

The Impact of COVID-19 and Muscle Fatigue on Cardiorespiratory Fitness and Running Kinetics in Female Recreational Runners

Jafarnezhadgero, Amir Ali; Noroozi, Raha; Fakhri Mirzanag, Ehsan; Granacher, Urs; Oliveira, Anderson Souza

Published in:
Frontiers in Physiology

DOI (link to publication from Publisher):
[10.3389/fphys.2022.942589](https://doi.org/10.3389/fphys.2022.942589)

Creative Commons License
CC BY 4.0

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

[Link to publication from Aalborg University](#)

Citation for published version (APA):
Jafarnezhadgero, A. A., Noroozi, R., Fakhri Mirzanag, E., Granacher, U., & Oliveira, A. S. (2022). The Impact of COVID-19 and Muscle Fatigue on Cardiorespiratory Fitness and Running Kinetics in Female Recreational Runners. *Frontiers in Physiology*, 13, Article 942589. <https://doi.org/10.3389/fphys.2022.942589>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.



The Impact of COVID-19 and Muscle Fatigue on Cardiorespiratory Fitness and Running Kinetics in Female Recreational Runners

Amir Ali Jafarnezhadgero¹, Raha Noroozi¹, Ehsan Fakhri¹, Urs Granacher^{2*} and Anderson Souza Oliveira³

¹Department of Sport Managements and Biomechanics, Faculty of Educational Sciences and Psychology, University of Mohaghegh Ardabili, Ardabil, Iran, ²Division of Training and Movement Sciences, Research Focus Cognition Sciences, University of Potsdam, Potsdam, Germany, ³Department of Materials and Production, Aalborg University, Aalborg, Denmark

OPEN ACCESS

Edited by:

Lawrence D Hayes,
University of the West of Scotland,
United Kingdom

Reviewed by:

Yaodong Gu,
Ningbo University, China
Stephanie Valentin,
University of the West of Scotland,
United Kingdom

*Correspondence:

Urs Granacher
urs.granacher@uni-potsdam.de
orcid.org/0000-0002-7095-813X

Specialty section:

This article was submitted to
Exercise Physiology,
a section of the journal
Frontiers in Physiology

Received: 12 May 2022

Accepted: 24 June 2022

Published: 18 July 2022

Citation:

Jafarnezhadgero AA, Noroozi R, Fakhri E, Granacher U and Oliveira AS (2022) The Impact of COVID-19 and Muscle Fatigue on Cardiorespiratory Fitness and Running Kinetics in Female Recreational Runners. *Front. Physiol.* 13:942589. doi: 10.3389/fphys.2022.942589

Background: There is evidence that fully recovered COVID-19 patients usually resume physical exercise, but do not perform at the same intensity level performed prior to infection. The aim of this study was to evaluate the impact of COVID-19 infection and recovery as well as muscle fatigue on cardiorespiratory fitness and running biomechanics in female recreational runners.

Methods: Twenty-eight females were divided into a group of hospitalized and recovered COVID-19 patients (COV, $n = 14$, at least 14 days following recovery) and a group of healthy age-matched controls (CTR, $n = 14$). Ground reaction forces from stepping on a force plate while barefoot overground running at 3.3 m/s was measured before and after a fatiguing protocol. The fatigue protocol consisted of incrementally increasing running speed until reaching a score of 13 on the 6–20 Borg scale, followed by steady-state running until exhaustion. The effects of group and fatigue were assessed for steady-state running duration, steady-state running speed, ground contact time, vertical instantaneous loading rate and peak propulsion force.

Results: COV runners completed only 56% of the running time achieved by the CTR ($p < 0.0001$), and at a 26% slower steady-state running speed ($p < 0.0001$). There were fatigue-related reductions in loading rate ($p = 0.004$) without group differences. Increased ground contact time ($p = 0.002$) and reduced peak propulsion force ($p = 0.005$) were found for COV when compared to CTR.

Conclusion: Our results suggest that female runners who recovered from COVID-19 showed compromised running endurance and altered running kinetics in the form of longer stance periods and weaker propulsion forces. More research is needed in this area using larger sample sizes to confirm our study findings.

Keywords: hospitalization, running mechanics, ground reaction forces, virus infection, COVID-19

1 INTRODUCTION

Previously infected SARS-CoV-2 patients may wish to return to normal life and sports practice as soon as possible. However, return-to-sports following SARS-CoV-2 might be challenging, as the disease substantially compromises cardiorespiratory fitness (Bansal, 2020). Recent studies have shown that COVID-19 causes arrhythmia, myocarditis, acute myocardial injury (Babapoor-Farrokhran et al., 2020; Guzik et al., 2020; Sapp et al., 2020), myalgia and arthralgia (Guan et al., 2020). There is evidence that different exercise types are effective as prevention and adjuvant therapy in patients with COVID-19 such as traditional Chinese intervention programs (e.g., Taiji, Baduanjin, Liuzijue, Yijinjing) (Yang et al., 2021). Further studies on the effects of exercise-based treatments on the post-COVID-19 syndrome are required to provide knowledge for practitioners and clinicians about the type of exercise that is particularly effective in the treatment of COVID-19 symptoms (Jimeno-Almazán et al., 2021). A recent review article suggested that a 10-months moderate aerobic training with three weekly sessions improves immune responses to influenza or pneumonia vaccination in older adults (Song et al., 2020). Due to the impact of COVID-19 on different body systems, several health agencies (e.g., National Strength and Conditioning Association and Collegiate Strength and Conditioning Coaches Association Joint committee) recommend a gradual and conservative return-to-sports approach, involving weeks of low-level activity following absence of symptoms (Caterisano et al., 2019; Salman et al., 2021). Therefore, COVID-19 infections may negatively affect sports performance even after full recovery. At the muscle level, the relatively short half-life of mitochondrial proteins (~1 week) (Hood, 2001) may cause decrements in mitochondrial function and capacity after a short period of training cessation. In line with this, decrements in muscle oxidative capacity (Gjøvaag and Dahl, 2008) and reductions in mitochondrial enzyme activities (Wibom et al., 1992) have been found after few days/weeks of training cessation. Due to interindividual heterogeneity of detraining and training effects, it is important to perform a battery of sport-specific tests aimed at evaluating the individual detraining status for planning an effective and safer return to sport activities (Girardi et al., 2020).

Running is a popular physical exercise, as it requires little equipment, is time-efficient and health beneficial (Mehl et al., 2011). Accordingly, there is evidence that running exercise can improve cardiorespiratory fitness and bone strength (Lee et al., 2017), brain function (Vivar and van Praag, 2017) and psychological well-being (Nezlek et al., 2018). At the same time, running is a demanding exercise for the cardiorespiratory system, and compromised energy supply and/or oxygen transport to the muscles might accelerate the fatigue process during exercising. Muscle fatigue has been defined as a decrease in maximal force or power production in response to contractile muscle activity, which affects performance of prolonged daily life activities and sports practice (Gandevia, 2001). Fatigue is multi-factorial, with components related to peripheral muscle contractile function, as well as central factors related to the descending drive to the active muscles

(Bigland-Ritchie et al., 1978; Gandevia, 2001; Wan et al., 2017). It has been suggested that COVID-19 affects oxygen transport to the skeletal muscles (Alayash, 2021; Böning et al., 2021), likely influencing the fatigue process. Some of the mechanisms of reduced oxygen availability are 1) the reduced hypercapnia/CO₂ retention that causes “happy hypoxemia” in patients with COVID-19 (Dhont et al., 2020); 2) the infection of O₂-sensing glomus cells by SARS-CoV-2, which affects central breathing regulation (Böning et al., 2021), and 3) the reduced hemoglobin concentration during the course of COVID-19 (Liu et al., 2020a; Kumar et al., 2020; Vogel et al., 2020). Thus, previous SARS-CoV-2 infections might influence essential mechanisms related to oxygen delivery to muscle cells during exercise, potentially accelerating the fatigue process which may lead to early termination of exercise (Amann and Calbet, 2008; Alayash, 2021).

