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Association between SARS-CoV-2 infection and the physical fitness of young-adult cadets: a retrospective case–control study

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ABSTRACT

Objectives To determine the association of symptomatic and asymptomatic mild COVID-19 and the SARS-CoV-2 viral load with the physical fitness of army cadets.

Design A retrospective case–control study.

Setting Officers' Training School of the Israel Defense Forces.

Participants The study included all cadets (age, 20.22±1.17 years) in the combatant (n=597; 514 males, 83 females; 33 infected, all males) and non-combatant (n=611; 238 males, 373 females; 91 infected, 57 females, 34 males) training courses between 1 August 2020 and 28 February 2021. COVID-19 outbreaks occurred in September 2020 (non-combatants) and January 2021(combatants).

Primary and secondary outcome measures The primary outcome measures were the aerobic (3000 m race) and anaerobic (combatant/non-combatant-specific) physical fitness mean score differences (MSDs) between the start and end of the respective training courses in infected and non-infected cadets. Secondary outcome measures included aerobic MSD associations with various COVID-19 symptoms and SARS-CoV-2 viral loads.

Results SARS-CoV-2 infection led to declined non-combatant and combatant aerobic fitness MSD (14.53±47.80 vs –19.19±60.89 s; p<0.001 and –2.72±21.74 vs –23.63±30.92 s; p<0.001), but not anaerobic. The aerobic physical fitness MSD decreased in symptomatic cadets (14.69±44.87 s) and increased in asymptomatic cadets (–3.79±31.07 s), but the difference was statistically insignificant (p=0.07). Symptomatic cadets with fever (24.70±50.95 vs –0.37±33.87 s; p=0.008) and headache (21.85±43.17 vs 1.69±39.54 s; p=0.043) had more positive aerobic physical fitness MSD than asymptomatic cadets. The aerobic fitness decline was negatively associated with viral load assessed by the RNA-dependent RNA polymerase (n=61; r = –0.329; p=0.010), envelope (n=56; r = –0.385; p=0.002) and nucleus (n=65; r = –0.340; p=0.010) genes.

Conclusions SARS-CoV-2 infection was associated with a lingering decline in aerobic, but not anaerobic, fitness in symptomatic and asymptomatic young adults, suggesting possible directions for individualised symptom-dependent and severity-dependent rehabilitation plans' optimisation.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study participants constituted a homogeneous group of similar-aged young adults and short, similarly positioned COVID-19 outbreaks, considerably reducing the possible confounders affecting the research outcomes.
⇒ Despite being a retrospective study, the uninfected cadets were a suitable control for the infected ones, as both groups underwent the same training and detraining periods.
⇒ Missing values for some of the participants, particularly for the viral load assessment, lowered the power of the statistical analysis.
⇒ Follow-up was limited to the duration of the respective training courses, hindering our ability to assess the association between physical fitness and long COVID-19.
⇒ Although fitness score differences in both sexes were similar, there were no females in the infected combatant group, limiting the generalisability of our findings.

INTRODUCTION

COVID-19, caused by the novel SARS-CoV-2, is a well-established multisystemic disease that primarily affects the lungs.[1 2] The pandemic has had a considerable impact on physical activity and sports, affecting professional and recreational athletes alike.[3–5] For both athletes and non-athletes, recovery varies depending on the extent and severity of the acute illness, premorbid conditions and other factors. However, the lasting association of SARS-CoV-2 infection with the physical fitness of those who had recovered from the disease remain largely unknown. Several small studies showed decreased peak oxygen uptake,[6 7] fatigue, impaired neuromuscular function and reduced muscle strength, leading to poor performance.[8 9]

