include any such details in their original manuscript. Working in a comprehensive stroke center does not excuse clinician-scientists from providing such crucial information to the readership. We are actually surprised that their paper passed the peer-review process in the first place, while omitting those very important details. How can anyone implicate COVID-19, a novel disease and unestablished cardiovascular risk factor, in the pathophysiology of stroke, without having unequivocally demonstrated that an extensive and thorough stroke workup had been undertaken and had failed to uncover alternative, well-established causes. It would be very helpful to the scientific readership to hear directly from the authors as to what constitutes "standard complete" workup in their stroke center, what workup exactly was obtained in those patients, and what were the specific results of that workup.</p>
6	See answer to query #5 above.

increase in unemployment ever recorded.^{29,30} According to the United Nations, a global economic depression of this magnitude could lead to the starvation of up to 130 million people.³¹ This brief summary is, by no means, an exhaustive account of the catastrophic, direct consequences of the pandemic. Nor is it one of the unintended, indirect consequences of the lockdown "guidelines" the authors seem to be promoting. However, we believe it illustrates very well how public statements emanating from us, physician-leaders in the field, could potentially have real consequences in the real world. A point-by-point response to the authors' query can be seen in [Table](#).

Finally, we concede that, in normal times, our hospital is a relatively "low-volume primary stroke center," contrasting with the authors' "busy ... comprehensive stroke center." However, as the authors point out, "Philadelphia was not hit as hard as New York," not even close. During the surge, New York City (NYC) experienced 10 times as many new cases per day as Philadelphia and, to date, NYC has 6 times as many total COVID-19 cases as Philadelphia.^{32,33} Moreover, among the 5 boroughs in NYC, the Bronx was the hardest hit, experiencing up to 1500 new cases per day.³² At the worst, Philadelphia experienced a maximum of 626 new cases a day.³³ To match the ongoing demand, our 400-bed hospital was practically converted into a COVID-19 treatment center. Several nonclinical areas were converted into

patient wards. Our 16-bed intensive care unit was expanded by a factor of 6 to 7, reaching a total capacity of more than 105 ventilator-equipped beds. At the height of the pandemic, over 95% of those beds were occupied by ventilated patients. Thus, we can confidently state that our experience with COVID-19 in the Bronx at least matches that of the authors in Philadelphia. Although firm conclusions cannot be drawn based on small, single-digit numbers, we invite the authors to reconsider their statement regarding our large vessel occlusion (LVO) rate having "quadrupled" during the height of the pandemic. In fact, based on the surge in critically ill patients in our center, a much higher LVO rate would have been expected. Strikingly, rather than increasing, the overall stroke volume decreased during the same time. An Institutional Review Board study protocol is currently underway at our institution, aiming to scientifically assess the occurrence rate, clinical and radiologic features, and pathophysiologic mechanisms of stroke in patients with COVID-19.

In summary, we strongly stand by our statement that, as of now, there is absolutely no scientific evidence that "young and middle-aged people, barely sick with COVID-19, are dying of strokes."¹ To suggest otherwise would be reckless and irresponsible at best.

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