Long-Term Recovery from SARS-CoV-2 (COVID-19)

Recent COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in physically active healthy people

Helena Batatinha,1 Forrest L. Baker,1,2 Kyle A. Smith,1 Tiffany M. Zúñiga,1 ☑ Charles R. Pedlar,3,4 Shane C. Burgess,5,6 ☑ Emmanuel Katsanis,2,6,7,8,9 and ☑ Richard J. Simpson1,2,6,7

1 School of Nutritional Sciences and Wellness, University of Arizona, Tucson, Arizona; 2 Department of Pediatrics, University of Arizona, Tucson, Arizona; 3 Faculty of Sport, Allied Health and Performance Science, St. Mary’s University, London, United Kingdom; 4 Institute of Sport Exercise and Health, University College London, London, United Kingdom; 5 Department of Animal and Comparative Biomedical Sciences, University of Arizona, Tucson, Arizona; 6 The University of Arizona Cancer Center, Tucson, Arizona; 7 Department of Immunobiology, University of Arizona, Tucson, Arizona; 8 Department of Medicine, University of Arizona, Tucson, Arizona; and 9 Department of Pathology, University of Arizona, Tucson, Arizona

Abstract

Athletes are advised to receive the COVID-19 vaccination to protect themselves from SARS-CoV-2 infection during major competitions. Despite this, many athletes are reluctant to get the COVID-19 vaccine due to concerns that symptoms of vaccinosis may impair athletic performance. This study aimed to determine the effects of COVID-19 vaccination on the physiological responses to graded exercise. Healthy physically active participants completed a 20-min bout of graded cycling exercise at intensities corresponding to 50%, 60%, 70%, and 80% of the predetermined VO2max before and ~21 days after receiving the COVID-19 vaccine (2-dose Pfizer mRNA or 1-dose Johnson & Johnson). Vaccination had no effect on a large number of physiological responses to exercise measured in blood (e.g., lactate, epinephrine, and cortisol) and by respiratory gas exchange (e.g., oxygen uptake, CO2 production, ventilation, respiratory exchange ratio, predicted VO2max, and ventilatory threshold) (P > 0.05). We did, however, find significant elevations in heart rate (~5 beats/min) and norepinephrine (P = 0.006 and 0.04, respectively) in response to vigorous (i.e., 70%–80% VO2max) intensity exercise after vaccination, particularly in those who received the two-shot Pfizer mRNA vaccine regimen. These findings held true when compared with demographically matched controls who completed identical bouts of exercise several weeks apart without receiving a vaccine; delta values for heart rate (P = 0.03) and norepinephrine (P = 0.01) were elevated in the second trial for those who received the Pfizer mRNA vaccine compared with the controls at the 70% and 80% VO2max stages, respectively. Recent COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in physically active healthy people. The small elevations in cardiovascular and neuroendocrine responses to exercise after the Pfizer mRNA vaccine regimen could have implications for athletes at the elite level and warrants investigation.

NEW & NOTEWORTHY Recent COVID-19 vaccination does not affect a large number of physiological responses to graded exercise, indicating that vaccination is unlikely to impair exercise capacity in normal healthy people. Heart rate and norepinephrine levels were elevated in response to exercise after the two-dose Pfizer mRNA vaccination compared to controls. Small elevations in cardiovascular and neuroendocrine responses to exercise after recent COVID-19 vaccination could have implications for exercise performance in elite athletes and warrants investigation.

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—etiologic agent of coronavirus disease 2019 (COVID-19)—was first identified in December 2019 in Wuhan, China, before being declared a global pandemic in March 2020 (1). As of November 2021, more than 250 million people worldwide have been infected with SARS-CoV-2, which has resulted in ~5.1 million deaths. The rapid production and distribution of mRNA (e.g., Pfizer and Moderna) and viral vector-based vaccines (e.g., Johnson & Johnson and AstraZeneca) were initiated in November 2020 and has greatly limited the spread of COVID-19 (2), with 40% of the world’s population now fully vaccinated (3). Several clinical trials have
demonstrated the safety and efficacy of the current COVID-19 vaccines (4–6), with reported side effects such as body aches, fever, arm soreness, malaise, and flu-like symptoms usually mild and typically resolving within 48 h (7). However, reports are emerging that COVID-19 vaccination in a minority of patients has been associated with more severe and longer-lasting symptoms including myocarditis, fatigue, shortness of breath, cough, joint, and chest pain (8, 9).

