SCIENCE
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BASIC STUDY

Cardiac involvement in athletes infected by SARS COV-2 disease

Atteinte cardiaque chez les athlètes infectés par le SARS COV-2

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Summary
Objectives. — The aim of the present study was to conduct a review of the current literature evaluating the available evidence to date in terms of epidemiology, pathophysiology and clinical presentation of COVID-19 in relation to cardiovascular involvement, with a special focus on the myocarditis model, in the population of athletes (professional and recreational) who are preparing to return to competitions, with the ultimate aim of guaranteeing maximum safety for resuming sports activities.
News. — The COVID-19 pandemic has resulted in the inevitable cancellation of most sports activities, practiced at both a professional and amateur level, in order to minimize the risk of spreading the infection. Since the number of athletes who tested positive was rather high, the potential cardiac involvement in this peculiar population of subjects contracting the disease in a mild (asymptomatic, slightly symptomatic) or moderate form, has recently raised concerns following the observation of cases of recorded myocardial damage, myocarditis, arrhythmias and a first reported case of Sudden Cardiac Death (SCD) in a 27-year-old professional basketball player. Several studies even seem to confirm the possibility of permanent impairment of the cardiorespiratory system following the infection. Medical history, biomarkers, electrocardiographical and cardiac imaging features appear to be crucial in distinguishing cardiovascular alterations related to COVID-19 infection from typical adaptations to exercise related to athletes' heart.

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Prospects and Projects. — Clarifications and prospective data based on long-term follow-ups on larger populations of athletes are still needed to exclude the development of myocardial damage capable of negatively affecting prognosis and increasing cardiovascular risk in athletes recovered from COVID-19 in asymptomatic (simple positivity to SARS-COV-2) or in a mild form.

Conclusion. — From a clinical point of view extreme caution is necessary when planning the return to sport (Return To Play—RTP) of athletes recovered from a mild or asymptomatic form of COVID-19: a careful preliminary medical-sports evaluation should be carried out in order to assess the potential development of myocardial damage that would increase their cardiovascular risk.

Résumé

Objectifs. — Le but cette étude était de mener une revue de la littérature actuelle évaluant les différents éléments disponibles en termes d'épidémiologie, de physiopathologie et de présentation clinique de l'atteinte cardio-vasculaire du COVID-19. Une attention particulière sera donnée aux lésions myocardiques dans la population des athlètes, à la fois de niveau professionnel et amateur, qui s'apprêtent à reprendre la compétition, dans le but de garantir une sécurité maximale dans la reprise des activités sportives.

Actualités. — La pandémie de COVID-19 a entraîné l'annulation inévitable de la plupart des activités sportives, pratiquées à la fois à un niveau professionnel et amateur, afin de minimiser le risque de propagation de l'infection. Le nombre d'athlètes testés positifs étant plutôt élevé, les répercussions cardiaques potentielles dans cette population particulière de sujets contractant la maladie sous une forme légère (asymptomatique, légèrement symptomatique) ou modérée, a récemment soulevé des inquiétudes suite à l'observation de cas de lésions myocardiques, de myocardites, d'arythmies et d'un premier cas signalé de mort subite chez un basketteur professionnel de 27 ans. De plus, plusieurs études semblent confirmer la possibilité d'une altération permanente du système cardiorespiratoire suite à l'infection. Les antécédents médicaux, les biomarqueurs, les caractéristiques électrocardiographiques et à l'imagerie cardiaque semblent ainsi être des éléments cruciaux pour pouvoir distinguer les altérations cardiovasculaires liées à l'infection au COVID-19 des adaptations typiques à l'exercice des cœurs d'athlètes.

Perspectives et projets. — Des précisions et des données prospectives basées sur des suivis à long terme sur des populations plus importantes d'athlètes sont encore nécessaires pour exclure le développement de lésions myocardiques capables d'affecter négativement le pronostic et d'augmenter le risque cardiovasculaire chez les athlètes en rémission d'une infection au COVID-19 asymptomatique (positivité simple au SARS-COV-2) ou sous une forme légère.

Conclusion. — D'un point de vue clinique, une extrême prudence est nécessaire lors de la planification du retour au sport des athlètes en rémission d'une forme légère ou asymptomatique de COVID-19: une évaluation médico-sportive minutieuse de ces patients doit être effectuée afin d'évaluer le développement potentiel de lésions myocardiques qui augmenteraient leur risque cardiovasculaire.

