JIM Editorial

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SARS-CoV-2 antibody titers at the time of hospital admission and risk for mortality

In this issue of the *Journal of Internal Medicine*, Mink et al. [1] evaluated if anti-SARS-CoV-2 Spike-antibody titers in SARS-CoV-2 positive individuals could be used to predict risk for inhospital mortality. In this context, they conducted a prospective, multicenter cohort study. In the study, anti-SARS-CoV-2 Spike antibodies were determined on hospital admission. The investigated endpoint was inhospital mortality of any cause. The authors found anti-Spike antibodies, upon hospital admission, to be significantly lower in non-survivors in both nonvaccinated and vaccinated patient groups. On the basis of their results, they conclude that anti-SARS-CoV-2 Spike-antibody levels on hospital admission are inversely associated with inhospital mortality. That is, hospitalized SARS-CoV-2 positive patients with lower antibody titers had a higher risk of mortality.

Anti-SARS-CoV-2 vaccinations have had a major impact on the prevention of severe disease and death in COVID-19 [2–4]. At the initiation of the present study, it was not known whether antibody levels against SARS-CoV-2 on the day of hospital admission could help identify patients at high risk of mortality. This question was especially pertinent considering the high number of SARS-CoV-2 positive patients with severe COVID-19 being admitted during the initial phases of the pandemic. The authors hence reasoned, a simple diagnostic parameter to assess the risk of mortality in COVID-19 could facilitate patient management and, possibly, could allow for timely adjustment of therapy in high-risk patients. The latter questions formed the rational for the present prospective, multicenter cohort study. In their study, including 1152 patients, they were able to demonstrate that SARS-CoV-2 Spike-antibody titers below 1200 U/mL (as assessed by the Elecsys Anti-SARS-CoV-2 S assay for antibodies against SARS-CoV-2 Spike) upon hospital admission could serve as a predictor for patient mortality. This is an interesting and important observation. Its full usefulness in clinical practice, however, remains to be evaluated. As such, the strength of the present study, and hence its results, is the clinical trial setting involving several hospitals allowing for high recruitment rates, which has minimized the risk of selection bias. In addition, the study is based on a hard primary endpoint (i.e., mortality). Adding value to the study, the results are also adjusted for multiple causes of potential bias, including age, body mass index, and SARS-CoV-2 variants.

The lower mortality observed in vaccinated patients with Spike-antibody titers above 1200 U/mL, the authors reason, may at least in part be due to higher levels of anti-SARS-CoV-2 neutralizing antibodies. However, indeed likely, it would be interesting to confirm this notion in further explorative studies. Likewise, it would be of interest, if possible, to assess similar correlates with respect to T-cell-mediated immune responses. In this context, the authors indeed also note that it is currently not fully proven that the observed associations between Spike antibodies and lower mortality specifically indicate protection by higher Spike-antibody titers per se or if they indicate a "generally better" immune response and thus a better general condition of the individual, which in turn improves chances of survival. The authors, in relation to their own findings, also describe that different models have been proposed for identifying patients at high risk of negative outcomes [5–7]. Although these findings are interesting, they (likely correctly) note some of these models may require measuring of a combination of different parameters and may, as such, have a more limited feasibility in clinical practice as predictive measures.

Finally, the authors note that although they did see significant differences in mortality above versus below 1200 U/mL of anti-SARS-CoV-2 Spike antibodies, additional and extended studies are required to define a clear cutoff for protection against mortality in COVID-19. They reason that, as an increasing percentage of the population is getting vaccinated against SARS-CoV-2, follow-up studies to evaluate the role of antibody titers and define a protective cutoff after additional booster

vaccinations are needed. It can, however, be discussed how feasible this is in practice on a populational level versus more generic advice toward the general populational with respect to needs for additional booster doses over time, for example, once a year for generally healthy individuals and perhaps twice a year for risk groups, including patients with immunocompromised disorders and/or high age. This said, measuring Spike antibodies on hospital admission of vaccinated (and/or previously infected) patients may, as concluded by the present study, facilitate risk stratification and serve toward identifying patients with high(er) risk of mortality upon hospitalization. As such, the present study provides valuable insights and a clinically important finding.

Conflict of Interests Statement

The author declares no conflict of interests.

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