Symptom Number and Reduced Preinfection Training Predict Prolonged Return to Training after SARS-CoV-2 in Athletes: AWARE IV

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ABSTRACT

SNYDERS, C., M. SCHWELLNUS, N. SEWRY, K. KAULBACK, P. WOOD, I. SEOCHARAN, W. DERMAN, C. READHEAD, J. PATRICIOS, B. OLIVIER, and E. JORDAAN. Symptom Number and Reduced Preinfection Training Predict Prolonged Return to Training after SARS-CoV-2 in Athletes: AWARE IV. *Med. Sci. Sports Exerc.*, Vol. 55, No. 1, pp. 1–8, 2023. **Purpose:** This study aimed to determine factors predictive of prolonged return to training (RTT) in athletes with recent SARS-CoV-2 infection. **Methods:** This is a cross-sectional descriptive study. Athletes not vaccinated against COVID-19 ($n = 207$) with confirmed SARS-CoV-2 infection (predominantly ancestral virus and beta-variant) completed an online survey detailing the following factors: demographics (age and sex), level of sport participation, type of sport, comorbidity history and preinfection training (training hours 7 d preinfection), SARS-CoV-2 symptoms (26 in 3 categories; "nose and throat," "chest and neck," and "whole body"), and days to RTT. Main outcomes were hazard ratios (HR, 95% confidence interval) for athletes with versus without a factor, explored in univariate and multiple models. HR < 1 was predictive of prolonged RTT (reduced % chance of RTT after symptom onset). Significance was $P < 0.05$. **Results:** Age, level of sport participation, type of sport, and history of comorbidities were not predictors of prolonged RTT. Significant predictors of prolonged RTT (univariate model) were as follows (HR, 95% confidence interval): female (0.6, 0.4–0.9; $P = 0.01$), reduced training in the 7 d preinfection (1.03, 1.01–1.06; $P = 0.003$), presence of symptoms by anatomical region (any "chest and neck" [0.6, 0.4–0.8; $P = 0.004$] and any "whole body" [0.6, 0.4–0.9; $P = 0.025$]), and several specific symptoms. Multiple models show that the greater number of symptoms in each anatomical region (adjusted for training hours in the 7 d preinfection) was associated

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Submitted for publication April 2022.
Accepted for publication August 2022.
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.acsm-msse.org).

0195-9131/22/5501-0001/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0000000000003027

with prolonged RTT ($P < 0.05$). **Conclusions:** Reduced preinfection training hours and the number of acute infection symptoms may predict prolonged RTT in athletes with recent SARS-CoV-2. These data can assist physicians as well as athletes/coaches in planning and guiding RTT. Future studies can explore whether these variables can be used to predict time to return to full performance and classify severity of acute respiratory infection in athletes. **Key Words:** PREDICTORS, COVID-19, RETURN TO SPORT, RESPIRATORY TRACT INFECTIONS

An acute respiratory tract infection is the most common cause of acute illness in athletes and accounts for approximately 50% of illness episodes during tournaments or competitions (1–3). The outbreak of the COVID-19 pandemic increased this burden of respiratory disease in the general population and in athletes. In athletes with acute respiratory infection, an important clinical decision is whether an athlete, who discontinued training for a period during the infection, can return to training (RTT) or sport.

The term "return to sport" (RTS) after injury in athletes is well established, although the definition varies (4). However, similar studies on RTS after illness are lacking. Historically, RTS was considered as a single end point when the athletes "return to competition or game," but it is now recognized that RTS is a continuum (5) starting from returning to participation (training) and is completed on return to previous levels of performance. The Sport and Exercise Medicine clinician is faced with two important clinical decisions along this continuum. The first clinical decision is related to the resumption of training after illness, and the measurable variable is the time (days) before an athlete starts training again after an infection, defined as days to RTT. Once an athlete starts training after an acute illness, the progression of training load is usually gradual. A second clinical decision is to determine when the athlete in training can return to previous levels of competitive sport and full performance. Full RTS is the end point of this continuum.

Data on RTS in athletes after SARS-CoV-2 infection, and studies on factors influencing decisions on the time course for RTT and the return to full performance, are limited (6). To date, most RTS guidelines after SARS-CoV-2 infection in athletes are based on expert opinion, with the majority of studies focused on the cardiovascular system (7,8). In the general population, symptom clusters are predictive of short- and long-term clinical outcomes of SARS-CoV-2 infection (9,10). Demographics, level of sport participation, type of sport, comorbidities, preinfection training, and characteristics of acute symptoms are factors that may determine RTT after SARS-CoV-2 infection, but these have not been explored.