1. Introduction

In March 2020, the World Health Organization (WHO) declared a pandemic state of emergency due to the spread of Coronavirus Disease (COVID-19), caused by the SARS-CoV-2.

This definition derives from the initial Severe Acute Respiratory Syndrome (SARS) outbreaks recorded in Wuhan, a Chinese city in Hubei province, in December 2019 [1].

Although clinical manifestations of COVID-19 are largely dominated by the now well-known respiratory symptoms [2,3], several patients have also reported significant consequences affecting the cardiovascular system [4].

Several studies involving patients hospitalized for COVID-19 and with underlying cardiovascular diseases have actually shown a higher mortality, under the same clinical conditions [4,5].

Parallel to the in-hospital finding of major arrhythmias, an increase in the incidence of cardiac arrest and sudden cardiac death has been reported in various geographic regions with a high prevalence of COVID-19: first of all Lombardy (Italy) which found a 77% increase in incidence compared to 2019 [6].

The COVID-19 pandemic has also resulted in the inevitable suspension/cancellation of most sports activities, practiced at both a professional and amateur level, in order to minimize the risk of spreading the infection.

Since the number of athletes who tested positive was rather high, the potential cardiac involvement in this particular population of subjects contracting the disease in

a mild (asymptomatic, slightly symptomatic) or moderate form, has recently raised concerns following the observation of recorded cases of myocardial damage [7], myocarditis [8], arrhythmias and a first reported case of Sudden Cardiac Death (SCD) in a 27-year-old professional basketball player [9].

Several studies even seem to confirm the possibility of permanent impairment to the cardiorespiratory system following the infection [10].

The goal is to examine the evidence available to date in terms of epidemiology, pathophysiology and clinical disease of COVID-19 in relation to cardiovascular involvement in the population of athletes (professional and recreational) who are preparing to return to competitions, with the ultimate aim of guaranteeing maximum safety for resuming sports activities.

2. Sars-CoV-2 and tropism for the cardiovascular system

What mainly distinguishes SARS-CoV-2 from other viruses of the *Coronaviridae* family is the marked tropism for the cardiovascular system. This is exerted through its ability to bind to the Angiotensin-converting enzyme 2 (ACE2) receptor, mainly expressed by myocardial, lung and endothelial tissue, through the *spike* protein and by the cooperation of different transmembrane proteases and heparansulfate [11].

The presence of SARS-CoV-2 RNA was actually proved, by autopsy, apart from in the lungs also in correspondence with the myocardial, renal and hepatic tissue, with the finding of high concentrations of viral copies in myocardiocytes in 16 of 22 deceased patients [12].

The SARS-CoV-2 infection would be able to affect the cardiovascular system in two basic ways:

- direct infection of myocardiocytes, binding to the ACE2 receptor by means of the spike protein and penetrating the cell through the fusion of the viral membrane with the cellular one, resulting in elevated levels of troponin (indicator of myocardial damage), acute alteration of the function of the heart muscle and potential development of residual and permanent scar tissue, increased vulnerability of cell substrate to malignant ventricular arrhythmias and to the development of heart failure. The virus has also shown a surprising ability to infect cardiomyocytes, deriving from induced pluripotent stem cells (iPSCs) in vitro, causing cellular apoptosis and cessation of contractile activity within 72 hours of exposure [13], and even fragmentation of muscle fibers and a complete dissolution of the structures responsible for the contraction [14]. Myocardial damage, defined by plasma troponin levels higher than the 99th percentile of the upper limit of the reference range [15], is commonly found in subjects affected by COVID-19, with a prevalence of at least 20—25% in hospitalized patients and 50% of those who already originally had risk factors or cardiovascular diseases [16]. Furthermore, troponin levels positively correlate with those of pro-inflammatory markers (C-Reactive Protein, Interleukin-6, Ferritin, LDH and Neutrophils), cardiac dysfunction (proBNP) and with in-hospital mortality [17];

- indirect ''cytokine storm'' that typically develops during the severe form of infection: consists of a systemic inflammatory response involving platelets, neutrophil granulocytes, macrophages and lymphocytes, which release proinflammatory cytokines into the circulation that contribute to the development of a endotheliitis and intravascular coagulation, responsible for a reduced blood supply to the tissues and consequent necrosis which can lead to a significant reduction in cardiac function, comparable to that found in other forms of sepsis.

