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Investigating the Effect of COVID-19 Infection on Professional Athletes' Post-Infection with a Focus on Fatigue and Chronic Fatigue Syndrome

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Abstract

Introduction and Objectives: COVID-19 has been reported to cause long-term sequela including persistent fatigue and Chronic Fatigue Syndrome (CFS) in the general population. However, it remains to be seen if similar effects are observed in an athlete population. The aetiology and pathophysiology are poorly understood but is thought to be multi-factorial. Patient reported outcome measures are commonly used to improve patient-centred outcomes (PROMs). They are essential to assess patient quality of life post-COVID infection. This paper aims to assess the effect of COVID-19 on athletes' long-term fatigue and CFS and identify the PROMs used to characterise this. **Methodology:** Articles were selected for extraction based on the eligibility criteria and PRISMA guidelines. The inclusion criteria required papers to assess competitive athletes over eighteen years of age who were clinically diagnosed with COVID-19. Articles were extracted to assess different variables including type of sport, type of athlete and ethnicity. Key terms were obtained using MeSH trees and utilised with Web of Science and NCBI Pubmed. Papers were graded by quality using the Hawker quality assessment tool. **Results and Discussion:** Forty articles (N = 40) were identified for full-text screening (N = 8). Eight were selected for extraction based on the eligibility criteria. Data was obtained on athlete characteristics, sport characteristics, properties of PROM measurement techniques and fatigue presentation. Male athletes were found to be 10% - 50% more likely than female athletes to suffer from persistent fatigue symptoms (N = 2). Persistent fatigue was present in 9% - 10% Athletes from mixed backgrounds and genders (N = 2). Initial fatigue was documented to be between 47% - 56% (N = 2). A heterogenous range of PROMs were utilised to assess symptoms including fatigue and excluded emotional or mental fatigue. **Conclusion:** COVID-19 is associated with signs of persisting fatigue and potentially CFS in athlete populations. More work needs to be done to develop standardised and validated PROMs specific to CFS.

Keywords

COVID-19, Fibromyalgia, Athlete, Quality of Life, Patient Reported Outcome Measures

1. Introduction

The COVID-19 pandemic resulted in millions of deaths worldwide despite national efforts to contain it by reducing transmission and increasing testing capabilities. The disease presentation and symptoms affect patient outcomes with severe disease (requiring hospitalisation) associated with negative patient outcomes and a poorer prognosis [1]. It is now clear that acute outcomes are not the only lasting effect of COVID-19. Following an infection with SARS-COV-2, individuals have reported a range of associated sequelae, also known as long-COVID including anosmia, ageusia, reduced forced expiratory volume/forced vital capacity ratio, persistent fatigue and Chronic Fatigue Syndrome (CFS) [2] [3]. These symptoms have also been reported in trained athletes' post-infection and occurred during the return of competitive sporting events [4]. This can decrease athletic performance and damage professional athletic careers if the effects are permanent.

Individuals affected by cardiomyopathies and heart failure have been found to be at an increased risk of adverse COVID-19 outcomes including myocarditis and fatigue [5] [6] [7]. Hypertrophic cardiomyopathy is ubiquitous amongst athletes due to cardiac remodelling and is the biggest cause of sudden cardiac death but there is no current link current to fatigue [8].

Chronic fatigue syndrome (CFS) is a diagnosis of exclusion characterised by severe fatigue without exertion lasting over six months and is also associated with asthenia, cognitive dysfunction, autonomic dysfunction and post-exertional malaise [9] [10]. The exact aetiology of CFS is unclear, with studies linking it to genetics, oxidative stress and immune dysregulation [9]. It is now clear that COVID-19 can cause CFS and long-term mild fatigue with the permanent effects to be determined [11] [12]. This can be extremely debilitating for patients as it is significantly associated with affective mental health disorders such as anxiety and depression [10] [13].

