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.

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Letter to the editor

Frequency of new seizures after SARS-CoV-2 infections may depend on the length of follow-up

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Letter to the Editor

We read with interest the article by Westman et\xA0al. about the seizure frequency among Swedish patients with an acute SARS-CoV-2 infection [1]. It was found that among 1,221,801 SARS-CoV-2 infected patients the seizure frequency was not significantly increased compared to an age- and sex-matched control cohort [1]. However, when focusing only on the age groups 60-80 years and 81-100 years, seizure frequency increased in these two age groups compared to controls [1]. It was concluded that considering the potential non-controllable bias and that COVID-19 patients on the intensive care unit (ICU) present with a lower risk of seizures than the general ICU population, the virus-induced epileptogenic effect is likely very small [1]. The study is promising but raises concerns that should be discussed.

A limitation of the study is that the latency between COVID-19 infection and onset of seizures was not determined. It cannot be ruled out that the likelihood of experiencing a seizure after a SARS-CoV-2 infection increases with the length of post-COVID-19 period. Structural cerebral lesions from an acute SARS-CoV-2 infection may be more likely to become symptomatic the longer they persist.

A further limitation is that the treatment COVID-19 patients were receiving during hospitalisation was not considered as trigger of seizures. From several compounds used for the treatment of COVID-19 it is known that they are potentially epileptogenic. Chloroquine and hydroxy-chloroquine have been reported to cause tonic clonic seizures [2]. Tocilizumab has been reported to even trigger a status epilepticus [3].

A further limitation of the study is that only four co-variates, the confounding comorbidities ischemic stroke, traumatic brain injury, and mechanical ventilation were used for Cox regression to assess the risk of epilepsy [1]. Neurological complications of the central nervous system (CNS) after a SARS-coV-2 infection are much more widespread and additionally include venous sinus thrombosis (VST), intracerebral bleeding (ICB), subarachnoid bleeding (SAB), acute, disseminated encephalomyelitis (ADEM), acute, hemorrhagic, necrotizing encephalopathy (AHNE), acute, hemorrhagic leukoencephalitis (AHLE), immune encephalitis, rhombencephalitis, ventriculitis, cerebellitis, hypophysitis, and reversible, cerebral vasoconstriction syndrome (RCVS) [4]. If any of these conditions may be present, the likelihood that an affected patient develops epilepsy is also increased.

A fourth limitation of the study is that cerebrovascular risk factors were not included in the evaluation. Because diabetes, arterial hypertension, hyperlipidemia, atrial fibrillation, and smoking increase the risk of cardio-embolism, and because embolic stroke can be a focus of seizures, it is crucial that the general cerebro-vascular risk to experience an embolic stroke is included in the evaluation.

A further limitation of the study is that readers were not informed about the frequency of cerebral lesions among those with seizures and that the number of those requiring anti-seizure dugs (ASDs) was not provided. There is also no mentioning of the seizure frequency. Furthermore, the long-term outcome of COVID-epilepsy was not provided.

Overall, the interesting study has limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study. There is ample evidence that SARS-CoV-2 can secondarily cause epilepsy most commonly through structural cerebral lesions occurring as a complication of a SARS-CoV-2 infection. Since SARS-CoV-2 is only rarely documented in the cerebro-spinal fluid (CSF) of SARS-CoV-2 infected patients, it is rather unlikely that seizures are directly caused by the virus.

Declarations

Ethical Approval

Not applicable

Abbreviations: ADEM, acute disseminated encephalomyelitis; AHNE, acute, henorrhagic, necrotising encephalitis; ICB, intracerebral bleeding; ICU, intensive care unit; RCVS, reversible, cerebral vasoconstrciton syndrome; SAB, subarachnoid bleeding; VST, venus sinus thrombosis.

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none

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