On a clinical level, a wide spectrum of cardiovascular manifestations would derive from this inflammatory form of non-ischemic myocardial damage: from necrosis limited to myocardiocytes — ''myocardial damage'' —, to acute inflammatory forms (myocarditis), major ventricular arrhythmias, biventricular heart failure and occasionally cardiogenic shock [18].

This type of inflammation is therefore characterized by an early acute phase of viral replication within myocardiocytes, followed by a sub-acute phase of immuno-inflammatory response and by a chronic phase that can swing from a complete recovery at best, up to fulminant heart failure in the worst cases.

The chronicization of this inflammatory process and the resulting pro-arrhythmic effect, capable of altering the electrical activity of the heart, may also persist even after the infectious episode has healed.

In fact, of the cohorts of patients admitted to hospital due to infection with bilateral interstitial pneumonia and respiratory failure, damage to the myocardium was demonstrable in 10%—28% of cases, with a mortality of 69.4%, and permanent cardiac alterations over time were documented in these subjects through cardiac magnetic resonance imaging (cMRI), even following discharge and recovery [19].

3. COVID-19 and the athletes' heart: the myocarditis model

Before the COVID-19 pandemic, myocarditis accounted for 7—20% of the causes of Sudden Cardiac Death (SCD) in both young athletes (under the age of 35) and physically active individuals [20], with a higher incidence during the course exercise, which proved to be a worsening factor in the clinical infectious picture [21,22].

Myocarditis, a widespread inflammation of the myocardium (more extensive than myocardial damage), is comparable to a mixture of myocardial damage and the systemic immune-inflammatory response to that damage, capable of extending to involve the pericardium and characterized by the typical autoptic finding of lymphocytic infiltrates. The involvement of myocardiocytes, largely responsible for the electrical conduction of the impulse, can result in conduction slowdowns/blocks and malignant ventricular arrhythmias, both of which can lead to cardiocirculatory arrest [23].

3.1. Etiology

The prevailing etiology, especially in the populations of athletes studied, is undoubtedly that of the viral type: the main pathogens capable of causing acute myocarditis are the same found in infectious episodes of the upper airways and the gastrointestinal system. Endomyocardial biopsy samples in fact revealed the presence of Adenovirus, Enterovirus (in particular Cytomegalovirus), Parvovirus B19 and Human Herpes Virus Type 6 (HHV6) [24,25].

Infectious bacterial, mycotic and protozoal causes are much less prevalent, particularly in the general population. Schistosomiasis has proved to be one of the main causes in Africa, the Far East and Central and South America; followed by Chagas disease (North America, Europe, Japan and Australia), Tuberculosis (Asia, Africa and Eastern Europe), Hepatitis C (Japan) [24].

The common finding of Lyme disease (Borreliosis) is interesting as a causative agent of myocarditis in athletes who practice outdoor sports.

Non-infectious agents, such as inflammatory bowel disease, rheumatoid arthritis, collagenosis, vasculitis and sarcoidosis (therefore pathologies with a marked autoimmune nature) should also be considered [24,26].

Furthermore, pharmacological agents such as some classes of antibiotics, diuretics, tricyclic antidepressants, cocaine and doping substances such as amphetamines, dissociation curve modulators and anabolic steroids can potentially induce myocardial inflammation and cardiomyopathy [27,28].

Elite athletes appear to have an increased risk of contracting viral infections and subsequent myocarditis due to the high probability of exposure to pathogenic microorganisms (travel and international competitions) and/or impaired immune function (failure to interrupt training during minor infectious episodes or return to training too early compared to an optimal period of convalescence, particularly strenuous training sessions and competitions or performed in extreme weather conditions) [29].

3.2. Clinical presentation

When SARS-Cov-2 is the viral agent responsible for the infection, the onset of symptoms may include fever (body temperature > 37.5 °C), cough, anosmia and ageusia/dysgeusia, nausea, vomiting and/or diarrhea, headache, sore throat, nasopharyngeal congestion, myalgia, asthenia and easy fatigue [2].