Athletes are recommended to receive all necessary vaccines before competition due to increased risks of viral exposure (10). A recent study in elite German athletes found that the quadrivalent inactivated influenza vaccine evoked a strong immune response with no reported side effects or loss of training (11). However, due to emerging reports (albeit mostly anecdotal) of adverse symptoms associated with COVID-19 vaccines, there is a growing concern among the athletic community that vaccination might hinder athletic performance. This has resulted in many athletes refusing to get vaccinated before or during competition, leaving them susceptible to SARS-CoV-2 infections during major sporting events. Indeed, during current/recent sporting events such as the 2021 European Championship and Copa America International Soccer tournaments, as well as the Tokyo Olympic Games, there were multiple incidences involving players/athletes having to miss games/competitions due to contracting SARS-CoV-2 or having been in contact with infected individuals.

To alleviate or confirm concerns regarding the potential negative effects of COVID-19 vaccination on athletic performance, there is a critical need to determine whether recent COVID-19 vaccination affects physiological responses to various intensities of exercise. Here, we investigated the effects of recent COVID-19 vaccination on metabolic and physiological responses to graded cycling exercise in physically active healthy individuals. We report that COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in healthy people, although small increases in the cardiovascular and neuroendocrine response to vigorous exercise that were observed after vaccination could have implications for athletes at the elite level.

### METHODS

#### Participants

A total of 18 (9 females, 9 males) healthy individuals between the ages of 24–43 yr participated in this study. Baseline anthropometric and cardiovascular characteristics are shown in Table 1. Twelve participants received a COVID-19 vaccine during the study period [Pfizer mRNA vaccine (n = 9), Johnson & Johnson viral vector-based vaccine (n = 3)], whereas six participants, who were involved in a parallel nonvaccine-related research study in our laboratory, served as controls. Prior to their enrollment, each subject completed the American Heart Association/American College of Sports Medicine (AHA/ACSM) preparticipation screening questionnaire and medical history survey (12) to verify that they had not been previously diagnosed with any cardiovascular, metabolic, renal, liver, pulmonary, asthmatic, rheumatic, or other inflammatory diseases/conditions and were not currently under the administration of medication known to alter their inflammatory or metabolic profiles. All participants were additionally screened for physical activity participation to ensure the enrollment of active individuals—physical activity rating score > 4 (13). Moreover, research participants were nonusers of tobacco products and consumed 10 or less standard alcoholic beverages per week on average. Participants were asked to abstain from alcohol, caffeine, and physical activity 24 h before exercise trials and complete an overnight (minimum 8 h and maximum 12 h) fast before each laboratory visit. Adherence to these pretesting procedures was confirmed verbally with the participants upon their arrival to the laboratory. All participants provided written informed consent and all procedures were performed in accordance with the ethical guidelines provided by the Belmont Report. The Institutional Review Board (IRB) of the University of Arizona granted ethical approval (No. 2102477676) and the trial was registered at www.clinicaltrials.gov (NCT05019456).

#### EXPERIMENTAL DESIGN

The study required participants to visit the laboratory on three separate occasions. Visit 1 involved a prescreening procedure to verify whether the participants were eligible for the study and healthy enough to perform vigorous intensity exercise and to provide written consent (AHA/ACSM questionnaire). Eligible participants then completed a submaximal graded exercise test on a cycling ergometer (Velotron, Quarq Technology, San Diego, CA) to determine predicted maximal oxygen consumption (V\text{O}_\text{2max}). Blood samples were also collected during this visit to confirm serological status against SARS-CoV-2 using a commercially available ELISA kit (SARS-CoV-2 Spike S1 Human IgG; BioLegend, San Diego). Visit 2

