Symptom cluster is associated with prolonged return-to-play in symptomatic athletes with acute respiratory illness (including COVID-19): a cross-sectional study—AWARE study I

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ABSTRACT

Background There are no data relating symptoms of an acute respiratory illness (ARI) in general, and COVID-19 specifically, to return to play (RTP).

Objective To determine if ARI symptoms are associated with more prolonged RTP, and if days to RTP and symptoms (number, type, duration and severity) differ in athletes with COVID-19 versus athletes with other ARI.

Design Cross-sectional descriptive study.

Setting Online survey.

Participants Athletes with confirmed/suspected COVID-19 (ARI_{COV}) (n=45) and athletes with other ARI (ARI_{OTH}) (n=39).

Methods Participants recorded days to RTP and completed an online survey detailing ARI symptoms (number, type, severity and duration) in three categories: *'nose and throat'*, *'chest and neck'* and *'whole body'*. We report the association between symptoms and RTP (% chance over 40 days) and compare the days to RTP and symptoms (number, type, duration and severity) in ARI_{COV} versus ARI_{OTH} subgroups.

Results The symptom cluster associated with more prolonged RTP (lower chance over 40 days; %) (univariate analysis) was *'excessive fatigue'* (75%; p<0.0001), *'chills'* (65%; p=0.004), *'fever'* (64%; p=0.004), *'headache'* (56%; p=0.006), *'altered/loss sense of smell'* (51%; p=0.009), *'Chest pain/pressure'* (48%; p=0.033), *'difficulty in breathing'* (48%; p=0.022) and *'loss of appetite'* (47%; p=0.022). *'Excessive fatigue'* remained associated with prolonged RTP (p=0.0002) in a multiple model. Compared with ARI_{OTH}, the ARI_{COV} subgroup had more severe disease (greater number, more severe symptoms) and more days to RTP (p=0.0043).

Conclusion Symptom clusters may be used by sport and exercise physicians to assist decision making for RTP in athletes with ARI (including COVID-19).

INTRODUCTION

Protecting the athlete against acute illness is a key consideration for health professionals involved in sport. About 50% of all acute illness in athletes during competitions and tournaments affect the respiratory system,[1 2] and the most frequent illness is an acute infection caused by a wide range of pathogens, mostly viruses.[3] At times, athletes can be more prone to acute respiratory illness (ARI), especially during times of increase training load, competitions or travel.[4–7]

In 2019, the SARS-CoV-2 was identified as a novel respiratory pathogen responsible for COVID-19. COVID-19 is associated with a broad range of symptoms, including symptom clusters localised to the upper respiratory tract (eg, anosmia, dysgeusia, coryzal symptoms and throat discomfort), general thoracic symptoms (eg, cough, shortness of breath, headache or chest pain) and systemic symptoms (eg, myalgia, fever or excessive fatigue).[8] In addition to causing acute respiratory disease (ie, a viral pneumonitis), data indicate that COVID-19 can impact multiple organ systems, including the cardiovascular, neurological, gastrointestinal and renal systems and can impede skeletal muscle function.[9 10] Even mild / moderate COVID-19 infection (ie, non-hospitalised individuals), can be associated with protracted or 'Long-COVID' symptoms in previously healthy individuals.[11] Serious potential complications, resulting from COVID-19, include myocarditis, which is also reported in athletic individuals[12] placing an athlete at significant health risk, when returning to vigorous exercise.

A key role within sport and exercise medicine is to provide guidelines for safe return to play (RTP) after illness. A number of expert position statements have been published to guide physicians in decision making on RTP after COVID-19 infection, but these focused on cardiovascular assessment and are based on expert opinion and experience.[13 14] There are limited published data that describe or characterise symptoms or groups of symptoms (ie, symptom clusters) in athletes, during the acute phase of an ARI in general, and COVID-19 specifically. In the general (ie, non-athletic) population, recently published data indicates that symptom clusters of COVID-19 are valuable and can predict probable infection[15] and other clinical outcomes such as need for respiratory support,[16] hospitalisation[17] and 'Long-COVID'.[18]

The primary aim of this study was to determine if symptoms experienced during the acute phase of an ARI in athletes was associated with days to RTP. A secondary aim was to determine if the number, type, duration and severity of ARI symptoms differ in athletes with confirmed or suspected COVID-19, compared with athletes with other causes of ARI

(non-COVID-19). These data could be used to develop a future prediction model (based on symptoms and other variables) to guide the RTP clinical decision making for athletes with recent ARI. This information is required urgently so that health professionals can advise competitive and recreational athletes and their coaching support systems as they return to play following COVID-19 or another ARI.

METHODS

The Athletes With Acute Respiratory InfEctions (AWARE studies) is a multicentre study, led by the Sport, Exercise Medicine and Lifestyle Institute at the University of Pretoria in South Africa, together with researchers from a number of academic institutions, sports federations and some members of 'subgroup 7' of the IOC Consensus group on 'Acute Respiratory Illness in the Athlete'. This is a descriptive cross-sectional study of data collected between 20 July 2020 and 13 October 2020.

Participants and data collection

Potential participants for this study were athletes (age 18–60 years), defined as 'competing at varying levels in any sport, training for a minimum of 3 hours per week'. Following informed electronic consent, participants completed an online survey using the Research Electronic Data Capture platform.[19 20] A link to the online survey was distributed to potential participants using existing databases of athletes and via several social media platforms. For participants to be included in this study, they had to report at least one symptom lasting ≥1 day. Details regarding participant recruitment is shown in online supplemental figure 1.

Survey instrument and data collection

Participants completed their history of respiratory health, including symptoms of a recent (<6 month period) ARI, including COVID-19. The survey evaluated athlete demographics, comorbidities, training history, RTP and residual symptoms. Participants reported the following details about ARI: number, type, severity and duration of symptoms (days). Symptom type consisted of 26 symptoms of ARI in three categories: (1) '*nose and throat*' (eight symptoms), (2) '*chest and neck*' (eight symptoms) and (3) '*whole body*' (10 symptoms, including gastrointestinal symptoms). Symptom severity was reported on a scale from 1 to 7, which was adapted from the validated Wisconsin Upper Respiratory Symptom Survey (WURSS).[21] The duration (days) that each symptom lasted was recorded. The days to RTP were reported by participants in response to the question '*How many days were there between the start of your symptoms and the return to your first training session*?'.

