Symptom number and reduced pre-infection training predict prolonged return to training after SARS-CoV-2 in athletes: AWARE IV

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ABSTRACT

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, sex), level of sport participation, type of sport, co-morbidity history and pre-infection training (training hours 7 days pre-infection), 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%CI) for athletes with vs. 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 co-morbidities were not predictors of prolonged RTT. Significant predictors of prolonged RTT (univariate model) were (HR;95%CI): female (0.6;0.4-0.9; $p=0.01$), reduced training in the 7 days pre-infection (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 days pre-infection) was associated with prolonged RTT ($p<0.05$).

Conclusion: Reduced pre-infection 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 other acute respiratory infection in athletes.

Key words

Predictors, COVID-19, return-to-sport, respiratory tract infections

INTRODUCTION

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 or sport.

The term "return to sport" (RTS) following 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 recognised 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 (SEM) clinician is faced with two important clinical decisions along this continuum. The first clinical decision is related to the resumption of training following illness, and the measurable variable is the time (days) before an athlete starts training again following an infection, defined as days to "return to training" (RTT). Once an athlete starts training following 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 following 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 following 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, co-morbidities, pre-infection training and acute symptoms characteristics, 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, sex), level of sport participation, type of sport, history of co-morbidities, pre-infection training (7 days 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 **A**thletes **W**ith **A**cute **R**espiratory Inf**E**ctions (AWARE studies) is a multi-centre 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 20 July 2020 and 20 May 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 due to the COVID-19 restrictions and only gradually re-introduced, 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).

Participants, Survey Instrument and Data Collection

Athletes are defined as "competing at varying levels in any sport, training for a minimum of 3 hours per week" and were recruited using social media platforms, existing databases and the SEMLI medical practice. Participants (n=207) were included if they were: 1) aged 18 to 60 years, 2) reported a SARS-CoV-2 infection, confirmed by positive Polymerase Chain Reaction (PCR) or antigen test in the past 6 months, 3) gave electronic informed consent on the online survey housed on the Research Electronic Data Capture (REDCap) 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 co-morbidities, 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 days 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 (ARinf), 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, sex), level of sport participation, type of sport, history of co-morbidities in organ systems (respiratory, cardiovascular, gastrointestinal, nervous, metabolic, renal systems and cancer), training history in the 7 days 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 co-morbidities and pre-infection 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%CI)], 2) the duration in days (median: Q1-Q3) and 3) the severity [number (%) 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), 0 days RTT were recorded. For the days to RTT analysis, 207 participants were used for this analysis. For the Cox regression modelling of factors associated with a prolonged RTT the analysis was done in stages. For the univariate modelling, the independent factors explored were: 1) demographics, level of sport participation, type of sport, history of co-morbidities and pre-infection 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 days before the onset of the infection. The Hazard Ratio (HR; 95%CI) was reported with Chi-Square (p-values) (type 3 test) for significance ($p<0.05$). Cox regression assumption of proportional hazards was checked. For these data, a HR<1 indicates a prolonged RTT after the onset of symptoms.

RESULTS

Demographics, level of sport participation, type of sport, history of co-morbidities and pre-infection training

The demographic variables, level of sport participation, type of sport, history of co-morbidities and pre-infection training in athletes with recent SARS-CoV-2 (n=207) are shown in Table 1.

Table 1: Demographics, level of sport participation, type of sport, history of co-morbidities and pre-infection 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 (cm) (mean, SD)[b]	178.3 (13.3)
Body weight (kg) (mean, SD)[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 co-morbidities	
Number of co-morbidities per participant (mean, SD)	0.7 (1.1)
Any co-morbidity (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)
Pre-infection training history	
Training 7 days prior to onset of symptoms (hrs/week) (mean, SD)	9.7 (6.9)
Weekly training 2-5 weeks prior to onset of symptoms (hrs/week) (mean, SD)	11.7 (7.6)

Number of participants with missing data: a=23, b=25, c=26

The mean age of the study population was 28 years, the majority were males (66%) and 45% were professional athletes. Participants mostly competed in mixed (53%) (including 3 athletes with skill sport) and endurance sports (41%). A history of any co-morbidity 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 is shown in Supplemental Digital Content 1. 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). 21 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 "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 days). 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 return to training (RTT)

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

Factors associated with prolonged return to training (RTT) following SARS-CoV-2 infection: Univariate models

Demographics, level of sport participation, type of sport, history of co-morbidities and pre-infection training history (univariate model)

The Hazard Ratio (HR and 95%CI) for demographics (age and sex), level of sport participation, type of sport, history of co-morbidities, and pre-illness training history is shown in Table 2. HR<1 indicates a lower chance of RTT (prolonged RTT) after the onset of the infection.

Table 2: Demographics, level of sport participation, type of sport, history of co-morbidities and pre-infection training history as possible factors associated with prolonged return to training (RTT) (n=207) (Univariate model)

Variable	**Hazard ratio* 95%CI**	**Chi-Square**	**p-value**
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 co-morbidities			
Number of co-morbidities	0.9 (0.8-1.0)	2.05	0.152
Any co-morbidities by organ system (No vs. Yes)^	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
Pre-infection training history			
Training 7 days prior to onset of symptoms (hrs/week)	1.03 (1.01-1.06)	8.74	**0.003**
Weekly training 2-5 weeks prior to onset of symptoms (hrs/week)	1.10 (0.99-1.03)	1.05	0.307

* Ratio of the hazard of an individual with the presence of the co-variate compared to the hazard of RTT for an individual without the presence of the co-variate

^ Co-morbidities in other organ systems were too few for further analyses (this included participants with a history of cardiovascular disease)

Age, level of sport participation, type of sport and history of co-morbidities 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 days prior to infection (p=0.003).