The main aim of this study was to determine if selected factors are predictive of prolonged RTT in athletes with recent SARS-CoV-2 infection. Factors that were explored include demographics (age and sex), level of sport participation, type of sport, history of comorbidities, preinfection training (7 d before onset of infection), and symptom characteristics of the acute infection (by specific symptoms, anatomical region, and number of symptoms). Physicians responsible for athlete medical care are faced with the challenge of providing guidance in the process of RTS after acute respiratory infection. These data could be used to guide RTT clinical decision making in athletes with a recent SARS-CoV-2 infection.

METHODS

Study design and setting. The Athletes with Acute Respiratory Infections (AWARE studies) is a multicenter study, led by the Sport, Exercise Medicine and Lifestyle Institute (SEMLI) at the University of Pretoria in South Africa, together with researchers from a number of academic institutions, sports federations and some members of a subgroup of the International Olympic Committee (IOC) Consensus group on "Acute Respiratory Illness in the Athlete." This is a descriptive cross-sectional study using data collected between July 20, 2020, and May 20, 2021, during the first (ancestral virus) and second waves (predominantly beta-variant) of SARS-CoV-2 infection. During this study period, competitive sport was limited because of the COVID-19 restrictions and only gradually reintroduced, initially for professional athletes, and later in recreational settings. At the start of the study, COVID-19 vaccines were not available. In 2021, vaccination became available in a phased roll out, initially only for higher risk and older individuals. Thus, at the time of closure for participant inclusion for this study (May 2021), no participants were vaccinated. Ethical clearance was obtained from the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria (REC 409/2020) (REC 751/2019).

Participants, survey instrument, and data collection. Athletes are defined as "competing at varying levels in any sport, training for a minimum of 3 $h \cdot wk^{-1}$" and were recruited using social media platforms, existing databases, and the SEMLI medical practice. Participants ($n = 207$) were included if they were 1) 18 to 60 yr old; 2) reported a SARS-CoV-2 infection, confirmed by positive polymerase chain reaction or antigen test in the past 6 months; 3) gave electronic informed consent on the online survey housed on the Research Electronic Data Capture platform (11,12); and 4) provided information on the number of days to RTT. Survey details have previously been described (6) and included questions on 1) demographics (age and sex), 2) level of sport participation (professional—elite level/full-time, or amateur—part time/hobby), 3) type of sport (power, endurance, skilled, or mixed) (13), 4) history of comorbidities, 5) symptoms of acute SARS-CoV-2 infection (type, number, duration, and severity) per anatomical region ("nose and throat," "chest and neck," and "whole body"[systemic]), and 6) training history (hours of training 0 to 35 d before onset of infection). SARS-CoV-2 vaccines were not available at the time the study commenced and was not included in this questionnaire. Participants were requested

to indicate if they 1) have started training again after recent infection (n = 138), 2) have not started training (n = 61), or 3) continued training throughout recent infection (n = 8). For those who have started training, the days to return to the first training session were reported in response to the following question: "How many days were there between the start of your symptoms and the return to your first training session?"

Patient and public involvement (PPI). PPI was considered for this study. Athletes who had experienced an acute respiratory infection, including SARS-CoV-2, and medical practitioners that regularly treat athletes with acute respiratory tract infections were asked to provide feedback on the questionnaire in the development stages (6).

Measures of outcome. The primary outcome measure was the self-reported number of days to return to the first training session (RTT) after recent SARS-CoV-2 infection. Factors explored as possible predictors of RTT included, demographics (age and sex), level of sport participation, type of sport, history of comorbidities in organ systems (respiratory, cardiovascular, gastrointestinal, nervous, metabolic, renal systems, and cancer), training history in the 7 d before acute infection, and symptoms of acute SARS-CoV-2 infection (by specific symptoms, anatomical region, and number of symptoms).

Statistical analysis of data. Demographics, level of sport participation, type of sport (13), history of comorbidities, and preinfection training history in athletes were described using n (%) or mean ± SD. The responses to the 26 types of SARS-CoV-2 symptoms (8 "nose and throat," 8 "chest and neck," and 10 "whole body") were described in three ways: 1) the presence of symptoms, number of athletes (n) (%, 95% confidence interval [CI]); 2) the duration in days (median, Q1–Q3); and 3) the severity, n (%) of mild and moderate or severe.

For the training resumption variable: 1) participants reporting RTT days (n = 138), the actual days to RTT were recorded; 2) participants that did not start training (n = 61), the days RTT with censoring were recorded; and 3) participants that continued training (n = 8), days to RTT were recorded as 0. For the days to RTT analysis, 207 participants were used for this analysis.