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**Table 1. Participant demographic data (n = 18)**

|                | Total, n = 18 | Pfizer Cohort, n = 9 | Controls, n = 6 |
|----------------|--------------|----------------------|---------------|
| Female         | 9/18         | 5/9                  | 3/6           |
| Age, yr        | 29 ± 5.4     | 29.1 ± 3.9           | 28 ± 8.4      |
| Height, cm     | 173.9 ± 11   | 170.1 ± 11           | 177.5 ± 11.7  |
| Weight, kg     | 67.4 ± 13.6  | 68.1 ± 10.9          | 70.2 ± 11.5   |
| Resting HR, beats/min | 70 ± 5.7 | 71.2 ± 5.6           | 70 ± 5.9      |
| Resting systolic blood pressure, mmHg | 115 ± 8.2 | 115.4 ± 6.4          | 119 ± 7.9     |
| Resting diastolic blood pressure, mmHg | 77 ± 6.7 | 75.7 ± 5.5           | 77 ± 4        |
| Predicted V\text{O}_\text{2max}, mL/kg/min | 40.7 ± 9.9 | 42.7 ± 7.2           | 44.1 ± 8.1    |
| Time between main exercise trials, days | 52.5 ± 21.6 | 54.6 ± 15.7        | 26 ± 18.5     |
| Time between final vaccine dose and last exercise trial, days | 14 ± 10.1 | 14.9 ± 6.5          | N/A           |

Vaccinated participants received either the two-dose Pfizer mRNA regimen (n = 9) or the single-dose Johnson & Johnson vaccine (n = 3). The remaining participants served as controls (n = 6). Median ± SD. HR, heart rate; V\text{O}_\text{2max}, maximal oxygen consumption.
EXERCISE RESPONSES AFTER COVID-19 VACCINATION

occurred 1–3 wk after the first visit and required the participants to complete a continuous 20-min graded cycling exercise with multiple blood collections from an intravenous catheter. Visit 3 required participants to perform the exact same trial that was performed during Visit 2 at 1–3 wk after receiving the final COVID-19 vaccine dose via their own healthcare provider. This corresponded to an elapsed time of 5–7 wk between Visit 2 and Visit 3. Participants arrived at our laboratory at the exact same time of day across all trials, which were performed between 06:00 and 09:00 local time.

Submaximal Exercise Testing Procedure (Visit 1)

Upon arrival at the laboratory, participants were briefed regarding the nature of the testing protocol, and height, weight, and resting blood pressure measurements were collected. Each participant was assessed for appropriate apparatus sizing (e.g., metabolic cart face mask) and cycling ergonomics (e.g., saddle height, handlebar reach, etc.) and these were recorded so they could be replicated during subsequent visits. Prior to initiating the test, all participants performed 3–5 min of seated rest on the cycling ergometer for the collection of resting heart rate and respiratory gas exchange data. This was followed by a 5-min warm-up period of cycling at 50 watts (W). Thereafter, resistance was increased by 15 Ws every minute and participants were asked to maintain a consistent cycling cadence throughout the entire exercise bout (≥60 rpm). Exercise continued until the participant reached 88% of age-predicted maximum heart rate (220-age). Estimated VO₂max was determined using the built-in algorithm contained within the metabolic cart software (Quark CPET, COSMED, Pabona di Albona Laziale, Italy). Heart rate and rating of perceived exertion [RPE; Modified BORG 0–10 scale (14)] were recorded during the final 15 s of each exercise stage. Individual linear regression equations were established for each participant and used to determine cycling power outputs corresponding to various percentages of the VO₂max for the main exercise trials performed during Visit 2 and Visit 3.