Patient Reported Outcome Measures (PROMS) are standardised questionnaires used as tools to assess outcomes from a patient's perspective. They can be used to measure mental health status, physical health, ailments, and quality of life. Validated PROMS allow for the quality of clinical interventions to be monitored as it is completed by the patient pre-intervention and post-intervention. The type and quality of PROM depends on the condition of interest and the administration method used.

Whilst studies have investigated the effects of COVID-19 on athletes' performances and physical status, extended studies using patient reported outcome measures to identify the prominence of fatigue were sparse. This paper aims to identify the effect of COVID-19 on athletes and report the PROMs used in this process.

2. Aims and Objectives

We aim to identify the effect of COVID-19 severity on competitive athletes with a focus on persistent fatigue and CFS. The type and administration of PROMs utilised in this population will be assessed.

3. Methodology

3.1. Search Strategy

Key terms were identified based on the targeted population and examined using MeSH trees. Web of Science and NCBI Pubmed were used as the databases of choice. These data sources were used in order to generate as many relevant papers to this topic as possible as seen in **Figure 1**. The following key words were used:

- COVID-19:
  2019 Novel Coronavirus Disease
  2019 Novel Coronavirus Infection
  2019-nCoV Disease
  2019-nCoV Infection
  COVID-19 Pandemic
  COVID-19 Pandemics
  COVID-19 Virus Disease
  COVID-19 Virus Infection
  COVID-19
  Coronavirus Disease 2019
  Coronavirus Disease-19
  SARS Coronavirus 2 Infection
  SARS-CoV-2 Infection COVID-19
- Athlete:
  Elite Athletes
  Professional Athletes
  Para-Athletes
  Sportsperson
  Sportsman
  Sportswomen
  Sports Person
- Fibromyalgia
  Diffuse Myofascial Pain Syndrome