Online survey validation and testing

The symptom list and severity score were adapted from the validated WURSS,[21] to which we added additional COVID-19 symptoms.[8] A pilot study of 16 participants, consisting of athletes and medical practitioners directed early development and assessed accessibility of the survey (the symptoms, the length of the questionnaire and terminology used).

Patient and public involvement (PPI)

PPI was included in this study. Athletes and medical practitioners treating athletes who had experienced an ARI (including COVID-19) were asked to provide feedback on the questionnaire in the development stages.

Definitions and criteria for subgroups

Participants (ARI_{ALL}) (n=84) in this study were divided into subgroups, based on their responses to questions in the survey that related to the diagnosis of the ARI (online supplemental figure 1).

- Confirmed COVID-19 (ARI_{COV+ve}) (n=40): participants who declared a positive COVID-19 test: positive PCR test on a nose/throat swab (n=37) or a positive antibody test (n=3).
- Suspected COVID-19 (ARI_{COV-S}) (n=5): participants who consulted a health professional but had no nasopharyngeal swab or blood test, where the diagnosis of 'likely COVID-19', was made by the health professional, based on reported symptoms.
- Other ARI (ARI_{OTH}) (n=39): participants with either a negative COVID-19 test (n=12) or symptoms not typical of COVID-19 (n=27).

For the purpose of our cross-sectional analysis of subgroups, we combined the ARI_{COV+ve} and the ARI_{COV-S} subgroups into one group: ARI with COVID-19 (ARI_{COV}) (n=45).

Measures of outcome

The primary outcome measure was the self-reported number of days to RTP. Secondary analyses included evaluation of the association between symptom type and the days to RTP. We also compare the number of symptoms/athlete (maximum of 26), type of symptoms (by region and individual symptoms), duration of each symptom (number of days) and the severity of each symptom in two categories (mild: score 1–3; moderate/severe: score 4–7) between the ARI_{COV} and ARI_{OTH} subgroups.

Statistical analysis of data

Demographic data were described for the ARI_{COV} (including ARI_{COV+ve} and ARI_{COV-S}) and ARI_{OTH} subgroups. The responses to the type of ARI symptoms were modelled using the log-binomial model, and the prevalence, 95% CI and prevalence ratios were

Table 1 Demographics of each of the different acute respiratory illness (ARI) subgroups

	ARI_{ALL} (n=84)	ARI_{COV}* (n=45)	ARI_{OTH} (n=39)	ARI_{COV} versus ARI_{OTH} (p value)
Age (mean (SD))	33.9 (13.8)	32.6 (14.0)	35.5 (13.5)	0.345
Sex (n, % males)	41 (48.8)	18 (40.0)	23 (59.0)	0.082
Height (mean (SD))†	172.8 (18.4)	170.7 (23.5)	175.2 (9.4)	0.241
Weight (mean (SD))	72.3 (14.5)	70.0 (14.2)	74.9 (14.6)	0.125
Sporting level (professional) (n (%))	26 (31)	14 (31.1)	12 (30.8)	0.973
Years sporting experience (mean, SD)†	12.7 (10.3)	11.4 (7.5)	14.2 (12.7)	0.247

*ARI_{COV} is the combined ARI_{COV+ve} (n=40) and ARI_{COV-S} (n=5) subgroups.
†For this variable, there are missing data for 1 participant

reported. χ^2 (p values) were used for significance testing (type 3). The negative binomial model was used for the comparison of the mean number of symptoms between the ARI_{COV} and the ARI_{OTH} groups.

The median number of days and IQRs were reported for describing the duration of symptoms. The comparison of duration of symptoms (median duration in days) between subgroups was done using non-parametric survival analysis. For participants that did not report a specific symptom, the days of a symptom was considered censored; that is, the comparison of days with a symptom between groups was for those participants reporting the symptom. Nelson-Aalen estimates were reported, and the log-rank χ^2 (p values) were reported for testing of the homogeneity of survival curves over the groups.

The Cochran-Armitage trend test was used to test for a difference in severity (no symptoms, mild and moderate/severe) of ARI symptoms between subgroups. A one-sided z test (p value) was reported.

For the days to RTP analysis, six participants did not report RTP days, resulting in 78 cases for this analysis. The training resumption variable had three responses: (1) '*Yes, I have started training again*', (2) '*No, I have not started training again*' and (3) '*I have continued training throughout my recent infection/COVID-19 with no interruptions*'. For the 49 participants reporting response 1, the actual days RTP were recorded. For the 23 participants reporting response (2) (above), censoring was indicated for their RTP days. For the six participants reporting response (3) above, 0 days RTP were recorded. Non-parametric survival analysis was done to compare the median duration (in days) between the two subgroups. The log-rank χ^2 (p values) were reported. A figure with separate Product-Limit Survival Estimates for the two subgroups was included.

For the analysis to predict the RTP from the 'type of symptom', a Cox regression was done including the individual ARI symptoms in the model. The interaction for ARI group × symptom was tested, and separate HRs for the groups were reported when the interaction was significant. Symptoms with less than 15 events were not analysed. The Firth's corrected estimates were computed but not reported since they were consistent with the uncorrected estimates.[22]

Three multiple models were presented, one for each subgroup of symptoms: nose and throat, chest and neck and whole body. For each model, significant variables from the univariate models were entered ($p<0.05$). However, the impact of multicollinearity

Table 2 The symptoms (type, number and percentage with 95% CI) by region and specific symptoms in the ARI_{ALL} and the subgroups (ARI_{COV} and ARI_{OTH})