Fatigue impacts on running kinematics in different ways such as increased loading on the medial arch of the foot (Fourchet et al., 2015), increased dorsiflexion velocity and knee internal rotation excursion (Radzak et al., 2017), as well as reduced plantar flexion and knee flexion moments (Radzak et al., 2017). In terms of kinetics, fatigue-related increases in peak vertical ground reaction forces (GRF) and loading rates have been reported during the performance of landing tasks (James et al., 2006; James et al., 2010) and running exercise (Nicol et al., 1991; Jafarnejadgero et al., 2019; Pircoveanu et al., 2021). Accordingly, the monitoring of running biomechanics in fatigued condition is relevant as increased early vertical impact loading has been associated with an increased risk of sustaining running-related injuries (Weist et al., 2004). Another external factor that appears to have an influence on running-related injuries is whether running is performed in shod condition or barefooted (Hobara et al., 2012). Of note, barefoot running has been associated with shorter stride length and higher cadence compared with rearfoot strike shod running (De Wit et al., 2000). It is well-known that reduced stride length results in lower instantaneous vertical loading that may protect runners from impact-related injuries (Hobara et al., 2012). Thus, barefoot running can be used as an experimental condition to test fatigued running. There is evidence that females have significantly greater knee abduction, knee internal rotation and ankle eversion angles compared with males (Sinclair et al., 2012). Males have greater hip flexion (Sinclair et al., 2012). In females, sex-specific anatomical (e.g., pelvic width), morphological (e.g., steroid hormones level), and biomechanical characteristics (e.g., ankle eversion) (Sinclair et al., 2012) appear to increase the risk of sustaining running-related injuries (Griffin et al., 2006). Accordingly, female runners were examined in this study.

It is likely that any type of hospitalization may lead to compromised performance when exercising shortly after recovery. Nonetheless, investigating the potential influence of COVID-19 infection on running performance is highly relevant, as COVID-19 might substantially affect cardiorespiratory fitness and running mechanics (Bansal, 2020). In fact, recovered SARS-CoV-2 patients showed increased peak lateral forces during initial contact, concomitant with a higher activation of the medial gastrocnemius and a lower activation of the vastus lateralis

TABLE 1 | Participant characteristics according to group allocation (controls = CTR, COVID-19 = COV).

| Characteristics | CTR | COV | p-value |
|--------------------------------------|-------------|------------|---------|
| Age (years) | 22.5 ± 1.9 | 22.3 ± 1.5 | 0.834 |
| Height (cm) | 171.4 ± 6.7 | 169.0 ± 85 | 0.366 |
| Body mass (kg) | 63.2 ± 10.9 | 60.0 ± 7.1 | 0.357 |
| Body mass index (kg/m ²) | 21.3 ± 2.3 | 20.9 ± 1.3 | 0.560 |
| Weekly mileage (km) | 16.2 ± 1.8 | 16.3 ± 1.5 | 0.941 |

p-values indicate between group differences in the respective parameters. NA stands for not applicable.

muscle (Jafarnejadgero et al., 2021). However, the effect of running-induced fatigue on running mechanics in recovered COVID-19 patients has not been scientifically investigated. Moreover, there is evidence that fully recovered COVID-19 patients usually resume physical exercise, but do not achieve the same intensity level as prior to infection. More specifically, ~50% of recovered COVID-19 patients reduce their exercise intensity level compared with that before infection (Garrigues et al., 2020), likely due to impaired cardiorespiratory fitness. Impaired cardiorespiratory fitness following COVID-19 infection might lead to reduced adherence to physical exercise, potentially leading to increased physical inactivity and/or an inability to exercise at health promoting intensity zones.

Therefore, the aim this study was to investigate the effects of fatigue and/or COVID-19 on cardiorespiratory fitness and running mechanics during barefoot running in female recreational runners. With reference to the relevant literature (Hortobágyi et al., 1993; Bloomfield, 1997; James et al., 2006; James et al., 2010; Musumeci, 2017; Tuzun et al., 2020; Giraudo et al., 2021; Jafarnejadgero et al., 2021), we hypothesized that recovered COVID-19 patients compared with healthy controls would fatigue earlier and show impaired running mechanics.

2 METHODS

2.1 Participants

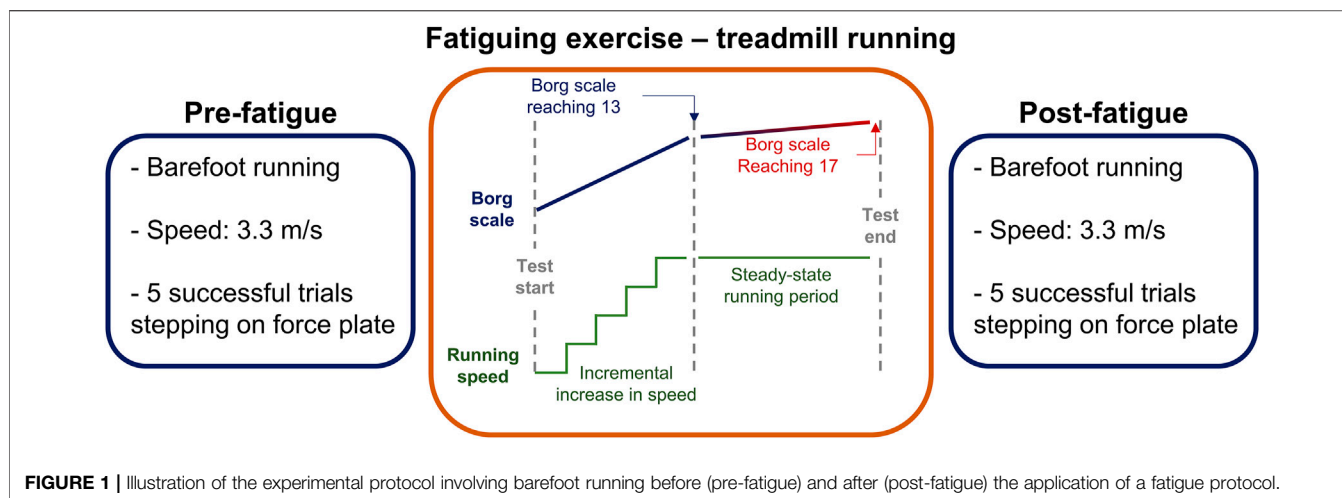
Thirty-five young recreational female runners (average weekly mileage before COVID infection ~16 km) were enrolled in this study (Table 1). The World Masters Association age grading performance tables were used to classify runners' performance levels. Recreational runners were classified as runners with an age-graded score of <60% (Clermont et al., 2019). An age-graded score was computed *via* (www.howardgrubb.co.uk/athletics/wmalookup06.html) according to the age, gender, recent race performance during the past 6 months (e.g., self-reported best time of 10 km, half-marathon or marathon race), and years of running practice (Liu et al., 2020b).