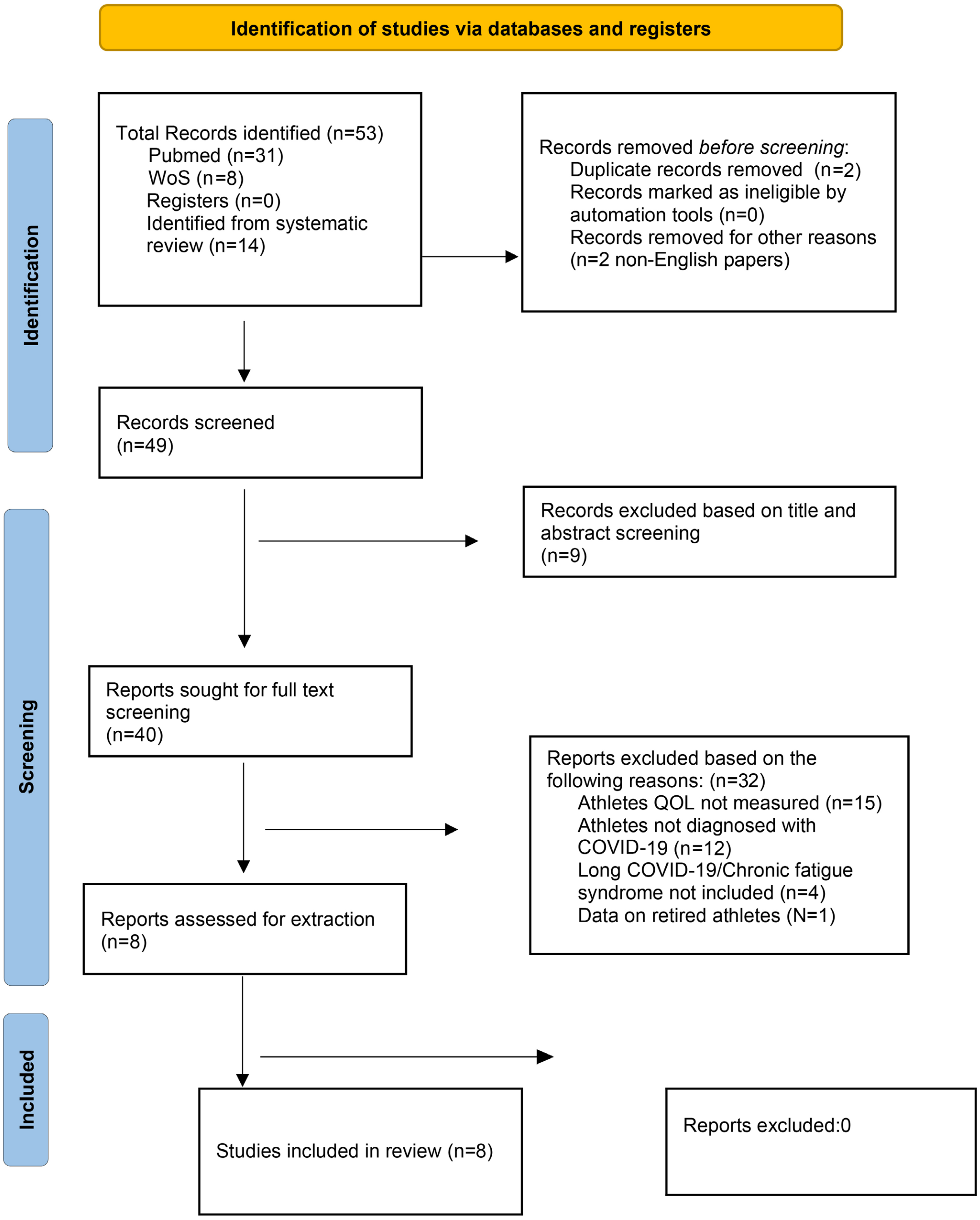

Figure 1. Flow diagram of study selection process.

Fibromyalgia, Primary
Fibromyalgia, Secondary
Fibromyalgia-Fibromyositis Syndrome
Fibromyositis-Fibromyalgia Syndrome
Fibrositis
Myofascial Pain Syndrome, Diffuse
Rheumatism, Muscular
Chronic Fatigue Syndrome

- Quality of Life:
  HRQOL
  Health-Related Quality Of Life
  Life Quality
  QOL
  Health Status
- Patient Reported Outcome Measures:
  Patient Reported Outcome
  Patient Reported Outcome Measure
  Patient Reported Outcomes
  Patient-Reported Outcome
  Patient-Reported Outcomes
  Patient-Reported Questionnaires

3.2. Sample Population

We focused on athletes with a confirmed diagnosis (symptomatic/asymptomatic) of COVID-19 (mild/moderate/severe disease) with either confirmed or suspected fatigue/chronic fatigue syndrome. Athletes were defined as adults over the age of eighteen that are currently registered with the appropriate sporting body/club or receive a monetary reward for their physical performances. Studies without a comparator were not considered.

3.3. Study Selection and Eligibility Criteria

Papers identified were then included/excluded by selected criteria. Published works (full text papers, systematic reviews, literature reviews, RCTs, meta-analysis papers, clinical trials/experimental studies, case reports/series and cross-sectional studies) from 2019-2021 only in English were accepted. Athletes must be diagnosed with COVID-19 either via antigen testing, antibody testing or PCR test (asymptomatic or symptomatic). Papers which include athletes diagnosed by a clinician based on symptoms will be accepted if it is a minor number of the overall participants. College level athletes were considered if playing competitively. Adults defined as individuals of any sex over the age of 18, there is no upper age limit if they fulfil the other criteria (monetary reward/affiliations). Ex-professional athletes/retired athletes were not considered. Published works were excluded if they were abstract only, study protocols, conference pieces, poster presentations or opinion pieces. Studies that reported athletes presenting with COVID-19 symptoms, but not yet diagnosed/excluded Influenza or other upper respiratory tract infections were included if assessed by a registered clinician to have COVID-19. PRISMA guidelines were followed to identify papers for extraction.