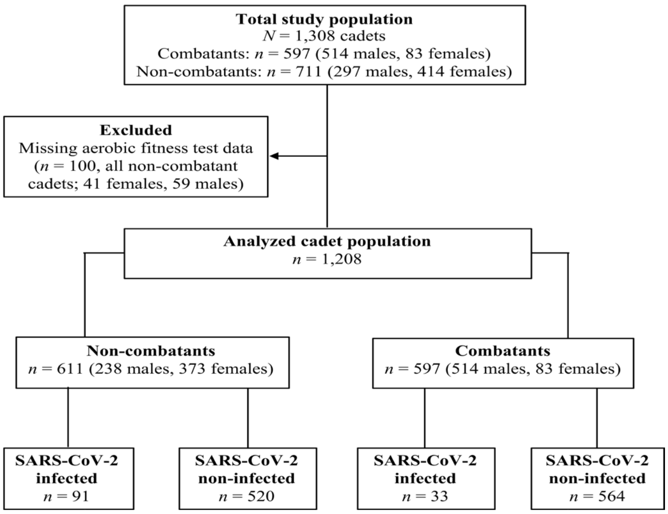

Figure 1 Participant selection flow chart. All cadets attending the non-combatant (1 August 2020–30 October 2020) and combatant (1 November 2020–28 February 2021) courses were included in this study. SARS-CoV-2 infection data were retrieved from the electronic medical record of the participants. Only those diagnosed during the respective course periods were considered infected cases in this study.

Similar to COVID-19 in clinical and pathological characteristics, the SARS global pandemic in 2003 led to low exercise capacity and health status of recovered patients.[3 10] Patients have demonstrated incomplete recovery of physical function, with some experiencing residual impairments 1–2 years postinfection.[11] The lasting associations of symptomatic and asymptomatic COVID-19 and SARS-CoV-2 viral load with the aerobic and anaerobic fitness of young adults have not been studied. This study aimed to assess these associations in a cohort of army cadets. The association between the viral load and COVID-19 severity and mortality is well documented,[12 13] but its association with physical fitness is not. An expanded understanding of the lasting associations between COVID-19 and the physical fitness of young adults could suggest customised rehabilitation approaches. We hypothesised that cadets recovering from the disease would show inferior aerobic and anaerobic fitness to those who tested negative for SARS-CoV-2, differing in their mean fitness test score differences between the end and start of the study. We further hypothesised that those recovering from symptomatic COVID-19 would perform poorer than cadets recovering from asymptomatic disease, and those with a higher viral load would perform poorer than those with a lower viral load. This study was designed to test these hypotheses.

METHODS

Study design

This study retrospectively examined the aerobic and anaerobic fitness test results of 1308 male and female cadets at the Officers' Training School of the Israel Defense Forces. COVID-19 outbreaks occurred in the training classes of non-combatant (September 2020) and combatant (January 2021) cadets. The infected cadets were isolated for 14 days until recovery, and the non-infected cadets were in quarantine for 14 days, following the Israeli Ministry of Health (IMoH) national guidelines (https://www.health.gov.il/LegislationLibrary/kor01.pdf). All cadets underwent an additional 14-day training pause for recovery before gradually returning to the training activity. This recovery period was recommended for all recovering soldiers by the Israeli Medical Corps and enacted for the non-infected cadets to ensure that all underwent the same training course. These resulted in matched 28-day quarantine/isolation and recovery sequences (without training) for the infected and non-infected populations. As the detraining period occurred in the middle of the cadets' training courses, all cadets underwent a similar layout of training, disease/quarantine course, recovery interval and gradual return to training, making them ideal for this comparative study. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines and checklist.

Study population

The study included 1308 cadets, 597 with combatant background (514 males, 83 females) and 711 with non-combatant background (297 males, 414 females). The study included all non-combatant cadets participating in a training course between 1 August 2020 and 30 October 2020 and all combatant cadets in a training course between 1 November 2020 and 28 February 2021. Cadets with missing baseline aerobic fitness test data (exempted from running due to medical or subjective limitations) were excluded from the study. The study participants handling process is shown in figure 1. The participant characteristics (age, sex, military unit, height, weight and body mass index) were retrieved from the Military Human Resources database.