Main Exercise Trial (Visits 2 and 3)

During Visit 2 and Visit 3, participants’ weight was recorded, and an indwelling catheter (BD, Franklin Lakes, NJ) was inserted into an antecubital vein so that serial blood draws could be collected before, during, and after exercise. The catheter was flushed with isotonic saline after each blood draw and a 2 mL volume was drawn and discarded before collecting the blood sample used for analysis. Blood was collected into a 6 mL vacuum tube containing a serum separator gel (BD Vacutainer blood collection tubes). Participants were then asked to complete a 5-min warm-up at 50 W before cycling continuously for an additional 20 min at graded intensities. The 20-min trial consisted of four incremental 5-min stages with power outputs corresponding to 50%, 60%, 70%, and 80% of the individual predicted VO₂max. Participants again were asked to maintain a consistent cycling cadence throughout the entire exercise session (≥60 rpm) and heart rate and respiratory gas exchange were measured throughout with RPE being recorded during the final 15 s of each exercise stage. To reduce the influence of a respiratory lag phase at the beginning of each incremental stage of the exercise protocol, the heart rate, and breath-by-breath respiratory data obtained during the final 3 min of each stage was averaged and processed for analysis (15).

Blood samples were collected at four separate time points during these visits: 1) at rest; 2) during the 60% VO₂max stage; 3) during the 80% VO₂max stage; and 4) at 1 h after exercise cessation. An exception to this was the control participants who performed identical exercise protocols as part of a parallel but separate research study in our laboratory had blood collected at rest and during the 80% VO₂max stage only. To maintain consistency, the absolute cycling power outputs for each individual were identical during Visit 2 and Visit 3. During Visit 3, the resting serum sample was also used to confirm whether all vaccinated individuals had seroconverted and presented with a positive SARS-CoV-2 IgG titer. To exclude the possibility of including participants who had been infected naturally between laboratory visits, whole blood samples collected in two lithium heparin coated tubes were stimulated with overlapping peptide pools spanning the breadth of the spike, membrane, and nucleocapsid antigens (10 μg/mL; Miltenyi) before measuring IFN-γ in plasma by ELISA (R&D Systems; Minneapolis, MN) following methods we recently described (16). No responses to membrane or nucleocapsid antigen were found post vaccine in the participants who had not been infected naturally (data not shown)(17).

Assessment of Serum Biomarkers

Blood collected into vacutainers containing a serum gel separator were allowed to rest for 30 min and subsequently centrifuged at 1,500 relative centrifugal force for 10 min. Serum was then collected and stored at −80°C until future analysis of cortisol (EIAHCHOR, INVITROGEN, Frederick, MD), lactate (MAK064, Sigma Aldrich, St Louis, MO), and catecholamine release (BA E-6500R, LDN, Nordhorn, Germany) by standard enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer’s instructions.

Statistical Analysis

All data are presented as means ± standard deviation (SD) unless otherwise stated. All statistical analyses were completed using GraphPad Prism 8.0. Linear mixed models (LMM) or repeated-measures ANOVA was used to analyze all metabolic and blood data, with Sidak post hoc test to determine differences between trials and groups. The model included main effects for group (vaccinated vs. control), time (exercise workload), and trial (Pre vs. Post vaccine, or Trial 1 vs. Trial 2 in the controls), and interaction (Group × Time × Trial) effects. Main effects for Time and Trial and interaction effects (Time × Trial) were also determined within each group. Paired sample t tests were used to detect differences in predicted VO₂max and time to ventilatory threshold between the trials performed during Visit 2 and Visit 3. Significance was set at P < 0.05.

RESULTS

COVID-19 Vaccination Is Associated with an Elevated Heart Rate and Norepinephrine Response to Graded Cycling Exercise in Healthy Individuals

To determine if COVID-19 vaccination is associated with changes in the physiological responses to exercise,
we, first of all, compared pre- and postvaccine exercise responses in the entire vaccinated cohort (n = 12) regardless of SARS-CoV-2 exposure status or vaccine type (Fig. 1). Overall, the physiological responses to exercise were similar between trials but we did find significant interaction (Time × Trial) effects for heart rate (HR) and serum norepinephrine levels, which were elevated during exercise after vaccination. Post hoc analysis revealed that HR was elevated at the 60% and 70% V\(_{O2\text{max}}\) stage (P = 0.02 and 0.0005, respectively) and norepinephrine levels were elevated at the 80% V\(_{O2\text{max}}\) stage (P = 0.002) compared with the prevaccine trial. The RPE tended to be lower post vaccine at the 50% V\(_{O2\text{max}}\) stage (P = 0.06) but not at the other exercise intensities. We found no pre-to-post vaccine differences for ventilation (V\(_E\)), oxygen uptake (V\(_O2\)), CO2 production (V\(_{CO2}\)), respiratory exchange ratio (RER), lactate, cortisol, epinephrine, and norepinephrine. Data are represented as means ± SD. Significant difference from the Pre-trial indicated by ***(P < 0.001), **(P < 0.01), and *(P < 0.05).

