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Expanding on the Neurologic Effects of COVID-19

Dr. Wilner:
You're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner, and I recently spoke with Dr. Jennifer Frontera, who's a neurocritical care specialist and professor of neurology at the NYU Grossman School of Medicine. Here's Dr. Frontera now, discussing her research on the neurologic symptoms that COVID-19 patients are facing today.

Dr. Frontera:
Yeah, so separately, with our NYU dataset, we have about 5,000 patients that we initially started looking at in the spring. About 14% of those had neurological events during their hospitalization. And we've continued to follow those patients longitudinally. So we did telephone interviews at six months, and we're gearing up to do one-year telephone interviews where we're asking things like looking at their functional status, their activities of daily living, whether they've been able to return to work if they were working prior to hospitalization. And then we're also doing Neuro-QoL, PROMIS batteries, which are NIH-type measures of self-reported health status for looking at things like sleep, fatigue, anxiety, and depression, and we're doing a telephone MoCA measure of objective cognitive function, to try to get a sense of how these people are doing after six months. Do people still have deficits at that time frame, whether or not they have a neurologic complication during hospitalization? And so, we're also going to hopefully be looking at the trajectory of recovery, from six months to one year, to see how long it takes for folks to really improve, after hospitalization, and we have seen some prolonged symptoms in certain proportion of patients.

We also did a citizen survey, which was basically indexed to match the demographics of the U.S. population. We had about 1,000 patients in that survey, but just to look at the prevalence of some of the symptoms reported in long-haul or long-COVID syndrome amongst the general population – because, of course, there's a concern that even folks without COVID-19 may have symptoms of anxiety, depression, fatigue, sleep issues, brain fog, etc. that are related to pandemic-related stressors, be that economic, social or other. So to really get a handle on how much is COVID-related versus pandemic-related, we wanted to look at kind of a citizen survey in the general population.

I'm also working with our Alzheimer's disease center. We've been looking at some blood markers that are common to dementia and Alzheimer's patients. We're looking at those in COVID patients to see what the correlation is with folks that develop brain fog or cognitive abnormalities after hospitalization. So, I think we'll have a little bit more information and that might give us a little bit of insight into neuropathology or what's happening with this brain fog that seems to be the most debilitating, and one of the most common symptoms amongst those who are feeling that they have long COVID or prolonged COVID symptoms.

Dr. Wilner:
I mean that's a really knotty problem, but it's a really important one to sort out. Are you gonna send these patients to the psychiatrist, you know, for their depression treatment? Or do we need to develop a medical treatment to reverse whatever injury is occurring or both. So, this is really great to try and get this sorted out. Very ambitious project, it seems to me.

Dr. Frontera:
And I know we had discussed in the past how much of what we're seeing in these patients is due to direct neurotropic effects of the virus, or direct viral invasion versus secondary effects of COVID or sequelae of COVID, so namely, hypoxia, renal failure with uremia, or the coagulopathy, or endothelial small vessel injury that we believe to be related to COVID-19, but not directly from neuroinvasiveness, perhaps from the inflammatory response that follows SARS-CoV-2 infection. So, I think from our perspective, most of what we've observed thus far has been sequelae, or secondary effects of COVID. We in our cohort did not find any evidence of direct viral invasion, meningitis, or encephalitis, and I think a lot of the reports that are out there, talking about meningitis or encephalitis, maybe are

not as rigorous as we would want them to be. We just published a review looking at CSF findings in COVID, which was very large, hundreds of papers included in that. And 5% of those had some PCR evidence of SARS-CoV-2 in the CSF. However, the cycle threshold was not reported in most of these papers, and then the two papers where it was reported it was a high cycle threshold, meaning that probably it was contamination from blood, either from a traumatic tap or, you know, a leaky blood-brain barrier with, entry of the viral particles through the blood-brain barrier, but not necessarily direct virulence. And then in terms of antibody production in the CSF of SARS-CoV-2, IGG or IGM or IGA, you know, the papers we've seen, there's only been one paper that reported an elevated IGG synthetic rate intrathecally, but again, that's not specific to SARS-CoV-2. That could be some other pathogen that is causing the elevated IGG synthetic rate. What you really want to see is an increased ratio of SARS-CoV-2 IGG, IGA, IGM in the CSF compared to the serum – drawn at the same time, done at the same dilution, looking at the same antibodied antigens, so same nucleocapsid antibodies, or same spike protein antibodies. And we have yet to see a paper demonstrating that in in a COVID patient. So, not to say that direct viral invasion definitively does not occur, but if it does occur, it's pretty rare and the neuropathological data has not substantiated that this is a frequent event or that the virus itself is causing damage.

Dr. Wilner:
That was Dr. Jennifer Frontera, discussing her current research on the neurologic symptoms of COVID-19. For ReachMD, I'm Dr. Andrew Wilner, and to hear my full conversation with Dr. Frontera and to find other programs in our series, visit ReachMD.com/NeuroFrontiers, where you can be part of the Knowledge. Thanks for listening!