Myocarditis in Athletes Recovering from COVID-19

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To assess the event rates of myocarditis detected by Cardiac Magnetic Resonance (CMR) in athletes who recovered from COVID-19. The prevalence of COVID-19-related myocarditis in the athletic population ranges from 1 to 4%. Even if the event rate is quite low, current screening protocols are helpful tools for a safe return to play to properly address CMR studies.

Keywords: COVID-19 ; myocarditis ; athletes

1. Introduction

COVID-19, which was first reported in the city of Wuhan, China, has been spreading rapidly worldwide since December 2019 [1][2]. The majority of the SARS-CoV-2 infection symptoms were respiratory in nature (including fever, cough, pharyngodynia, fatigue, and complications related to pneumonia and acute respiratory distress syndrome) [3]. Children and adolescents often experience asymptomatic or paucisymptomatic infection [4]. Cardiac involvement, mainly consisting of myopericarditis, has been described by several authors on patients both with severe disease and with asymptomatic or paucisymptomatic infection [5][6]. Even if the true prevalence of COVID-19-related myocarditis is difficult to establish, due to the lack of the specific diagnostic assessment modalities in early reports, a recent study reported a prevalence between 15% and 27.8% among cases of severe COVID-19 pneumonia [7]. As for cardiac involvement, autopsy reports published so far demonstrated cardiac dilatation, necrosis, lymphocytic infiltration of the myocardium and small coronary vessel microthrombosis as the main cardiac pathological findings [8], with increasing evidence that direct infiltration of SARS-CoV-2 into myocardial cells is possible and frequently accompanied by a strong inflammatory cytotoxic T-cell response [9] and by an interferon-mediated hyperactivation of the innate and adaptive immune system [7]. However, all anatomopathological data may still be influenced by the lack of a uniform post-mortem COVID-19 diagnostic protocol, which has not yet been proposed [10]. The main clinical manifestations of COVID-19 cardiac involvement described so far have been arrhythmias, coronary thrombotic events, acute heart failure and even cardiogenic shock [7].

At the beginning of the pandemic, cases of myocarditis had been frequently described in hospitalized patients, but no information was available regarding cardiac involvement in athletes [5]. As assessed in a recent systematic review, several studies have subsequently investigated the possible cardiovascular complications of COVID-19 infection in young athletes [11]. This because myocarditis is recognized as a cause of sudden death in athletes [12].

For this reason, International Sports Cardiology Expert Panels have developed a set of guidelines on returning to sport in athletes who have had a COVID-19 infection. Cardiopulmonary screening, in this context, has been considered of paramount importance [13][14].

2. Myocarditis in Athletes Recovering from COVID-19

2.1. Pathophysiology of the COVID-19 Myocarditis

The pathophysiology of myocardial involvement during COVID-19 infection is still debated. Some hypotheses include direct damage to cardiomyocytes, systemic inflammation, myocardial interstitial fibrosis, interferon-mediated immune response, exaggerated cytokine response by T helper cells type 1 and 2, coronary plaque destabilization, hypoxia [15], and molecular mimicry [16], among others. However, the two main theories at present are (1) the direct role of angiotensin-converting enzyme 2 (ACE2) receptors; and (2) a hyperimmune response [17]. Teresa Castiello et al. reported that included 38 case reports, showed only in one case the presence of SARS-CoV-2 in endomyocardial biopsy (EBM). In the other cases, histology showed inflammation of the myocardium with a predominance of macrophages, whereas myocyte necrosis was limited.

2.2. Importance of the Diagnosis of Myocarditis in Athletes

Myocarditis plays an important role in the pathogenesis of sudden cardiac death (SCD) in athletes [19]. Physical exertion is probably a trigger for dangerous arrhythmias and may have the potential to further propagate myocardial damage in athletes with myocarditis [20]. In adjunct, exercise has an important impact on immune function and may therefore lead to changes in the biological response of athletes to myocarditis. Exercise of moderate intensity can significantly improve the immune response [21], whereas intense exercise (and a lack in restoration) can lead to a dramatic decline in immune function [22]. Myocarditis represents a potential cause of SCD in athletes: in acute myocarditis, myocardial inflammation represents an arrhythmogenic substrate that predisposes patients to ventricular arrhythmias (VAs); in chronic myocarditis, on the other hand, myocardial fibrosis promotes VAs through the creation of re-entry circuits around the myocardial scar [23]. For these reasons, current guidelines recommend a rest period of three to six months after the diagnosis of myocarditis [24].

Nowadays, as stated above, it is well known that COVID-19 may predispose to myocarditis, even in athletes, and this is the reason that leads International Sports Cardiology authors and societies to propose screening protocols aimed to assess the cardiopulmonary system in athletes who recovered from COVID-19 [14][25][26][27].

2.3. Cardiac Magnetic Resonance' Abnormalities in Athletes

ITo date, observational data suggest that LGE in the midwall and septal segments carries the highest risk of SCD in the context of both reduced and preserved left ventricular ejection fraction (LVEF), independently from clinical symptoms, and LGE seems to be superior to other prognostic factors such as LVEF, left ventricular end diastolic volume, or NYHA functional class [23]. Zorzi et al. demonstrated that isolated, non-ischemic left ventricular LGE may be associated with life-threatening arrhythmias and SCD in athletes and that, due to its subepicardial/myocardial location, left ventricular scarring is often not detected by echocardiography [28]. Further interpretation of these findings, even in SARS-CoV-2 infection, needs follow-up data, which are not always provided in all available studies: in fact, only a few studies [29][30][31][32][33] reported short-term follow-up data with a control CMR, with a small number of athletes involved. As for arrhythmias, the issue is still present: only three studies [34][35][36] evaluated the presence of arrhythmias after COVID-19 (two of them comparing it with a pre-COVID ECG) and none had an arrhythmic follow-up through time.

2.4. SARS-CoV-2 Vaccination and Myocarditis or Myopericarditis

In a recent large cohort study by A. Husby et al. [37] the association between mRNA-1273 vaccination and an increased rate of myocarditis or myopericarditis compared to unvaccinated individuals was confirmed; an increased rate of myocarditis or myopericarditis was also observed among female individuals with BNT162b2 vaccination. However, in contrast to the Israeli [38][39][40] study and the USAstudy [41], showed an overall low absolute rate of myocarditis or myopericarditis cases after SARS-CoV-2 mRNA vaccination among female participants and younger age groups. It also highlighted that clinical outcome after myocarditis or myopericarditis events are predominantly mild, providing evidence to support the overall safety of SARS-CoV-2 mRNA vaccines.

3. Conclusions

The prevalence of COVID-19-related myocarditis in the athletic population varies in different studies, but the overall estimate rate is quite low, around 1%. However, if CMR study is requested based on a clinical-instrumental suspicion, the estimate rate is around 4%. Even if the rate remains relatively low, as myocarditis remains one of the causes of SCD in athletes, recognizing and treating it is of paramount importance [14][25][26]. Current screening protocols are helpful tools for a safe return to play in athletes who recovered from COVID-19 and, guided by a good clinical practice, should lead a decision in CMR studies. As for the relationship between CMR and other laboratory or instrumental abnormalities (ECG, ECHO, and hs-TN), there is not any strong association between these parameters.

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