	ARI_{ALL} (n=84)		ARI_{COV} (n=45)		ARI_{OTH} (n=39)		ARI_{COV} versus ARI_{OTH}	
Symptom	**n**	**%**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**PR**	**P value***
Nose and throat								
Sore/scratchy throat	44	52.4	23	51.1 (38.4 to 68.0)	21	53.9 (40.3 to 72.0)	0.95 (0.63–1.43)	0.802
Hoarseness	16	19.1	10	22.2 (12.9 to 38.4)	6	15.4 (7.4 to 32.1)	1.44 (0.58–3.62)	0.424
Blocked/plugged nose	52	61.9	26	57.8 (45.0 to 74.2)	26	66.7 (53.4 to 83.2)	0.87 (0.62–1.21)	0.402
Runny nose	36	42.9	17	37.8 (26.0 to 55.0)	19	48.7 (35.3 to 67.2)	0.78 (0.47–1.27)	0.312
Sinus pressure	34	40.5	15	33.3 (22.1 to 50.4)	19	48.7 (35.3 to 67.2)	0.68 (0.41–1.16)	0.152
Sneezing	28	33.3	13	28.9 (18.3 to 45.7)	15	38.5 (25.9 to 57.2)	0.75 (0.41–1.38)	0.354
Altered/loss sense of smell	37	44.1	31	68.9 (56.6 to 83.8)	6	15.4 (7.4 to 32.1)	4.48 (2.10–9.59)	**0.0001**
Altered/loss sense of taste	36	42.9	29	64.4 (51.9 to 80.1)	7	18.0 (9.2 to 35.1)	3.59 (1.77–7.27)	**0.0001**
Chest and neck								
Dry cough	40	47.6	23	51.1 (38.4 to 68.0)	17	43.6 (30.5 to 62.3)	1.17 (0.74–1.85)	0.491
Wet cough	20	23.8	13	28.9 (18.3 to 45.7)	7	18.0 (9.2 to 35.1)	1.61 (0.71–3.62)	0.237
Difficulty in breathing	31	36.9	17	37.8 (26.0 to 55.0)	14	35.9 (23.6 to 54.6)	1.05 (0.60–1.85)	0.859
Fast breathing or shortness of breath	29	34.5	17	37.8 (26.0 to 55.0)	12	30.8 (19.2 to 9.3)	1.23 (0.67–2.24)	0.500
Chest pain/pressure	25	29.8	14	31.1 (20.1 to 48.1)	11	28.2 (17.1 to 46.5)	1.10 (0.57–2.14)	0.771
Chest tightness	23	27.4	14	31.1 (20.1 to 48.1)	9	23.1 (13.0 to 40.9)	1.35 (0.66–2.77)	0.409
Headache	54	64.3	35	77.8 (66.5 to 90.9)	19	48.7 (35.3 to 67.2)	1.60 (1.12–2.28)	**0.005**
Red/watery/scratchy eyes	19	22.6	10	22.2 (12.9 to 38.4)	9	23.1 (13.0 to 40.9)	0.96 (0.44–2.13)	0.926
Whole body								
Fever	22	26.2	17	37.8 (26.0 to 55.0)	5	12.8 (5.7 to 29.1)	2.95 (1.20–7.25)	**0.008**
Chills	24	28.6	17	37.8 (26.0 to 55.0)	7	18.0 (9.2 to 35.1)	2.10 (0.98–4.54)	**0.042**
Excessive fatigue	62	73.8	35	77.8 (66.5 to 90.9)	27	69.2 (56.2 to 85.3)	1.12 (0.87–1.46)	0.375
General muscle aches and pains	40	47.6	24	53.3 (40.6 to 70.1)	16	41.0 (28.2 to 59.8)	1.30 (0.82–2.07)	0.259
Skin rash†	5	6.0	4	8.9 (3.5 to 22.7)	1	2.6	–	
Abdominal pain†	14	16.7	12	26.7 (16.4 to 43.3)	2	5.1	–	
Nausea	16	19.1	9	20.0 (11.2 to 35.9)	7	18.0 (9.2 to 35.1)	1.11 (0.46–2.71)	0.811
Vomiting†	6	7.1	3	6.7	3	7.7	–	
Diarrhoea	13	15.5	9	20.0 (11.2 to 35.9)	4	10.3 (4.1 to 26.0)	1.95 (0.65–5.84	0.233
Loss of appetite	35	41.7	25	55.6 (42.8 to 72.2)	10	25.6 (15.0 to 43.8)	2.17 (1.19–3.93)	**0.005**

*χ^2 test.
†Symptoms where the numbers were too small to analyse between groups or produce CIs.
ARI, acute respiratory illness; ARI_{COV}, acute respiratory illness COVID-19 subgroup that is the combined ARI_{COV+ve} and ARI_{COV-S} subgroups.; ARI_{OTH}, acute respiratory illness Other subgroup; PR, prevalence ratio.

Table 3 The duration (median number of days; 95% CI) of symptoms by region and specific symptoms in the ARI_{ALL}, and the ARI_{COV} and the ARI_{OTH} subgroups

	ARI_{ALL} (n=84)	ARI_{COV} (n=45)	ARI_{OTH} (n=39)	ARI_{COV} versus ARI_{OTH}
Symptom	**Median days (95% CI)**	**Median days (95% CI)**	**Median days (95% CI)**	**P value***
Nose and throat				
Sore/scratchy throat	7 (5 to 10)	7 (5 to 9)	7 (4 to 10)	0.361
Hoarseness	5 (4 to 14)	5 (3 to 10)	9.5 (2 to 20)	0.709
Blocked/plugged nose	7 (5 to 10)	10 (7 to 15)	5 (3 to 7)	**0.006**
Runny nose	5 (3 to 6)	5 (2 to 10)	4 (3 to 7)	0.356
Sinus pressure	8 (5 to 10)	10 (6 to 15)	6 (4 to 10)	0.342
Sneezing	5 (3 to 6)	5 (3 to 10)	4 (2 to 6)	0.100
Altered/loss sense of smell	10 (7 to 14)	7 (7 to 14)	17 (2 to 61)	0.451
Altered/loss sense of taste	9.5 (5 to 14)	9 (5 to 14)	10 (1 to 20)	0.784
Chest and neck				
Dry cough	9.5 (6 to 12)	9 (6 to 10)	10 (4 to 29)	0.107
Wet cough	6.5 (3 to 7)	6 (3 to 7)	7 (2 to 7)	0.603
Difficulty in breathing	14 (6 to 20)	10 (4 to 20)	14 (5 to 30)	0.887
Fast breathing or short of breath	14 (5 to 20)	15 (5 to 27)	10.5 (3 to 32)	0.684
Chest pain/pressure	8 (6 to 13)	9 (3 to 14)	7 (3 to 14)	0.429
Chest tightness	7 (5 to 15)	7 (4 to 21)	10 (3 to 21)	0.578
Headache	6 (4 to 8)	5 (4 to 8)	7 (4 to 10)	0.877
Red/watery/scratchy eyes	10 (5 to 15)	10 (4 to 24)	8 (3 to 30)	0.597
Whole body				
Fever	5.5 (2 to 9)	5 (2 to 9)	6 (2 to 14)	0.766
Chills	3 (2 to 5)	3 (2 to 5)	4 (2 to 5)	0.465
Excessive fatigue	11 (8 to 20)	14 (9 to 21)	8 (5 to 20)	0.263
General muscle aches and pains	7 (5 to 10)	7 (5 to 10)	5.5 (4 to 14)	0.628
Skin rash†	4 (3 to 10)	3.5	5	
Abdominal pain†	4.5 (2 to 7)	4	7	
Nausea	7 (2 to 14)	7 (2 to 20)	7 (2 to 31)	0.532
Vomiting†	4.5 (1 to 10)	6	1	
Diarrhoea†	4 (3 to 7)	4	7	
Loss of appetite	7 (5 to 12)	10 (5 to 14)	6.5 (2 to 8)	0.390