3.4. Assessment of Study Quality

The quality assessment tool utilised was the Hawker tool, papers were rated to assess credibility, dependability, confirmability and transferability. These ratings were used to grade the papers from low quality to high quality.

3.5. Assessment of Measurement Properties

The type of PROM used, the time period covered and its implementation to measure the health of athletes was assessed.

4. Results

4.1. Overview of Literature

Eight articles were selected for extraction following the eligibility criteria and were graded by quality using the Hawker quality assessment tool [14]-[21]. The majority of papers (N = 6) were published in the USA with no papers published from Asia or South America. They were published in medium-high impact journals and have been cited elsewhere. In terms of study design, there were three observational studies, three cross-sectional studies, one retroactive case review and one case report.

4.2. Content Description and Validity

Four articles indirectly obtained information on athlete's health from databank institutions [15] [17] [18] [19]. These databanks used routine medical screening questions to assess fatigue in athletes. The other articles (N = 4) directly obtained information from athletes via either a questionnaire or online survey [14] [16] [19] [21].

4.3. Quality Rating of Measurement Properties and Construct Validity

Petracek *et al.*, (2021) used the unidimensional wellness score which rated physical health from 0 (lowest) to 100 (highest) [19]. Schwellnus *et al.*, (2021) used the Wisconsin respiratory symptom survey which is a standardised and validated method used to evaluate patient quality of life post-upper respiratory tract infections [21]. Moulson *et al.*, (2021) and Petek *et al.*, (2021) used the Updated Lake Louise imaging criteria which is recommended prior to cardiac magnetic resonance for suspicion of myocarditis as a cause of systemic symptoms such as fatigue [18] [19]. Martinez *et al.*, (2021) used the ACC RTP cardiac screening protocol while also using databanks for patient symptoms [17].

5. Discussion

5.1. Summary

Persistent fatigue and CFS currently have no standardised validated PROMs, with large discrepancies between clinician and patient standards. The majority of PROMs focus on physical symptoms and exclude patient emotional or mental well-being which affects patients QOL the most [22] [23] [24]. A lack of knowledge on the underlying pathophysiology makes it difficult to create specific

PROMs. Roberts in 2017 determined that the WHOQoL-Bref26 can offer an accurate snapshot of patient condition during the course of treatment but offers little in terms of long-term value or symptom severity [24]. New frameworks have been proposed by Parslow *et al.*, in 2020 to assess CFS but it is limited to a children population [25]. Each group used a different PROM tool to assess fatigue in athletes (**Table 1**). This lack of standardisation makes it difficult to cross-reference results from different athlete populations to accurately assess the effect of COVID-19 on fatigue or CFS.

Table 1. Properties of PROM measurement techniques.

***Authors* (*in order*)**	Schwellnus *et al.*, (2021)	Petracek *et al.*, (2021)	Petek *et al.*, (2021)	Moulsen *et al.*, (2021)	Martinez *et al.*, (2021)	Krzywanski *et al.*, (2021)	Hull *et al.*, (2021)	Brito *et al.*, (2021)
Country/ place of study	South Africa	USA	USA	USA	USA	Poland	UK	USA
Study design	Cross-sectional	Case report	Observational cohort study	Prospective observational	Cross-sectional	Observational	Retroactive case review	Cross-sectional
PROMs/ QOL used	Wisconsin respiratory symptom survey for severity, self-reported number of days to RTP	Unidimensional Wellness score	Outcome from Updated Lake Louise Imaging criteria	Outcome from Updated Lake Louise Imaging criteria	Cardiac screening protocol in line with ACC RTP recommendations	Routine medical screening to assess symptoms	Dataset obtained from English institute of sport performance data management system	Used a monitoring protocol to assess symptoms
Type of PROM	Physical symptoms	Physical symptoms	Physical symptoms	Physical symptoms	Physical symptoms	Physical symptoms	Physical symptoms	Physical symptoms
When PROM was used	July - October 2020	June 2020 - Jan 2021	September 2020 - May 2021	September - December 2020	May - October 2020	July - October 2020	February 2020 - August 2020, August 2020 - Jan 2021	July 2020
Method of application	Online survey	Questionnaire	Data from National Collegiate athletic association institutions using ORCCA registry	Data obtained from 42 colleges/ universities	Data obtained from North American professional sports leagues and players associations	Routine medical screening	Data obtained from data from UK sport institutes	Smartphone app
Grade	High quality	Medium quality	High quality	High quality	High quality	Medium quality	High quality	High quality