In case of involvement of the cardiovascular system, the evolution of the clinical picture can acquire characteristics of acute myocarditis, whose symptoms can however be extremely variable and highly non-specific, if not absent. Although the clinical findings are almost overlapping between populations of sedentary and physically active individuals, the latter, especially if professional athletes, by virtue of greater awareness and body sensitivity, complain of a rather wide spectrum of symptoms.

In this case, the following symptoms are noted: asthenia and fatigue, reduced performance, widespread arthromyalgia, headache, mood deflection. Added to these are new atrial and/or ventricular arrhythmias which can lead to vertigo, dizziness and pre-syncopal symptoms, especially in athletes practicing endurance activities with a heart rate (HR) at rest of less than or equal to 50 bpm. At rest or following the training session, muscle pain or general malaise not related to exercise may also arise.

An increase of 5—10 bpm in the usual average HR at rest could indicate the potential presence of a subclinical infection. In the more severe (and much less frequent) cases of myocarditis, the initial presentation is characterized by dyspnea on exertion, extreme fatigue, signs of heart failure or even cardiogenic shock, as well as rhythm alterations or an aborted SCD [20,24].

In the acute phase of the disease, physical exercise can cause the acceleration of viral replication and the amplification of the immune-inflammatory response, resulting in an increased risk of myocardial damage and consequent myocardiocyte necrosis. Based on the extent of necrosis, scar tissue that will develop as a result of myocarditis can potentially increase the risk of developing atrial and/or ventricular tachyarrhythmias.

The difficulty in interpreting the symptoms, in combination with undefined diagnostic findings, results in a variety of possible diagnoses: from COVID-19 infection with exclusive involvement of the airways and/or respiratory system without involvement of the cardiovascular system, to mild myocarditis, without excluding a clinical picture purely correlated to sports practice, such as muscle fatigue and soreness, therefore only in the presence of a positive SARS-CoV-2 molecular swab.

3.3. Diagnosis

3.3.1. Surface electrocardiography

Typical surface electrocardiogram (ECG) findings are [30]: 1. Supraventricular and ventricular arrhythmias, 2. Diffuse ST-segment elevation in several leads (with associated signs of pericarditis), 3. T-wave inversion, 4. Left Branch Blocks, 5. Ventricular ectopic beats, 6. High-grade atrioventricular blocks (especially Grade 2, Mobitz 2 and Grade 3 - complete) and 7. Low voltages (often related to pericardial effusion and/or myocardial edema) [31,32]. However, the sensitivity of the ECG in diagnosing myopericarditis using the aforementioned criteria is rather limited (Sn = 47%) [33]; more than 70% of athletes have repolarization anomalies characterized by elevation of the J point, ascending and concave ST segment in the inferior-lateral precordial leads and high T waves, characteristics that can be mistaken for myo-pericarditis. On the other hand, the specificity of ECG changes in diagnosing myocarditis has not yet been established, but it is estimated to be rather limited. In fact, in most of the subjects tested with acute myocarditis, the ECG may appear completely normal, especially when the differential diagnosis is complicated by the presence of ''athlete's heart'' characteristics (particularly in endurance athletes), with electrocardiographic patterns of cardiac adaptation to long-standing physical exercise that can mimic the typical ECG findings of myocarditis (Table 1): primarily low-grade atrioventricular blocks, sinus bradycardia and ST segment elevation in the anterior precordial leads V2-V3 [34]. In these cases a comparison with previous ECGs is particularly useful [35].

Table 1 Characteristics that can help differentiate physiological adaptation from pathological change in athletes with suspected COVID-19 cardiac involvement.

