

## Critical Review: Methodological and Interpretative Issues in COVID-19 and Acute Coronary Syndrome Study

To the Editor,

Recently, I came across this wonderful article titled "Comparison of the Effects of Recent Coronavirus 2019 Infection and Vaccination on the Prognosis of Acute Coronary Syndrome: A Retrospective Study Conducted in a Single Center in Türkiye" by Özbek and Can<sup>1</sup> which was recently published in your journal. The authors were successful in bringing out the interlink between COVID-19 infection, vaccination, and acute coronary syndrome (ACS). However, there are certain methodological and interpretative issues that need to be discussed further.

To begin with, the study has a retrospective design, and the data collected were from a single center. This raises questions about the generalizability of its findings. Even though the authors acknowledge these limitations, the extent to which these results can be applied to other populations remains unclear. Also, the study relies on hospital records and national databases for its data. This may result in inconsistencies, particularly concerning the accuracy of retrospective data collection. Similar studies by Alharbi et al<sup>2</sup> and Rashid et al<sup>3</sup> demonstrates the fact that multicenter data were needed to ensure broader applicability and validate findings.

The authors point out that there are increased mortality and major adverse cardiovascular event (MACE) rates in post-COVID groups compared to other groups. Even though this finding is critical, the authors fail to rule out the potential confounders such as the severity of coronavirus disease 2019 (COVID-19) infection, preexisting conditions, and the timing of infection relative to ACS onset, which could have influenced the outcomes. The significance of these variables on the mortality and MACE rates in ACS patients was demonstrated in a study by Milovančev et al.<sup>4</sup> This suggests that more granular data are needed to draw definitive conclusions.

Also, the study finds that hyperlipidemia was independently associated with decreased chances of MACE. This was contradictory to our preexisting knowledge. This unexpected result suggests that anti-inflammatory and antioxidant effects possibly exerted by antilipidemic therapy could have played a protective role; however, prospective studies are required to support this hypothesis. This suggestion blends with existing literature on the potential benefits of such treatments but requires more robust evidence to shift current clinical paradigms.

Also, the study does not properly address the importance of certain factors like difference in vaccination regimens, time since the last vaccine dose, etc., which could have influenced the ACS outcomes. A comprehensive analysis including these factors are essential for reaching accurate interpretations of vaccine efficacy and safety concerning ACS.

In summary, while the study by Özbek and Can<sup>1</sup> has added great insight into the interplay between COVID-19, vaccination, and ACS, it has certain issues as highlighted above. Addressing these concerns through further research, preferably with multi-center and prospective designs, will be crucial in validating these

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findings and improving our understanding of ACS management in the context of COVID-19.

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