For the Cox regression modeling of factors associated with a prolonged RTT, the analysis was done in stages. For the univariate modeling, the independent factors explored were as follows: 1) demographics, level of sport participation, type of sport, history of comorbidities, and preinfection training history; 2) the presence of specific individual symptoms; 3) the presence of any symptoms by anatomical region; and 4) the number of symptoms by anatomical region. The individual symptoms were not considered in the multiple regression model, but instead the variables "presence" and "number" of symptoms by anatomical region were considered. Separate multiple regression models for "presence" and "number" of symptoms were conducted, adjusting for training hours in the 7 d before the onset of the infection. The hazard ratio (HR, 95% CI) was reported with χ^2 (P values) (type 3 test) for significance ($P < 0.05$). Cox regression assumption of proportional hazards was checked. For these data, HR < 1 indicates a prolonged RTT after the onset of symptoms.

RESULTS

Demographics, Level of Sport Participation, Type of Sport, History of Comorbidities, and Preinfection Training

Demographic variables, level of sport participation, type of sport, history of comorbidities, and preinfection training in athletes with recent SARS-CoV-2 (n = 207) are shown in Table 1.

The mean age of the study population was 28 yr, the majority were males (66%), and 45% were professional athletes. Participants mostly competed in mixed (53%) (including three athletes with skill sport) and endurance sports (41%). A history of any comorbidity was reported by 42% of participants.

Symptoms (Number, Duration, and Severity) of SARS-CoV-2 Infection in Study Participants

The mean number of SARS-CoV-2 symptoms (out of 26) in the acute infective phase was 7.3 per athlete (95% CI = 6.7–7.9). The number (n [%], 95% CI), duration (days), and severity of symptoms by anatomical region and specific symptoms are shown in Supplemental Table 1 (see Supplemental Digital Content, http://links.lww.com/MSS/C702). The mean number of "nose and throat" symptoms was 2.8 (2.6–3.1), and "chest and neck" symptoms was 2.1 (1.9–2.4). Twenty-one participants reported "other whole body" symptoms that were included in the questionnaire as "free text." The mean number of "whole body" (inclusive of "other whole body") symptoms was 2.3 (2.1–2.6). The four most common symptoms were

TABLE 1. Demographics, level of sport participation, type of sport, history of comorbidities, and preinfection training history in athletes with recent SARS-CoV-2 (n = 207).

Variable	SARS-CoV-2 (n = 207)
Demographics	
Age, mean ± SD	27.9 ± 9.9
Male sex, n (%)[a]	121 (65.8)
Height, mean ± SD, cm[b]	178.3 ± 13.3
Body weight, mean ± SD, kg[a]	80.2 ± 19.1
Level of sport participation	
Professional sports, n (%)[a]	82 (44.6)
Years sporting experience, mean ± SD[b]	11.0 ± 7.4
Type of sport[c]	
Power	10 (5.5)
Endurance	75 (41.4)
Mixed (including skills, n = 3)	96 (53.0)
History of comorbidities	
Number of comorbidities per participant, mean ± SD	0.7 ± 1.1
Any comorbidity (yes), n (%)	87 (42)
Respiratory	45 (22.7)
Cardiovascular risk factors	20 (9.7)
Gastrointestinal	32 (15.5)
Nervous system	22 (10.6)
Allergies (yes), n (%)	36 (17.4)
Preinfection training history	
Training 7 d before onset of symptoms, mean ± SD, h·wk^{-1}	9.7 ± 6.9
Weekly training 2–5 wk before onset of symptoms, mean ± SD, h·wk^{-1}	11.7 ± 7.6

[a]Number of participants with missing data = 23.
[b]Number of participants with missing data = 25.
[c]Number of participants with missing data = 26.

TABLE 2. Demographics, level of sport participation, type of sport, history of comorbidities, and preinfection training history as possible factors associated with prolonged RTT (n = 207) (univariate model).