Twenty-one runners with a history of COVID-19 hospitalization were recruited for this study from the local rehabilitation centers, Ardabil city. Seven participants were excluded after clinical examination by a cardiologist because they showed signs of hypertension, thyroid disease, cardiovascular and cerebrovascular disease, malignancy, and chronic kidney disease and rheumatologic diseases. The

remaining 14 participants of the COVID-19 group (COV) stayed on average 18 ± 3 days (range: 15–23 days) in pulmonary and cardiovascular hospitals. Participants were recruited for study participation during their final day of hospital stay. An inclusion criteria was the engagement in recreational long-distance running for at least 2 years prior to COVID-19 hospitalization. The average weekly mileage before the COVID infection was 16 ± 2 km. If participants engaged in other systematic training (dancing, team sports and/or racket sports), they were not included in this study (Lun et al., 2004). All participating individuals were familiar and experienced with barefoot running. Nine participants from each group used a forefoot striking pattern while the remaining participants used a rear foot striking pattern. Forefoot strikers generate only one peak value in the vertical force (the active peak), whereas rearfoot strikers generate an early impact peak and the active peak. The striking pattern was determined post-hoc using the ground reaction force data.

Four participants from COV received mechanical ventilation. Overall, disease severity at the time of hospitalization was “mild-to-moderate” for COV individuals based on the American Thoracic Society Guidelines for community-acquired pneumonia (Metlay et al., 2019). COVID-19 infection was defined as a positive result on real-time reverse-transcription polymerase chain reaction analysis of throat swab specimens, and/or radiologic assessments including chest computer tomography according to the classification of the Radiological Society of North America (RSNA) (Simpson et al., 2020; World Health Organization, 2020). COVID individuals received rehabilitation including low-dosed running protocols as they left hospital (Caterisano et al., 2019). An experienced physiotherapist from the hospital staff provided instructions on the low-dose running protocols upon hospital discharge. The conditioning volume for the first week was reduced by at least 50% of the normal exercise load, followed by 30%, 20%, and 10% in the following 3 weeks if COVID individuals felt comfortable at the end of each week (Caterisano et al., 2019). The exercise load was defined using a combination of the parameters “running distance” and “intensity”. A researcher of this study contacted COVID patients on the final day of their hospital stay and asked them whether they would be willing to participate in this study. Compliance with the low-dose training was verified by asking the study participants before testing. Biomechanical testing of COVID-19 participants took place between 14 and 21 days after hospitalization.

A control group (CTR, *n* = 14) consisting of age, body height, and weekly mileage matched runners with no history of COVID-19 infection was also investigated. Examiners were blinded for group allocation to avoid research bias. Leg dominance was determined using the kicking ball test. The right leg was the dominant limb for all subjects. Written informed consent was provided from all participants prior to the start of the study. The study was conducted in accordance with the latest version of the Declaration of Helsinki. Ethical approval was obtained from the local ethical committee (IR.UMA.REC.1400.078).



2.2 Experimental Protocol

Initially, participants performed 4 min of stretching and 2 min of warm-up in the form of jogging. Before and after the fatigue protocol, participants were asked to run barefoot at a constant speed of ~ 3.3 m/s over an 18 m overground straight walkway with an embedded force plate. The proposed running speed was chosen following previous studies investigating running-related injury risk factors (Willems et al., 2005; Anbarian and Esmaeili, 2016). The average running speed was computed by dividing the running distance (i.e., 18 m) by the running time which was assessed using a chronometer. To reach ~ 3.3 m/s, participants were expected to run the 18 m in 5.6 s. To reach this speed consistently or within a 10% variability in time, participants were familiarized with the walkway by performing several trials prior to data recording. Participants were instructed to ideally land with their right foot on the middle of the force plate (Jafarnejadgero et al., 2019) to minimize the risk that participants step outside the limits of the force platform. After participants were familiarized with running speed and foot placement on the force plate, five running trials were performed. Trials were repeated if the runner did not step on the force plate, altered their stride to hit the force plate, or if the running speed was above or below 10% of the targeted speed. **Figure 1** illustrates the experimental protocol.

2.3 Heart Rate Measurements

The heart rate (Polar RS100, Polar Electro Oy, Woodbury, NY) was monitored continuously during the fatigue protocol. Maximum heart rate was determined using the Tanaka equation as follows: $208 - (0.7 \times \text{Age})$ (Tanaka et al., 2001).

2.4 Ground Reaction Force Recordings

Vertical and anterior-posterior ground reaction forces were recorded using a force plate (Bertec Corporation, Columbus, 4060–07 Model, OH, United States). The force plate recorded data at a 1,000 Hz sampling frequency. Kinetic data were analyzed during the stance phase of running, defined as the interval from ground contact (vertical GRF > 10 N) to toe off (vertical GRF < 10 N). Kinetic data were filtered using a fourth-order low-pass Butterworth filter with a cutoff frequency of 20 Hz (determined by residual analysis) (Winter,

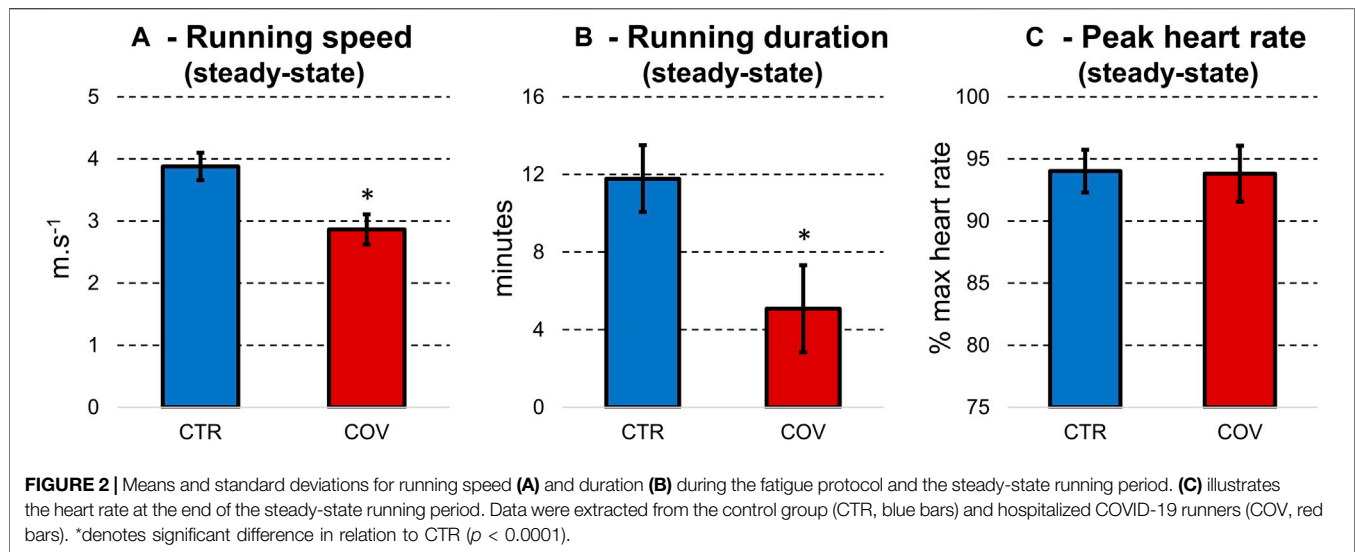
2009). All ground reaction forces were normalized to the individual's body weight (xBW).

2.5 Fatigue Protocol

The fatigue protocol consisted of running on a motorized treadmill with no inclination (Horizon Fitness, Omega GT, United States), while the heart rate was monitored continuously (Polar RS100, Polar Electro Oy, Woodbury, NY). Participants started the test at 6 km/h, and the treadmill speed was increased 1 km/h every 2 min. The rating of perceived exertion was collected from participants at the end of each stage using the 6–20 Borg scale (Borg, 1998). As soon as participants reported a perceived exertion of 13 or higher, the treadmill speed was fixed to allow steady-state running until exhaustion. Throughout the steady-state period, rating of perceived exertion and heart rate were collected every 30 s. The fatigue protocol was terminated after 2 minutes of steady-state running beyond 17 on the Borg scale or $\geq 80\%$ of the maximum heart rate (Koblbauer et al., 2014).

