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Addressing Selection Bias and Risk Factors in COVID-19 and CAD Research: Critical Considerations

LETTER TO THE EDITOR

To the Editor,

We read with interest the article by Çetinkaya and Taş[1] examining the relationship between COVID-19 infection, vaccination, and severe coronary artery disease (CAD) in a center in Türkiye.[1] Their study makes a valuable contribution to observations on the cardiovascular outcomes of the pandemic period. However, we believe that several methodological aspects warrant further discussion.

Pandemic-related changes in clinical practice have likely influenced the severity of observed CAD. During periods of high COVID-19 transmission, coronary angiography was often restricted to patients presenting with overt acute myocardial infarction, whereas elective procedures were postponed.[2,3] Consequently, regardless of any direct effect of COVID-19 infection or vaccination, patients undergoing angiography during this time were more likely to have advanced disease. This context complicates attributing the temporal increase in severe CAD solely to pandemic-related biological effects.

Another limitation relates to the study's definition of severe CAD based on clinical decision-making, namely the need for percutaneous coronary intervention or surgical referral. Although clinically practical, such criteria introduce subjectivity, as intervention preferences may vary according to physician judgment, patient comorbidities, and institutional protocols. The reproducibility and comparability of the results would be strengthened if objective angiographic scoring systems, such as SYNTAX or Gensini scores, were employed.

Furthermore, the lack of basic demographic characteristics and cardiovascular risk profiles further limits interpretation. Factors such as hypertension, diabetes, dyslipidemia, and smoking are critical determinants of CAD severity.[4] Without adjustment for these variables, it is difficult to exclude the possibility that differences in the underlying comorbidity burden confounded the findings. Pandemic-related healthcare disruptions associated with poorer risk factor control may also have contributed to more advanced coronary disease presentations.[3]

In addition, the study does not clarify the clinical context leading to angiography. It does not specify whether patients underwent angiography for acute coronary syndromes or for elective evaluation. Given that CAD severity varies considerably by clinical presentation, this missing information complicates the interpretation of severity trends.

The exclusion of patients who died due to missing immunization data also introduces potential selection bias. Fatal cases, which may have involved more severe cardiovascular disease, were not represented, potentially underestimating associations between COVID-19, vaccination status, and CAD severity.

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In conclusion, although the study by Çetinkaya and Taş[1] provides important data, its findings should be interpreted cautiously due to variations in clinical practice, subjective definitions of disease severity, incomplete risk factor adjustments, potential selection bias, and lack of clinical presentation details. Future studies incorporating objective CAD severity, comprehensive risk factor adjustments, and stratification by clinical presentation would offer greater clarity regarding the cardiovascular outcomes of COVID-19 infection and vaccination.

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