*Log-rank test.
†Symptoms where the numbers were too small to analyse between groups or produce CIs.
ARI, acute respiratory illness; ARI_{COV}, acute respiratory illness COVID-19 subgroup that is the combined ARICOV+ve and ARICOV-S subgroups; ARI_{OTH}, acute respiratory illness Other subgroup.

was considered in the modelling.[23] Tetrachoric correlations were calculated for variables within each subgroup of symptoms and variables with a correlation ≥0.8 were not entered together. The three final models were presented without doing any stepwise selection.

RESULTS

Demographics

Data from 181 participants were available, and 97 were excluded because they had no ARI symptoms, including 11 participants who had a positive COVID-19 test but were asymptomatic (online supplemental figure 1). The remaining 84 participants were included in this analysis and their demographics are shown in table 1.

There was no significant difference in the demographic variables (age, sex, height and weight), professional sporting level and years of sporting experience between ARI_{OTH} and the ARI_{COV} subgroups.

Number of symptoms of ARI

The mean number of ARI symptoms (out of 26) in the ARI_{ALL} group was 9.2 (95% CI 8.1 to 10.3).

The mean number of symptoms was significantly higher in the ARI_{COV} subgroup (10.4 (95% CI 8.9 to 12.1) compared with the ARI_{OTH} subgroup (7.8; 95% CI 6.5 to 9.2) (p=0.016). The mean number of '*nose and throat*' symptoms for ARI_{ALL} was 3.4 (95% CI 3.0 to 3.8), and this was not different between the ARI_{COV} (3.6; 95% CI 3.1 to 4.2) and ARI_{OTH} (3.1; 95% CI 2.5 to 3.7) (p=0.139). The mean number of '*chest and neck*' symptoms for ARI_{ALL} was 2.9 (95% CI 2.5 to 3.4), and this was not different between subgroups (ARI_{COV}: 3.2; 95% CI 2.6 to 3.9); ARI_{OTH}: (2.5; 95% CI 2.0 to 3.2) (p=0.14). The mean number of '*whole body*' symptoms for ARI_{ALL} was 2.8 (95% CI 2.4 to 3.4), and the number of symptoms was higher for the ARI_{COV} subgroup (3.4; 95% CI 2.8 to 4.3) compared with the ARI_{OTH} subgroup (2.1; 95% CI 1.6 to 2.8) (p=0.007).

Type of symptoms of ARI

The symptoms (type, number and percentage with 95% CI) by region and specific symptoms of ARI in the ARI_{ALL} and the subgroups (ARI_{COV} and ARI_{OTH}) are shown in table 2.

In the ARI_{ALL} group, the four most common symptoms were '*excessive fatigue*' (73.8%), '*headache*' (64.3%), '*blocked/plugged nose*' (61.9%) and '*sore/scratchy throat*' (52.4%). The following

Table 4 The number and percentage (N, %) of athletes with mild (score 1–3) and moderate/severe (score 4–7) symptoms by region and specific symptoms in the ARI_{COV} and the ARI_{OTH} subgroups (athletes who did not report the symptom, had a severity of 0 and make up the rest to 100%)

	ARI_{COV} (n=45)				ARI_{OTH} (n=39)				ARI_{COV} versus ARI_{OTH} (% mild vs % moderate/severe)
	Mild		Moderate/severe		Mild		Moderate/severe		
Symptom	n	%	n	%	n	%	n	%	P value
Nose and throat									
Sore/scratchy throat	12	25.7	11	24.4	11	28.2	10	25.6	0.413
Hoarseness	1	2.3	7	16.3	1	2.8	2	5.6	0.075
Blocked/plugged nose	8	17.8	18	40	11	28.2	15	38.5	0.351
Runny nose	13	28.9	4	8.9	15	38.5	4	10.3	0.198
Sinus pressure	3	6.7	12	26.7	5	15.4	13	33.3	0.131
Sneezing	8	17.8	5	11.1	15	38.5	0	0	
Altered/loss sense of smell	5	11.1	26	57.8	2	5.1	4	10.3	**0.0001**
Altered/loss sense of taste	8	17.8	21	46.7	2	5.1	5	12.8	**0.0001**
Chest and neck									
Dry cough	15	33.3	8	17.8	8	20.5	9	23.1	0.449
Wet cough	6	13.3	7	15.6	4	10.3	3	7.7	0.104
Difficulty in breathing	8	17.8	9	20	0	0	14	35.9	
Fast breathing or short of breath	6	13.3	11	24.4	2	5.1	10	25.6	0.379
Chest pain/pressure	4	8.9	10	22.2	2	5.1	9	23.1	0.455
Chest tightness	7	15.6	7	15.6	3	7.7	6	15.4	0.307
Headache	6	13.3	29	64.4	7	18	12	30.8	**0.0008**
Red/watery/scratchy eyes	3	6.7	7	15.6	4	10.3	5	12.8	0.453
Whole body									
Fever	7	15.6	10	22.2	1	2.6	4	10.3	**0.013**
Chills	6	13.3	11	24.4	2	5.1	5	12.8	**0.035**
Excessive fatigue	5	11.1	30	66.7	6	15.4	21	53.9	0.13
General muscle aches and pains	7	15.6	17	37.8	7	18	9	23.1	0.082
Skin rash*	2		2		0		1		
Abdominal pain*	5		7		0		2		
Nausea	3	6.7	6	13.3	4	10.3	3	7.7	
Vomiting*	1		2		1		2		
Diarrhoea*	0		9		1		3		
Loss of appetite	6	13.3	19	42.2	5	12.8	5	12.8	**0.001**

