Reply to: "To conclude that BNT162b2 does not worsen echocardiographic indices, well-powered multicenter studies are required"

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DEAR EDITOR,

We thank Dr. Josef Finsterer and Claudia Stollberger C for the valuable comments and questions on our study named "Echocardiographic function evaluation in adolescents following BNT162b2 Pfizer-BioNTech mRNA vaccination: a preliminary prospective study" published in *Journal of the Chinese Medical Association* in October 2023.[1] We acknowledge the concerns raised and provide the following responses to address these points.

Small group size: We acknowledge the limitation of the small sample size in our study, attributed primarily to constraints imposed by the government's unified vaccination program and challenges in recruiting additional participants for this particular investigation. We concur with the suggestion of multicenter and international collaborations to expand the cohort and enhance the robustness of our findings. Future studies with larger, more diverse populations are indeed warranted to provide more definitive conclusions.

Explanation of the increase in systolic function: The observed steady increase in systolic function postvaccination raises important questions. Although we hypothesized that this may be attributable to heightened self-care postvaccination or a compensatory mechanism in response to subclinical myocardial stress, we acknowledge that without concrete evidence of myocardial damage or a direct link to vaccination, these interpretations remain speculative. The referenced study on isolated rat cardiomyocytes provides valuable insights, suggesting possible cellular mechanisms that warrant further investigation in humans.[2]

Analysis of autonomic function: We appreciate the suggestion to include autonomic function in our analysis. Due to the limited time interval between participant enrollment and vaccination, influenced by government policy during the Coronavirus Disease 2019 (COVID-19) pandemic, our study did not measure sympathetic activation levels, such as urinary catecholamines or serum norepinephrine. These measurements could indeed provide a more comprehensive understanding of the vaccine's impact on cardiac function and represent an interesting avenue for future research.

Explanation of decreased Left Ventricular Internal Diameters (LVIDs) in females on day 2: The decrease in LVIDs in females from baseline to day 2 postvaccination was an interesting finding. The potential influence of baseline differences in cardiac dimensions between males and females warrants further investigation. The decision to initiate echocardiographic assessments on day 2 postvaccination was based on previous reports indicating that myocarditis symptoms typically manifest around this time.[3,4] Although this approach limited our ability to detect immediate changes on day 1, it was chosen to balance participant compliance with the need for timely evaluation.

We acknowledge the limitations of our study, including the small sample size, lack of autonomic function analysis, and potential selection bias. These constraints are addressed in our discussion, and we underscore the necessity for further research in this area. Well-designed, multicenter studies with comprehensive cardiac evaluations, including biochemical and autonomic function assessments, are crucial to confirm our findings and expand our understanding of the cardiac effects of the BNT162b2 vaccine.

We trust these explanations adequately address both the readers' and the authors' expectations. We appreciate your continued interest.

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