SARS-CoV-2 infection

SARS-CoV-2 infection was diagnosed by a positive SARS-CoV-2 real-time reverse transcription-quantitative PCR (RT-qPCR) test in an authorised IMoH laboratory. All real-time RT-qPCR test results were gathered from a national IMoH database. The infection date was defined as the date of the diagnostic positive SARS-CoV-2 real-time RT-qPCR test result during the respective study periods. Data on viral loads (cycle thresholds) were extracted from the IMoH database (n=61, 65 and 56 for RNA-dependent RNA polymerase (RdRp), nucleus (N) and envelope (E) genes, respectively). Fewer cycles indicated a higher viral load. These limited data are attributed to differences in testing kits in the laboratories and a selective documentation protocol customary in Israel at that time.

Symptomatic patients were those presenting symptoms at the time of diagnosis or at any time during the following 14 days. Symptoms included rhinorrhoea, cough, sore throat, shortness of breath, systemic fever, chill, loss of the sense of taste and/or smell, headache, weakness, fatigue or myalgia, gastrointestinal symptoms, chest pain and disturbance to the vital signs (oxygen saturation <95% (desaturation), blood pressure <120/90 mm Hg and pulse rate >100 beats per minute).

The recovery date was defined following the IMoH guidelines enforced at the time as 14 days from diagnostic real-time RT-qPCR for all patients.

Residual COVID-19 symptoms documented in the electronic medical records among some recovering individuals included headache, weakness, loss of the sense of taste and/or smell, shortness of breath and chest pain.

Aerobic and anaerobic fitness tests

Physical fitness test results were retrieved from the database at the Physical Training Section of the officers' school. The cadets underwent fitness tests at the start and end of their respective courses. The tests were subdivided into aerobic and anaerobic segments. The aerobic test was a 3000 m race. The anaerobic tests included push-ups for non-combatant individuals and pull-ups, parallel bars, squat-thrusts, 150 m×2 sprint runs and postexercise shooting performance for combatant individuals.

Outcome measures

The primary outcome measure was the mean fitness test score differences between the end and the start of the respective courses. The secondary outcome measures included the mean aerobic fitness test score differences under the influence of each disease symptom and the associations between the viral loads and the aerobic fitness test mean score differences (MSD) in those infected by SARS-CoV-2.

Statistical analysis

Normally distributed quantitative data are presented as mean±SD. Categorical variables are displayed as counts and percentages. Comparisons between MSDs were made using paired-samples or independent-samples t-tests, as appropriate. Non-parametric assessments were made by the Wilcoxon signed-rank test. Categorical variables were compared by the χ^2 test.

A multivariable linear regression model estimated the significance of the infection status, baseline aerobic fitness test score, combatant status and sex on the aerobic fitness test results at the end of the study period. The significance level was set at $p<0.05$. All hypothesis tests were two sided. Statistical analysis was performed using IBM SPSS Statistics for Windows, V.25.0 (IBM).

Patient and public involvement

No patient was involved.

RESULTS

Participant characteristics

The study included 1308 cadets. One hundred non-combatant cadets with missing baseline aerobic fitness tests were excluded, leaving 1208 cadets, 597 combatants and 611 non-combatants (figure 1). These comprised 456 (37.7%) females and 752 (62.3%) males. SARS-CoV-2 infection was detected in 33 (5.5%) combatant and 91 (14.9%) non-combatant cadets. There were no females among the infected combatants. The study population mean age was 20.22±1.19 years. Except for sex in the combatant group, the study and control groups were similar in all participant characteristics, as presented in table 1.

Fitness test outcomes

Tables 1 and 2 present comparisons within and among the combatant and non-combatant cohorts according to COVID-19 disease status.

The study and control groups' baseline mean running times were similar in the non-combatant cohort (16:50:32±02:39:92 vs 16:52.06±02:51:66 min; p=0.93) but differed significantly in the combatant cohort (12:26:10±00:56:70 vs 13:09:84±01:36:81; p<0.001). The baseline aerobic fitness performance test results showed that the combatants (n=581; 13:07:58±01:35:61 min) were more fit and aerobically capable than their non-combatant counterparts (n=609; 16:51:81±02:49:85 min; p<0.001; table 1).