Variable	HR, 95% CI[a]	x^2	P
Demographics			
Age	0.99 (0.98–1.01)	1.09	0.297
Sex: females (vs males)	0.6 (0.4–0.9)	6.66	**0.010**
Level of sport participation			
Professional sport (vs recreational)	1.4 (1.0–2.0)	3.58	0.058
Type of sport			
Power (reference)	–		
Endurance	1.06 (0.51–2.19)	0.026	0.872
Mixed (including skills)	0.94 (0.46–1.92)	0.032	0.857
History of comorbidities			
Number of comorbidities	0.9 (0.8–1.0)	2.05	0.152
Any comorbidities by organ system (no vs yes)[b]	0.8 (0.6–1.2)	0.959	0.328
Respiratory	1.0 (0.6–1.4)	0.054	0.816
Cardiovascular risk factors	0.8 (0.5–1.4)	0.528	0.467
Gastrointestinal	0.7 (0.5–1.1)	2.31	0.129
Nervous	0.8 (0.5–1.4)	0.764	0.382
Allergies	0.9 (0.6–1.3)	0.458	0.499
Preinfection training history			
Training 7 d before onset of symptoms ($h \cdot wk^{-1}$)	1.03 (1.01–1.06)	8.74	**0.003**
Weekly training 2–5 wk before onset of symptoms ($h \cdot wk^{-1}$)	1.10 (0.99–1.03)	1.05	0.307

P values presented in bold represent statistically significant differences.
[a]Ratio of the hazard of an individual with the presence of the covariate compared with the hazard of RTT for an individual without the presence of the covariate.
[b]Comorbidities in other organ systems were too few for further analyses (this included participants with a history of cardiovascular disease).

"excessive fatigue" (58%), "headache" (57%), "altered/loss of sense of smell" (54%), and "blocked nose" (51%). Symptoms with the longest duration were "fast breathing/shortness of breath," "excessive fatigue," "loss of appetite," "red watery eyes," and "altered/loss of smell or taste" (all median of 7 d). The following symptoms were most commonly reported as moderate or severe: "excessive fatigue" (43%), "loss/altered sense of smell and taste" (42% and 36% respectively), "headache" (38%), and "muscle aches" (29%).

Days to RTT

The median duration of RTT for the participants who had started training was 14 d (interquartile range, 10–21 d), with a minimum of 0 d (for those who continued training throughout the infection period), and the maximum duration of RTT was 87 d (for those who had not started training at the time of completing the questionnaire).

Factors Associated with Prolonged RTT after SARS-CoV-2 Infection: Univariate Models

Demographics, level of sport participation, type of sport, history of comorbidities, and preinfection training history (univariate model). HR and 95% CI for demographics (age and sex), level of sport participation, type of sport, history of comorbidities, and pre-infection training history are shown in Table 2. HR < 1 indicates a lower chance of RTT (prolonged RTT) after the onset of the infection.

Age, level of sport participation, type of sport, and history of comorbidities were not associated with a more prolonged RTT. In this univariate model, the following variables were significantly associated with a prolonged RTT: females (P = 0.01) and reduced hours of training in the 7 d before infection (P = 0.003).

The association between the presence of specific symptoms and the prolonged RTT (univariate model). HR was derived as the ratio of the hazard of RTT for an individual with the symptom compared with the hazard of RTT for an

TABLE 3. HR (95% CI) for the presence of specific symptoms in athletes and prolonged RTT (n = 207) (univariate model).

Anatomical Region	Symptom	n	HR (95% CI)[a]	x^2	P
Nose and Throat	Sore/scratchy throat	102	1.0 (0.7–1.4)	0.03	0.863
	Hoarseness	26	0.6 (0.3–1.0)	4.09	**0.043**
	Blocked/plugged nose	105	0.9 (0.6–1.2)	0.72	0.397
	Runny nose	45	0.7 (0.5–1.1)	2.03	0.154
	Sinus pressure	65	0.7 (0.5–1.1)	2.73	0.098
	Sneezing	32	0.9 (0.5–1.4)	0.24	0.569
	Altered/loss sense of smell	111	0.7 (0.5–1.0)	3.41	0.065
	Altered/loss sense of taste	98	0.7 (0.5–1.0)	3.34	0.068
Chest and Neck	Dry cough	75	0.7 (0.5–1.0)	3.54	0.060
	Wet cough	47	1.1 (0.7–1.6)	0.06	0.813
	Difficulty in breathing	46	0.6 (0.4–1.0)	4.7	**0.030**
	Fast breathing/shortness of breath	46	0.7 (0.5–1.0)	3.22	0.073
	Chest pain/pressure	42	0.6 (0.4–1.0)	4.08	**0.044**
	Chest tightness	42	0.8 (0.5–1.2)	1.33	0.248
	Headache	118	0.9 (0.6–1.2)	0.49	0.480
	Red/watery/scratchy eyes	27	0.9 (0.5–1.4)	0.4	0.527
Whole body	Fever	73	0.8 (0.5–1.1)	2.64	0.104
	Chills	43	0.5 (0.3–0.8)	7.24	**0.007**
	Excessive fatigue	119	0.7 (0.5–1.0)	4.95	**0.026**
	General muscle aches and pains	88	1.1 (0.8–1.5)	0.08	0.784
	Skin rash^	6	–	–	–
	Abdominal pain	19	0.5 (0.2–0.9)	4.78	**0.029**
	Nausea	27	0.6 (0.4–1.1)	2.72	0.099
	Vomiting[b]	1	–	–	–
	Diarrhea	19	1.0 (0.6–1.7)	0.006	0.936
	Loss of appetite	63	0.6 (0.4–0.8)	9.31	**0.002**
	Other whole body symptoms	21	0.8 (0.5–1.3)	0.88	0.347