P value: Cochran Armitage one-sided test.
*Symptoms where the numbers were too small to analyse between groups or produce CIs.
ARI, acute respiratory illness; ARI_{COV}, acute respiratory illness Other subgroup; ARI_{OTH}, acute respiratory illness - other subgroup.

symptoms were significantly more common in the ARI_{COV} compared with the ARI_{OTH} subgroup: '*altered/loss of sense of smell*' (prevalence ratio (PR)=4.48; p=0.0001), '*altered/loss of sense of taste*' (PR=3.59; p=0.0001), '*fever*' (PR=2.95; p=0.008), '*loss of appetite*' (PR=2.17; p=0.005), '*chills*' (PR=2.1; p=0.042) and '*headaches*' (PR=1.6; p=0.005). Other symptoms included: dry eyes, hives, hunger, racing heart beats, vertigo and insomnia (all n=1).

Duration of symptoms

The duration of symptoms (days) by region and specific symptoms in ARI_{ALL} and the ARI_{COV} and the ARI_{OTH} subgroups is shown in table 3 (for ARI_{ALL} the median and IQR is presented in online supplemental table S1).

For '*nose and throat*' symptoms, '*altered/loss sense of smell*' and '*altered/loss sense of taste*' took the longest to recover (median 10 and 9.5 days, respectively). For '*chest and neck*' symptoms, '*difficulty in breathing*' and '*fast breathing or shortness of breath*' took the longest to recover (median 14 days), and for '*whole body*' symptoms, '*excessive fatigue*' took the longest to recover (median 11 days). The only symptom with a significantly longer duration in the ARI_{COV} versus the ARI_{OTH} subgroup was '*blocked/plugged nose*' (median of 10 days vs 5 days, p=0.006).

Severity of symptoms

The number and percentage (%) of athletes with mild (score 1–3) versus moderate/severe (score 4–7) symptoms by region and specific symptoms in the ARI_{COV} and the ARI_{OTH} subgroups is shown in table 4 (the 'no symptom' group is not noted in table 4 but is included in the analyses).

The % moderate/severe symptoms was higher in the ARI_{COV} subgroup compared with the ARI_{OTH} subgroup for the following symptoms: '*altered/loss of smell*' (58% vs 10%; p=0.0001), '*altered/loss of taste*' (47% vs 13%; p=0.0001), '*headache*' (64% vs 31%; p=0.0008), '*fever*' (22% vs 10%; p=0.013), '*chills*' (24% vs 13%; p=0.035) and '*loss of appetite*' (42% vs 13%; p=0.001).

Days to RTP analysis for ARI_{ALL} and for ARI_{COV} versus ARI_{OTH}

Of the 84 ARI_{ALL} athletes, six did not report number of days to RTP, resulting in 78 data points for the analysis of days to RTP

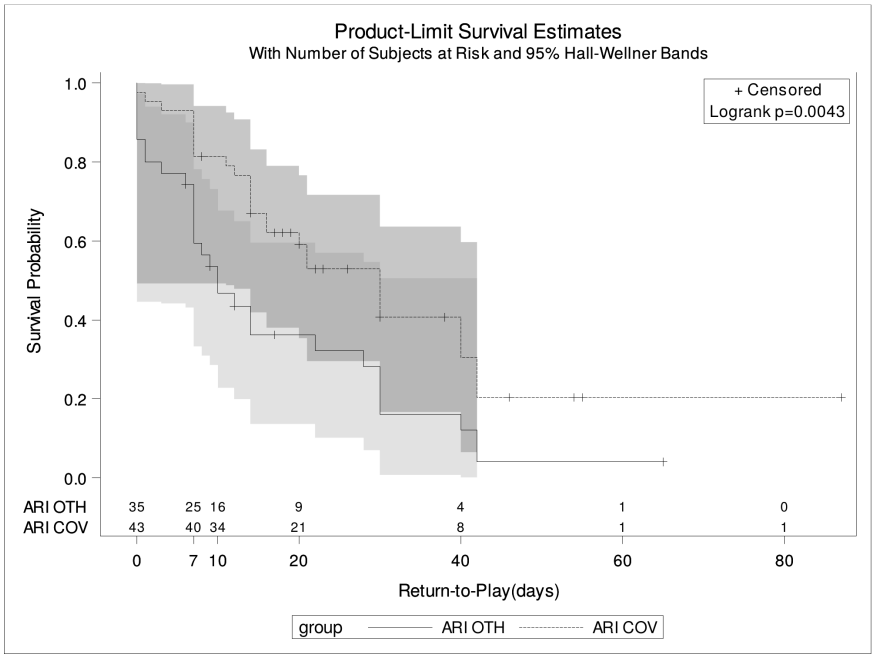

Figure 1 The survival probability of days to return to play in the ARI_{COV} (n=43) and the ARI_{OTH} group (n=35) (p=0.004). Shaded areas depict the 95% CIs. Numbers above the x-axis represent the number of athletes who have not yet returned to play in their respective groups at that time point. ARI, acute respiratory illness.

(ARI_{COV}: n=43; ARI_{OTH}: n=35). In the ARI_{ALL} group, the estimated median days to RTP was 20 (95% CI 14 to 30), indicating that 50% of athletes would have returned to play by day 20, and 75% of athletes would have returned to play by day 30.

The survival probability (%) of athletes in the ARI_{COV} and the ARI_{OTH} group after the onset of symptoms and RTP is shown in figure 1.