2.6 Data Analyses

As dependent variables, we measured steady-state running duration and speed during the fatigue protocol and heart rate at the end of the steady-state running period. The vertical force component provided the ground contact time, representing the time period between ground contact and toe-off. Moreover, the vertical force provided the active peak (defined as the higher vertical force value) and the impact peak (defined as the first peak in the vertical force). The time to reach the impact peak was computed from ground contact to the time of impact peak. If no impact peak was present in the vertical force, the force value at 13% of the stance period was used as reference for calculating the vertical loading rate (Oliveira and Pircoveanu, 2021). The vertical average loading rate (LR) was computed as the average slope from 20% to 80% of the impact peak force (Jafarnejadgero et al., 2019; Oliveira and Pircoveanu, 2021). The vertical impulse was calculated by extracting the area under the vertical force curve. In addition, peak braking and propulsion forces were recorded from the anterior-posterior force measurement. The



time-to-peak braking and propulsion forces were computed from the ground contact times until the occurrence of the peak events. All running variables were averaged across five trials (Jafarnejadgero et al., 2019).

2.7 Statistical Analyses

The sample of this study was a convenience sample due to the availability of incoming COVID-19 patients. Our post-hoc power analysis for the parameter loading rate with eta squared = 0.146 (Cohen's $f = 0.413$) demonstrated 98% power with the applied characteristics of our study design (28 subjects). The Shapiro-Wilk-Test confirmed normal data distribution. Accordingly, data were presented as group mean values and standard deviations. The effect of group (CTR vs. COV) as between-subject factor and fatigue (Pre vs. Post) as within-subject factor were assessed with a mixed-model 2-way ANOVA with repeated measures. Sphericity was confirmed using a Mauchly's test and homogeneity was confirmed using the Levene's test. The following variables were evaluated using this ANOVA model: Ground contact time, loading rate, impact peak, time to impact peak, active peak, vertical impulse, peak and time-to-peak braking force, peak and time-to-peak propulsion force. In addition, between group differences were assessed using a 2-tailed Student t-tests for independent samples for the fatiguing exercise duration and the maximum heart rate achieved during the fatiguing exercise. Cohen's d effect sizes were estimated for the paired comparison. The significance level was set at $p < 0.05$. The Statistical Package for Social Sciences (SPSS) version 27.0 was used to calculate inferential statistics.

3 RESULTS

3.1 Fatiguing Exercise

Also, we quantified perceived exertion using the 6–20 Borg scale (Borg, 1998). During the fatiguing task, CTR perceived a score of 13 on the 6–20 Borg scale (which determined the steady-state running period) while running at a ~25% higher speed ($p <$

0.0001, $d = 1.8$, **Figure 2A**). In addition, the steady-state running period was significantly longer ($p < 0.0001$, $d = 1.89$, ~56%, **Figure 2B**) in CTR when compared to COV. However, the heart rate at the end of the steady-state running period was not different between the two groups ($p > 0.05$, **Figure 2C**).

3.2 Ground Reaction Force Parameters

The COV group presented greater ground contact time when compared to CTR ($p = 0.002$, $d = 1.58$, **Table 2**). Significant main effects of fatigue in the form of reductions were found for loading rate ($p = 0.004$, $d = 1.45$) and impact peak ($p = 0.015$, $d = 1.19$). Moreover, the time-to-reach the impact peak was greater for COV when compared to the CTR ($p = 0.049$, $d = 0.93$). The variables active peak and vertical impulse showed no effects of fatigue or group. No fatigue-by-group interactions were found for any of the above-mentioned parameters.

3.3 Braking and Propulsion Forces

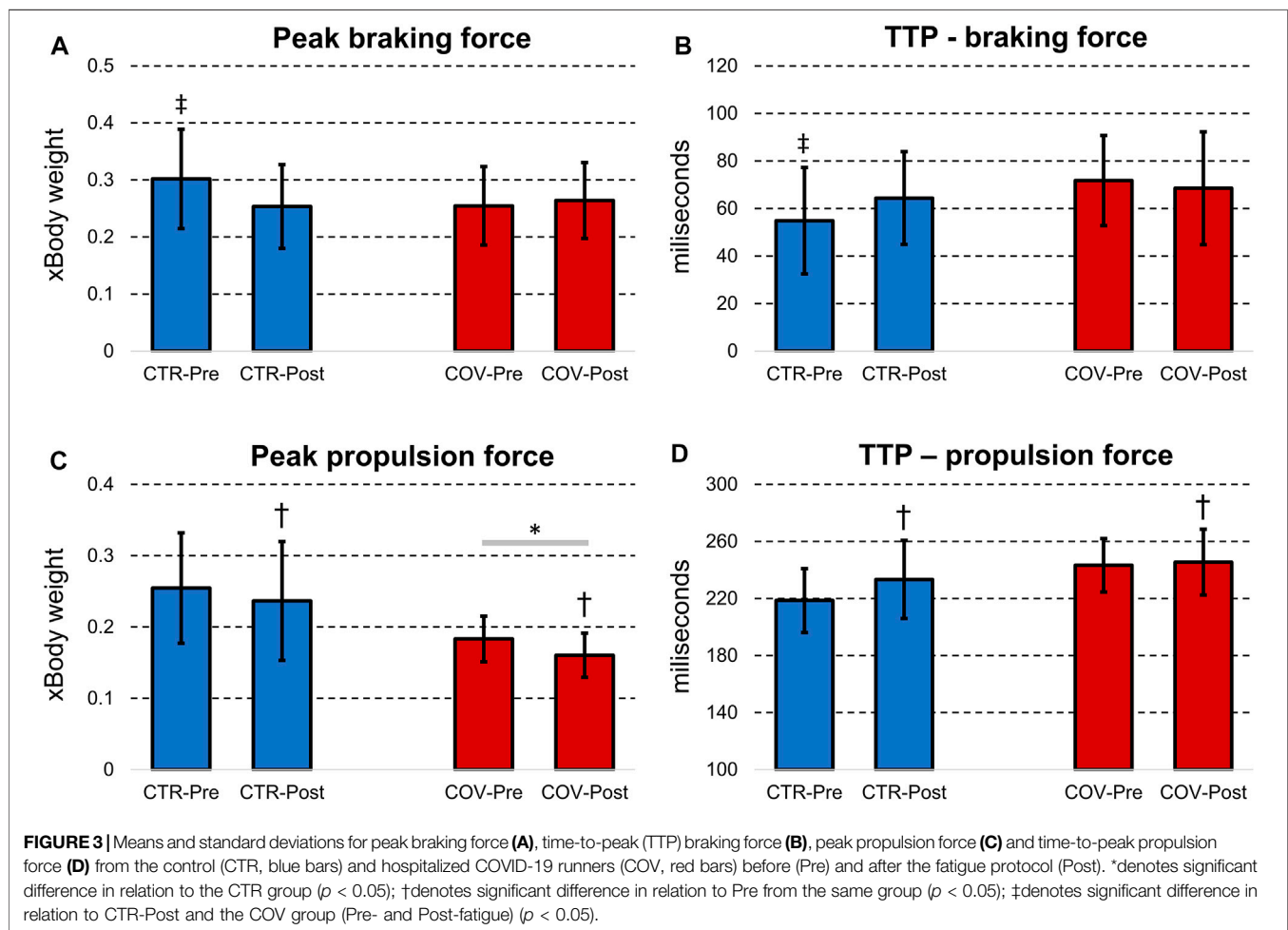
Significant group-by-fatigue interactions were detected for peak braking force ($p = 0.04$, $d = 0.93$, **Figure 3A**) and time-to-reach the braking force ($p = 0.03$, $d = 1.04$, **Figure 3B**). The post-hoc analyses revealed that both parameters were greater pre compared with postfatigue for CTR as well as to the Pre- and Post-measurement from COV ($p < 0.001$, $d = 1.00$ – 1.78). In addition, COV compared with CTR presented lower peak propulsion force ($p = 0.005$, $d = 1.39$, **Figure 3C**). Regarding fatigue, both groups showed after the fatigue protocol lower peak propulsion force ($p = 0.025$, $d = 1.09$) and time to peak propulsion force ($p = 0.046$, $d = 0.95$, **Figure 3D**). No fatigue-by-group interaction was found for time to peak propulsion forces ($p > 0.05$).