P values presented in bold represent statistically significant differences.
[a]HR is the ratio of the hazard of RTT for an individual with the symptom compared with the hazard of RTT for an individual without the symptom. HR < 1 indicates a lower chance of RTT after the onset of infection for an individual with the symptom compared with an individual without the symptom, i.e., prolonged RTT.
[b]Numbers were too few for further analyses.

TABLE 4. HR (95% CI) for symptoms (presence and number) by anatomical region and prolonged RTT (n = 207) (univariate models).

Symptoms by Anatomical Region	n (%) or Q1;Median;Q3	HR (95% CI)[a]	x^2	P
Presence of symptoms[b] (univariate model 1)				
Nose and throat	190 (91.8)	0.9 (0.5–1.6)	0.07	0.791
Chest and neck	169 (79.7)	0.6 (0.4–0.8)	8.34	**0.004**
Whole body[c]	165 (79.7)	0.6 (0.4–0.9)	5.03	**0.025**
Number of symptoms[d] (univariate model 2)				
Nose and throat	2;3;4	0.89 (0.81–0.98)	6.2	**0.013**
Chest and neck	1;2;3	0.88 (0.80–0.97)	6.45	**0.011**
Whole body[c]	1;2;4	0.86 (0.79–0.94)	10.26	**0.001**
All symptoms	4;6;10	0.94 (0.90–0.98)	10.8	**0.001**

P values presented in bold represent statistically significant differences.
[a]HR of the hazard of RTT for an individual with either the presence or an increased number of symptoms in each anatomical region. HR < 1 indicates a lower chance of RTT after the onset of infection.
[b]Hazard of RTT for the presence of any symptoms compared with the hazard of RTT without the presence of any symptoms in each anatomical region.
[c]Includes 160 participants with "whole body" symptoms plus 5 with "other whole body" symptoms.
[d]For number of symptoms, HR indicates the change in the risk for 1 more symptom.

individual without the symptom. HR and 95% CI for the presence of specific symptoms are shown in Table 3.

The following specific symptoms were associated with a more prolonged RTT (% lower chance) compared with athletes without the symptom: "chills" (50%; P = 0.007), "abdominal pain" (50%; P = 0.029), "loss of appetite" (40%; P = 0.002), "difficulty in breathing" (40%; P = 0.030), "hoarseness" (40%; P = 0.043), "chest pain/pressure" (40%; P = 0.044), and "excessive fatigue" (30%; P = 0.026).

The association between the presence and the number of symptoms by anatomical region and prolonged RTT (univariate models). Associations between the presence and the number of symptoms by anatomical region and prolonged RTT were explored in two univariate models. HR and 95% CI for the presence and number of symptoms by anatomical region and prolonged RTT are shown in Table 4.

The presence of any "nose and throat" symptoms (HR = 0.9; 95% CI = 0.5–1.6: P = 0.791) was not associated with more prolonged RTT. The presence of any "chest and neck" (HR = 0.6; 95% CI = 0.4–0.8: P = 0.004) and "whole body" symptoms (HR = 0.6; 95% CI = 0.4–0.9: P = 0.025) were associated with more prolonged RTT.

In athletes with recent SARS-CoV-2 infection, the number of symptoms in each anatomical region was significantly associated with more prolonged RTT as follows: "nose and throat" symptoms (HR = 0.89, 95% CI = 0.81–0.98, P = 0.013), "chest and neck" symptoms (HR = 0.88, 95% CI = 0.80–0.97, P = 0.011), "whole body" symptoms (HR = 0.86, 95% CI = 0.79–0.94, P = 0.001), and "all symptoms" (HR = 0.94, 95% CI = 0.90–0.98, P = 0.001).