A significant linear association was found between the baseline 3000 m race scores and the running time difference between the end and start tests for the entire population (r = −0.133; p<0.001), confirming the hypothesis that the less fit cadets at the start of the course were more likely to improve than the fit ones when going through the same training programme and duration. Among the cadets with 3000 m race results at the start and end of the study, the MSD of the infected (n=76; 00:08:85 min) and non-infected (n=816; −00:21:41 min) groups in the entire study populations differed significantly (p<0.001). The infected and non-infected combatant and non-combatant cadets showed no difference in the anaerobic tests (table 2).

Analysis of fitness test results by sex indicated that males completed the 3000 m race faster than females at baseline (table 1) and the end of the course (table 2) in the combatant and non-combatant cohorts. However, the 3000 m race MSDs for female and male non-combatant infected (9.15 vs 20.53 s; p=0.399) and non-infected (−19.19 vs −19.19 s; p>0.999) were similar. Female and male non-infected combatants also had similar 3000 m race MSDs (−27.62 vs −22.84 s; p=0.377). While non-infected male and female combatants and infected non-combatants had similar MSDs in all anaerobic fitness tests, push-up MSDs of non-infected male and female non-combatants differed significantly (table 2), with the male MSD indicating improvement (−7.73) and the female MSD indicating deterioration (3.07). Analysis of symptomatic and asymptomatic infected cadets found that the symptom status was not associated with the aerobic MSD, except fever and headache (table 3). Significant negative linear associations were found between the viral load and the difference

Table 1 Baseline (preinfection) participant characteristics and aerobic physical fitness test results, stratified by combatant status

Variable	Infected combatant	Non-infected combatant	P value	Infected non-combatant	Non-infected non-combatant	P value	Total
n	33 (5.5%)	564 (94.5%)		91 (14.9%)	520 (85.1%)		1208
Age (year)	20.67±1.05	20.35±1.04	0.09	20.04±1.21	20.08±1.33	0.82	20.22±1.192
Sex			**0.020***			0.74*	
Female	0 (0%)	83 (14.7%)		57 (62.6%)	316 (60.8%)		456 (37.7%)
Male	33 (100%)	481 (85.3%)		34 (37.4%)	204 (39.2%)		752 (62.3%)
Height (cm)	172.4±5.6	172.9±10.0	0.77	168.7±8.3	167.7±8.9	0.35	170.4±9.3
Weight (kg)	66.33±9.97	67.04±10.88	0.72	62.12±11.50	60.96±11.24	0.36	64.03±11.43
BMI (kg/m^2)	22.30±2.88	22.36±2.80	0.90	21.78±3.32	21.62±3.14	0.65	22.00±3.02
Baseline aerobic physical fitness capacity							
Mean 3000 m race (min:s:ms)							
Female	–	16:10:29±01:11:80	**<0.001†**	18:27:19±01:39:63	18:27:77±02:23:37	**<0.001†**	
Male	12:26:10±00:56:70	12:37:84±00:57:62		14:03:00±01:30:38	14:24:28±01:25:08		
All	12:26:10±00:56:70	13:09:84±01:36:81	**<0.001**	16:50:32±02:39:92	16:52:06±02:51:66	0.93	15:02:33±02:58:28
Cohort	13:07:58±01:35:61‡			16:51:81±02:49:85‡		**<0.001‡**	

Values are presented as mean±SD or counts (percentages).
Bold values in this table are statistically significant
*Categorical variables were compared using the χ^2 test, all other continuous variables were compared using independent-samples t-test.
†Statistical tests performed to compare between the sexes.
‡Running times of combatants (n=581) and non-combatants (n=609) were compared, irrespective of the disease status and after excluding participants with missing data.
BMI, body mass index.

