Acute and post-acute COVID-19 presentations in athletes: a systematic review and meta-analysis

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ABSTRACT
Objective To describe acute/postacute COVID-19 presentations in athletes.
Design Systematic review and meta-analysis.
Data sources The search was conducted in four databases (MEDLINE, EMBASE, SCOPUS, SPORTDiscus) and restricted to studies published from 2019 to 6 January 2022.
Eligibility criteria for selecting studies Studies were required to (1) include professional, amateur or collegiate/university athletes with COVID-19; (2) present data on acute/postacute COVID-19 symptoms and (3) have an observational design. Risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal tools.
Results 43 studies with 1158 athletes were included. For acute presentation, the pooled event rates for asymptomatic and severe COVID-19 were 25.5% (95% CI: 21.1% to 30.5%) and 1.3% (95% CI: 0.7% to 2.3%), respectively. For postacute presentations, the pooled estimate of persistent symptoms was 8.3% (95% CI: 3.8% to 17.0%). Pooled estimate for myocardial involvement was 5.0% (95% CI: 2.5% to 9.8%) in athletes undergoing any cardiac testing, and 2.5% (95% CI: 1.0% to 5.8%) in athletes undergoing MRI, although clinical symptoms were not characterised. None of the studies with a control group (eg, non-infected athletes) could confirm a causal relationship between COVID-19 and myocardial involvement.
Conclusion This broad characterisation of COVID-19 presentations in athletes indicates that ~94% exhibited mild or no acute symptoms. The available evidence did not confirm a causal relationship between COVID-19 and myocardial involvement. A small proportion of athletes experienced persistent symptoms while recovering from infection, which were mostly mild in nature, but could affect return-to-play decisions and timing.

INTRODUCTION
The estimated prevalence of COVID-19 symptoms among competitive athletes remains unknown. Some studies show that most infections are asymptomatic or result in a mild form of the disease (ie, self-limiting symptoms not requiring medical attention).1–3 Although severely ill hospitalised patients are at greater risk for postacute sequelae of COVID-19 (also referred as post-COVID-19 condition or long COVID-19),4 low-risk individuals, such as athletes, may also have persistent symptoms and abnormal findings, regardless of their acute symptomatology.5 In fact, there is evidence that athletes may also face postacute COVID-19 complications.

WHAT IS ALREADY KNOWN ON THIS TOPIC
⇒ Athletes mostly experience mild COVID-19; however, postacute complications may affect their health and performance. A better understanding of COVID-19 presentations in athletes is essential to inform safe measures and return-to-play protocols.

WHAT THIS STUDY ADDS?
⇒ This systematic review and meta-analysis showed that the vast majority (~94%) of athletes with COVID-19 are asymptomatic or exhibit mild acute symptoms.
⇒ A variable proportion of athletes (3.8%–17.0%) may exhibit some persistent symptoms (eg, anosmia/dysgeusia, cough, fatigue, chest pain, headache), which are usually mild in nature but could affect return-to-play decisions and timing. Importantly, the available evidence could not confirm a causal relationship between COVID-19 and myocardial involvement.
⇒ Future studies should incorporate control athletes (ie, non-infected) and systematically follow athletes with COVID-19 to better understand the predictors and natural course of postacute symptoms among athletes.

Among mild symptomatic and asymptomatic athletes recently recovered from COVID-19, 27% (n=13) presented with pericardial involvement (ie, presence of late enhancement with pericardial effusion).5 Conversely, there are studies showing no abnormal findings among professional athletes following COVID-19.5–9 A recent review on cardiac sequelae and risk of sudden cardiac arrest/death showed an overall low risk (0%–2.1%) of pericardial and/or myocardial involvement among athletes recovered from COVID-19.10
To the best of our knowledge, there is no systematic review characterising acute and postacute COVID-19 manifestations in athletes. A better understanding of COVID-19 presentation in athletes is essential to inform safe return-to-sport protocols, as well as to allow adequate screening and monitoring of potentially at-risk individuals. Therefore, the aim of this systematic review and meta-analysis is to report on acute and postacute COVID-19 presentations in athletes.

