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Commentary

Do not Forget the Brain When COVID-19 Patients Die

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We read with interest the article by Grassi *et al*. on a retrospective analysis of the autopsy findings of 60 patients who died from coronavirus disease-19 (COVID-19) at a single Italian centre [1]. It was found that 92% of patients had at least one comorbidity, that 67% had pulmonary intravascular coagulation with an inflammatory pattern, that 73% had myocardio-sclerosis, 55% had liver involvement, 20% had renal tubular epithelial exfoliation, and 7% intravascular coagulation [1]. The study is compelling but has limitations that should be discussed.

The major limitation of the study is that the central nervous system (CNS), the peripheral nervous system (PNS), and the skeletal muscles were not considered in the autopsy of the 60 patients who died from COVID-19. Death can only be attributed to COVID-19 when alternative causes of death are ruled out. Since neuro-COVID is the most common non-pulmonary manifestation of SARS-CoV-2 infection, it is crucial to assess whether or not the CNS or PNS was affected by the infection. In general, neuro-COVID can occur with or without COVID-19. In patients dying with COVID-19 and neuro-COVID, it can be difficult to assess whether the one or the other was responsible for the death. Patients with severe COVID-19 are frequently intubated and ventilated, which is why neuro-COVID often goes unrecognised unless these patients are actively evaluated for neurological impairment. Non-convulsive seizures or non-convulsive status epilepticus often go undetected, unless an electroencephalogram (EEG) is recorded. Ischemic stroke, intracerebral bleeding, venous sinus thrombosis (VST), acute, disseminated encephalomyelitis (ADEM), posterior reversible encephalopathy syndrome (PRES), acute hemorrhagic, necrotising encephalopathy (AHNE), immune encephalitis, or hypophysitis can easily be missed without cerebral imaging. Because cerebral imaging is usually performed only when indicated and not prospectively, cerebral involvement may be missed if patients remain asymptomatic. If comatose patients with COVID-19 do not undergo cerebrospinal fluid (CSF) investigations or nerve conduction studies (NCSs), Guillain Barre syndrome (GBS) and its subtypes may go unrecognised in these patients.

We disagree that the included patients underwent full autopsy, as stated in the introduction [1]. Since the brain, spinal cord, nerve roots, plexus, and peripheral nerves were not autopsied, it cannot be classified as “complete”.

There is no mention whether or not the 60 patients were intubated and ventilated at the time of death and therefore monitored. Knowing whether they were monitored or not is crucial for assessing whether malignant ventricular arrhythmias (MVAs) could be responsible for death.

There is also no discussion about the possibility that at least some of the included patients died from Takotsubo syndrome (TTS) also known as stress cardiomyopathy. TTS is usually a reversible condition but in case of severe stress, acute heart failure or MVAs may develop and may lead to death.

In summary, the interesting study has limitations that put the results and their interpretation into perspective. Addressing these issues would strengthen the conclusions and could improve the status of the study. In COVID-19 patients, death can be misattributed to pulmonary involvement if “silent” neurological manifestations are not actively ruled out.

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Keywords: Autopsy, Brain, SARS-CoV-2, COVID-19, Death

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