

Response to the reviewers

Reviewer#1

Reviewer response 1: All possible stressors can cause Takotsubo cardiomyopathy (TTC), including addiction, which is also a natural cause of TTC and not uncommon. There is nothing new about the clinical features and treatment of TTC after it has occurred, and it is unlikely to be of much interest to the reader.

Authors response 1: Thank you for the suggestion. We agree that several stressors can precipitate TTC. In this review article, we highlight the multiple reported cases of TTC following envenomation which has not been reviewed before. We have included this in the discussion and have highlighted it in red. (Line 220 to 222)

Reviewer response 2: You mention poisoning and animal bites, but in fact you describe bites caused by insects and other organisms. It seems that a more detailed description of how it was investigated should be provided.

Authors response 2: We agree with the reviewer and have changed the wording to insects and reptiles. We have incorporated the same in the abstract and in the manuscript. (Line 60,80,317,374)

Reviewer response 3: Is this all-case reports as listed in Table 1? Are there any characteristics in terms of gender, age, etc.? Also, the authors should add a reference to each report.

Authors response 3: All case reports are present in the table. As per the reviewer's recommendation, we have included another table with multiple demographic characteristics. (Table -1) (Lines: Multiple)

Reviewer response 4: Line 105-106, it is stated that it is more common in males in Japan, but there is no mention of the source. This seems incorrect, since it is definitely more common among elderly women in Japan.

Authors response 4: In their review article "Takotsubo cardiomyopathy: Review of broken heart syndrome" Boyd et al reported that TTC is more common in males in Japan. However, as per the reviewer's concern, we looked at the recent demographics of TTC in Japan. Recent articles on gender differences in TTC in Japan have reported that its prevalence is higher in elderly females. We agree with the reviewer's response. We have modified the manuscript and have removed the old citation. We have also incorporated the recent article by Murakami et al (Line 105 modified, Citation 3)

Citation: Murakami T, Komiyama T, Kobayashi H, Ikari Y. Gender Differences in Takotsubo Syndrome. *Biology (Basel)*. 2022 Apr 24;11(5):653. doi: 10.3390/biology11050653. PMID: 35625378; PMCID: PMC9138502.

Reviewer#2

Reviewer response 1: This review summarized the various mechanisms, clinical features, management, and outcome following envenomation's precipitating Takotusbo cardiomyopathy (TTC). The manuscript provides another unique perspective on TTC, which is helpful for clinical treatment.

Authors response 1: We thank the reviewer for the positive response to our manuscript

Reviewer response 2: The minor comments are: i) provide the full names when acronyms first appear in the text, such as TCM, ECMO.

Authors response 2: We have incorporated the same in the manuscript and have highlighted the same in red. (Lines: Multiple)

Reviewer response 3: ii) Please introduce the key components of venom that could lead to TTC from different species, if possible.

Authors response 3: We have included the details of the 2 venoms under the mechanism section. We agree with the reviewer that consistently the component of the venom precipitating TTC has not been reported. Hence, we have included the same in the limitation and in future recommendations. (Lines: 268-270, 354,355, 361,363)

Reviewer response 4: iii) Please improve the readability of diagrams.

Authors response 4: We have enhanced the image quality further. (Image 1 and 2)

Response to the Editor

Editors response 1: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Cardiology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Authors response 1: Thank you for your positive response. We have incorporated all the modifications as suggested by the reviewers. We have included an additional table, removed 1 citation, and have included 5 more additional citations and have highlighted all the modifications in red.

Editor response 2: Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Authors response 2: We have enhanced the quality of our images and have incorporated the modifications within a Power point presentation. (Image 1 and 2)

Editor response 3: In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is

‘original’, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

Authors response 3: These are the author’s original images. We have incorporated the copyright as required. (Image 1 and 2)

Editor response 4: Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Authors response 4: We have submitted the table as per the requirements of the journal (Table 1 and Table 2)

Editor response 5: Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

Authors response 5: We will provide highlights of this research results on acceptance of our manuscript

Editor response 6: To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Authors response 6: We have utilized the RCA database and have incorporated the same in our manuscript (Line 127)