Factors Associated with Prolonged RTT after SARS-CoV-2 Infection: Multiple Model

In a multiple model including the significant demographic factors, only hours of training in the 7 d before infection was significant (P = 0.017). Thus, associations between 1) the presence and 2) the number of symptoms by anatomical region and prolonged RTT were explored in two multiple models adjusting for training hours in the 7 d before the onset of the infection. The adjusted HR and the 95% CI for presence (model 1) and number of symptoms (model 2) by anatomical region in athletes are shown in Table 5.

In the first multiple model, "nose and throat" symptoms and "whole body" symptoms were not predictive of prolonged RTT, but the presence of "chest and neck" symptoms was indicative of prolonged RTT (P = 0.014). In the second multiple model, the increasing number of symptoms in each anatomical region remained predictors of prolonged RTT ("nose and throat," HR = 0.89, 0.81–0.98, P = 0.018; "chest and neck," HR = 0.89, 0.81–0.99, P = 0.025; "whole body," HR = 0.88, 0.80–0.96, P = 0.005). The increasing number of "all symptoms" was also a predictor of prolonged RTT (HR = 0.94; 0.91–0.98; P = 0.003).

Finally, we explored the interaction of the total number of symptoms and number of symptoms in the three anatomical regions with

TABLE 5. HR (95% CI) for symptoms (presence and number) by anatomical region and prolonged RTT adjusted for training hours in the 7 d before the onset of infection (n = 207) (multiple models).

Symptoms by Anatomical Region	n (%) or Q1;Median;Q3	HR (95% CI)[a]	x^2	P
Presence of symptoms[b] (multiple model 1)				
Nose and throat	190 (91.8)	0.87 (0.52–1.48)	0.28	0.597
Chest and neck	169 (79.7)	0.60 (0.40–0.90)	6.08	**0.014**
Whole body[c]	165 (79.7)	0.71 (0.47–1.08)	2.55	0.11
Number of symptoms[d] (multiple model 2)				
Nose and throat	2;3;4	0.89 (0.81–0.98)	5.59	**0.018**
Chest and neck	1;2;3	0.89 (0.81–0.99)	5.04	**0.025**
Whole body[c]	1;2;4	0.88 (0.80–0.96)	7.84	**0.005**
All symptoms	4;6;10	0.94 (0.91–0.98)	8.73	**0.003**

P values presented in bold represent statistically significant differences.
[a]HR of the hazard of RTT for an individual with either the presence or an increased number of symptoms in each anatomical region. HR < 1 indicates a lower chance of RTT after the onset of infection.
[b]Hazard of RTT for the presence of any symptoms compared with the hazard of RTT without the presence of any symptoms in each anatomical region.
[c]Includes 160 participants with "whole body" symptoms plus 5 with "other whole body" symptoms.
[d]For number of symptoms, HR indicates the change in the risk for 1 more symptom.

the covariate "training hours in the 7 d before the onset of symptoms." None of the interactions were significant ($P > 0.1$).

DISCUSSION

The aim of this study was to identify factors predictive of prolonged RTT after SARS-CoV-2 infection in athletes. Overall, in athletes that did start training, the median RTT was 14 d (interquartile range, 10–21 d). In our univariate models, we first show that females, symptoms by anatomical region ("chest and neck" or "whole body"), and specific symptoms of SARS-CoV-2 were associated with prolonged RTT. Specific symptoms associated with more prolonged RTT were "chills," "abdominal pain," "loss of appetite," "difficulty in breathing," "hoarseness," "chest pain/pressure," and "excessive fatigue." Second, our univariate analysis showed that the number of symptoms in each anatomical region and reduced training in the 7 d before infection were predictive of prolonged RTT. In multiple models, including reduced training in the 7 d before infection, an increase in the number of symptoms in each anatomical region remained predictive of prolonged RTT. Factors not associated with prolonged RTT were age, level of sport participation, type of sport, and history of comorbidities.