PROMS were used by all papers over the course of one to six months to obtain information regarding athlete physical condition post-infection (**Table 1**). Mental state of athletes was not assessed despite brain fog commonly reported in patients with long-COVID or diagnosed with COVID-19 associated CFS [26] [27]. Brito *et al.*, (2021), Petraceck *et al.*, (2021) and Schwellnus *et al.*, (2021) used a questionnaire format to obtain information about athlete quality of life directly [14] [20] [21]. Krzywanski *et al.*, (2021) carried out routine medical screenings and the rest of the papers obtained data indirectly via institutional data banks [16].

Associations between ethnicity and CFS have been previously reported in literature [28] [29]. Of the papers reviewed, little attempt was made to link athlete ethnicity and fatigue although Petek *et al.*, (2021) reported that black athletes were five times more likely to have exertional symptoms than white and white-Hispanic athletes (**Table 2**) [19]. Moulson *et al.*, (2021) reported higher rates of myocardial disease in the same population [18]. 50% of the papers reviewed did not disclose patient ethnicity (N = 4). The relationship between

Table 2. Study characteristics.

***Authors* (*in order*)**	Schwellnus *et al.*, (2021)	Petracek *et al.*, (2021)	Petek *et al.*, (2021)	Moulsen *et al.*, (2021)	Martinez *et al.*, (2021)	Krzywanski *et al.*, (2021)	Hull *et al.*, (2021)	Brito *et al.*, (2021)
Number of participants	N = 45	N = 1	N = 3597	N = 3018	N = 789	N = 111	N = 147	N = 60
Ethnicity	Not mentioned	Not mentioned	White non-Hispanic (N = 2301), Black (N = 983), White-hispanic (N = 110), Mixed (N = 73), Other (N = 91)	White non-Hispanic (N = 1922), Black (N = 829), White-hispanic (N = 87), Mixed (N = 62), Other (N = 80)	Not mentioned	All Caucasian	Not mentioned	White (N = 3), African American (N = 36), Other (N = 3)
Type of sport	Not mentioned	Track and cross-country athlete	Not mentioned	Not mentioned	Major League soccer (N = 70), Major League baseball (N = 181), National hockey league (N = 68), National football league (N = 349), National basketball association (N = 121)	Strength (N = 33), Endurance (N = 29), Team sports (N = 38), Technical (N = 10)	Summer sport (N = 36), Winter sport (N = 11)	American Football (N = 35), Basketball (N = 13), Vollleyball (N = 1), Soccer (N = 2), Swimming (N = 1), Other (N = 2)

COVID-19 severity and type of sport on fatigue level was also unclear. Krzywanksi *et al.*, (2021) categorised the different types of sports but there was no cross-analysis to determine if fatigue varied between the different sporting populations [16]. Hull *et al.*, (2021) carried out a similar approach but divided their athlete population by summer and winter sports [15]. Additionally, they were the only group to clarify about the type of athlete with twenty-five para-athletes included in the study population. Para-athletes and were found to have a greater risk ratio of symptoms impacting more than twenty-eight days when compared to athletes (1.2 to 0.8).