4 DISCUSSION

The aim of this study was to evaluate the impact of COVID-19 infection and recovery as well as muscle fatigue on cardiorespiratory fitness and running biomechanics in female

TABLE 2 | Means and standard deviations for ground reaction force parameters extracted from the control and the COVID-19 group before (Pre) and after fatigue (Post). The significance level (p) and effect size (partial eta-squared, η^2) illustrate main effects of fatigue, group and the fatigue-by-group interactions. Significant effects are expressed in bold.

| | CTR | | COV | | Significance (η^2) | | |
|---|-------------------|-------------------|-------------------|-------------------|---------------------------|----------------------|-----------------|
| | Pre | Post | Pre | Post | Fatigue | Group | Group x fatigue |
| Ground contact time (s) | 0.295 \pm 0.020 | 0.313 \pm 0.031 | 0.335 \pm 0.024 | 0.338 \pm 0.024 | 0.089 (0.138) | 0.002 (0.384) | 0.192 (0.084) |
| Loading rate ($\text{N.kg}^{-1}.\text{s}^{-1}$) | 77.84 \pm 37.39 | 62.72 \pm 29.43 | 49.54 \pm 21.80 | 45.41 \pm 21.57 | 0.004 (0.344) | 0.061 (0.165) | 0.079 (0.146) |
| Impact peak (xBW) | 1.288 \pm 0.392 | 1.095 \pm 0.251 | 1.134 \pm 0.251 | 1.096 \pm 0.178 | 0.015 (0.264) | 0.489 (0.024) | 0.090 (0.137) |
| Time to impact peak (ms) | 18.54 \pm 7.408 | 20.56 \pm 6.529 | 25.85 \pm 10.69 | 28.03 \pm 10.38 | 0.220 (0.074) | 0.049 (0.179) | 0.961 (0.000) |
| Active peak (xBW) | 2.083 \pm 0.219 | 2.031 \pm 0.238 | 1.937 \pm 0.149 | 1.947 \pm 0.152 | 0.238 (0.069) | 0.165 (0.094) | 0.083 (0.142) |
| Vertical impulse (xBW.s $^{-1}$) | 0.376 \pm 0.029 | 0.383 \pm 0.029 | 0.388 \pm 0.038 | 0.382 \pm 0.032 | 0.862 (0.002) | 0.693 (0.008) | 0.250 (0.066) |



recreational runners. The main findings of this study were that fatigue induced larger decrements in running speed (26%) and running duration (56%) in female runners previously hospitalized due to COVID-19 compared with healthy age-matched controls. Moreover, these previously hospitalized runners presented increased foot contact time and peak braking force concomitant with reduced peak propulsion forces. However, the effects of fatigue were similar for running

mechanics between groups, with reductions in loading rate and peak propulsion force for both groups.

4.1 Physiological Aspects of Running Performance

Our results demonstrated that runners from the COVID-19 group performed the steady-state running for a shorter period

despite achieving lower running speed. Nonetheless, these runners achieved similar peak heart rate at the end of the exercise. Altogether, these results demonstrated the substantial deficit in cardiorespiratory capacity of previous COVID-19 runners shortly after the disappearance of disease symptoms. Athletes recovered from COVID-19 might present an overall low risk of pericardial/myocardial disorders, arrhythmias and sudden cardiac arrest/sudden cardiac death (Babapoor-Farrokhran et al., 2020; Guzik et al., 2020; Sapp et al., 2020; van Hattum et al., 2021), myalgia and arthralgia (Guan et al., 2020). Moreover, diffusion capacity is the most common abnormality of lung function in discharged COVID-19 patients, followed by restrictive ventilatory defects, which are both associated with the severity of the disease (Mo et al., 2020).

The premature termination of the underperformed running test reflects the physiological impact of the disease in trained individuals. The previously referred impaired blood oxygen transportation in runners from the COVID-19 group might explain the compromised running capacity, in which elevated heart rates and perceived effort can be related to an early transition to anaerobic metabolism (Alayash, 2021; Böning et al., 2021). Therefore, our results highlight the significant drop in endurance capacity caused by COVID-19 in recreational runners, with an augmented effort perception caused by the deteriorated physiological status. In practice, these results corroborate the recommendations to avoid exercising within 2 weeks from the end of quarantine. Moreover, it may be suggested that the return to running practice should take into account the difficulty in performing moderate-to-intense exercises.

4.2 Running Biomechanical Parameters

Our results demonstrated that the effects of fatigue were similar between groups, with reductions in loading rate during barefoot running. Literature shows agreement (Willson and Kernozek, 1999) and disagreement (Nicol et al., 1991; Jafarnejadgero et al., 2019) with respect to our findings of increased early vertical impact forces with fatigue during running.

The peculiar fatiguing conditions exhibited by the runners recovered from COVID-19 demonstrate that they were close to exhaustion without performing either a very intense or long exercise. Therefore, usual factors associated with fatigue, such as metabolite accumulation, reduced pH and others may not be as influenced as for the control group (Wan et al., 2017). Such distinct fatigue state may help explain divergent results from running kinetics (e.g., loading rate) between our study and the literature. As mentioned above, the reasons for disagreement may be due to methodological differences (e.g., barefoot running versus shod running (Nicol et al., 1991; Jafarnejadgero et al., 2019), running intensity during fatiguing exercise (Jafarnejadgero et al., 2019), type of fatigue protocol (marathon race versus running on a motorized treadmill) (Nicol et al., 1991), and the type disorders [pronated feet runners (Jafarnejadgero et al., 2019) or healthy marathon runners (Nicol et al., 1991) versus COVID runners] (Jafarnejadgero et al., 2019) between the studies. It is noteworthy that the fatigue in our study has been exacerbated

by the highly compromised cardiorespiratory capacity rather than peripheral fatigue (metabolites accumulation in lower limb muscles etc.). Moreover, our running protocol involved barefoot trials instead of shod running, which may cause mechanical modifications of running patterns (Divert et al., 2005). It has been demonstrated that the main role of running shoes is to attenuate the foot-ground impact by adding damping material (Divert et al., 2005). However, these changes may lead to a decrease of the storage and restitution of elastic energy capacity which could explain the lower net efficiency reported in shod running (Divert et al., 2005).

