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Letter to the Editor

The difference of inhospital outcome of COVID-19 in vaccinated and unvaccinated not only depends on the vaccination status

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We read with interest the article by Balian *et al.* on a retrospective, single centre, observational, study of the inhospital outcome of vaccinated and unvaccinated patients admitted for acute COVID-19 infection ^[1]. It was concluded that vaccination status correlates with patient demographics and differences in inpatient treatment ^[1]. The study is excellent but has limitations that are cause of concern and should be discussed.

A parameter not included in the analysis is the latency period between the last vaccination and the onset of symptoms that lead to hospital admission ^[1]. Knowing this latency is crucial to be able to assess whether the symptoms could also be due to side effects of the vaccination and to assess whether the vaccination is still effective or not. Side effects of SARS-CoV-2 vaccines can be serious and life-threatening in individual patients, such as venous sinus thrombosis, stroke, immune encephalitis, myocarditis, or cerebral bleeding ^[2].

Another limitation is that the group sizes were small and the study design was retrospective, single-centre, and observational^[1]. The quality of the data in a study based on electronic records depends on the quality of the record and documentation, and the quality of the data cannot be easily controlled.

Another limitation is that the case allocation excluded more unvaccinated than vaccinated patients. The large number of excluded patients in the vaccinated group may have contributed to the favourable assessment of the vaccination. A 1:2 ratio of vaccinated to unvaccinated subjects would probably have produced a more realistic result.

Another limitation is that the virus variant and variant lines with which the included patients were infected were not included in the analysis. Knowledge of virus variants and lineages would be helpful, since the pathogenicity and thus the outcome of the infection can depend heavily on the pathogenicity of the causative virus variants and lineages.

Overall, the interesting study has limitations that put the results and their interpretation into perspective. Clarifying these limitations would strengthen the conclusions and could improve the study. The conclusion that vaccinated patients have a better outcome from COVID-19 infection than unvaccinated patients' needs to be reconsidered given that the two cohorts compared in this index study were inhomogeneous in terms of age. In addition, key parameters to assess the effectiveness of vaccination with regard to the outcome of a COVID-19 infection, such as the latency period between vaccination and the onset of COVID-19 symptoms, number of doses, and viral pathogenicity, were not included in the evaluation.

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Compliance with Ethics Guidelines: This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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