V\(_{CO2}\), carbon dioxide consumption; Q, cardiac output; HR, heart rate; V\(_{O2\text{max}}\) maximal oxygen consumption; V\(_{O2}\), oxygen consumption; RPE, rating of perceived exertion; RER, respiratory exchange ratio; SV, stroke volume; VT, time to ventilatory threshold; V\(_E\), ventilation.

**Figure 1.** The physiological responses to graded exercise before (Pre) and after (Post) COVID-19 vaccination (n = 12). Endpoint measures include (A) V\(_{O2}\), (B) V\(_{CO2}\), (C) RER, (D) predicted V\(_{O2\text{max}}\), (E) V\(_E\), (F) V\(_E\)/V\(_{O2}\), (G) V\(_{E}\)/V\(_{CO2}\), (H) Time to VT, (I) HR, (J) SV, (K) Q, (L) RPE, (M) lactate, (N) cortisol, (O) epinephrine, and (P) norepinephrine. Data are represented as means ± SD. Significant difference from the Pre-trial indicated by ***(P < 0.001), **(P < 0.01), and *(P < 0.05).
ratio (RER), ventilatory equivalents of oxygen uptake ($\dot{V}E$/\dot{V}O$_2$), carbon dioxide production ($\dot{V}E$/\dot{V}CO$_2$), stroke volume (SV), cardiac output (Q), predicted \dot{V}O$_{2\text{max}}$, time to ventilatory threshold (VT), rating of perceived exertion (RPE), serum lactate, serum epinephrine, or serum cortisol ($P > 0.05$).

Elevations in Heart Rate and Norepinephrine Responses to Graded Exercise Were Found in Those Receiving the Pfizer mRNA COVID-19 but Not in Controls

As the majority of our vaccinated participants received the Pfizer mRNA vaccine (9/12), we decided to test if the

| Vaccine | Control |
|---------|---------|
| **HR (bpm)** | | |
| 50 | 60 | 70 | 80 | 50 | 60 | 70 | 80 |
| 0 | 50 | 100 | 150 | 200 | 0 | 50 | 100 | 150 |
| **SV (mL)** | | |
| 50 | 60 | 70 | 80 | 50 | 60 | 70 | 80 |
| 0 | 10 | 20 | 30 | 40 | 0 | 10 | 20 | 30 |
| **Lactate (ng/μl)** | | |
| 50 | 60 | 70 | 80 | 50 | 60 | 70 | 80 |
| 0 | 500 | 1000 | 1500 | 2000 | 0 | 500 | 1000 | 1500 |
| **Cortisol (ng/ml)** | | |
| 50 | 60 | 70 | 80 | 50 | 60 | 70 | 80 |
| 0 | 0.2 | 0.4 | 0.6 | 0.8 | 0 | 0.2 | 0.4 | 0.6 |
| **Epinephrine (ng/ml)** | | |
| 50 | 60 | 70 | 80 | 50 | 60 | 70 | 80 |
| 0 | 2 | 4 | 6 | 8 | 0 | 2 | 4 | 6 |
| **Noradrenaline (ng/ml)** | | |
| 50 | 60 | 70 | 80 | 50 | 60 | 70 | 80 |
| 0 | 2 | 4 | 6 | 8 | 0 | 2 | 4 | 6 |

