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## Correspondence

# Rising trends in Takotsubo syndrome during the COVID-19 pandemic: A single center experience



### Keywords:

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Takotsubo syndrome (TTS) is a major psychosomatic cardiovascular disease (CVD), and it has been estimated that it represents 1–3% of patients presenting with a suspected acute coronary syndrome (ACS)<sup>1</sup>. There are reports suggesting that TTS has been associated with increased long-term morbidity and mortality, despite it being considered to be a benign condition<sup>1,2</sup>.

TTS is characterized by acute reversible left ventricular (LV) dysfunction, typically affecting LV apex with hypercontractile basal segments, in the setting of unobstructed or obstructed coronary arteries not corresponding to the pattern of LV dysfunction. Although the precise pathophysiological mechanisms remain unknown, it has been proposed that a catecholamine surge, precipitated by physical or emotional stress, plays a principal role<sup>1</sup>.

The ongoing coronavirus disease 2019 (COVID-19) pandemic has brought major consequences to the physical and mental health of the population. It has been suggested that in the current COVID-19 pandemic era, the psychological and physical consequences of the restrictive measures taken to combat the pandemic are likely to make individuals more vulnerable to TTS<sup>3</sup>. In our study, we investigated whether TTS incidence, as a percentage of ACS patients admitted to a major tertiary hospital, has increased during the COVID-19 era.

The study population included 316 consecutive patients admitted to the coronary care unit (CCU) of the University General Hospital “Attikon” in Athens throughout the 16 months (March 2020–June 2021) of COVID-19 pandemic period with an initial diagnosis of ACS. For comparison, we retrospectively analyzed medical records of 342 patients with ACS admitted to the CCU during the 16 months period preceding the COVID-19 pandemic (November 2018–February 2020). All ACS patients underwent coronary angiography within 48 h of admission. A prerequisite for admission to CCU of all ACS patients during the pandemic period was a negative reverse transcription-polymerase chain reaction test for COVID-19. For the diagnosis of TTS, the proposed by the Position Statement from the Taskforce on TTS of the Heart Failure

Association of the European Society of Cardiology criteria were applied<sup>4</sup>.

Table 1 shows the characteristics of TTS patients. There was a significant increase in the incidence of TTS during the 16 months of COVID-19 period (6.3%, i.e., 20 TTS among 316 ACS patients) compared with the corresponding incidence of TTS 16 months prior to COVID-19 pandemic (2.6%, i.e., 9 TTS among 342 ACS patients) [Fig. 1]. The incidence rate ratio comparing the TTS cases of COVID-19 pandemic period to the pre-pandemic period was 2.22 (95%CI: 0.97–5.54,  $p = 0.021$ ). Among the 20 TTS patients presented during the pandemic period, 2 (10%) had normal ECG at admission, 9 (45%) had T wave inversion, 5 (25%) had ST-segment elevation, and 4 (20%) had ST-segment depression. There was no difference in the type of ECG changes between the TTS cases presented prior compared to those presented during the pandemic ( $p > 0.05$ ).

Although there are several reports of TTS among COVID-19 patients<sup>5,6</sup> suggesting a direct “detrimental” triggering role of new coronavirus in the development of TTS, there are few and conflicting data on the impact of COVID-19 pandemic in the incidence of TTS among “non-COVID-19” patients<sup>6,7</sup>. In line with our results, Jabri et al. reported a significant increase in the incidence of TTS among ACS patients presented during the COVID-19 pandemic compared with the incidence in the pre-pandemic period<sup>6</sup>. On the contrary, Delmas et al. did not find an increase in TTS cases admitted to their institution between March 1st and April 15th, 2020 compared with the same period of previous years<sup>7</sup>. The difference in the results between the studies may be due to different quarantine policies and diverse levels of pandemic severity of the studied populations and the length of the study period<sup>8</sup>.

The current pandemic has renewed the interest in TTS, as one of the most characteristic psychosomatic manifestations of CVD. Quarantine and self-isolation can elicit feelings of social deprivation, anxiety, fear of infection, economic catastrophe, and depression, which in turn may lead to severe emotional stress, activating the hypothalamus–pituitary–adrenal axis and provoking increased catecholamines secretion, which is a pathophysiological cornerstone of TTS development<sup>1,3</sup>. Therefore, TTS increase among “non-COVID-19” individuals may be secondary to the additional psychological overload imposed by the COVID-19 pandemic.