		Physiology	Pathology
History	Gandhi 2020 Halle 2020, Kindermann 2012	Asymptomatic Mild symptoms Muscle fatigue Soreness Mood deflection	Limiting symptoms (dyspnea—on exertion—, chest pain, palpitations, syncopal event concerning for arrhythmia, exertional intolerance) Increase of 5—10 bpm in the usual average HR at rest
Biomarkers	Halle 2020, Donnellan 2018, Kleiven 2019, Bardajì 2018	Absence of troponin elevation Troponin peak with complete resolution in 24—48 h post-exercise	Sustained troponin elevation of two samples >9 percentile
EKG	Pelliccia 2019, Maron 2015, Sharma 2018, Corrado 2020	White athletes TWI V1—V2 Black athletes TWI V1—V4, often accompanied by J point ST elevation Low grade AV blocks	New or evolving: TWI (especially lateral) ST depression or elevation Q waves Complex VEBs Supraventricular and/or ventricular arrhythmias (at rest or on exertion) High grade AV blocks LBBs
Echo	Felker 2000, Churchill 2020, Inciardi 2020, Szekely 2020, Kim 2016, Phelan 2020	Left heart Symmetric remodeling No regional structural or functional wall motion abnormalities Symmetric wall thickening <12 mm (< 15 mm in black male athletes) Normal or low-normal EF Increase in LVEF > 10% with exercise Right heart RVEDD:LVEDD < 1.0 Coordination and consistency of regional RV wall motion, contraction and deformation Increase in RVEF with exercise No signs of pericardial diffusion	Left heart Disproportionate/severe LV dilation Regional LV wall motion abnormalities Asymmetric wall thickening LVEF < 50% Failure to increase LVEF with exercise Right heart RVEDD:LVEDD > 1.0 RV segmental wall motion abnormalities and mechanical dysynchrony Reduced RVEF augmentation with exercise More than trivial pericardial diffusion
CMR	Phelan 2020, Ferreira 2018, Rajpal 2020, Brito 2020, Malek 2021	LGE as a sign of patchy fibrosis Isolated myocardial edema	LGE in pathological distribution (subepicardial or mid-myocardial) with other clinical investigations/history suspicious of pathology

TWI: t wave inversion; AV: atrioventricular; VEB: ventricular ectopic beat; LBB: left branch block; LV: left ventricle; LVEF: left ventricular ejection fraction; RVEDD: right ventricle end-diastolic diameter; LVEDD: left ventricle end-diastolic volume; RV: right ventricle; RVEF: right ventricular ejection fraction; LGE: Late Gadolinium Enhancement; CMR: cardiac magnetic resonance.

3.3.2. Electrocardiography in 24 hours

The execution of a Holter-ECG in 24 hours can reveal the presence of rhythm anomalies, such as ventricular arrhythmias with morphological characteristics and complexity not common to those typically found in athletes, anomalies which should therefore be placed in differential diagnosis with arrhythmias with benign prognosis [36].

3.3.3. Humoral biomarkers

Currently, certain data on the real prevalence of myocardial damage, myocarditis and pericarditis in athletes affected by and recovered from COVID-19 are limited to a few observational studies on case series.

Evaluation of suspected myocarditis in athletes, especially those with mild or asymptomatic symptoms, can be challenging. Even in cases with a variety of skewed diagnostic findings, myocarditis cannot always be diagnosed with certainty.

In any case, it is assumed that in athletes affected by COVID-19, even asymptomatic or with mild symptoms (without the need to be hospitalized), there is still a subclinical damage to the myocardium, despite the fact that anomalies that have emerged as markers of COVID-19-correlated myocardial damage may overlap the well-known characteristics of the athlete's heart, an anatomical-physiological picture arises resulting from adaptation to training (Table 1) [37].

In elite athletes it is essential to consider the influence that intense and prolonged exercise exerts on the kinetics of cardiac troponin secretion [38]. For example, exercise sessions in healthy athletes often induce, physiologically, a temporary increase in plasma concentration of troponins, which reaches a peak and complete resolution in a time interval of approximately 24–48 hours [39,40].

Troponin dosage (High-Sensitivity cardiac Troponin—hs-cTn) as a screening test for COVID-19 related myocardial damage should be performed at least 48 hours after the end of the last exercise session, repeating it after another 24–48 hours of rest in case the first dosage is high.

However, myocardial damage associated with COVID-19 and its long-term consequences in athletes could be significantly underestimated if the assessment of damage was based solely on the presence of elevated troponin levels. It is necessary to underline that there is still no established reference range for a population of athletes: the prognostic value of high hs-cTn concentrations below the 99th percentile has been demonstrated, emphasizing that normal hs-cTn values cannot exclude the presence of subclinical myocardial damage [15,41].