The median days to RTP for the ARI_{COV} subgroup (30 days; 95% CI 16 to 40) was significantly longer than the ARI_{OTH} subgroup (10 days; 95% CI 7 to 22) (log-rank test: p=0.0043). The survival curves for the two groups both drop substantially at around day 7 (13 athletes returning to play by day 7). After 7 days, the rate of RTP was lower in the ARI_{COV} group than the ARI_{OTH} group.

The association between symptoms and RTP in the ARI_{ALL} group (univariate model)

The HR (HR and 95% CI) for symptoms (by region and specific symptoms) in the ARI_{ALL} group is shown in table 5 (Univariate model). The HR was derived as the ratio of the hazard of RTP for an individual with the symptom, compared with the hazard of RTP for an individual without the symptom. An HR <1 indicates a lower % chance of RTP in the 40-day period after the onset of symptoms for an individual with the symptom compared with an individual without the symptom, indicating a more prolonged RTP. The interaction for group × symptom was tested when analysing the individual symptoms, and separate HRs were reported for the two groups where the interaction was significant.

Over the 40-day period, athletes with the following specific symptoms had a lower chance (% lower chance) and thus a more prolonged RTP compared with athletes without the symptom: '*excessive fatigue*' (75%; p<0.0001), '*chills*' (65%; p=0.004), '*fever*' (64%; p=0.004), '*headache*' (56%; p=0.006), '*altered/loss sense of smell*' (51%; p=0.009), '*chest pain/pressure*' (48%; p=0.033), '*difficulty in breathing*' (48%; p=0.022) and '*loss of appetite*' (47%; p=0.022). Athletes with altered loss of taste or chest pain experienced a marginal but potentially clinically significantly longer RTP compared with athletes without the symptoms. '*Difficulty in breathing*' was the only symptom that had a significant interaction effect (p=0.029), with the separate HR estimates for ARI_{OTH} (0.18; 95% CI 0.08 to 0.45, p=0.0002) and ARI_{COV} (0.67; 95% CI 0.30 to 1.49, p=0.328). In the ARI_{OTH} RTP was significantly longer in those reporting '*difficulty in breathing*' (median 30 days; 95% CI 10 to 40) versus those not reporting the symptom (median 7 days; 95% CI 1 to 10).

The association between symptoms and RTP in the ARI_{ALL} group (multiple model)

The HR (95% CI) of days to RTP for symptoms in the ARI_{ALL} group is shown in online supplemental table S2 (multiple model) (further details on the collinearity are shown in online supplemental table S3). The multiple model included six significant symptoms from the univariate analysis (without correlation >0.8). Of these included symptoms, '*altered/loss sense of smell*', '*headache*' and '*excessive fatigue*' remained significant. '*Excessive fatigue*' was associated with a 70% lower chance of RTP over the 40-day period, compared with not reporting '*excessive fatigue*'. '*Altered/loss sense of smell*' was significant (p=0.009), with a 51% lower chance of RTP, as well as '*headache*' having a 49% lower chance of RTP.

DISCUSSION

The novel and clinically most important finding of this study is that the following cluster of symptoms of ARI are significantly associated (univariate model) with a longer RTP (listed in order by the % chance of more prolonged RTP in the 40-day period

Table 5 The HR (95% CI) for symptoms by region and specific symptoms in the ARI_{ALL} group (n=78) (univariate model)

Symptom	HR (95% CI)* (ratio of the hazard of RTP for an individual with the symptom compared with the hazard of RTP for an individual without the symptom RTP)	P value †
Nose and throat		
Sore/scratchy throat	1.01 (0.59 to 1.71)	0.986
Hoarseness	0.68 (0.34 to 1.34)	0.262
Blocked/plugged nose	1.23 (0.70 to 2.16)	0.476
Runny nose	1.29 (0.76 to 2.20)	0.344
Sinus pressure	0.96 (0.57 to 1.65)	0.907
Sneezing	1.06 (0.61 to 1.85)	0.843
Altered/loss sense of smell	0.49 (0.28 to 0.84)	**0.009**
Altered/loss sense of taste	0.58 (0.34 to 1.00)	0.050
Chest and neck		
Dry cough	0.64 (0.37 to 1.10)	0.104
Wet cough	1.01 (0.54 to 1.89)	0.978
Difficulty in breathing	0.52 (0.30 to 0.91)	**0.022**
Fast breathing or shortness of breath	0.65 (0.37 to 1.13)	0.121
Chest pain/pressure	0.52 (0.29 to 0.95)	**0.033**
Chest tightness	0.96 (0.54 to 1.68)	0.875
Headache	0.44 (0.25 to 0.79)	**0.006**
Red/watery/scratchy eyes	0.90 (0.49 to 1.65)	0.729
Whole body		
Fever	0.36 (0.18 to 0.73)	**0.004**
Chills	0.35 (0.17 to 0.72)	**0.004**
Excessive fatigue	0.25 (0.13 to 0.47)	**<0.0001**
General muscle aches and pains	0.83 (0.49 to 1.41)	0.496
Skin rash†	–	–
Abdominal pain†	–	–
Nausea	0.51 (0.25 to 1.04)	0.063
Vomiting†	–	–
Diarrhoea†	–	–
Loss of appetite	0.53 (0.31 to 0.91)	**0.022**

*An HR <1 indicates a lower chance of RTP in the 40-day period after the onset of symptoms for an individual with the symptom compared with an individual without the symptom, that is, prolonged RTP.
†Symptoms where the numbers were too small (<15 events) to analyse between groups or produce CIs.
‡Type 3 test.
ARI, acute respiratory illness; ARI_{COV}, acute respiratory illness COVID-19 subgroup; ARI_{OTH}, acute respiratory illness Other subgroup; RTP, return to play.

after the onset of symptoms): '*excessive fatigue*' (75%), '*chills*' (65%), '*fever*' (64%), '*headache*' (56%), '*altered/loss sense of smell*' (51%), '*chest pain/pressure*' (48%), '*difficulty in breathing*' (48%) and '*loss of appetite*' (47%). All these associations were valid in the ARI_{OTH} and the ARI_{COV} subgroups, with the exception of the symptom '*difficulty in breathing*' that was significantly associated with a longer RTP only for the ARI_{OTH} subgroup. From our multiple model, we show that the most important ARI symptom associated with a longer RTP was '*excessive fatigue*'—a 70% lower chance of RTP over the 40-day period. The symptoms '*altered/loss sense of smell*' and '*headache*' were also significantly associated with a longer RTP, a 51% and 49% less chance of RTP over the 40-day period, respectively. We are not aware of data from any other study that relate individual symptoms or clusters of ARI symptoms to RTP in athletes.

