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Letters to the Editor

Takotsubo Syndrome in COVID-19 Requires Elucidation of the Pathophysiological Background

Josef Finsterer^{a,*}, Claudia Stollberger^b^a Klinik Landstrasse, Messerli Institute, Vienna, Austria^b 2nd Medical Department with Cardiology and Intensive Care Medicine, Klinikum Landstrasse, Vienna, Austria

With interest we read the article by Kong et al. about two SARS-CoV-2 infected patients with Takotsubo syndrome (TTS) complicated by cardiogenic shock [1]. Patient-1 (88yo male with metastatic prostate cancer) deceased but patient-2 (79yo female with multiple sclerosis) recovered [1]. It was concluded that TTS should remain on the differential in the setting of arrhythmias, systolic dysfunction, cardiac biomarker elevation, or ST-elevation [1]. We have the following comments and concerns.

The main shortcoming of the study is that the possible causes of TTS in the patients were not extensively discussed and that the pathophysiology of TTS remained elusive. Though it is mentioned that the SARS-CoV-2 induced cytokine storm may cause myocardial oedema, there was no evidence provided that either of the two patients had myocardial oedema. Other pathophysiological scenarios that should be considered in the context of a SARS-CoV-2 infection include myocarditis [2], secondary leading to TTS or autonomic dysfunction [3], leading to impaired sympathetic myocardial innervation. Since evidence is emerging that SARS-CoV-2 can trigger the development of Guillain Barre syndrome (GBS) [4] and GBS frequently affects the autonomic fibers, it is crucial that GBS is excluded in the two presented patients. GBS may develop within –10 to 90 days before or after onset of COVID-19 why it is conceivable that TTS can be an early complication of the viral infection. There is also increasing evidence that SARS-CoV-2 may cause myocarditis, why it is crucial that myocarditis is appropriately excluded. We should know if there was late enhancement on cardiac MRI or if *endo*-myocardial biopsy was carried out in either patient.

Since TTS is a frequent complication of seizures and since cerebral metastasis complicated by seizures were not excluded in patient-1 and since multiple sclerosis may go along with seizures as well, it would be interesting to know if the history in either patient was positive for seizures. Single patients have been reported in whom multiple sclerosis per se was made responsible for the development of TTS.

Missing are the autopsy finding in patient-1 [1]. We should know if there was histological evidence for virus particles within the

myocardium, the endocardium, the pericardium, or the cardiac conduction system, if there was an inflammatory response within the myocardium, or if there were micro-thrombi within the myocardial capillaries.

Missing is also the assessment of the severity of the COVID-19 infection. We should know if the severity of the viral infection was classified as mild, moderate, or severe.

We agree that the prevalence of TTS may be underestimated in COVID-19 patients. In a recent review, however, it was documented that as per the end of September 2020, only 38 patients with SARS-CoV-2 associated TTS have been reported [5]. In accordance with previous findings it was concluded that the general prevalence of TTS has not increased during the pandemic as reported by Jabri et al. and Delmas et al. [6,7], that the clinical presentation, epidemiology, treatment, and outcome of SARS-CoV-2-associated TTS is similar to COVID-19-unrelated TTS, and that TTS can mimic myocarditis [5].

Overall, the interesting report has some limitations, which should be addressed to strengthen the conclusions. Particularly, the pathophysiology of TTS in the two reported patients should be elucidated.

Declarations

Statement of ethics was in accordance if ethical guidelines.
Informed consent was obtained.
The study was approved by the institutional review board.

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Author contribution

JF: design, literature search, discussion, first draft, critical comments, final approval,

Declaration of competing interest

None.

* Corresponding author at: Postfach 20, 1180 Vienna, Austria.
E-mail address: fifigs1@yahoo.de (J. Finsterer).

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