It was found that previously hospitalized runners presented increased foot peak braking force concomitant to reduced peak propulsion force. Changes in anterior-posterior ground reaction forces are highly relevant to modulating forward running speed (Nummela et al., 1994; Luo et al., 2019), as increases in braking force and reductions in propulsion force may cause slower running speed. In addition to the fact that these runners presented increased time to reach the peak braking force and increased foot contact time at similar running speed, it is evident that there were adjustments to their motor patterns to run following the COVID-19 hospitalization. Limitations in cardiorespiratory capacity influences muscle activation due to compromised oxygen delivery (Alayash, 2021; Böning et al., 2021), potentially influencing runners to achieve optimal running style even in non-fatigued conditions. Since the fatigue protocol was substantially shorter for the recovered runners, no relevant fatigue-related differences in running biomechanics were found. In other words, the running performance of runners recovered from COVID-19 was already compromised without the fatiguing exercise. This result is further supported by the fatigue-by-group interactions found for the peak braking force and time-to-peak braking force, in which the COVID-19 group has similar performance when compared to the control group post-fatigue. Therefore, the compromised cardiorespiratory function in runners recovered from COVID-19 might directly influence running technique, elevating the effort to maintain the exercise and causing more fatigue during shorter periods of time.

There are some limitations that should be acknowledged the future studies. Firstly, the control group in this study consisted of healthy individuals. It is plausible that any hospitalization caused by viral infections might affect cardiorespiratory function, subsequently deteriorating running performance shortly after the absence of symptoms. Therefore, our results are not able to demonstrate that COVID-19 infection induces greater or lower effects than other types of viral infections, or other types of hospitalizations in general. Future studies comparing COVID-19 patients and patients affected by other types of viral infections and/or hospitalization causes are necessary to elucidate this issue. Secondly, the previously hospitalized runners performed an intense exercise shortly after being clinically recovered from the disease. The conduction of this protocol was only possible due to the previous clinical examination assuring medical clearance to perform exercises. It is not recommended that runners perform similar running protocols following COVID-19 infection/hospitalization without performing clinical

examinations. Third, running kinematics were not investigated in this study. Future studies could analyze kinematic parameters to clarify the impact of COVID-19 or other viral infections on running kinematics. Future studies are needed to elucidate the physiological mechanisms responsible for performance decrements in recreational runners who are fully recovered from COVID infection. Combining the investigation of biomechanical and physiological parameters would provide greater knowledge on the timeline of the recovery of runners following COVID-19 infection. Overground running speed was accessed by simply dividing the running distance by the running duration, which is a method prone to measurement errors. Ideally, future studies should access running speed using a motion capture system or timing gates. Finally, runners were instructed to land with their right foot in the middle of the force plate, potentially requiring subtle adjustments of foot position prior to landing. Trials presenting such type of adjustments were discarded by the experimenters.

5 CONCLUSION

In summary, this study demonstrated that fatigue has a major impact on cardiorespiratory fitness and rating of perceived exertion but not on running mechanics of female runners previously hospitalized due to COVID-19 compared with healthy controls. More specifically, irrespective of fatigue, runners who recovered from COVID-19 presented longer foot contact time and peak braking forces concomitant with reduced peak propulsion forces, suggesting a shift in the running style towards a poorer technique. Therefore, our results suggest that COVID-19 infections compromise cardiorespiratory fitness and perceived effort, which may lead to a sub-optimal running style. The gathered knowledge will help to better program return-to-sport protocols following SARS-CoV-2 infections, as well as other viral infections.

REFERENCES

- Alayash, A. I. (2021). The Impact of COVID-19 Infection on Oxygen Homeostasis: A Molecular Perspective. *Front. Physiology* 12, 1575. doi:10.3389/fphys.2021.711976
- Amann, M., and Calbet, J. A. L. (2008). Convective Oxygen Transport and Fatigue. *J. Appl. physiology* 104 (3), 861–870. doi:10.1152/jappphysiol.01008.2007
- Anbarian, M., and Esmaeili, H. (2016). Effects of Running-Induced Fatigue on Plantar Pressure Distribution in Novice Runners with Different Foot Types. *Gait Posture* 48, 52–56. doi:10.1016/j.gaitpost.2016.04.029
- Babapoor-Farrokhran, S., Gill, D., Walker, J., Rasekhi, R. T., Bozorgnia, B., and Amanullah, A. (2020). Myocardial Injury and COVID-19: Possible Mechanisms. *Life Sci.* 253, 117723. doi:10.1016/j.lfs.2020.117723
- Bansal, M. (2020). Cardiovascular Disease and COVID-19. *Diabetes & Metabolic Syndrome Clin. Res. Rev.* 14 (3), 247–250. doi:10.1016/j.dsx.2020.03.013
- Bigland-Ritchie, B., Jones, D. A., Hosking, G. P., and Edwards, R. H. T. (1978). Central and Peripheral Fatigue in Sustained Maximum Voluntary Contractions of Human Quadriceps Muscle. *Clin. Sci. Mol. Med.* 54 (6), 609–614. doi:10.1042/cs0540609
- Bloomfield, S. A. (1997). Changes in Musculoskeletal Structure and Function with Prolonged Bed Rest. *Med. & Sci. Sports & Exerc.* 29 (2), 197–206. doi:10.1097/00005768-199702000-00006

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the University of Mohaghegh Ardabili. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AJ participated in the design of the study, contributed to data collection and data analysis; RN, participated in the design of the study; EF, participated in the design of the study and contributed to data collection; AO, contributed to data analysis and interpretation of results; UG, contributed to data analysis and interpretation of results. All authors contributed to the manuscript writing. All authors have read and approved the final version of the manuscript.

FUNDING

Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - Projektnummer 491466077.

ACKNOWLEDGMENTS

We gratefully thank all participants for having volunteered to participate in this study.

- Böning, D., Kuebler, W. M., and Bloch, W. (2021). The Oxygen Dissociation Curve of Blood in COVID-19. *Am. J. Physiology-Lung Cell. Mol. Physiology* 321, L349–L357. doi:10.1152/ajplung.00079.2021
- Borg, G. (1998). *Borg's Perceived Exertion and Pain Scales*. Champaign, IL: Human Kinetics.
- Caterisano, A., Decker, D., Snyder, B., Feigenbaum, M., Glass, R., House, P., et al. (2019). CSCCa and NSCA Joint Consensus Guidelines for Transition Periods: Safe Return to Training Following Inactivity. *Strength & Cond. J.* 41 (3), 1–23. doi:10.1519/ssc.0000000000000477
- Clermont, C. A., Benson, L. C., Osis, S. T., Kobsar, D., and Ferber, R. (2019). Running Patterns for Male and Female Competitive and Recreational Runners Based on Accelerometer Data. *J. Sports Sci.* 37 (2), 204–211. doi:10.1080/02640414.2018.1488518
- De Wit, B., De Clercq, D., and Aerts, P. (2000). Biomechanical Analysis of the Stance Phase During Barefoot and Shod Running. *J. Biomechanics* 33 (3), 269–278. doi:10.1016/s0021-9290(99)00192-x
- Dhont, S., Derom, E., Van Braeckel, E., Depuydt, P., and Lambrecht, B. N. (2020). The Pathophysiology of 'happy' Hypoxemia in COVID-19. *Respir. Res.* 21 (1), 198–199. doi:10.1186/s12931-020-01462-5
- Divert, C., Mornieux, G., Baur, H., Mayer, F., and Belli, A. (2005). Mechanical Comparison of Barefoot and Shod Running. *Int. J. Sports Med.* 26 (07), 593–598. doi:10.1055/s-2004-821327

