

## Reply to Letter to the Editor: "Critical Review: Methodological and Interpretative Issues in COVID-19 and Acute Coronary Syndrome Study"

To the Editor,

We recently received a comment<sup>1</sup> to our study 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,"<sup>2</sup> which was recently published in your journal. We thank the authors of the comment for their interest and detailed evaluation. In this study, we aimed to elucidate the relationship between Coronavirus Disease 2019 (COVID-19) infection, vaccination, and acute coronary syndrome (ACS).

For this retrospective study, data were collected from a single center based on hospital records and national databases. As expected, this may have led to some deficiencies in data collection. However, apart from acknowledging their possibility, it is evident that these deficiencies are unlikely to alter the outcomes or the content of the article.

In the results section, we found increased mortality and major adverse cardiovascular events (MACE) rates in the post-COVID group compared to other groups. Of course, there may be confounding factors that bias these outcomes. However, data such as the severity of COVID-19 infection and pre-existing conditions, which have been mentioned in the critique, were not included in the study because it would be very difficult to ensure the reliability of these data in a retrospective review. Furthermore, these data could also introduce other forms of bias since there were numerous definitions of COVID-19 severity, which changed considerably within short intervals during the pandemic. Therefore, including this data may have been inefficient and insufficient.

Our study found that hyperlipidemia was independently associated with lower rates of MACE. Although this was contradictory to pre-existing knowledge, this unexpected result can be attributed to the protective role of antilipidemic therapy due to its anti-inflammatory and anti-oxidant effects.<sup>3,4</sup>

Finally, we evaluated other factors that could affect the interpretation of the results, such as differences in vaccination regimens and the time that had elapsed since the most recent vaccination. However, vaccine types, their combinations, and temporal relationships were not considered suitable for evaluation due to their complexity and the paramount difficulty in characterization.

In conclusion, considering all these issues and contradictions, it is clear that larger-scale research can improve our understanding of ACS management in the context of COVID-19, given that strict exclusion criteria are applied to only include patients with characteristics that can be reliably stratified into meaningful groups. We believe that the main outcomes of our study contribute to the literature to a certain extent, despite the marginal limitations and the need for further data collection.

### LETTER TO THE EDITOR REPLY

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