Table 2 Mean differences in aerobic and anaerobic physical fitness test results of SARS-CoV-2-infected and non-infected combatant and non-combatant cadets*

	Infected, MSD (n)†				Non-infected, MSD (n)†				
Variable	M	F	P value	Total	M	F	P value	Total	P value‡
Non-combatant cadets (n)				91				520	
Aerobic physical fitness test									
3000 m race (s)	20.58 (24)	9.15 (27)	0.399	14.53 (51)	−19.19 (265)	−19.19 (145)	>0.999	−19.19 (410)	<0.001
Anaerobic physical fitness test									
Push-ups (n)	2.67 (34)	1.68 (54)	0.536	2.07 (88)	−7.73 (198)	3.07 (309)	<0.001	−1.15 (507)	0.80§
Combatant cadets (n)				33				564	
Aerobic physical fitness test									
3000 m race (s)	−2.72 (25)	0		−2.72 (25)	−22.84 (339)	−27.62 (67)	0.377	−23.63 (406)	<0.001
Anaerobic physical fitness tests									
Pull-ups (n)	2.65 (26)	0		2.65 (26)	1.81(365)	1.20 (70)	0.08	1.71 (435)	0.08
Parallel bars (n)	−0.85 (26)	0		−0.85 (26)	0.22 (367)	0.71 (70)	0.255	−0.30 (437)	0.11
Squat-thrust (n)	0.001 (26)	0		0.001 (26)	0.24 (367)	0.001 (70)	0.348	0.19 (437)	0.60
Sprint run, 150 m×2 (n)	−0.52 (25)	0		−0.52 (25)	−0.24 (339)	−1.29 (67)	<0.001	−0.41 (406)	0.82
Postexercise shooting hits (n)	0.22 (27)	0		0.22 (27)	−0.04 (402)	−0.25 (65)	0.47	−0.07 (467)	0.44

*MSD: the mean result at the end minus the mean result at baseline. Positive values indicate deterioration, while negative values indicate improvement.
†The number of cadets whose results were recorded.
‡Outcomes of comparisons between the totals of the two cohorts.
§The Wilcoxon signed-rank test compared the MSDs due to asymmetric distribution, all other continuous variables were compared using independent-samples t-test.
F, female; M, male; MSD, mean score difference.

between the mean end and start 3000 m race times for the RdRp (n=61; r = −0.329; p=0.010), E (n=56; r = −0.385; p=0.002) and N (n=65; r = −0.340; p=0.010) genes (figure 2), indicating a significant deterioration in the aerobic physical fitness capacity of all infected subjects with increasing SARS-CoV-2 viral loads.

Table 3 COVID-19 symptom presentation and 3000 m race mean score difference comparisons between infected cadets with and without each symptom*

	Symptomatic, n (%)		Aerobic MSD†				
Variable	Combatant	Non-combatant	Sympt. (n)	MSD±SD	Asympt. (n)	MSD±SD	P value
Symptomatic infection	18 (54.5)	70 (76.9)	52	14.69±44.88	24	−3.79±31.07	0.07
Fever (>38°C)	3 (9.1)	25 (27.5)	20	24.70±50.95	56	−0.37±33.87	0.008
Cough	4 (12.1)	25 (27.5)	11	26.45±41.93	65	5.88±41.27	0.13
Sore throat	4 (12.1)	16 (17.6)	13	−1.00±33.54	63	10.89±43.17	0.35
Rhinorrhoea	3 (9.1)	12 (13.2)	8	−4.50±39.29	68	10.43±41.99	0.34
Headache	10 (30.3)	31 (34.1)	27	21.85±43.17	49	1.69±39.54	0.040
Chills	2 (6.1)	5 (5.5)	5	14.80±20.33	71	8.44±42.88	0.74
Anosmia or dysgeusia	12 (36.4)	30 (33.0)	28	9.21±38.51	48	8.64±43.89	0.96
Chest pain	0 (0.0)	2 (2.2)	2	45.50±61.52	74	7.86±41.22	0.21
Dyspnoea	2 (6.1)	13 (14.3)	8	15.50±47.99	68	8.07±41.26	0.67
Gastrointestinal‡	1 (3.0)	10 (11.0)	5	23.60±45.62	71	7.82±41.59	0.42
Fatigue, malaise or myalgia	8 (24.2)	22 (24.2)	23	14.00±33.85	53	6.62±44.83	0.48
Major symptoms§	2 (6.1)	14 (15.4)	8	13.50±48.21	68	8.31±41.27	0.74
Residual COVID-19 symptoms	1 (3.0)	27 (29.7)	8	9.63±39.31	68	8.76±42.28	0.96