Age has been reported to be one of the greatest independent risk factors for adverse COVID-19 outcomes [30] [31]. Papers reviewed opted to either use mean or median ages rather than sort symptoms by age groups (**Table 3**). Hull *et al.*, (2021) and Petek *et al.*, (2021) both reported little difference of age on symptom duration including fatigue [15] [19]. Males have a higher unadjusted COVID-19 mortality rate than females [32]. Furthermore, men are more likely to be hospitalised and develop long-term sequalae including fatigue [33]. All studies reviewed, bar one, included a mix of genders, but none assessed the effect of athlete gender on COVID-19 outcomes. *Hull et al.*, (2021) demonstrated that males were almost twice as likely to suffer from short term fatigue symptoms post-infection, however, there was no statistical difference after twenty-eight days [15]. Petek *et al.*, (2021) however reported that male athletes were 10% more likely to have persistent symptoms including fatigue [19]. Kryzywanski

Table 3. Athlete characteristics.

Authors (in order)	Schwellnus *et al.*, (2021)	Petracek *et al.*, (2021)	Petek *et al.*, (2021)	Moulsen *et al.*, (2021)	Martinez *et al.*, (2021)	Krzywanski *et al.*, (2021)	Hull *et al.*, (2021)	Brito *et al.*, (2021)
Type of athlete	Athletes training for minimum 3 hours a week	College student athlete	College athletes	College athletes	Professional athletes	Professional athletes	Able-bodied (N = 122) Para-athletes (N = 25)	College student athletes
Age of athlete	Mean age = 32.6	19	Mean age = 20	Mean age = 20	Mean age = 15	Mean age = 25	Mean age = 24.7	Median age = 19
Sex of athlete	M: (N = 18) F: (N = 27)	M	M: (N = 2410) F: (N = 1187)	M: (N = 957) F: (N = 2061)	NBA: M: (N = 109) F: (N = 12)	Strength: M: (N = 10) F: (N = 23) Endurance: M: (N = 21) F: (N = 8) Team Sports: M: (N = 15) F (N = 23) Technical: M: (N = 6) F: (N = 5)	M: (N = 93) F: (N = 53)	M: (N = 46) F: (N = 14)

et al., (2021) also found that females were more likely to have asymptomatic cases across all sporting brackets [16].

A large proportion of athletes screened suffered from fatigue post-COVID-19 infection (Table 4). The majority of papers assessed fatigue spanning a time period of several months post-infection. Brito *et al.*, (2021) demonstrated that 25% of athletes with symptomatic COVID-19 symptoms had fatigue [14]. A higher figure of 56% was reported by Krzywanski *et al.*, (2021) [16]. A similar figure was reported by Hull *et al.*, (2021) with 47% reporting fatigue post-infection and 10% showing signs of persistent fatigue after 28 days [15]. Schwellnus *et al.*, (2021) reported the highest fatigue rates but included athletes presumed to have COVID-19 adding a confounding bias [21]. A large cohort study including 3597 participants by Petek *et al.*, (2021) demonstrated that 9% of athletes had exertion fatigue, which decreased to 4% after three weeks [19]. A cross-sectional study by Martinez *et al.*, (2021) assessed fatigue in thirty athletes with abnormal heart conditions with five reporting fatigue [17]. These studies indicate that persistent

Table 4. The effects of COVID-19 on fatigue in athletes.