METHODS
The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)15 and
Prisma in Exercise, Rehabilitation, Sport medicine and SporTs science (PERSiST) guidelines were followed for reporting of this review. The protocol for this review was prospectively registered in the PROSPERO database (CRD42022301817).

Eligibility criteria
Eligibility criteria were defined according to the Population, Exposure, Outcome and Study design. Studies were eligible if they (1) included professional, amateur or collegiate athletes with COVID-19; (2) presented data on symptoms/sequela during and after the acute phase of infection and (3) had an observational design. Single case reports and studies involving recreational (ie, non-competitive) athletes or investigating the relationship between physical activity levels and COVID-19 symptoms and were not included.

Information sources and search strategy
The search for relevant studies was performed in four databases (MEDLINE (via OVID), EMBASE (via embase.com), SCOPUS (via Elsevier) and SPORTDiscus (via EBSCO)), without language restrictions. We screened the reference list of included studies and consulted experts in the field (Coalition SPORT-COVID-19) on their awareness of possible non-selected studies. The search strategy used a combination of terms related to COVID-19, athlete and symptom (online supplemental table 1). The multipurpose (mp) option was used to simultaneously search using a combination of free text and subject-specific headings. The search was restricted to studies published from 2019 to 6 January 2022.

Selection and data collection
Two independent reviewers applied the inclusion criteria and screened all titles and abstracts. Full texts were read, evaluated and assessed for inclusion independently by both reviewers. Disagreements were resolved by consensus, with a third reviewer being consulted in the lack of consensus. Two independent reviewers performed the data extraction of included studies using a standardised data extraction form and compared the extracted data for consistency. All inconsistencies were resolved by discussion between the two reviewers. We extracted the following information from each included study: country, participants’ characteristics (ie, age, sex and competitive level), number of infected athletes, sport modality, method for COVID-19 diagnosis, criteria for defining disease severity, characteristics of acute and postacute symptoms. Symptom severity was extracted as reported within the original study.

Results

Risk of bias assessment
The risk of bias was evaluated by two reviewers using the Joanna Briggs Institute (JBI) Critical Appraisal tool with the specific tool selected based on the design of each study included in the review (ie, cohort, cross-sectional, case series and case-control).

Data synthesis
Pooled estimates (number of events/total sample size of infected athletes in each study) of (1) asymptomatic, mild, moderate or severe cases; (2) presence of postacute symptoms; (3) type of acute and postacute symptoms and (4) myocardial involvement were obtained using random-effect models (DerSimonian and Laird approach) to account for heterogeneity across individual studies and presented as event rate and 95% CI. Heterogeneity was examined as between-study variance and calculated as the I² statistic measuring the proportion of variation in the combined estimates due to study variance. An I² value of 0% indicates no inconsistency, and an I² of 100% indicates maximal inconsistency. Pooled estimates of type of acute and postacute symptoms and myocardial involvement were based only on studies reporting one or more symptoms/events. Meta-analyses were conducted using the Comprehensive Meta-Analysis software, V.3 (Biostat, Englewood, New Jersey, USA, 2013).

Deviation from protocol
Post hoc sensitivity analyses following the same statistical procedures above described were performed to investigate the pooled event rates of acute symptom presentations when including only professional/elite athletes and only college/university athletes.

Results

Study selection
The search strategy identified 3344 studies. After removal of duplicates, 2215 studies remained. Title and abstract screening identified 69 potentially eligible studies. Twenty-nine of these were excluded owing to: lack of outcomes of interest (n=12), wrong population (n=4), conference abstracts (n=11) or editorials (n=2) (online supplemental table 2). Forty original studies met the inclusion criteria. Four additional studies were included on checking the references of included studies and consulting experts in the field (figure 1). Two studies may have had overlapping participants considering the study designs and athletes’ characteristics; therefore, we decided to retain only the study with the largest sample size in the data synthesis. In total, 43 studies were included in the review.