*Mean score difference: the mean result at the end minus the mean result at the start of the course. Positive values indicate deterioration, while negative values indicate improvement.
†Values are presented after excluding participants with missing data. The independent-samples t-test compared the mean score differences.
‡Gastrointestinal symptoms included nausea, vomiting, abdominal discomfort, diarrhoea and constipation.
§Major symptoms included chest pain, dyspnoea and desaturation <95%.
Asympt, asymptomatic; MSD, mean score difference; Sympt, symptomatic.

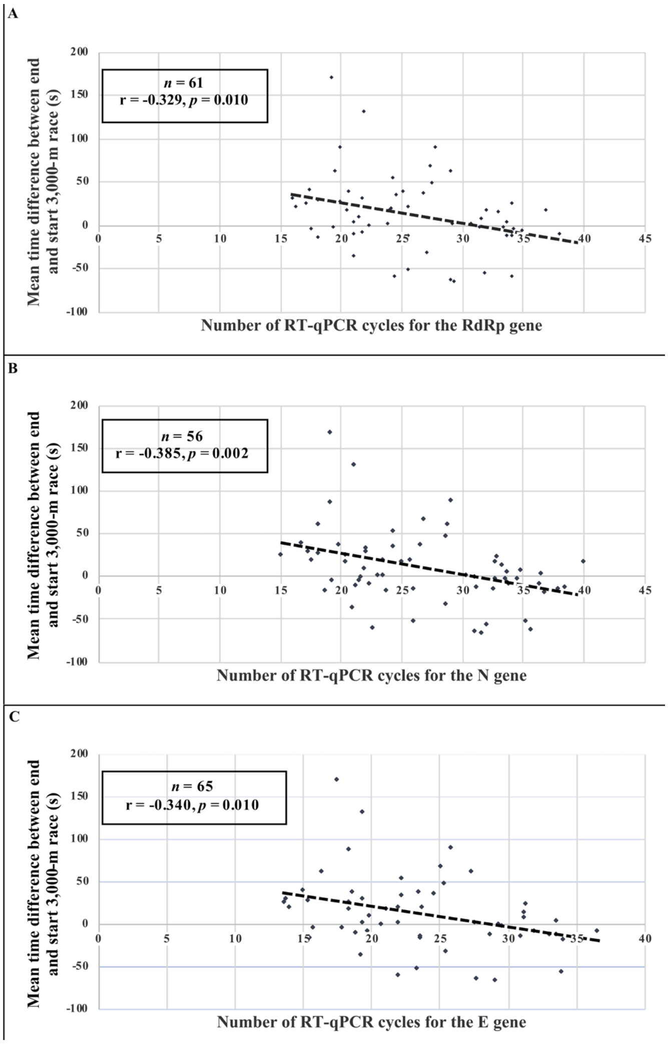

Figure 2 Correlations between real-time RT-qPCR cycles for selected SARS-CoV-2 genes and the difference between the end and start 3000 m race time means (aerobic fitness) in the entire cadet population. (A) Correlation between real-time RT-qPCR cycles for the RdRP (A), N (B), or E (C) genes and the difference between the end and start 3000 m race time means. The linear regression lines are represented by dashed lines. E, envelop; N, nucleus; RdRP, RNA-dependent RNA polymerase; RT-qPCR, reverse transcription-quantitative PCR.

A stepwise multivariable linear regression model was constructed to assess whether the infection status independently affected the aerobic MSD after controlling for baseline aerobic capacity, combatant status and sex, all of which were significant contributors (table 4). The model indicated that SARS-CoV-2 infection was a significant independent contributor (R^2=0.150; R^2 change=0.014; B=20.93; β=0.120; p<0.001).