In conclusion, we found that COVID-19 pandemic was associated with a significant increase in the incidence of TTS probably due to the additional psychological burden imposed by the pandemic. However, larger studies are needed to confirm the association of TTS with the COVID-19 pandemic.

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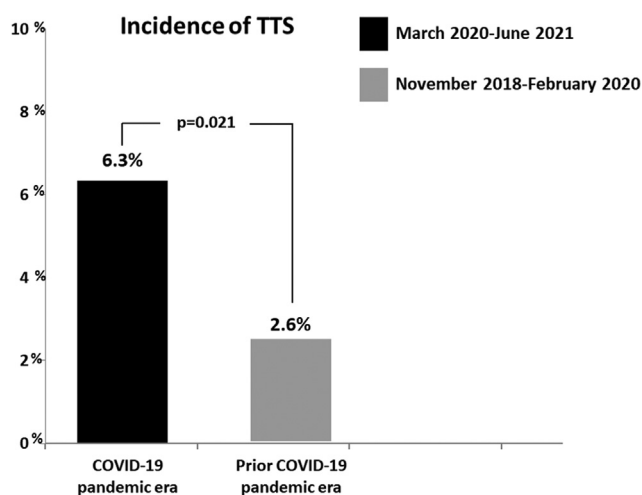
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**Table 1**

Characteristics of patients with Takotsubo syndrome (TTS). Patients with TTS during COVID-19 pandemic (n = 20) were compared with all TTS cases (n = 21) admitted to the coronary care unit during a period of 3 years prior the pandemic

Characteristics	All TTS patients (n = 41)	TTS patients during 16 months of pandemic (n = 20)	TTS patients during 3 years prior to pandemic (n = 21)	P-value*
Age (yrs)	69.9 ± 14.6	71.1 ± 15.4	68.7 ± 14.1	0.621
Women (n, %)	38 (92.7)	19 (95.0)	19 (90.5)	0.578
Ejection fraction at admission (%)	39.8 ± 7.9	40.8 ± 9.3	38.7 ± 6.1	0.438
Ejection fraction at follow-up (%)	47.2 ± 5.5	48.9 ± 4.9	46.1 ± 5.7	0.196
In-hospital mortality (n, %)	1 (2.4)	0	1 (4.7)	NA
Smoking (n, %)	9 (22.0)	5 (25.0)	4 (19.0)	0.645
Hypertension (n, %)	23 (56.1)	11 (55.0)	12 (57.1)	0.890
Diabetes mellitus (n, %)	9 (22.0)	5 (25.0)	4 (19.1)	0.645
Hypercholesterolemia (n, %)	16 (39.0)	8 (40.0)	8 (38.1)	0.901
Family history of premature CAD (n, %)	3 (7.3)	1 (5.0)	2 (9.5)	0.578
Triggering factor (n, %)	15 (36.6)	11 (55.0)	4 (19.0)	0.017
Previous psychiatric history (n, %)	6 (14.6)	4 (20.0)	2 (9.5)	0.343
Chest pain (n, %)	24 (60.0)	10 (50)	14 (66.7)	0.279
Dyspnea (n, %)	10 (24.4)	6 (30.0)	4 (19.0)	0.414
Syncope (n, %)	7 (17.0)	5 (25.0)	2 (9.5)	0.188
Abnormal ECG at admission (n, %)	37 (90.2)	18 (90.0)	19 (90.5)	0.955
Peak hs-cTnT (pg/mL)	517 ± 532	367 ± 399	620 ± 605	0.395
Peak NT-proBNP (pg/mL)	9861 ± 9567	9048 ± 9940	10964 ± 9284	0.578
Ratio: hs-cTnT/NT-proBNP	29.4 ± 26.5	30.4 ± 27.5	28.5 ± 26.3	0.817

Abbreviations: Hs = high sensitivity; CAD = coronary artery disease; NT-proBNP = N-terminal-prohormone of brain natriuretic peptide, cTnT = cardiac troponin T. \* Comparison between TTS patients During 16 months (March 2020–June 2021) of COVID-19 pandemic and TTS patients during 3 years prior to the pandemic.



**Figure 1.** Incidence of Takotsubo syndrome (TTS) among patients with initial diagnosis of acute coronary syndrome (ACS) during the 16 months of coronavirus disease 2019 (COVID-19) pandemic and among ACS patients during the 16 months preceding the pandemic.

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**Conflicts of interest**

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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