**Figure 2.** The physiological responses to graded exercise before (Pre) and after (Post) vaccination in the Pfizer mRNA vaccine cohort ($n = 9$) and nonvaccinated controls ($n = 6$) who were tested on two separate occasions. Endpoint measures include (A) $\dot{V}O$_2, (B) $\dot{V}CO$_2, (C) RER, (D) predicted $\dot{V}O$_{$2\text{max}}$, (E) $\dot{V}E$, (F) $\dot{V}E$/\dot{V}O$_2$, (G) $\dot{V}E$/\dot{V}CO$_2$, (H) Time to VT, (I) HR, (J) SV, (K) Q, (L) RPE, (M) lactate, (N) cortisol, (O) epinephrine, and (P) norepinephrine. Data are represented as means ± SD. Significant difference from the Pre-trial indicated by **$P < 0.01$** and *$P < 0.05$*. $\dot{V}CO$_2, carbon dioxide consumption; Q, cardiac output; HR, heart rate; $\dot{V}O$_{$2\text{max}}$, maximal oxygen consumption; $\dot{V}O$_2, oxygen consumption; RPE, rating of perceived exertion; RER, respiratory exchange ratio; SV, stroke volume; VT, time to ventilatory threshold; VE, ventilation.
increased heart rate and norepinephrine responses to exercise after vaccination were unique to this cohort. We found that the elevation in HR at the 70% \( V_{O_{2\text{\max}}} \) stage and norepinephrine response at the 80% \( V_{O_{2\text{\max}}} \) stage was still significant \((P = 0.006\) and 0.04, respectively) \((\text{Fig. 2})\). As with the entire cohort, we did not find differences in any other physiological endpoint post vaccine. As this study was not randomized, we decided to include data collected from a parallel study being performed in our laboratory whereby two bouts of graded exercise were performed by healthy participants \(~5\) wk apart (i.e., similar to the time elapsed between Visit 2 and Visit 3 for the vaccinated cohort) without receiving a vaccine. All participants in the control group were found to be seronegative for SARS-CoV-2 at the time of testing \((\text{Fig. 2})\) and the exercise bouts performed by these control participants were identical to the vaccinated cohorts described here. When the control participants and the Pfizer mRNA vaccine cohort were included in the same LMM, we found no Group \(\times\) Time \(\times\) Trial interactions for HR or norepinephrine \((P > 0.05)\). However, due to the preliminary nature of this study and the fact that we had only six control participants compared with nine vaccinated participants, we were concerned that our small sample size and variability across groups could be causing a type II statistical error. To address this, we decided to compare delta values \((\text{Trial B} - \text{Trail A})\) between the vaccinated and the control cohorts for heart rate and norepinephrine and analyzed these in the same LMM \((\text{Fig. 3})\). In doing this, we found that both HR \((P = 0.03)\) and norepinephrine \((P = 0.01)\) were elevated in the second trial for those who received the Pfizer mRNA vaccine compared with the controls at the 70% and 80% \( V_{O_{2\text{\max}}} \) stages, respectively.

**DISCUSSION**

Vaccination is strongly recommended to safeguard athletes from infection during training and competition \((\text{10})\). Several major sporting events (e.g., European and Copa America international soccer tournaments, Tokyo Olympic Games) have been held during the COVID-19 pandemic, increasing the risk of SARS-CoV-2 infection for nonvaccinated athletes. Although both vaccination \((\text{18})\) and natural immunity (e.g., from prior infection) \((\text{19})\) can protect against COVID-19 disease, nonvaccinated athletes are at an increased risk of contracting SARS-CoV-2 during training and competition. This could cause athletes to miss major sporting events and initiate isolation protocols for other athletes they were in close contact with. Despite this risk, anecdotal reports have emerged of athletes refusing the COVID-19 vaccine due to perceived negative impacts it may have on both their health and performance.