In our study, we clustered symptoms by anatomical region and added both the presence of any symptoms and the number of symptoms in each anatomical region into the multiple models. This analysis showed that not the presence of symptoms in anatomical regions but rather a greater number of symptoms in each region remained a significant predictor of prolonged RTT when adjusted for preinfection training (hours in the 7 d before onset of infection). In the general population, a greater number of symptoms during acute phase are associated with increased risk of prolonged symptoms ("Long-COVID") (14,15). Our finding that greater number of symptoms is a predictor of prolonged RTT may have potential clinical application in determining the severity of acute respiratory infections in athletes. Our study population was unvaccinated against SARS-CoV-2, and the predominant variants of SARS-CoV-2 during our study period were the ancestral virus (first wave) and the beta-variant (second wave). We acknowledge that previous SARS-CoV-2 infection, vaccination status, and the variant could influence predictors of RTT after SARS-CoV-2 infection in athletes. Our results are thus strictly applicable only 1) to an unvaccinated SARS-CoV-2 naïve athletic population and 2) to infection with the SARS-CoV-2 variants that were predominant during our study period. There are data indicating that both the variant and the vaccination status may have an influence on the symptoms experienced and disease severity (16,17). Despite this limitation of generalizability, we believe that the findings of predictors of RTT in athletes are of value because they are novel and are valid for an investigation of this nature. We strongly encourage future studies to determine if these predictors are applicable to other athlete populations (vaccinated and unvaccinated) that are infected with other SARS-CoV-2 variants or with other pathogens causing acute respiratory infections.

Reduced training hours in the 7 d before symptom onset was associated with prolonged RTT in our univariate analysis. In our multiple models, reduced hours of training in the 7 d before the onset of SARS-CoV-2 infection remained an independent predictor of prolonged RTT. This finding is of particular interest and is in keeping with several recently published findings that higher levels of physical activity per week are associated with reduced severity of SARS-CoV-2 infections (18,19,20). The potential mechanism/s for this is not well established but may be related to the immunoprotective effect of regular exercise (21,22). However, we acknowledge that in this cross-sectional study, we cannot infer causality and athletes with higher preinfection hours of training might, for example, be more determined to continue with sporting activity after acute infection and, therefore, resume training sooner.

In our univariate analysis of symptoms, we found that regional symptoms (any "chest and neck" symptoms and "whole body" symptoms) as well as selected specific symptoms were predictive of delayed RTT. These findings correlate with data from our previous AWARE study (6). In support of this finding, other published data also show that "chest pain" is associated with a higher likelihood of time loss (days from symptom onset to full training and competition) for more than 28 d, and athletes presenting with the presence of chest-related symptoms ("chest pain," "dyspnoea," and "cough") and "fever" were 2.1 (95% CI = 1.2–3.5) times more likely to have a prolonged time loss from training (more than 28 d). The same study showed an association between symptom duration lasting more than 28 d, with time loss for longer than 28 d (23). The presence of symptoms indicative of regional or systemic illness, and their duration, may thus have an impact on time to RTT.

Finally, from our univariate analysis, we show that females have a higher chance of prolonged RTT after SARS-CoV-2 infection, but this was not significant in the multiple model analysis. To our knowledge, female sex has not been associated with delayed RTT in the current literature. However, previous studies have found female athletes have a longer duration of symptoms during acute infection (24). More specifically, the duration of SARS-CoV-2 symptoms lasted longer in females international-level athletes compared with their male counterparts (23). A study in the general population also found females to be more prone to "Long-COVID" (symptoms lasting for more than 28 d) (14). Furthermore, in an epidemiological study on the incidence of illness in athletes, females have been found to be more prone to infection (1,25). Although these studies may indicate increased likelihood for females to have symptoms for longer and thus possibly delayed resumption of sport, we could not confirm this finding, and it requires further investigation.

A strength of our study is that we included data from a sample of athletes with SARS-CoV-2 infection that was large enough to determine independent factors predictive of more prolonged RTT using multiple models. We acknowledge that our study has several limitations. First, our sample was a convenience sample with potential selection bias. Second, participants were reliant on recall to document self-reported symptoms on an electronic questionnaire. However, this survey

was conducted at a time of global heightened awareness of COVID-19, including COVID-19-related symptoms. Athletes, specifically professional and high level athletes, are particularly aware of their training schedules and any symptoms they experience (presence, duration, and severity), and we are reasonably confident that recall of training data and symptoms is accurate. We also note that most published manuscripts reporting COVID-19 symptoms, in the general population and in athletes, relied on self-reporting of symptoms. Third, we acknowledge that during data collection, 23 participants (11%) did not disclose their sex, and this could have influenced our finding on female sex as a possible predictor of prolonged RTT in our univariate analysis. Although we do note that the median RTT was not significantly different between the groups that reported sex and those who did not ($P = 0.160$), we still suggest that the finding of sex as a possible predictor of RTT should be interpreted with caution. Our study design was cross-sectional, and although we show significant associations with prolonged RTT, these do not infer a cause-and-effect relationship.