Study characteristics
Of the 43 studies and 11518 infected athletes included in this systematic review, the median number (IQR) of participants per study was 26 (15–101). The included studies were conducted in Argentina, Australia, Brazil, Denmark, Finland, Germany, Hungary, Italy, Poland, Qatar, Russia, Serbia, Turkey, UK and USA. One study was a multicentre collaboration led by researchers in South Africa, and one study was conducted across different countries in Europe.

Eleven (25%) studies included only male athletes, and 22 (51%) studies included both male and female athletes. Eight (19%) studies did not report data on sex. All studies included young adults, except one that included youth athletes (mean age 14.0±1.9). Fourteen studies did not report the
age of participants. Two studies included only amateur athletes, 12 studies included only college/university athletes, and 23 studies included only professional/elite athletes. Three studies included both professional and non-professional athletes, and 1 study included professional, college and amateur athletes. One study included professional, semi-professional and youth athletes. Regarding COVID-19 diagnosis, 28 studies used PCR tests only (either real-time or reverse transcription), 9 studies used PCR and antibody/antigen tests and 2 studies used PCR, antibody/antigen and clinical features. In 4 studies, the authors stated that participants had COVID-19, but did not provide information on the diagnostic testing.

Among the studies meta-analysed for disease severity (n=26), five of them clearly reported on criteria used for defining mild/moderate/severe disease, 6, 21, 24, 27 whereas 19 studies did not provide this information. 1, 3, 14–16, 25, 29–31, 33–35, 38–41, 43, 47, 48, whereas 2 studies had only asymptomatic infections. 18, 22

Fifteen studies reported on infections among athletes following reopening or during sport competitions, 12, 15, 16, 18, 22, 23, 26, 29, 31, 32, 36, 49 9 studies reported on infections following return-to-play/campus protocols, 7, 27, 28, 38–40, 41, 43, 44, 46 11 studies included analyses of previously collected data (ie, medical records), 6, 9, 14, 21, 35, 37, 41, 42, 45, 47, 48 7 studies enrolled previously infected athletes 8, 24, 25, 30, 33, 34 and 1 study was an online survey. 35 An overview of the included studies is provided in online supplemental table 3.

**Risk of bias**

The specific JBI tool was applied according to the study design (ie, cross-sectional (n=7), case–control (n=5), case series (n=3), cohort (n=28)). Among the cross-sectional studies, 86% did not describe participants and settings in detail, identify confounding factors and define strategies to deal with confounding factors. Nonetheless, exposure was measured in a valid and reliable way and appropriate statistical analysis was used in most cross-sectional studies (86%). As for case–control studies, confounding factors and strategies to deal with them were not identified in 80%, whereas all studies had exposure measured in a standard, valid and reliable way, had exposure period long enough to be meaningful and used appropriate statistical analysis. Among case-series designs, no study presented clear inclusion criteria and site-specific demographic information; however, all studies had the condition measured in a standard, valid and reliable way, and clearly reported outcomes or follow-up results. Regarding cohort studies, 89% of them did not identify confounding factors and 96% did not inform the strategies to deal with them; however, 89% had exposure measured in a valid and reliable way. Detailed information on risk of bias of each study can be found in online supplemental tables 4–7.

**Acute COVID-19 presentations**

Thirty-five (n=5709) studies provided data of asymptomatic athletes, and 26 (n=5091) of these also reported data on symptomatic athletes (ie, mild, moderate, severe). Eight studies did not describe the disease severity and were not included in the pooled event rate estimate. 7, 9, 19, 23, 34, 37, 42, 48 Asymptomatic and paucisymptomatic athletes from the study by Martinez et al 41 were grouped as asymptomatic in this review.