This is the first study, to our knowledge, to report physiological responses to exercise before and after COVID-19 vaccination. We found that recent COVID-19 vaccination in a group of physically active healthy individuals had no impact on a large number of physiological endpoints measured in blood and by respiratory gas exchange during graded cycling exercise. Principally, reliable markers of metabolism and aerobic capacity including blood lactate, oxygen uptake, carbon dioxide production, time to ventilatory threshold, and predicted \( V_{O_{2\text{\max}}} \) were unaffected by recent COVID-19 vaccination. These findings indicate that COVID-19 vaccination is unlikely to affect exercise capacity in normal healthy people and should alleviate concerns regarding potential negative effects of vaccination on the ability to carry out daily physically demanding tasks or in meeting recommended physical activity guidelines. We did, however, find significant elevations in heart rate \((~5 \text{ beats/min})\) and norepinephrine responses to vigorous (e.g., 70%–80% \( V_{O_{2\text{\max}}} \)) intensity exercise after vaccination, particularly in those who received the two-dose Pfizer mRNA vaccine regimen. Neither heart rate nor norepinephrine changed in demographically matched control participants who completed identical bouts of exercise several weeks apart without receiving a vaccine. Although it is possible that these effects are due to reduced physical activity levels after vaccination (e.g., due to symptoms of vaccinosis), we deem a detraining effect unlikely as, despite reporting many of the common symptoms associated with COVID-19 vaccination, our participants did not report significant changes to their physical activity levels during the study period. The mechanisms by which recent COVID-19 vaccination might increase cardiovascular responses to graded exercise in healthy people are not known, although the elevated heart response after vaccination may have been driven by the concomitant elevation in the norepinephrine response to exercise \((\text{20})\). A more detailed examination of the cardiovascular and neuroendocrine responses to graded exercise after COVID-19 vaccination would be illuminating.

Despite finding that most physiological responses to exercise were unaffected by recent COVID-19 vaccination in these physically active healthy people, it should be noted that the small increases in heart rate and norepinephrine response to exercise after vaccination could have implications for athletic performance at the elite level. Repeating this work in a group of elite athletes with an additional

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**Figure 3.** Delta (Trial B – Trial A) HR and norepinephrine responses during exercise trial 1 (prevaccine) compared with trial 2 (postvaccine) for the Pfizer vaccine cohort \((n = 9)\) vs. nonvaccinated controls tested on two separate occasions \((n = 6)\). Data are represented as means ± SD. Significant difference from controls indicated by *\(P < 0.05)\). HR, heart rate.
because athletes are often vaccinated in close proximity to exercise observed after the Pfizer mRNA vaccine could have implications for athletes and more consideration should be given when it comes to administering vaccines in close proximity to competition (10). Finally, we acknowledge that our VO2max assessments were made using submaximal as opposed to maximal tests, which may have affected the accuracy of the exercise intensity prescriptions. This was to alleviate concerns associated with maximal exercise testing in naturally infected and/or vaccinated individuals with undiagnosed myocarditis (22).

We conclude that recent COVID-19 vaccination has minimal effects on the physiological responses to graded exercise in physically active healthy people. However, small elevations in the cardiovascular and neuroendocrine responses to exercise observed after the Pfizer mRNA vaccine could have implications for athletes and more consideration should be given when it comes to administering vaccines in close proximity to major sporting events. Future studies are required to determine if these effects of COVID-19 vaccination will impact athletic performance at the elite level, particularly because booster shots or new vaccines may be required for continuous protection against SARS-CoV-2 and its evolving variants (23).

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[DISCLOSURES]
No conflicts of interest, financial or otherwise, are declared by the authors.

[AUTHOR CONTRIBUTIONS]
F.L.B., C.R.P., S.C.B., E.K., and R.J.S. conceived and designed research; H.B., F.L.B., K.A.S., and T.M.Z. performed experiments; H.B., F.L.B., K.A.S., T.M.Z., and R.J.S. analyzed data; H.B., F.L.B., C.R.P., S.C.B., E.K., and R.J.S. interpreted results of experiments; H.B. and F.L.B. prepared figures; H.B. and R.J.S. drafted manuscript; F.L.B., K.A.S., T.M.Z., C.R.P., S.C.B., E.K., and R.J.S. edited and revised manuscript; H.B., F.L.B., K.A.S., T.M.Z., C.R.P., S.C.B., E.K., and R.J.S. approved final version of manuscript.

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