To date, the so-called neck check has been used in clinical decision making on RTP in athletes with ARI.[24] This guideline is not based on any scientific data, and its validity has recently been challenged also in the context of athletes with confirmed COVID-19.[25] We do note that the symptom cluster significantly associated with prolonged RTP in our study includes 'above the neck' and 'below the neck' symptoms. The simplified 'neck check' as a tool to guide RTP is not supported by our preliminary data, and we will investigate this in future AWARE studies, as we accumulate more data.

The symptom cluster is associated with prolonged RTP in the ARI_{ALL} group and holds for the ARI_{COV} subgroup and the ARI_{OTH} subgroup, where we do not have data on the specific pathogen causing the ARI. We therefore tentatively suggest that this symptom cluster can be used by sport and exercise physicians to assist their decision making for RTP in athletes with COVID-19 and athletes with any ARI. Further research is needed to determine if this or other symptom clusters are associated with prolonged RTP in ARI caused by other pathogens, for example, adenovirus or influenza virus. We also suggest testing these preliminary findings in a predictive model of RTP for all ARI and pathogen-specific ARI and to refine such a model by including other variables, for example, age, sex, sport type, treatment modalities used and existing comorbidities.

The second novel finding of this study is that the clinical presentation of symptoms and the RTP was significantly different in athletes with confirmed or suspected COVID-19 (ARI_{COV}), compared with the ARI_{OTH} subgroup. Compared with ARI_{OTH}, athletes in the ARI_{COV} subgroup: (A) had significantly greater number of symptoms, (B) were more likely to have '*altered/loss of sense of smell*' (PR=4.48) and '*altered/loss of sense of taste*' (PR=3.59), '*fever*' (PR=2.95), '*chills*' (PR=2.1), '*loss of appetite*' (PR=2.17) and '*headaches*' (PR=1.6), (C) reported higher % of more moderate/severe symptoms, specifically for '*altered/loss of smell*', '*altered/loss of taste*', '*headache*', '*fever*', '*chills*' and '*loss of appetite*' and (D) reported a longer RTP (median days=30 vs 10 in the ARI_{OTH} subgroup). The number, type and severity of symptoms differed between athletes with COVID-19 and the ARI_{OTH} subgroup, which is not surprising as there are data to show that COVID-19 is a more severe disease that is associated with specific symptoms (eg, '*altered/loss of smell and taste*'),[26] greater number of symptoms and more severe symptoms.[8] The RTP in our COVID-19 subgroup is longer because many of the symptoms in the cluster associated with prolonged RTP were more common in the ARI_{COV} subgroup.

Finally, we show that in our population of symptomatic athletes (n=84), the mean number of ARI symptoms per athlete was 9.2; the four most common symptoms were '*excessive fatigue*' (73.8%), '*headache*' (64.3%), '*blocked/plugged nose*' (61.9%) and '*sore/scratchy throat*' (52.4%) and that 20 days after the onset of symptoms, 50% of the athletes returned to their first training session. These data are of interest, but we recognise that this is a self-selected sample of athletes with ARI that we recruited during the COVID-19 pandemic and that the sample is not necessarily representative of a general population of athletes with ARI.

The main strength of our study is the novel data relating symptoms of ARI to RTP in a population of athletes with confirmed / suspected COVID-19 (only 5/45 were suspected but not confirmed). Although we compare the number, type, duration and severity of symptoms in athletes with COVID-19 to a subgroup of athletes with other ARI, we recognise that this ARI_{OTH} subgroup could have included athletes with non-infective illness or COVID-19, despite not presenting with more

typical symptoms of COVID-19. This is a limitation, but it was not possible to obtain data to confirm an infective illness or the specific pathogen in this subgroup. Other study limitations are that this is an observational study showing an association and does not demonstrate cause–effect, that factors other than symptom type could have influenced days to RTP, that data are self-reported and was reliant on recall and that our sample was heterogeneous with potential selection bias, that is, athletes with more severe illness completing the questionnaire. We also recognise that about a third of our study participants (all and in the two subgroups) were professional athletes, and in future studies, with a larger sample size, we can analyse this group separately. These are preliminary findings from a small sample of data collected over a short period, and this study is ongoing. In future, with a larger sample, we will be able to address many of the limitations in this study, including adjusting for possible confounders in the models. We do feel that the main practical clinical finding of the relationship between a symptom cluster and days to RTP holds for our sample of athletes with ARI and that it is important to communicate this finding at this stage of the COVID-19 pandemic. Further research is needed to determine possible differences in symptom clusters and days to RTP for other specific ARI pathogens.

SUMMARY AND CONCLUSIONS

In summary, we show that in our population of symptomatic athletes with ARI symptoms, a cluster consisting of '*excessive fatigue*', '*chills*', '*fever*', '*headache*', '*altered/loss sense of smell*', '*chest pain/pressure*', '*difficulty in breathing*' and '*loss of appetite*' was associated with a more prolonged RTP. The most important symptom of ARI associated with a longer RTP was '*excessive fatigue*', with a 70% lower chance of RTP over the 40-day period. We show that athletes with COVID-19 presented with a greater number and more severe symptoms, compared with a subgroup of athletes with other ARI. These findings may be used by sport and exercise physicians to assist their decision making for RTP in athletes with ARI. For example, in athletes presenting with ARI, clinicians can document the type, duration and severity of symptoms at the time of acute illness and then use the symptom cluster to identify athletes that may be at higher risk for a more prolonged RTP. The data on the % chance of RTP in the 40-day period can assist clinicians to assign a relative 'weighting' to specific symptoms in the cluster; for example, the most important symptom is '*excessive fatigue*'.