- Fourchet, F., Kelly, L., Horobeanu, C., Loepelt, H., Taiar, R., and Millet, G. (2015). High-Intensity Running and Plantar-Flexor Fatigability and Plantar-Pressure Distribution in Adolescent Runners. *J. Athl. Train.* 50 (2), 117–125. doi:10.4085/1062-6050-49.3.90
- Gandevia, S. C. (2001). Spinal and Supraspinal Factors in Human Muscle Fatigue. *Physiol. Rev.* 81, 1725–1789. doi:10.1152/physrev.2001.81.4.1725
- Garrigues, E., Janvier, P., Kherabi, Y., Le Bot, A., Hamon, A., Gouze, H., et al. (2020). Post-Discharge Persistent Symptoms and Health-Related Quality of Life After Hospitalization for COVID-19. *J. Infect.* 81 (6), e4–e6. doi:10.1016/j.jinf.2020.08.029
- Girardi, M., Casolo, A., Nuccio, S., Gattoni, C., and Capelli, C. (2020). Detraining Effects Prevention: A New Rising Challenge for Athletes. *Front. Physiol.* 11, 588784. doi:10.3389/fphys.2020.588784
- Giraud, C., Librizzi, G., Fichera, G., Motta, R., Balestro, E., Calabrese, F., et al. (2021). Reduced Muscle Mass as Predictor of Intensive Care Unit Hospitalization in COVID-19 Patients. *Plos One* 16 (6), e0253433. doi:10.1371/journal.pone.0253433
- Gjovaag, T. F., and Dahl, H. A. (2008). Effect of Training with Different Intensities and Volumes on Muscle Fibre Enzyme Activity and Cross Sectional Area in the M. Triceps Brachii. *Eur. J. Appl. Physiology* 103 (4), 399–409. doi:10.1007/s00421-008-0725-7
- Griffin, L. Y., Albohm, M. J., Arendt, E. A., Bahr, R., Beynon, B. D., DeMaio, M., et al. (2006). Understanding and Preventing Noncontact Anterior Cruciate Ligament Injuries. *Am. J. Sports Med.* 34 (9), 1512–1532. doi:10.1177/0363546506286866
- Guan, W.-j., Ni, Z.-y., Hu, Y., Liang, W.-h., Ou, C.-q., He, J.-x., et al. (2020). Clinical Characteristics of Coronavirus Disease 2019 in China. *N. Engl. J. Med.* 382 (18), 1708–1720. doi:10.1056/nejmoa2002032
- Guzik, T. J., Mohiddin, S. A., Dimarco, A., Patel, V., Savvatis, K., Marelli-Berg, F. M., et al. (2020). COVID-19 and the Cardiovascular System: Implications for Risk Assessment, Diagnosis, and Treatment Options. *Cardiovasc. Res.* 116 (10), 1666–1687. doi:10.1093/cvr/cvaa106
- Hobara, H., Sato, T., Sakaguchi, M., Sato, T., and Nakazawa, K. (2012). Step Frequency and Lower Extremity Loading During Running. *Int. J. Sports Med.* 33 (04), 310–313. doi:10.1055/s-0031-1291232
- Hood, D. A. (2001). Invited Review: Contractile Activity-Induced Mitochondrial Biogenesis in Skeletal Muscle. *J. Appl. Physiology* 90 (3), 1137–1157. doi:10.1152/jappl.2001.90.3.1137
- Hortobágyi, T., Houmard, J. A., Stevenson, J. R., Fraser, D. D., Johns, R. A., and Israel, R. G. (1993). The Effects of Detraining on Power Athletes. *Med. Sci. Sports Exerc.* 25 (8), 929–935.
- Jafarnejadgero, A. A., Hamlabadi, M. P., Sajedi, H., and Granacher, U. (2021). Recreational Runners Who Recovered from COVID-19 Show Different Running Kinetics and Muscle Activities Compared with Healthy Controls. *Gait Posture* 91, 260–265. doi:10.1016/j.gaitpost.2021.11.002
- Jafarnejadgero, A. A., Sorkhe, E., and Oliveira, A. S. (2019). Motion-Control Shoes Help Maintaining Low Loading Rate Levels During Fatiguing Running in Pronated Female Runners. *Gait Posture* 73, 65–70. doi:10.1016/j.gaitpost.2019.07.133
- James, C. R., Scheuermann, B. W., and Smith, M. P. (2010). Effects of Two Neuromuscular Fatigue Protocols on Landing Performance. *J. Electromyogr. Kinesiol.* 20 (4), 667–675. doi:10.1016/j.jelekin.2009.10.007
- James, R. C., Dufek, J. S., and Bates, B. T. (2006). Effects of Stretch Shortening Cycle Exercise Fatigue on Stress Fracture Injury Risk During Landing. *Res. Q. Exerc. Sport* 77 (1), 1–13. doi:10.1080/02701367.2006.10599326
- Jimeno-Almazán, A., Pallarés, J. G., Buendía-Romero, Á., Martínez-Cava, A., Franco-López, F., Sánchez-Alcaraz Martínez, B. J., et al. (2021). Post-COVID-19 Syndrome and the Potential Benefits of Exercise. *Int. J. Environ. Res. Public Health* 18 (10), 5329.
- Koblbauer, I. F., van Schooten, K. S., Verhagen, E. A., and van Dieën, J. H. (2014). Kinematic Changes During Running-Induced Fatigue and Relations with Core Endurance in Novice Runners. *J. Sci. Med. Sport* 17 (4), 419–424. doi:10.1016/j.jsams.2013.05.013
- Kumar, A., Arora, A., Sharma, P., Anikhindi, S. A., Bansal, N., Singla, V., et al. (2020). Clinical Features of COVID-19 and Factors Associated with Severe Clinical Course: A Systematic Review and Meta-Analysis. *Soc. Sci. Res. Netw.* 2020, 3566166. doi:10.2139/ssrn.3566166
- Lee, D.-c., Brellenthin, A. G., Thompson, P. D., Sui, X., Lee, I.-M., and Lavie, C. J. (2017). Running as a Key Lifestyle Medicine for Longevity. *Prog. Cardiovasc. Dis.* 60 (1), 45–55. doi:10.1016/j.pcad.2017.03.005
- Liu, Q., Mo, S., Cheung, V. C. K., Cheung, B. M. F., Wang, S., Chan, P. P. K., et al. (2020). Classification of Runners' Performance Levels with Concurrent Prediction of Biomechanical Parameters Using Data from Inertial Measurement Units. *J. Biomechanics* 112, 110072. doi:10.1016/j.jbiomech.2020.110072
- Liu, X., Zhang, R., and He, G. (2020). Hematological Findings in Coronavirus Disease 2019: Indications of Progression of Disease. *Ann. Hematol.* 99 (7), 1421–1428. doi:10.1007/s00277-020-04103-5
- Lun, V., Meeuwisse, W., Stergiou, P., and Stefanyshyn, D. (2004). Relation Between Running Injury and Static Lower Limb Alignment in Recreational Runners. *Br. J. Sports Med.* 38 (5), 576–580. doi:10.1136/bjsm.2003.005488
- Luo, Z., Zhang, X., Wang, J., Yang, Y., Xu, Y., and Fu, W. (2019). Changes in Ground Reaction Forces, Joint Mechanics, and Stiffness During Treadmill Running to Fatigue. *Appl. Sci.* 9 (24), 5493. doi:10.3390/app9245493
- Mehl, A. J., Nelson, N. G., and McKenzie, L. B. (2011). Running-Related Injuries in School-Age Children and Adolescents Treated in Emergency Departments from 1994 through 2007. *Clin. Pediatr. (Phila)* 50 (2), 126–132. doi:10.1177/0009922810384719
- Metlay, J. P., Waterer, G. W., Long, A. C., Anzueto, A., Brozek, J., Crothers, K., et al. (2019). Diagnosis and Treatment of Adults with Community-Acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am. J. Respir. Crit. Care Med.* 200 (7), e45–e67. doi:10.1164/rccm.201908-1581st
- Mo, X., Jian, W., Su, Z., Chen, M., Peng, H., Peng, P., et al. (2020). Abnormal Pulmonary Function in COVID-19 Patients at Time of Hospital Discharge. *Eur. Respir. J.* 55 (6). doi:10.1183/13993003.01217-2020
- Musumeci, G. (2017). Sarcopenia and Exercise “The State of the Art”. *Jfmk* 2 (4), 40. doi:10.3390/jfmk2040040
- Nezlek, J. B., Cyprińska, M., Cypriński, P., Chlebowski, K., Jencylik, K., Sztacharńska, J., et al. (2018). Within-Person Relationships Between Recreational Running and Psychological Well-Being. *J. Sport Exerc. Psychol.* 40 (3), 146–152. doi:10.1123/jsep.2017-0244
- Nicol, C., Komi, P., and Marconnet, P. (1991). Fatigue Effects of Marathon Running on Neuromuscular Performance: I. Changes in Muscle Force and Stiffness Characteristics. *Scand. J. Med. Sci. Sports* 1 (1), 10–17.
- Nummela, A., Rusko, H., and Mero, A. (1994). EMG Activities and Ground Reaction Forces During Fatigued and Nonfatigued Sprinting. *Med. Sci. Sports Exerc.* 26 (5), 605–609. doi:10.1249/00005768-199405000-00013
- Oliveira, A. S., and Pircoveanu, C. I. (2021). Implications of Sample Size and Acquired Number of Steps to Investigate Running Biomechanics. *Sci. Rep.* 11 (1), 1–15. doi:10.1038/s41598-021-82876-z
- Pircoveanu, C.-I., Dam, P., Brandi, A., Bilgram, M., and Oliveira, A. S. (2021). Fatigue-Related Changes in Vertical Impact Properties During Normal and Silent Running. *J. Sports Sci.* 39 (4), 421–429. doi:10.1080/02640414.2020.1824340
- Radzak, K. N., Putnam, A. M., Tamura, K., Hetzler, R. K., and Stickley, C. D. (2017). Asymmetry Between Lower Limbs During Rested and Fatigued State Running Gait in Healthy Individuals. *Gait Posture* 51, 268–274. doi:10.1016/j.gaitpost.2016.11.005
- Salman, D., Vishnubala, D., Le Feuvre, P., Beaney, T., Korgaonkar, J., Majeed, A., et al. (2021). Returning to Physical Activity after Covid-19. *bmj* 2021, 372. doi:10.1136/bmj.m4721
- Sapp, J. L., Alqarawi, W., MacIntyre, C. J., Tadros, R., Steinberg, C., Roberts, J. D., et al. (2020). Guidance on Minimizing Risk of Drug-Induced Ventricular Arrhythmia During Treatment of COVID-19: A Statement from the Canadian Heart Rhythm Society. *Can. J. Cardiol.* 36 (6), 948–951. doi:10.1016/j.cjca.2020.04.003
- Simpson, S., Kay, F. U., Abbata, S., Bhalla, S., Chung, J. H., Chung, M., et al. (2020). Radiological Society of North America Expert Consensus Document on Reporting Chest CT Findings Related to COVID-19: Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *Radiol. Cardiothorac. Imaging* 2 (2), e200152. doi:10.1148/ryct.2020200152