Table 4 Stepwise forward multivariable linear regression analysis for significant predictors of the aerobic mean score difference

Model*	R^2	R^2 change	B	β	P value
Model 1	0.018	0.018	–0.038	–0.133	<0.001
Model 2	0.070	0.053	–31.18	–0.321	<0.001
Model 3	0.136	0.066	–46.28	–0.468	<0.001
Model 4	0.150	0.014	20.93	0.120	<0.001

*Model 1: 3000 m race time at baseline; model 2: model 1+combatant status; model 3: model 2+sex; model 4: model 3+infection status.

DISCUSSION

Understanding the long-term effects of SARS-CoV-2 infection could apply to any training young adult athletes and encourage vaccination and adherence to the COVID-19-related restrictions, which could potentially reduce infections and disease severity, thereby preventing the need for quarantine and loss of training days. As expected, the aerobic fitness of the combatant cadets was superior to that of the non-combatant ones. The baseline aerobic fitness of combatant and non-combatant male cadets was superior to that of the respective female cadets. This difference could explain our finding that the infected combatant cadets (only males) were significantly more aerobically fit at baseline than the non-infected combatant cadets (males and females). Regardless of the initial fitness level, we showed that SARS-CoV-2 infection was an independent predictor of declined aerobic, but not anaerobic, physical fitness capacity, partially confirming our hypothesis that cadets recovering from the disease would show inferior aerobic and anaerobic fitness to those tested negative to SARS-CoV-2.

Our secondary hypothesis, stating that those recovering from symptomatic COVID-19 will achieve inferior fitness test results to those recovering from asymptomatic disease, was marginally rejected (p=0.07; table 3). However, the PCR assessment indicated a negative association between the viral load and the decline in the aerobic fitness scores at the end of the training course, suggesting further investigation of this aspect is needed.

There were no females among the infected combatants. During the wild-type SARS-CoV-2 outbreak, global trends in the WHO database indicated a 2:3 female-to-male ratio among infected individuals.[14] Moreover, there were few female combatant cadets in this study, and they used separate dormitories from the males, explaining the lower likelihood of infection among females in this cohort.

The aerobic fitness performance test results confirmed the baseline assumption that the combatants were fitter and aerobically capable than their non-combatant counterparts (table 1). Combatants frequently exercise to enhance their athletic abilities and combative performance, as they are expected to endure aerobic challenges.

Contrary to our hypothesis, we found COVID-19 to affect the aerobic but not the anaerobic fitness capacity of the cadets. Aerobic fitness is an indicator of the body's capacity for oxygen uptake (respiratory system), delivery to the muscles (cardiovascular system) and the oxidative mechanisms in the muscles (musculoskeletal system). Conversely, anaerobic fitness indicates the muscles' ability to generate energy independently of inhaled oxygen. Under anaerobic conditions, ATP is generated through glycolysis, a less efficient energy production route than the aerobic one, leading to lactic acid accumulation, decreased pH, and a further reduction in energy production efficiency.[15] Considering the differences between the two energy production routes and the known effects of COVID-19, it becomes clear why aerobic fitness, reflecting the sum of the effects on the respiratory, cardiovascular and musculoskeletal systems, is affected by the disease far more than anaerobic fitness. While the disease might have a lingering association with the aerobic capacity of recovered individuals, the infected cadets may have fully regained their anaerobic capacity during the weeks of training after recovery.

Except for headaches and fever, the various symptoms during illness showed no association with the cadets' fitness capacity at the end of the training course; however, the symptom-related assessments were performed on just a few individuals each and consequently are of low confidence level. Studies have shown that disease sequelae persist in a sizeable proportion of individuals months after recovering from non-severe COVID-19.[16] Even young, otherwise healthy individuals have often reported not returning to their old selves after recovering from the disease.[17] We assume that similar lingering post-COVID-19 associations occurred in our study population and that at least some cadets did not fully return to their preillness state of health by the end of the training course. As a retrospective study, we could not verify this assumption. Future prospective studies will need to address this question. It is possible that such studies would detect further differences between symptomatic and asymptomatic recovering individuals in their lingering disease sequelae and an association between the symptoms in symptomatic individuals and the ability to recover their preillness aerobic fitness.

