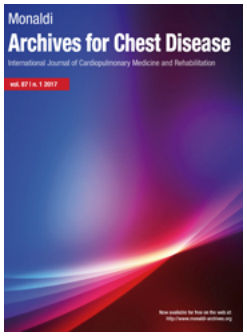

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Comments on "Tako-Tsubo syndrome in patients with COVID-19: a single centre retrospective case series"

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Dear Editor,

We read with interest the article by Alonzo et al. about a retrospective study of four patients with Takotsubo syndrome (TTS), which was attributed to SARS-CoV-2 infection (SC2I) [1]. All four patients had acute COVID-19 disease, which was confirmed by a PCR positive for SARS-CoV-2 and lung CT [1]. All four developed the classic TTS type and met the InterTAK diagnostic criteria [1]. It was concluded that COVID-19 may be a trigger for TTS, but the underlying pathophysiology remained unclear and may be multifactorial in nature [1]. The work is compelling, but some points should be discussed.

We disagree that none of the four patients had known triggers of TTS [1]. Since two of the four included patients had Alzheimer's disease (patient 1, patient 2), we wonder how the authors ruled that TTS was due to Alzheimer's disease and not due to SC2I. Alzheimer's disease has been repeatedly reported to trigger TTS [2]. It has been suggested that the underlying pathophysiology of TTS in these patients is anxiety [2]. In particular, a change of location such as a hospital admission can lead to massive stress in Alzheimer patients.

Furthermore, patient 2 had a history of permanent atrial fibrillation [1]. Atrial fibrillation is known to occur more frequently in TTS patients without triggers than in patients with an identified TTS trigger [3]. Therefore, it cannot be excluded that in patient 2 Alzheimer's disease in combination with atrial fibrillation triggered TTS and not SC2I.

Patient 3 had a history of colon cancer [1]. Since oncological patients are at increased risk of developing TTS due to the emotional stress as well as the physical stress after complete cancer therapy, it cannot be ruled out that SC2I was not the trigger for TTS. In this context, we should know the latency period between the diagnosis and treatment of colorectal cancer and the development of TTS.

Regarding patient 4, who had a coronary fistula to the pulmonary artery, there are several case reports of patients with coronary fistula and TTS. Coronary fistulas can be congenital or acquired from trauma or invasive cardiovascular procedures. Half of the patients with coronary fistulas suffer from angina pectoris while the other half are discovered incidentally on echocardiography or coronary angiography performed for another reason.

A limitation of the study is that patient 2 did not undergo coronary angiography to rule out coronary artery disease. At least according to the Mayo Clinic criteria, coronary artery stenosis must be ruled out as an alternative pathophysiology.

Overall, the interesting study has limitations which challenge the results and their interpretation. Addressing these limitations could further strengthen and reinforce the statement of the study. Contrary to the main message of the work, triggers other than the SC2I were present in all four presented patients and could be responsible for the occurrence of TTS.

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