

LETTER TO THE EDITOR

SARS-CoV-2 triggered Takotsubo in 38 patients

To the Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) predominantly affects the lungs but direct or indirect involvement of other organs is increasingly recognized.¹ There are a number of publications available showing that in addition to the lungs, the urinary, cardiovascular, gastrointestinal, hematological, hematopoietic, neurological, or reproductive systems may be affected.¹ Cardiac involvement reported in SARS-CoV-2 infected patients includes myocardial infarction, myocarditis, heart failure, ventricular arrhythmias, or cardiogenic shock.²⁻⁴ Additionally, there is increasing evidence that also Takotsubo syndrome (TTS) may be a complication of the viral infection.⁵

TTS, also known as stress cardiomyopathy, broken heart syndrome, or stunned myocardium, is characterized by transient hypokinesia/dyskinesia/akinesia of the left ventricular myocardium leading to systolic dysfunction. TTS is believed to be triggered by excessive catecholamine release and overstimulation of myocardial

adrenergic receptors. TTS predominantly affects females and is triggered by physical respectively emotional stress in one-third of the cases each.⁶ Depending on the location of dyskinesia/akinesia/hypokinesia, four types of TTS are delineated: the apical type, the mid-ventricular type, the basal type, and the global type. TTS mimics myocardial infarction clinically, chemically, and electrocardiographically.⁶ Clinical manifestations of TTS include anginal chest pain and dyspnea.⁶ Creatine-kinase, troponin, catecholamines and proBNP are frequently elevated. Electrocardiography shows ST-elevation and negative T-waves. However, coronary angiography is usually normal. TTS is diagnosed according to the Mayo Clinic criteria. The outcome of TTS is usually fair and more favorable in TTS triggered by emotional than by physical stress.⁷

Though generally believed to be a rare complication of the SARS-CoV-2 infection, 38 cases with SARS-CoV-2 associated TTS have been reported so far (Table 1).^{5,8-20} The first patient with TTS associated with a SARS-CoV-2 infection was a 83-year-old Swiss

TABLE 1 Patients with SARS-CoV-2-associated TTS so far reported

Age (year)	Sex	OC	TTST	Treatment	Outcome	Origin	Reference
83	F	T	Classical	Heart failure therapy	Recovery	Swiss	Meyer et al. ⁸
67	F	B	Classical	Pericardio-centesis	Recovery	US	Dabbagh et al. ⁹
48	F	B	Classical	Dobutamine	Improvement	US	Minhas et al. ¹⁰
71	F	T	Mid-ventricular	nr	nr	Belgium	Nguyen et al. ¹¹
87	F	B	Classical	Bisoprolol, heparin	Recovery	Italy	Roca et al. ¹²
59	F	B	Classical	BB, DR, nitrate	Recovery	Italy	Moderato et al. ¹³
39-65	M (n = 5)	B	Classical (n = 4), Basal (n = 1)	nr	Recovery (n = 3) Death (n = 2)	US	Giustino et al. ¹⁴
84	M	B	Classical	ASS, nitro, BB,	Recovery	Italy	Pasqualetto et al. ¹⁵
85	F	B	Classical	ASS, inotropes	Death	Italy	Pasqualetto et al. ¹⁵
81	M	B	Classical	ASS, BB, heparin	Recovery	Italy	Pasqualetto et al. ¹⁵
52	M	B	Classical	Heparin, tocilizumab	Recovery	US	Taza et al. ¹⁶
nr	n = 19	nr	nr	nr	nr	Europe	Dweck et al. ¹⁷
59	F	B	Mid-ventricular	Ventilation, lidocaine	Recovery	US	Tsao et al. ⁵
50	M	B	Basal	nr	Recovery	Spain	Solano-López et al. ¹⁸
72	F	B	Classical	ASS, statins	Death	US	Theetha Kariyanna et al. ¹⁹
67	F	B	Classical	DAPT, statins, OAC	Recovery	US	Sattar et al. ²⁰

Abbreviations: A, after TTS; B, before TTS; BB, beta-blocker; COVID-19, coronavirus disease 2019; DAPT, dual antiplatelet treatment; DR, diuretics; nr, not reported; OAC, oral anticoagulation; OC, onset of COVID-19; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; T, together with TTS; TTS, Takotsubo syndrome; TTST, TTS-type.

female described by Meyer et al.⁸ Since then, several other SARS-CoV-2 infected patients with TTS have been reported. In a patient reported by Chadha et al. TTS was triggered by the fear from becoming infected without being actually infected with SARS-CoV-2. This patient was not included in the current evaluation. Also the patient reported by Kir et al. was not included as echocardiography was normal throughout hospitalization.

In 17 patients, TTS developed after onset of the SARS-CoV-2 infection, in two patients together with the infection, and in 19 patients onset of TTS was not reported (Table 1). Age ranged between 39 and 87 years among 19 patients. In 19 patients age was not reported. Ten patients were females, 9 were males, and in 19 patients gender was not reported. Fifteen patients presented with the classical type, two with the mid-ventricular type of TTS, and two patients with the basal type. In 19 patients, the TTS type was not reported (Table 1). Treatment for TTS was quite variable but most patients received beta-blockers, diuretics, heparin, or acetyl-salicylic acid (Table 1). Only a single patient received oral anticoagulation. One patient required pericardiocentesis because of immune-mediated pericarditis.⁹ Thirteen patients recovered, four died, one patient improved, and in 20 patients the outcome was not reported (Table 1). Twenty-seven patients originated from Europe and 11 from the US.

This mini-review shows that TTS can be associated with the SARS-CoV-2 infection but whether this association is accidental or causal remains speculative. There are indications that the general prevalence of SARS-CoV-2 associated TTS is not increased compared to the pre-COVID-10 era as reported by Jabri et al. and Delmas et al. Clinical presentation, epidemiology, treatment, and outcome of SARS-CoV-2-associated TTS is similar to COVID-19-unrelated TTS. In some patients, as reported by Sala et al., TTS may mimic myocarditis. TTS should be suspected in a SARS-CoV-2 infected patient if symptoms and signs of a myocardial infarction or heart failure develop in addition to the pulmonary compromise.

In conclusion, TTS in the context of a SARS-CoV-2 infection is more frequent than anticipated. Whether the general prevalence of TTS is truly increased compared with non-COVID-19 times requires further investigations.

AUTHOR CONTRIBUTIONS

Josef Finsterer: design, literature search, discussion, first draft, and critical comments. Claudia Stöllberger: literature search, discussion, and critical comments.

KEYWORDS

coronavirus, SARS-Cov-2, stress cardiomyopathy, stunned myocardium

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