We will now extend our work in a larger sample size and test these preliminary findings in a predictive model of RTP. We will also refine the model by including other variables, for example age, sex, sport type, treatment modalities used and existing comorbidities.

What are the findings?

- The most important symptom of acute respiratory illness (ARI) associated with a longer return to play (RTP) was '*excessive fatigue*', with a 70% lower chance of RTP in the 40-day period after the onset of symptoms.
- We also recommend that clinicians consider the following symptom cluster as indicators of a more prolonged RTP in their athletes presenting with symptomatic ARI: '*excessive fatigue*', '*chills*', '*fever*', '*headache*', '*altered/loss sense of smell*', '*Chest pain/pressure*', '*difficulty in breathing*' and '*loss of appetite*'.
- The association between these symptoms of ARI hold for athletes with confirmed/suspected COVID-19 and athletes with other (non-COVID-19) ARI.
- Athletes with COVID-19 present with more severe disease (greater number of symptoms and higher % of moderate/severe symptoms) compared with a subgroup of athletes with other ARI.
- Athletes with COVID-19 have a significantly longer RTP compared with a subgroup of athletes with other ARI.

How might it impact on clinical practice in the future?

- We suggest that a specific symptom cluster can be used by sport and exercise physicians to assist their decision making for RTP in athletes with ARI (including COVID-19).

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REFERENCES

1 Engebretsen L, Soligard T, Steffen K, *et al*. Sports injuries and illnesses during the London summer Olympic Games 2012. *Br J Sports Med* 2013;47:407–14.
2 Engebretsen L, Steffen K, Alonso JM, *et al*. Sports injuries and illnesses during the winter Olympic Games 2010. *Br J Sports Med* 2010;44:772–80.
3 Valtonen M, Waris M, Vuorinen T, *et al*. Common cold in team Finland during 2018 winter Olympic Games (PyeongChang): epidemiology, diagnosis including molecular point-of-care testing (POCT) and treatment. *Br J Sports Med* 2019;53:1093–8.
4 Schwellnus M, Soligard T, Alonso J-M, *et al*. How much is too much? (Part 2) International Olympic Committee consensus statement on load in sport and risk of illness. *Br J Sports Med* 2016;50:1043–52.
5 Gleeson M, Bishop N, Oliveira M, *et al*. Influence of training load on upper respiratory tract infection incidence and antigen-stimulated cytokine production. *Scand J Med Sci Sports* 2013;23:451–7.
6 Svendsen IS, Taylor IM, Tønnessen E, *et al*. Training-related and competition-related risk factors for respiratory tract and gastrointestinal infections in elite cross-country skiers. *Br J Sports Med* 2016;50:815
7 Schwellnus MP, Derman WE, Jordaan E, *et al*. Elite athletes travelling to international destinations >5 time zone differences from their home country have a 2-3-fold increased risk of illness. *Br J Sports Med* 2012;46:816–21.
8 Burke RM, Killerby ME, Newton S, *et al*. Symptom Profiles of a Convenience Sample of Patients with COVID-19 - United States, January-April 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:904–8.
9 Zaim S, Chong JH, Sankaranarayanan V, *et al*. COVID-19 and multiorgan response. *Curr Probl Cardiol* 2020;45:100618.
10 Mokhtari T, Hassani F, Ghaffari N, *et al*. COVID-19 and multiorgan failure: a narrative review on potential mechanisms. *J Mol Histol* 2020;51:613–28.
11 Dennis A, Wamil M, Kapur S. Multi-Organ impairment in low-1 risk individuals with long COVID. *medRxiv* 2020.
12 Rajpal S, Tong MS, Borchers J. Cardiovascular magnetic resonance findings in competitive athletes recovering from COVID-19 infection. *JAMA Cardiol* 2020;132.
13 Kim JH, Levine BD, Phelan D, *et al*. Coronavirus disease 2019 and the athletic heart: emerging perspectives on pathology, risks, and return to play. *JAMA Cardiol* 2021;6:219-227.
14 Wilson MG, Hull JH, Rogers J, *et al*. Cardiorespiratory considerations for return-to-play in elite athletes after COVID-19 infection: a practical guide for sport and exercise medicine physicians. *Br J Sports Med* 2020;54:1157–61.
15 Menni C, Valdes AM, Freidin MB, *et al*. Real-Time tracking of self-reported symptoms to predict potential COVID-19. *Nat Med* 2020;26:1037–40.
16 Sudre C, Lee K, Lochlainn M. Symptom clusters in Covid19: a potential clinical prediction tool from the COVID symptom study APP. *medRxiv* 2020.
17 Lochlainn MN, Lee KA, Sudre CH. Key predictors of attending hospital with COVID19: an association study from the COVID symptom Tracker APP in 2,618,948 individuals. *medRxiv* 2020.
18 Sudre C, Murray B, Varsavsky T. Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid symptoms study APP. *medRxiv* 2020.
19 Harris PA, Taylor R, Thielke R, *et al*. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.
20 Harris PA, Taylor R, Minor BL, *et al*. The REDCap Consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
21 Barrett B, Brown R, Mundt M, *et al*. The Wisconsin upper respiratory symptom survey is responsive, reliable, and valid. *J Clin Epidemiol* 2005;58:609–17.
22 Greenland S, Mansournia MA, Altman DG. Sparse data bias: a problem hiding in plain sight. *BMJ* 2016;352:i1981.
23 Vatcheva KP, Lee M, McCormick JB, *et al*. Multicollinearity in regression analyses conducted in epidemiologic studies. *Epidemiology* 2016;6. doi:10.4172/2161-1165.1000227. [Epub ahead of print: 07 Mar 2016].
24 Scharhag J, Meyer T. Return to play after acute infectious disease in football players. *J Sports Sci* 2014;32:1237–42.
25 Hull JH, Loosemore M, Schwellnus M. Respiratory health in athletes: facing the COVID-19 challenge. *Lancet Respir Med* 2020;8:557–8.
26 Gerkin RC, Ohla K, Veldhuizen MG, *et al*. Recent smell loss is the best predictor of COVID-19: a preregistered, cross-sectional study. *medRxiv* 2020. doi:10.1101/2020.07.22.20157263. [Epub ahead of print: 26 Jul 2020].