Stroke

EDITORIAL

Stroke, Research and Science in the Time of COVID

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The incidence of acute stroke during the coronavirus disease 2019 (COVID-19) pandemic is either increasing, decreasing, or neither.[1–3] Published data fails to support a firm conclusion, whereas anecdotal reports and nonpeer-reviewed case series posted on preprint servers—although newsworthy—do not help clarify the effect of severe acute respiratory syndrome-corona virus-2 (SARS-Cov-2) infection on the frequency of thrombotic events.[1,4] One can speculate that fear of infection may lead potential stroke patients to refuse or delay calling for emergency medical services.[5] However, the virus may be linked to thrombotic risk, which, in turn, could lead to an increased incidence of stroke, especially severe stroke.[4] Therefore, a crucial need for data exists to characterize and understand the effect of the COVID-19 pandemic on stroke care.

See related article, p 2664

In this issue of our Journal, Jasne et al[6] provide an insightful and helpful comparison of stroke rates before and during (don't you wish we could say "and after") the pandemic. The community survey included a relatively circumscribed catchment area with reasonably good data capture. The 3 participating medical centers included a Comprehensive Stroke Center, a Primary Stroke Center, and a thrombectomy capable Primary Stroke Center; all 3 are near the US COVID-19 epicenter of New York City. A total of 822 Stroke Code activations were collected between January 1, 2020 and April 28, 2020. Data from February 2020 was selected as the pre-COVID period to be compared with 2019 and to a during-COVID period March 1 to April 28. The investigators could document an obvious drop in code stroke volumes beginning around the week of February 18 to 24, which was statistically significant. The data are likely overfit, but some univariate statistically significant differences comparing pre and during suggest that patients presenting during the pandemic were sicker, with more comorbidities. On the other hand, comparing pre to during, treatment rates remained constant for intravenous thrombolysis (5.4% versus 8.1%) and mechanical thrombectomy (9.6% versus 14.2%). The results confirm the impression many stroke specialists have suspected: although global rates of code stroke activations have declined markedly, the overall rates of both tpa use and thrombectomy remained constant. This finding, taken with confirmatory findings elsewhere, suggest that some stroke patients avoided coming in emergently but that the virus may not promote thrombosis and ischemic stroke.

However, the biological rationale underlying a stroke risk with SARS-Cov-2 viremia is quite strong. During presymptomatic or early symptomatic stages, infection with SARS-Cov-2 resembles any other viral syndrome, and such infections are associated with elevated stroke risk.[7,8] The mechanism may include mechanical factors, such as dehydration, but may also include activation of the coagulation cascade during the acute-phase inflammatory response. In later phases, as COVID-19 enters a severe stage characterized by the cytokine storm, obvious links to in situ thrombosis include both a procoagulopathy as well as overt thrombosis in the microcirculation.[9] Knowing the central role played by the PAR (protease activated receptor)

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EDITORIAL

in mediating neuroinflammatory toxicity, we proposed a speculative hypothesis that therapy targeting PARs may prove useful in managing a variety of SARS-Cov-2 complications.[10]

Given these background, mechanistic considerations, the stroke community was poised to accept reports of increased stroke rates and severity in patients with COVID-19. The effect of fear and community angst on scientific investigation has been documented, both anecdotally and rigorously. None of us need data, however, to know that our decision making—especially our readiness to accept preprint, nonpeer-reviewed data as valid—has been impaired, globally. Now would be an appropriate time to reinstitute our principles of rigor and peer-review; to reclaim our role as arbiters of scientific fact; and rechallenge the notion that personal anecdote trumps validated, well buttressed scientific investigation.

The reality is that scientific research is hard: we all would prefer to avoid time-consuming, challenging elements of rigor, such as placebo controls; randomization; proper design with adequate sample size; statistical consideration for type II, and worse, type I error rates. Before the present pandemic, we in hard science were already under scrutiny: we were investigating ourselves for outright fraud, but also less obvious but quite serious issues such as p-hacking.[11,12] In stroke, we were examining our own methods and drawing up plans to readdress rigor in translational stroke research.[13,14] In the grip of the global pandemic, perhaps it became easier to publish first and impose rigor later.

The well-presented data from Jasne et al[6] provide a good step forward, and undoubtably more groups will assemble properly curated and rigorously analyzed retrospective data. In larger datasets, perhaps advanced statistical methods such as propensity score matching can be applied because it is crucial to determine with confidence whether the SARS-Cov-2 virus does or does not promote stroke risk and to accomplish this before the next wave arrives upon us. Community education efforts must focus on the message that stroke still occurs, time is brain, and stroke can be treated.[15] Just as importantly, we must reestablish our commitment to rigor and properly executed scientific method.

Rigorous science is the only tool available to find treatments for diseases—for example to defeat a pandemic—and ultimately to understand the world around us.

ARTICLE INFORMATION

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