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Letter to the Editor

### Before attributing Takotsubo to SARS-CoV-2 vaccinations alternative triggers should be ruled out

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We eagerly read the article by Ahmed et al. about a systematic review of patients experiencing Takotsubo syndrome (TTS) after SARS-CoV-2 vaccinations <sup>[1]</sup>. Until the end of May 2022, 10 cases were extracted from five databases meeting the inclusion criteria <sup>[1]</sup>. It was concluded that pain should be considered an alarming symptom, especially in those who have received the first and second doses of the COVID-19 vaccine <sup>[1]</sup>. The study is appealing but raises concerns that should be discussed.

According to the exclusion criteria, articles providing only incomplete data were excluded from the evaluation <sup>[1]</sup>. However, according to table 1 the listed data are incomplete in patients 1, 2, 8, 9, and 10 <sup>[1]</sup>. This discrepancy should be solved.

A number of essential data are missing. There is no information about creatine-kinase (CK) or CK-MB <sup>[1]</sup>. Nonetheless, it was concluded that CK-MB and troponin are better biomarkers to confirm myocarditis than CRP, ESR, and NT-proBNP. Such conclusions cannot be drawn upon the provided data.

Missing are the results of coronary angiography <sup>[1]</sup>. According to the Mayo clinic criteria <sup>[2]</sup>, coronary angiography is a prerequisite to diagnose TTS. It is also not mentioned which subtype of TTS (classical, reverse, basal, global) was found in each of the 10 patients.

The spectrum of severe side effects to SARS-CoV-2 vaccines is much wider than thrombosis, anaphylaxis, Bell's palsy, myocarditis, and capillary leak syndrome <sup>[1]</sup>. It also includes Guillain-Barre syndrome, ischemic stroke, immune encephalitis, transverse myelitis, acute disseminated encephalomyelitis, myasthenia gravis, deep venous thrombosis, pericarditis, autoimmune hepatitis, pancreatitis, uveitis, thyroiditis, Graves' disease, arthritis, and several others <sup>[3]</sup>.

There were no data provided about myocarditis but it is concluded that CK-MB and troponin are better biomarkers to confirm myocarditis than CRP, ESR, and NT-proBNP <sup>[1]</sup>. This discrepancy should be solved.

It is stated that all 10 patients recovered from their symptoms but it is not indicated at what time ECG or echocardiography normalised after TTS.

The vasospasms of micro-vessels theory is only one pathophysiological concept to explain TSS. Catecholamine storm, downregulation of adrenergic receptors, sympathetic overstimulation, inflammation, estrogen deficiency, spasm of the epicardial coronary vessels, and aborted myocardial infarction should be also considered <sup>[4]</sup>.

We should know if the history was positive for TTS in any of the cases? In rare cases, recurrence of TTS has been reported <sup>[5]</sup>.

We should know if an acute SARS-CoV-2 infection was excluded in all patients. SARS-CoV-2 vaccinations do not prevent from infection in each case.

TTS is triggered by physical triggers in about one third of the cases, by psychological triggers in about one third of the cases, and in one third of cases the trigger remains unknown. We should how triggers, such as fear from side effects, fear from acquiring SARS-CoV-2 despite the vaccination, or other psychological stress was ruled out as the trigger of TTS.

Overall, the interesting study has limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study.

#### Declarations

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**Consent to participate:** was obtained from the patient  
Consent for publication: was obtained from the patient

**Availability of data:** All data are available from the corresponding author

**Code availability:** Not applicable

**Author contribution:** JF: design, literature search, discussion, first draft, critical comments, final approval.

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