Authors (in order)	Schwellnus *et al.*, (2021)	Petracek *et al.*, (2021)	Petek *et al.*, (2021)	Moulsen *et al.*, (2021)	Martinez *et al.*, (2021)	Krzywanski *et al.*, (2021)	Hull *et al.*, (2021)	Brito *et al.*, (2021)
COVID-19 status	PCR +ve (N = 37), Positive antibodies (N = 3)	PCR and antibody test	Tests via PCR, antigen or antibodies	PCR (N = 2465), Antigen (N = 234) or antibody (N = 263) testing, Asymptomatic excluded	Asymptomatic excluded, PCR and antibody testing used	Asymptomatic excluded	Assumed positive (N = 76), PCR or antibody testing (N = 71), Asymptomatic excluded	Symptomatic (N = 38), Asymptomatic (N = 16)
Severity of COVID-19	Full list of COVID symptoms	Mild symptoms including anosmia, cough, sore throat, headache and fatigue	Categorised symptoms as Mild, Moderate and cardio-pulmonary	Asymptomatic (N = 887), Mild (N = 839), Moderate (N = 663), Cardio-pulmonary (N = 337)	Preceding viral symptoms (N = 460), Asymptomatic (N = 329)	Mild (N = 93), Moderate (N = 2)	Not mentioned	Not mentioned
Fatigue outcome	Extensive fatigue (N = 45), Moderate fatigue (N = 30)	40 on Wellness score, 6 months post infection diagnosed with CFS	Exertional fatigue (N = 32), Persistent symptoms 3 weeks disease onset (N = 15)	Assessed fatigue as mild symptoms	Fatigue observed (N = 5)	Tiredness (N = 62)	N = 69 (<28 days), N = 15 (>28 days)	1/4 symptomatic patients had fatigue

fatigue is a relatively common long-term complication of COVID-19 in athletes. A case review by Petraceck *et al.*, (2021) highlighted a case of CFS in young athlete but other studies assessed fatigue on a shorter time frame [20].

Developing persistent fatigue is thought to be independent of COVID-19 severity across all age groups and genders [34] [35]. Most papers excluded asymptomatic patients whilst some omitted severity. Brito *et al.*, (2021) found no significant difference in cardiovascular activity between asymptomatic and symptomatic athletes [14]. The majority of papers used either lateral flow testing or PCR swabs to determine COVID-19 status. Petek *et al.*, (*2021*) and Schwellnus *et al.*, (2021) used an LFT, PCR swab and antibody test [19] [21]. Schwellnus *et al.*, (2021) assessed a large number of symptoms including fatigue along with median duration but included athletes assumed to have COVID-19 without a formal diagnosis [21]. Hull *et al.*, (2021) also included seventy-six athletes clinically assumed to be positive [15].

5.2. Limitations and Future Implications

Despite the clear association between COVID-19 and symptoms of long term COVID-19 sequela, the absence of standardised and validated PROMs to assess CFS or persistent fatigue results in a large heterogeneity within literature regarding this topic. The effect of lockdowns on sporting cancellations can also have a compounding factor on athlete fatigue due to decreased fitness levels. The effects of factors such as the type of athlete, type of sport and ethnicity of athlete on fatigue was equally unclear as the studies assessed either omitted or did not differentiate inter-variably. It was difficult to assess the impact of age as competitive athletes are generally younger rendering a selection bias. There is also an inherent sparse-data bias due to the difficulty assessing CFS as it takes six months to diagnose, thus requiring a large number of participants over a prolonged period. This study excluded non-English papers as well as non-competitive athletes, such as amateur bodybuilders, which could have yielded further insight. The emergence of new variants was also not assessed despite the different effects they confer.

Sparse-data bias meant that further follow-up studies are required to assess if the prevalence of CFS in athletes is similar to the general population. The potential impact on the commercial and marketing value of the players was not assessed and further studies are required to investigate this.

6. Conclusion

Across cohorts of elite athletes from different sporting backgrounds, COVID-19 is associated with persistent COVID-19 symptoms including fatigue. There is currently little evidence of CFS, but this could be due to a lack of relevant PROMs. Male athletes were found to be overall more likely to suffer from adverse COVID-19 outcomes including fatigue than female athletes although the cause is unclear. Additional work is required to further investigate these findings as well as develop new PROMS specific to CFS. This paper provides some insight regarding the effect of COVID-19 on athletes and can help with the associated fatigue symptoms to aid athlete recovery.

Data Is Available Upon Request

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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