The association between the presence of specific symptoms and prolonged return to training (univariate model)

The hazard ratio (HR) was derived as the ratio of the hazard of RTT for an individual with the symptom, compared to the hazard of RTT for an individual without the symptom. The Hazard Ratio (HR and 95%CI) for the presence of specific symptoms is shown in Table 3.

Table 3: The Hazard Ratio (95%CI) for the presence of specific symptoms in athletes and prolonged return to training (RTT) (n=207) (Univariate model)

Anatomical region	**Symptom**	**n**	**Hazard Ratio (95%CI)***	**Chi-Square**	**p-value**
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 ^	1	-	-	-
	Diarrhoea	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

*HR is the ratio of the hazard of RTT for an individual with the symptom compared to the hazard of RTT for an individual without the symptom. A HR<1 indicates a lower chance of RTT after the onset of infection for an individual with the symptom compared to an individual without the symptom i.e. prolonged RTT
^Numbers were too few for further analyses

The following specific symptoms were associated with a more prolonged RTT (% lower chance) compared to 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 number of symptoms by anatomical region and prolonged return to training (univariate models)

Associations between the presence and number of symptoms by anatomical region and prolonged RTT were explored in two univariate models. The Hazard Ratio (HR and 95%CI) for the presence and number of symptoms by anatomical region and prolonged return to training (RTT) is shown in Table 4.

Table 4: The Hazard Ratio (95%CI) for symptoms (presence and number) by anatomical region and prolonged return to training (RTT) (n=207) (Univariate models)

Symptoms by anatomical region	n (%) or Q1;median;Q3	Hazard Ratio (95%CI)*	Chi-Square	p-value
Presence of symptoms$^{\beta}$ (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^	165 (79.7)	0.6 (0.4-0.9)	5.03	**0.025**
Number of symptoms$^{\varphi}$ (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^	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**

*Hazard Ratio 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
$^{\beta}$Hazard of RTT for the presence of any symptoms compared to the hazard of RTT without the presence of any symptoms in each anatomical region
$^{\varphi}$For number of symptoms the hazard ratio indicates the change in the risk for 1 more symptom
^ Includes 160 participants with "whole body" symptoms plus 5 with "other whole body" symptoms

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 return to training (RTT) following SARS-CoV-2 infection: Multiple model

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

Table 5: The Hazard Ratio (95%CI) for symptoms (presence and number) by anatomical region and prolonged return to training (RTT) adjusted for training hours in the 7 days before the onset of infection (n=207) (Multiple models)

Symptoms by anatomical region	n (%) or Q1;median;Q3	Hazard Ratio (95%CI)*	Chi-Square	p-value
Presence of symptoms$^{\beta}$ (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^	165 (79.7)	0.71 (0.47-1.08)	2.55	0.11
Number of symptoms$^{\varphi}$ (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^	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**

*Hazard Ratio 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

$^{\beta}$Hazard of RTT for the presence of any symptoms compared to the hazard of RTT without the presence of any symptoms in each anatomical region

$^{\varphi}$For number of symptoms the hazard ratio indicates the change in the risk for 1 more symptom

^ Includes 160 participants with "whole body" symptoms plus 5 with "other whole body" symptoms

In the first multiple model the presence of symptoms in the "nose and throat" as well as "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, 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). 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 3 anatomical regions with the covariate "*training hours in the 7 days 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 following SARS-CoV-2 infection in athletes. Overall, in athletes that did start training, the median RTT was

14 days (interquartile range of 10-21 days). In our univariate models, we firstly 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". Secondly our univariate analysis showed that the number of symptoms in each anatomical region and reduced training in the 7 days prior to infection were predictive of prolonged RTT. In multiple models, including reduced training in the 7 days prior to 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 a history of co-morbidities.

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 that a greater number of symptoms in each region remained a significant predictor of prolonged RTT when adjusted for pre-infection training (hours in the 7 days before onset of infection). In the general population, a greater number of symptoms during acute phase is 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 following SARS-CoV-2 infection in athletes. Our results are thus strictly applicable only to 1) 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 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 days before symptom onset was associated with prolonged RTT in our univariate analysis. In our multiple models, reduced hours of training in the 7 days 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 pre-infection 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 days, 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 days). The same study showed an association between symptom duration lasting more than 28 days, with time loss for longer than 28 days.(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 to 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 days).(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. Firstly, our sample was a convenience sample with potential selection bias. Secondly, 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. Thirdly, 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 return to sport (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.

CONCLUSION

In summary, our study shows that decreased hours of training in the 7 day-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 co-morbidities 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 co-morbidities are not predictive of prolonged return to training (RTT)
- Reduced hours of training in the 7-day period before the onset of infection can predict prolonged RTT
- 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 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

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Competing Interests

None declared. The results of the present study do not constitute endorsement by ACSM and are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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List of Supplementary Digital Content

- Supplementary Digital Content 1.docx

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