The pooled event rate for asymptomatic COVID-19 was 25.5% (95% CI: 21.1% to 30.5%); I²=85.5%, while the pooled estimates for mild, moderate and severe forms of the disease were 68.6% (95% CI: 58.4% to 77.2%); I²=96.0%, 6.7% (95% CI: 4.0% to 11.1%); I²=88.9% and 1.3% (95% CI: 0.7% to 2.3%); I²=39.0%, respectively (figure 2).

**Figure 1** Flow diagram of the included studies.
Figure 2  Pooled event rate (95% CI) for (A) asymptomatic, (B) mild, (C) moderate and (D) severe COVID-19 in athletes.
(95% CI: 22.6% to 34.3%); I² = 79.8%) (Figure 3A and online supplemental figure 1). Types of symptoms in each study are thoroughly described in online supplemental table 8.

Sensitivity analysis
The pooled event rates restricted to studies with professional/elite athletes were 19.3% (95% CI: 11.5% to 30.6%); I² = 85.3% for asymptomatic, 76.3% (95% CI: 61.6% to 86.6%); I² = 88.5% for mild, 4.0% (95% CI: 1.1% to 13.0%); I² = 84.5% for moderate and 2.2% (95% CI: 1.0% to 4.8%); I² = 30.6% for severe COVID-19, while the estimates for college/university athletes were 26.2% (95% CI: 21.0% to 32.1%); I² = 84.5%, 58.4% (95% CI: 41.8% to 73.2%); I² = 96.9%, 17.8% (95% CI: 11.0% to 27.5%); I² = 89.3% and 0.4% (95% CI: 0.3% to 0.7%); I² = 0.0%, respectively (online supplemental figure 2).

Post-acute COVID-19 presentations
Eleven studies reported on post-acute COVID-19 symptoms.7 14 27 29 30 33 35 38–40 42 Of these, six found no persistent symptoms,7 27 29 33 39 40 whereas five reported persistent symptoms in 1.2% (44/3529),42 5.9% (10/170),38 14% (21/147),35 18% (20/111)14 and 79% (19/24)30 of the participants. In these studies, the timeframe for postacute symptoms ranged from at least 10 days after positive test and end of self-isolation period30 to >28 days.35 The pooled event rate for postacute symptoms was 8.3% (95% CI: 3.8% to 17.0%; I² = 92%) (online supplemental figure 3). The most common

Figure 3  Summary of acute (A: 18 studies, n=4115) and postacute and (B: 4 studies, n=3879) COVID-19 symptoms in athletes. Data are pooled estimates for all studies reporting symptomatic cases. GI, gastrointestinal.
symptoms reported were anosmia/dysgeusia (29.9% (95% CI: 9.9% to 62.4%)); $\Gamma=97.9\%$, cough (16.2% (95% CI: 4.2% to 46.0%)); $\Gamma=97.9\%$, fatigue (9.1% (95% CI: 1.0% to 49.9%)); $\Gamma=98.9\%$, chest pain (8.3% (95% CI: 2.0% to 28.9%)); $\Gamma=94.1\%$ and headache (6.4% (95% CI: 0.8% to 38.2%)); $\Gamma=98.9\%$ (figure 3B and online supplemental figure 4). In the longest follow-up study, persistent symptoms were not resolved in 3% of Olympic and Paralympic athletes 90 days following symptom onset, with a range of 0–148 days for symptoms resolution. In the largest study involving 3597 collegiate athletes, 44/3529 (1.2%) had persistent symptoms >3 weeks, 28 (0.8%) had symptoms >4 weeks and 2 (0.06%) had symptoms >12 weeks. Detailed information on type of symptoms for individual studies can be found in online supplemental table 9.

Assessment of myocardial involvement following the recovery from COVID-19 (on average 3 weeks after COVID-19 diagnosis or the isolation period, varying from 10 days to 27 weeks) was available in 25 studies. Seven studies included a control group (eg, non-infected athletes, healthy non-athletes, preinfection data). The pooled estimate for myocardial involvement was 5.0% (95% CI: 2.5% to 9.8%); $\Gamma=92.5\%$ (online supplemental figure 5). When considering only studies with CMRI, the pooled estimate for myocardial involvement was 2.5% (95% CI: 1.0% to 5.8%); $\Gamma=90.2\%$ (online supplemental figure 6). The available evidence, from the studies that included controls, could not confirm whether myocardial involvement was caused by COVID-19. Further details on myocardial involvement can be found in online supplemental table 10.