Evaluation of humoral biomarkers should therefore be performed in conjunction with additional diagnostic criteria. Persistently high levels of troponin necessarily require a thorough characterization of the myocardium through imaging tests.

3.3.4. Echocardiography

Performing an echocardiogram on athletes suffering from a mild form of COVID-19 has been suggested in various risk stratification and Return-To-Play protocols [36].

Non-COVID-19 myocarditis has typical characteristics of dilated, hypertrophic (due to edema) and/or restrictive cardiomyopathy, with concomitant left ventricular dysfunction or diastolic dysfunction with preserved ejection fraction [42].

Understanding and defining the spectrum of echocardiographic findings in the context of COVID-19 infection in athletes is still evolving, as most systematic studies of echocardiographic abnormalities have been conducted on hospitalized patient populations and often with serious conditions [43–45].

Benign consequences of cardiac adaptation to training include, among others, mild reduction in left ventricular ejection fraction [46] and non-ischemic myocardial fibrosis, further complicating the diagnosis of COVID-19 related myocardial injury [47]. Echocardiographic evaluation in athletes has the primary goal of distinguishing cardiovascular alterations related to COVID-19 infection from cardiac adaptations resulting from intense, prolonged and long-standing training (Table 1).

In the case of myocarditis affecting the left heart, alterations of the regional parietal kinetics, systolic dysfunction of the left ventricle, isolated diastolic dysfunction and segmental increases in the wall thickness due to edema are found. As regards the right heart, right ventricular dysfunction is one of the main anomalies described in patients with COVID-19, due to pulmonary and vascular complications that dominate the clinical picture of acute disease: any increase in pulmonary vascular resistance can determine right ventricular dysfunction over time [36].

The typical cardiac remodeling induced by physical exercise is instead characterized by a symmetrical and balanced increase of all heart chambers, with symmetrical hypertrophy (with eccentric mode in most cases), especially in athletes practicing endurance sports or alternating aerobic-anaerobic sports (mixed); moreover, the ejection fraction is often normal in athletes, with the exception of endurance athletes who may express a slight reduction in FE at rest, associated in any case with a normal diastolic function, a consensual increase in FE and a supra-normal functional capacity revealed by exercise [48,49]. In athletes, it is even more difficult to distinguish exercise-induced right remodeling from that resulting from an increase in pulmonary vascular resistance: therefore, both qualitative and quantitative evaluation is appropriate. For example, a potentially useful distinctive parameter that has been suggested is the ratio between the end-diastolic diameter between right ventricle and left ventricle (acquired in the apical window): in the athlete this parameter settles on the value of 0.8 ± 0.1 and frequently does not exceed 1.0 [36].

3.3.5. Cardiac Magnetic Resonance (CMR)

To complete the cardiac evaluation, in support of both biohumoral and echocardiographic data, Cardiovascular Magnetic Resonance (CMR) is proving extremely useful for an accurate characterization of myocardial damage and the inflammatory picture, net of remodeling characteristics of the athlete's heart [36].

For example, in the absence of myocardial damage or inflammation documented by CMR, in the presence of an increase in troponins, other systemic causes of this biohumoral finding should be sought [50].

In addition, CMR is able to document imaging findings suggestive of myocardial damage, myocardial inflammation and even tissue edema resulting from intense, prolonged and long-standing exercise [38,51].

Numerous recently published studies have evaluated cardiac abnormalities found through CMR on athletes recovered from COVID-19 infection. Cardiac MRI performed on 26 asymptomatic or mild COVID-19 athletes (average age 19 years), with normal ECG, negative humoral biomarkers (hs-cTn) and normal echocardiogram, revealed the presence of Late-Gadolinium-Enhancement (LGE) in 46% of cases, with evidence of myocarditis in 15% [52]. However, the absence of an appropriate control group and standardized CMR Imaging data on populations of young athletes significantly limits the accuracy in distinguishing minimal scarring regions from acquisition artifacts and partially nullify the clinical use of such data [19,36].

In another observational study involving 46 athletes with an average age of 19 years and recovered from the disease, screening by CMR showed the presence of pericardial hyperintensity in 41% of cases and LGE in the myocardium in only 2% of cases (1 athlete out of 46) [53].