These data are of clinical value to physicians responsible for athlete medical care and may develop into a predictive tool for RTT that can be used at the time of the initial consultation with the athlete. Future studies are needed to determine if the type and number of symptoms can be used to classify disease severity in athletes. The return to the first training session (RTT) after an infection is only the first step in a continuum to full RTS. We are not aware of any studies that relate RTT to RTS. For example, do athletes that RTT early after an infection also have a rapid RTS? Other factors that may influence the duration between RTT and return to full performance should be investigated in future studies, as this is the last step for an athlete's complete RTS after an acute infection.

CONCLUSIONS

In summary, our study shows that decreased hours of training in the 7-d period before the onset of infection, as well as total number of symptoms and number of symptoms by anatomical region at the time of the acute infection, can predict prolonged RTT in an unvaccinated athlete with recent SARS-CoV-2 infection (ancestral virus and beta-variant). Age, level of sport participation, type of sport, and history of comorbidities were not predictive of RTT. These data can assist physicians responsible for athlete medical care as well as athletes or coaches, in planning and guiding RTT in athletes after SARS-CoV-2 infection. Future studies are needed to determine if these predictors are applicable to other athlete populations, e.g., 1) vaccinated/unvaccinated, 2) athletes infected with other SARS-CoV-2 variants, and 3) athletes infected with other pathogens causing acute respiratory infections.

What are the new findings?. In unvaccinated athletes with recent SARS-CoV-2 infection (ancestral virus and beta-variant),

- age, level of sport participation, type of sport, and history of comorbidities are not predictive of prolonged RTT;
- reduced hours of training in the 7-d period before the onset of infection can predict prolonged RTT; and
- an increase in the total number of symptoms and the number of symptoms by anatomical region at the time of the acute infection can predict prolonged RTT.

Practical implications. In the initial assessment of the athlete with a recent SARS-CoV-2 infection, the history of the total number of symptoms and the number of symptoms per anatomical region during the acute phase, as well as training history in the period before the acute infection, may identify athletes with prolonged time course to RTT.

Data sharing statement. No additional data are available.

This study was funded by the International Olympic Committee (IOC) Research Centre (South Africa) (partial funding) and the South African Medical Research Council (SAMRC) (partial funding, statistical analysis).

The authors thank the following persons in South Africa (Dr. Jeremy Boulter, Dr. Darren Green, Prof. Christa Janse van Rensburg, Dr. Lervasen Pillay, Ms. Sonja Swanevelder, Dr. Phathokuhle Zondi, and SA Rugby doctors) and international colleagues (Dr. Paolo Emilio Adami, Dr. Addy Bamberg, Dr. Richard Budgett, Prof. Lars Engebretsen, Dr. Eanna Falvey, Prof. Jonathan Finnoff, A/Prof. Jane Fitzpatrick, Dr. Zhan Hui, Prof. James Hull, Prof. Guoping Li, Dr. Andrew Massey, Dr. Sergio Migliorini, Dr. Katja Mjosund, A/Prof. Lars Pedersen, Dr. Nirmala Perera, Prof. David Pyne, Dr. Torbjorn Soligard, and Dr. Maarit Valtonen) for their willingness to assist this study group with the ongoing distribution of the link containing the survey. In some cases, colleagues have now formally joined as collaborators, following approvals by their respective institutions. They also sincerely thank all the athletes for their participation in this study.

C. S. contributed in study planning, data collection, data interpretation, manuscript (first draft), and manuscript editing. M. S. was responsible for the overall content as guarantor, study concept, study planning, data collection, data interpretation, manuscript editing, and facilitating funding. N. S. contributed in study planning, data collection, data cleaning, data interpretation, manuscript (first draft), and manuscript editing. K. K. contributed in study planning, data collection, and manuscript editing. P. W. contributed in study planning, data collection, and manuscript editing. I. S. contributed in study planning, development of the data management system, data collection, data cleaning, and manuscript editing. W. D. contributed in data interpretation and manuscript editing. C. R. contributed in data collection, data interpretation, and manuscript editing. J. P. contributed in data collection, data interpretation, and manuscript editing. B. O. contributed in data collection, data interpretation, and manuscript editing. E. J. contributed in study planning, data cleaning, data management, data analysis including statistical analysis, data interpretation, and manuscript editing.

C. S. received a scholarship made possible through funding by the South African Medical Research Council through its Division of Research Capacity Development under the SAMRC Clinician Researcher Programme. This research project was supported by the South African Medical Research Council (SAMRC) under a Self-Initiated Research Grant awarded to M. S. The content hereof is the sole responsibility of the authors and does not necessarily represent the official views of the SAMRC.

The authors declare no competing interests. The results of the present study do not constitute endorsement by the American College of Sports Medicine. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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