DISCUSSION

Statement of principal findings

This comprehensive systematic review and meta-analysis compiled evidence on COVID-19 manifestation in athletes. The pooled event rates for asymptomatic, mild, moderate and severe diseases were 25.5%, 68.6%, 6.7% and 1.3%, respectively. While a growing body of knowledge reviewed herein indicates that acute symptoms are often mild or absent in this population (~94% of the cases), emerging evidence suggests that a considerable proportion of athletes (3.8%–17.0%) may experience persistent symptoms that may be potentially detrimental to performance, hence influencing the return-to-play decisions and timing. Myocardial involvement (ie, abnormal myocardium manifest by ECG, echocardiographic, and/or CMRI, with or without elevated cTn) were identified in 5% of the available sample, but this could not be causally linked to COVID-19, given that none of the 11 studies that had control parameters (eg, non-infected athletes, preinfection imaging) could confirm that reported cardiac events related to COVID-19 infection. This review also reveals that the absence of control groups or previous baseline (ie, preinfection) data for the assessment of COVID-19 cardiac involvement, small sample sizes, lack of clear strategies to identify and deal with potential confounders (eg, pre-existing diseases, smoking, previous COVID-19, vaccination status) and inconsistency or lack of clarity in how symptom severity was defined in several included studies are relevant limitations of the literature that should be addressed in subsequent investigations.

Clinical implications

This review brings a relevant characterisation of acute symptom presentations among competitive athletes, showing that approximately a quarter of those tested were asymptomatic, which is less than the one-third estimate from population-based studies. This is possibly because athletes in general tend to be closely followed by medical staff, possibly resulting in a more effective detection of oligosymptomatic cases; also, symptomatic athletes may be more inclined to participate in a screening study than those who are asymptomatic (selection bias). On the other hand, severe cases among athletes (1.3%) were slightly less frequent than in the young population (eg, 2.7%), which could underscore the potential role of high physical activity levels and/or physical fitness as protective factors against severe COVID-19, although other factors, such as nutrition and sleep quality, may also play a role in the immune response to infections.

Of relevance, we found that a small proportion of athletes (5.0%) had myocardial involvement after recovery from infection, corroborating previous observations. However, our systematic review could not confirm whether these abnormalities were caused by COVID-19, given that among 25 studies reporting postacute COVID-19 cardiac assessments, only 11 had control parameters (eg, non-infected athletes, healthy controls, baseline imaging). In fact, none of these studies employing controls found compelling evidence to indicate that cardiac abnormality was attributable to COVID-19. It is known that the prevalence of cardiac abnormalities in non-COVID-19 athletes is heterogeneous and may reach up to 12% in runners, based on CMRI findings suggestive of myocarditis on the basis of the presence of late gadolinium enhancement. This heterogeneity may be explained by site-specific technical variability and interpretation aspects. As knowledge evolves, CMRI has been recommended when there is clinical suspicion of cardiac involvement, and not as a primary screening tool. This is supported by the fact that there has not been a single case of cardiac complication reported to be clearly related to COVID-19, which is confirmed in the present review. However, further studies using appropriate controls remain necessary to investigate the role of COVID-19 on myocardial involvement among athletes.

