



## Monaldi Archives for Chest Disease

eISSN 2532-5264

<https://www.monaldi-archives.org/>

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Monaldi Arch Chest Dis 2023 [Online ahead of print]

*To cite this Article:*

Alonzo A, Di Fusco SA, Colivicchi F. **Authors' Response.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2023.2835

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## Authors' Response

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**Key words:** COVID-19, Tako-Tsubo syndrome, stress.

**Contributions:** all the authors made a substantive intellectual contribution. All authors have read and approved the final version of the manuscript.

**Conflict of interest:** the authors declare that they have no competing interests.

**Ethics approval and consent to participate:** institutional review board approval was not required for this study as only de-identified compliant data were used in the analysis. The Data Protection Act and the Helsinki Declaration's principles were followed in the study.

**Patient consent for publication:** not applicable.

**Funding:** no funding is provided for the study.

**Availability of data and material:** all the data mentioned in the paper are available in the medical records.

Dear Editor,

We thank Dr. Finsterer and Dr. Stollberger for their interest in our published manuscript which is focused on the collected data from patients hospitalized in our multidisciplinary COVID-19 department who experienced a Tako-Tsubo syndrome (TTS) during the second and third wave of the pandemic [1]. This response represents an opportunity to highlight some limitations of the study and to further discuss the cases we have presented in the paper.

As regards the potential triggers of TTS in our cases, although it is not possible to establish with certainty the specific cause of TTS, it is worth noticing that all our patients don't experience only a SARS-CoV2 infection, but a full-blown COVID-19 with the known correlated symptoms and related interstitial pneumonia confirmed by computed tomography, which can represent in itself a trigger like several other infectious diseases. In addition, although as specified by Finsterer et al, psychiatric and neurologic disorders may be triggers of TTS, the majority of TTS cases associated with neurological disorders that are reported in the literature are described after a stroke or subarachnoid haemorrhage or seizure [2]. Moreover, the literature's cases of TTS associated with Alzheimer's disease are anecdotal. For this reason, it is difficult to consider Alzheimer's disease a classical trigger for TTS. Nevertheless, we reported this information in the manuscript in order to highlight the association, which can also be interpreted as an additive predisposing condition to TTS. Larger clinical records are necessary to better clarify this interesting association. Although we recognize that anxiety may be a further potential trigger underlying the pathophysiology of TTS in these patients, the mechanisms of TTS in COVID-19 patients remain unclear and might be multifactorial.

The case 2 with atrial fibrillation (AF) was a case of permanent AF with a normal ventricular response and no symptoms. It is unlikely that a chronic and stable condition can represent in itself a trigger for TTS. However, we think that AF, in particular the paroxysmal form reported for patient n.4, may be considered as a complication of TTS.

For what concerns the patients with a history of colorectal cancer, the diagnosis was dated three years before and it was treated only with surgery at that time. Following, the patient underwent to serial oncological controls that resulted negative. As for the case of permanent AF, it is unlikely that a three-year dated diagnosis of colorectal cancer can be considered a trigger of TTS.

Regarding the patient 4, a coronary artery fistula (CAF) is diagnosed in 0.2- 0.4% of patients undergoing coronary angiography. Moreover, a recent paper collected clinical data of 9 patients with concomitant TTS and CAF, concluding that coexistence of TTS and CAF may be considered coincidental [3]. We agree with the colleagues that a limitation of the study is the missed

coronary angiography for patient n.2, but our choice was forced by an intercurrent episode of haemorrhagic shock due a spontaneous psoas muscle haematoma, which required red blood cells transfusions. Furthermore, we want to point out that several limitations of our study must be interpreted in light of the pandemic context we were forced to work.

With the present letter's response, we wish that our paper is more comprehensive. In conclusion, we would like to think about our work as a small piece of a wider puzzle, which is the pathophysiology of TTS in COVID-19 and that remains still to be defined. Further and larger studies will certainly help to better understand this interesting association.

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