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Letter to the Editor

Response to the letter to the Editor regarding the article “Vaccine versus infection - COVID-19-related loss of training time in elite athletes”

We thank Rujittika Mungmunpantipantip and Viroj Wiwanitkit for their interest in our article¹ and for taking the time to comment. We would like to respond to the points raised in their letter and explain aspects of our work related to these points.

Mungmunpantipantip and Wiwanitkit suggest that the observed outcomes of our study might be incorrectly interpreted because the extent and intensity of the side effects of COVID-19 vaccines can be related to confounding factors. They imply that our investigation should have been more robust and that we have not complied with issues such as the efficacy of vaccines, comorbidities of vaccine recipients, and other confounders.

In particular, they believe that the absence of clinical symptoms after vaccination may be associated with previous asymptomatic SARS-CoV-2 infection, and undiagnosed COVID-19 at the time of vaccination may cause the observed side effects and affect the loss of training after vaccination, not the vaccination itself. They accuse us of not ruling out past or active COVID-19 at the time of vaccination.

In addition, Mungmunpantipantip and Wiwanitkit think that we should have investigated the genetic polymorphisms related to the immune response to vaccination in our subjects since genetic variation can influence how individuals within a population respond to vaccination.

We concur that the ideal way to solve the problem raised in our study would be to start a clinical trial with a large group of athletes, to the fullest extent examined, who have not yet had COVID-19. The athletes would have been randomly and proportionally assigned to receive an intramuscular injection of selected vaccines or saline placebo. Then, at least a one-year follow-up should have been commencing. Such a perfect study would provide important data for future planning to manage the COVID-19 problem and post-COVID-19 consequences among athletes. But we must come down to earth and return to the reality of the advancing pandemic.

Our study has limitations because we retrospectively analyzed information from an ongoing real-world experiment. It was no longer possible to start the perfect clinical trial described above. But the study has strengths too. It was carried out on a large group of elite athletes, including Olympians, in a medical center that cares for them continuously. We had full access to their demographic data and medical history; the problem of comorbidities as potential confounding factors could be neglected in this group. The primary tool used in the study was a questionnaire, but the answers were given during a medical visit and directly inspected by the physician. The understanding of the problem was high, as virtually no one refused to participate in the study.

Vaccinations were performed as part of a national program, following the rules established by WHO, with vaccines registered by the European Medicines Agency, with standard dosage and administration. The safety and efficacy of these vaccines had already been evaluated in large clinical trials.^{2,3} We did not include an evaluation of the efficacy of the used vaccines in our analysis. Perhaps it would be worth addressing the issue of the efficacy of the vaccines in the discussion section of the article, noting that despite the vaccination, there is still an estimated risk of infection and loss of training days due to COVID-19.

As to the association between past COVID-19 and adverse symptoms after vaccination, the studies published so far indicate that it is the opposite of what Mungmunpantipantip and Wiwanitkit suggest. Although research on athletes is lacking, research on healthcare workers has shown that the occurrence of adverse symptoms after the first dose of mRNA BNT162b2 vaccine was more frequent in individuals with previous COVID-19, and after the second dose was similar in individuals with and without previous COVID-19.⁴ Similar conclusions were drawn after the study on the general population that evaluated factors potentially associated with participant-reported adverse effects after COVID-19 vaccination - subjects with prior COVID-19 had greater odds of adverse effects.⁵ We did not address this problem in our study. However, given the studies cited above, this issue could not have affected our observations in the way suggested by Mungmunpantipantip and Wiwanitkit.

The authors of the letter raise the issue of undiagnosed COVID-19 at the time of vaccination and in the first days after vaccination and its potential impact on the observed loss of training but go no further to show the potential magnitude of the problem. In the study cited in the letter, which included healthcare workers caring for COVID-19 patients, post-vaccination SARS-CoV-2 infection occurred within 14 days of the initial dose in 67 of 7109 (0.9%).⁶ These rates are up to five times lower in the clinical trials cited above.^{2,3} Even if, in a few cases, we incorrectly classified the disease symptoms as adverse effects of vaccination, this bias would not work in favor of vaccines.

However, we firmly refute the allegation that no examination has been conducted to rule out the likelihood of such incidents. During the period covered by the study, it was a rule in Poland that every vaccine recipient underwent a medical evaluation that included medical history and physical examination before the vaccination. An important part of this evaluation was ruling out COVID-19 symptoms and assessing infection risk related to exposure to infected people.

And finally, on the association between genetic polymorphisms and vaccine outcomes. Mungmunpantipantip and Wiwanitkit point to the lack of genetic background assessment in our study, but they do not indicate what exactly we should assess given the study's objectives.

Certainly, genetic factors contribute to the heterogeneity of vaccine response. Recognizing these genetic factors would contribute to more effective, personalized treatment and prevention strategies. But these genetic factors are not yet identified to the extent to allow clinical translation. The studies on the association between host genetics and SARS-CoV-2 infection have identified many DNA variants associated with COVID-19, but this is only the starting point to explain the mechanisms underlying the immune response.⁷

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Confirmation of ethical compliance

The authors declare that the Bioethics Committee at the Medical University of Warsaw on October 4, 2021, received information about the subject of the study entitled "Assessment of young athletes' attitudes towards vaccinations against COVID-19 and their impact on the implementation of the training program." The above-mentioned study is consistent with the principles of ethics of scientific research.

Declaration of interest statement

All authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence the present work.

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