Contrary to the previous two studies, a CMR survey conducted on 12 Hungarian athletes (median age 23 years) did not show any evidence of myocardial damage or inflammation [36,54].

Cardiac Magnetic Resonance is the most suitable imaging modality for the evaluation of global and regional ventricular function, with a specific focus on the presence, degree and extent of inflammation, edema and ventricular fibrosis resulting from myocardial damage and/or myocarditis, due to its peculiar ability to provide a precise characterization of myocardial tissue.

LGE is able to provide an accurate assessment of the presence, localization and transmural extension of fibrosis and/or myocardial scarring [55]. A pattern of signal hyper-intensification on LGE acquisitions at the parietal and/or subepicardial level, without coronary artery disease and in association with an increased hs-cTn is highly suggestive of acute myocarditis and is a significant marker of poor prognosis (heart failure, major ventricular arrhythmias, and mortality) in patients with myocarditis [56].

In a recent retrospective cohort study that included 26 professional athletes with COVID-19 with a mainly asymptomatic course or mild symptoms, the execution of CMR 1—2 months after diagnosis did not demonstrate the presence of criteria for active myocarditis. However, myocardial abnormalities were still found in 19% of cases (5 athletes), of which 4 with borderline findings of isolated myocardial edema and one characterized by non-ischemic LGE with pleuropericardial effusion [57].

Isolated myocardial edema, in the absence of additional markers of acute myocarditis or other CMR abnormalities and in the presence of normal biohumoral levels of markers of myocardial damage in asymptomatic individuals, is an entity to be considered with extreme caution. First of all because it has a rather limited specificity as a marker of myocarditis [58]; secondly, findings of transient myocardial edema were observed in the days following a marathon, proving to be totally reversible after three months without further complications and without interrupting the activity [59]; finally isolated myocardial edema in the absence of signs of fibrosis has not been shown to independently influence the prognosis in subjects with suspected myocarditis [60].

For these reasons, it seems reasonable to assume that in the case of asymptomatic subjects or those with mild symptoms, in the absence of high levels of hs-cTn and in the presence of normal ECG and preserved systolic function, the finding of isolated signs of myocardial edema through CMR should not constitute a restrictive criterion for the return to activity.

In contrast, the presence of LGE regardless of its location or pattern of presentation (with the exception of fibrosis of the septum-ventricular junction) has largely been correlated with a worse prognosis [61]. This pattern of fibrosis has been frequently observed in asymptomatic athletes even with negative medical history for previous myocarditis [57,62]. In any case, it should suggest further investigations to exclude the risk of underlying cardiomyopathy and/or arrhythmias by means of detailed family history, 24 h Holter-ECG and Maximal Ergometric Test [63].

The CMR as a first-line examination is now globally over-estimated: the anomalies that can be found are often difficult to discriminate from the physiological adaptations connected to the ''athlete's heart'', enjoying in fact a poor diagnostic and prognostic significance if not related to the clinical-anamnestic picture (Table 1) [36,55].

The most recent evidence and reviews are confirming the usefulness of CMR as an exclusive second-line examination and/or for research purposes only in subjects with a high clinical pretest probability or symptoms prolonged over time.

4. Conclusions

The foregoing shows a clear involvement of the cardiovascular system in subjects who have contracted COVID-19. The main difficulty consists in the importance to be attributed to signs, symptoms and laboratory and instrumental findings in individuals recovered from the disease and practicing sports at a professional and amateur level for diagnostic and especially prognostic purposes.

Despite the various aspects and doubts that have yet to be clarified regarding the repercussions of the disease on the cardiovascular system, in a population with peculiar characteristics such as that of athletes (professional and non-professional), there is still a lot of pressure to return to sports competitions.

From a purely clinical point of view, however, it would be premature to return to sports without having carried out a careful preliminary medical-sports evaluation, since clarifications and prospective data based on long-term follow-ups are still needed to exclude the development of myocardial damage capable of negatively affecting prognosis and increasing cardiovascular risk in athletes recovered from COVID-19 in asymptomatic form (simple positivity to SARS-COV-2) or in a mild form.

At present, extreme caution is recommended when planning the post-COVID-19 Return To Play, emphasizing the importance of involving all key figures (Sports Doctor and staff, coach, athletic trainers and athletes themselves) in the decision-making process.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgment

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