Many studies have reported an association between viral load and COVID-19 severity and mortality.[12 13] Although not all researchers agree with this assertion,[18] the nasopharyngeal swab used to collect the samples for the real-time RT-qPCR studies opens a window to the respiratory system and the status of its viral infection. Even if an association does not exist between disease severity or mortality and the viral load, our findings suggest that higher viral loads take a heavier toll on the respiratory system and the ability to recover aerobic fitness than lower loads.

An unexpected finding of this study was that individuals infected by SARS-CoV-2 among the combatant cadets were fitter at baseline than the healthy controls, contradicting previous reports.[19] It is known that one of the main routes SARS-CoV-2 uses to enter cells is through the ACE2 receptor.[20] By binding to this receptor, the virus effectively downregulates the ACE2-angiotensin (Ang) 1–7-Mas receptor axis and activates the ACE-Ang II-AT1 axis. It is also known, predominantly from animal studies, that exercises, particularly the moderate-intensity long-term ones as often used in combat training, upregulate the ACE2-Ang 1–7-Mas receptor axis and downregulate the ACE-Ang II-AT1 receptor axis, effectively endowing anti-inflammatory and antifibrosis effects on the body.[21 22] It would thus be expected that fitter individuals would be better-protected and less prone to contracting COVID-19. Why the infected group was fitter than the healthy control in this cohort remains unknown. However, the anti-inflammatory and antifibrosis effects of the ACE2-Ang 1–7-Mas receptor axis suggest that beyond their already widely acknowledged benefits, exercises could benefit those who had COVID-19 and recovered by reducing fibrosis in their lungs.

The male predominance in our cohorts created a sex difference. Consequently, the fitness capacity did not adequately represent the female fitness contribution. However, a comparison of the MSDs found no difference between males and females, suggesting that the aerobic fitness decline in infected combatant and non-combatant cadets was not attributed solely to the biased sex ratio. Statsenko *et al* found a higher COVID-19 disease severity in males and older patients with a non-mild disease,[23] suggesting a more substantial pulmonary function and, presumably, aerobic physical fitness decline in male than female patients. All infected cadets in our study population had mild COVID-19. Univariate analysis found no sex difference in the MSDs. However, the multivariable linear regression model demonstrated that baseline aerobic fitness, sex, combatant status and disease status significantly contributed to the change in the aerobic MSD. These results support the conclusion that SARS-CoV-2 infection was an independent predictor of fitness deterioration after controlling for the other three variables.

Our study had several limitations. Missing values for some of the participants, particularly for the viral load assessment, lowered the power of the statistical analysis. However, the considerable similarity between the study and control groups within each cohort strengthened the reliability of our findings and the conclusions derived from them. Based on table 2, the association between aerobic fitness decline and the presence of residual symptoms was insignificant. However, among those who recovered, 3% of the combatants and 29.7% of the non-combatants exhibited residual symptoms. These rates demonstrated that those with a better baseline physical fitness were less likely to experience lingering symptoms. Moreover, the higher rates of residual symptoms in the non-combatant cohort may have contributed to a subjective incapacity to train and perform the final aerobic test, leading to prominent missing data in this group. We did not include the smoking status of the participants in our analysis. While this could have affected the outcomes, the young age of the participants suggests that smoking would have a relatively minor accumulated effect. It is important to note that the study population was not vaccinated against SARS-CoV-2 as such vaccines were not available at the time. It could be hypothesised that vaccinated infected individuals will show a milder decrease in their fitness than non-vaccinated ones, an aspect to be assessed in future studies.

CONCLUSION

We showed that SARS-CoV-2 infection was an independent predictor of decreased aerobic fitness in recovered young adults. A negative association was noted between the initial viral load and aerobic fitness after recovery and resumption of training. Our findings, relevant to athletes and active young adults, could help formulate individualised symptom-dependent and severity-dependent optimisation of rehabilitation plans to allow a gradual return to fitness. Future long-term studies could investigate the effect of COVID-19, including long COVID-19, on the body physiology under various conditions, illuminating possible preventive and recovery routes for athletes and non-athletes alike.

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