A finding of concern is that the literature showed a significant and variable proportion of COVID-19-infected athletes (3.8%–17.0%) who experienced postacute symptoms, including anosmia/dysgeusia (30%), cough (16%), fatigue (9%), chest pain (8%) and headache (6%). Persistent symptoms are also frequently reported in the general population. Among healthcare workers, for example, 32% reported persistent symptoms 3–4 months after COVID-19, with moderate-to-severe fatigue being the most reported symptom. In addition, dyspnoea was the most reported symptom among non-critical (30%) and non-hospitalised (~18%) patients at 2.0 and 3.9 (range: 1.5–6.0) months after infection, respectively. Importantly, as highlighted by Hull et al, the proportion of not fully recovered athletes from COVID-19 seems to be significantly higher than that for other acute respiratory illnesses (roughly 4%). In professional sport, many athletes commonly return-to-play within 5–10 days after an asymptomatic or mild infection, which may be challenging for those experiencing some kind of symptoms on training/competition resumption. The mid-to-long-term (ie, weeks to months) impact of long COVID-19 on athletes’ health and performance as well as their predictors remain to be investigated.

Limitations of the available evidence and the review

Our assessment exposed several limitations within the evidence base, which may impact interpretation of results, and should be addressed in forthcoming studies. For instance, more than 80% of included studies did not identify potential confounders (eg, pre-existing diseases, vaccination status) and did not state strategies to deal with them; many outcomes, such as the criteria by which symptom severity was judged, were poorly defined in many studies, which makes comparison across studies difficult;
comparators such as non-infected control groups or preinfection data were scant for postacute COVID-19 assessments, which renders it difficult to ascertain whether results are directly attributable to COVID-19. Although in most studies (n=28) COVID-19 diagnosis was made using valid methods (eg, PCR, antibody/antigen), four studies failed to provide information on diagnostic testing. Further studies should clearly describe how participants were diagnosed. Selection bias may have contributed to the heterogeneous and possibly overestimated acute symptom event rate, which should be mitigated with large-scale cohort studies that could provide a more accurate denominator. The lack of clear and standardised criteria to define symptom presentations, along with variability in participants’ characteristics and study designs, may explain the substantial heterogeneity in pooled estimates, as evidenced by generally high I² values. In addition, our sensitivity analysis testing professional/elite and college/university athletes separately suggest a relatively similar rate of asymptomatic, mild and moderate cases, with overlapping CIs; although severe cases were slightly different between these two subgroups, caution should be exercised when interpreting these data considering the very low number of cases (n=12).

Further studies should investigate whether COVID-19 presentations change as a function of competitive levels. Furthermore, all the original studies evaluated in this review were conducted before the emergence of Omicron; therefore, the role of this variant on acute and postacute COVID-19 presentations in athletes warrants investigation. As scant information was available on vaccination status of the athletes, this review was unable to test the effect of immunisation on COVID-19 symptoms in the athletic population, another topic that merits new studies. Finally, the absence of studies that systematically applied clearly defined serial assessments of infected athletes preclude any inferences on the resolution of persistent symptoms in this population. These limitations should be considered when interpreting the findings of this review. Correction of these issues in forthcoming studies will improve understanding of the impact of COVID-19 on athletes and support the development of safety measures and return-to-play recommendations.

Conclusions and perspectives

In conclusion, this systematic review provides a broad characterisation of COVID-19 presentations in athletes and indicates that most (~94%) exhibit mild or no acute symptoms. The available evidence could not confirm a causal relationship between COVID-19 and myocardial involvement. Pooled analysis suggests that a variable proportion of athletes (3.8%-17.0%) may experience persistent symptoms after recovering from infection, which may affect the decision-making process of returning the affected individual to practice or competition. Future studies should incorporate comparators, clearly define their criteria and outcomes, identify potential confounders and systematically follow infected athletes to better understand the predictors and natural course of COVID-19 in this population.

Correction notice This article has been corrected since it published Online First. A collaborator’s name has been updated.

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Contributors BG, IRL and ED conceived and designed the study. IRL conducted the search. IRL, FIS, WDJR and NKF performed the screening, study selection and data extraction. IRL, BG and ED analysed and interpreted the data, and drafted the manuscript with input from FIS, WDJR, NKF, LDNdM, ALdSP and the Coalition SPORT-COVID-19. All authors have read and approved the final version.

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