- Sinclair, J., Greenhalgh, A., Edmundson, C. J., Brooks, D., and Hobbs, S. J. (2012). Gender Differences in the Kinetics and Kinematics of Distance Running: Implications for Footwear Design. *Int. J. Sports Sci. Eng.* 6 (2), 118–128.
- Song, Y., Ren, F., Sun, D., Wang, M., Baker, J. S., István, B., et al. (2020). Benefits of Exercise on Influenza or Pneumonia in Older Adults: A Systematic Review. *Ijerp* 17 (8), 2655. doi:10.3390/ijerp17082655
- Tanaka, H., Monahan, K. D., and Seals, D. R. (2001). Age-Predicted Maximal Heart Rate Revisited. *J. Am. Coll. Cardiol.* 37 (1), 153–156. doi:10.1016/s0735-1097(00)01054-8
- Tuzun, S., Keles, A., Yildiran, T., and Palamar, D. (2020). Assessment of Musculoskeletal Pain, Fatigue and Grip Strength in Hospitalized Patients with COVID-19. *Eur. J. Phys. Rehabil. Med.* 57, 653–662. doi:10.23736/S1973-9087.20.06563-6
- van Hattum, J. C., Spies, J. L., Verwijs, S. M., Verwoert, G. C., Planken, R. N., Boekholdt, S. M., et al. (2021). Cardiac Abnormalities in Athletes After SARS-CoV-2 Infection: A Systematic Review. *BMJ Open Sport Exerc. Med.* 7 (4), e001164. doi:10.1136/bmjsem-2021-001164
- Vivar, C., and van Praag, H. (2017). Running Changes the Brain: The Long and the Short of it. *Physiology* 32 (6), 410–424. doi:10.1152/physiol.00017.2017
- Vogel, D. J., Formenti, F., Retter, A. J., Vasques, F., and Camporota, L. (2020). A Left Shift in the Oxyhaemoglobin Dissociation Curve in Patients with Severe Coronavirus Disease 2019 (COVID-19). *Br. J. Haematol.* 191 (3), 390–393. doi:10.1111/bjh.17128
- Wan, J.-j., Qin, Z., Wang, P.-y., Sun, Y., and Liu, X. (2017). Muscle Fatigue: General Understanding and Treatment. *Exp. Mol. Med.* 49 (10), e384. doi:10.1038/emmm.2017.194
- Weist, R., Eils, E., and Rosenbaum, D. (2004). The Influence of Muscle Fatigue on Electromyogram and Plantar Pressure Patterns as an Explanation for the Incidence of Metatarsal Stress Fractures. *Am. J. Sports Med.* 32 (8), 1893–1898. doi:10.1177/0363546504265191
- Wibom, R., Hultman, E., Johansson, M., Matherei, K., Constantin-Teodosiu, D., and Schantz, P. G. (1992). Adaptation of Mitochondrial ATP Production in Human Skeletal Muscle to Endurance Training and Detraining. *J. Appl. Physiology* 73 (5), 2004–2010. doi:10.1152/jap.1992.73.5.2004
- Willems, T., Witvrouw, E., Delbaere, K., De Cock, A., and De Clercq, D. (2005). Relationship between Gait Biomechanics and Inversion Sprains: A Prospective Study of Risk Factors. *Gait Posture* 21 (4), 379–387. doi:10.1016/j.gaitpost.2004.04.002
- Willson, J. D., and Kernozek, T. W. (1999). Plantar Loading and Cadence Alterations with Fatigue. *Med. Sci. Sports Exerc.* 31 (12), 1828–1833. doi:10.1097/00005768-199912000-00020
- Winter, D. A. (2009). *Biomechanics and Motor Control of Human Movement*. New Jersey, US: John Wiley & Sons.
- World Health Organization (2020). *Clinical Management of Severe Acute Respiratory Infection When Novel Coronavirus (nCoV) Infection Is Suspected: Interim Guidance, 25 January 2020*. Geneva, Switzerland: World Health Organization.
- Yang, S., Liu, T., Xiong, J., Teng, Y., Guo, Y., Yu, S., et al. (2021). Traditional Chinese Exercise Potential Role as Prevention and Adjuvant Therapy in Patients with COVID-19. *Complementary Ther. Clin. Pract.* 43, 101379. doi:10.1016/j.ctcp.2021.101379

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Jafarnejadgero, Noroozi, Fakhri, Granacher and Oliveira. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.