



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Disponible en ligne sur

ScienceDirect
www.sciencedirect.com

Elsevier Masson France

EM|consulte
www.em-consulte.com



Clinical research

Cardiac screening before returning to elite sport after SARS-CoV-2 infection

Christophe Hédon^{a,*}, Frédéric Schnell^b, Philippe Sosner^{c,l,m,n}, Frédéric Chagué^d,
Iris Schuster^e, Marc Julia^f, Alexandre Duparc^g, Jean-Michel Guy^h, Nicolas Molinariⁱ,
Lionel Michaux^j, Frédéric Cransac^k, Stéphane Cade^k

^aPhyMedExp, University Montpellier, Inserm, CNRS; Cardiology and Physiology departments, University hospital Montpellier, Montpellier, France

^bDepartment of Sport Medicine, University hospital Pontchaillou; University Rennes 1, Inserm, LTSI-UMR 1099, Rennes, France

^cSport Medicine Center "Mon Stade", Paris, France

^dCardiology Department, University Hospital of Dijon, Physiopathology and brain cardiovascular epidemiology (PEC2), EA7460, University of Bourgogne Franche-Comté, Dijon, France

^ePhyMedExp, University Montpellier, Inserm, CNRS, University hospital Nîmes, Nîmes, France

^fDepartment of Sport medicine, Hospital of Perpignan, Perpignan, France

^gCardiology Department, Rangueil University Hospital, Toulouse, France

^hCardio-respiratory rehabilitation center of Loire, St Priest en Jarez, France

ⁱIDESP, Inserm, University Montpellier, University hospital Montpellier, Montpellier, France

^jCardiology practice, Montigny les Metz, France

^kCardiology Department, Clinique du Millénaire, Montpellier, France

^lAP-HP Hôtel-Dieu University Hospital, Diagnosis and Therapeutic Center, Paris, France

^mINSEP, medical center, Paris, France

ⁿMOVE laboratory (UR 20296), Poitiers University of sciences and technology of physical activity and sports, Poitiers, France

ARTICLE INFO

Article history:

Received 8 March 2022

Accepted 13 June 2022

Available online xxx

Keywords:

SARS-CoV-2

Screening

Athletes

Return-to-play

Myocarditis

ABSTRACT

Background: SARS-CoV-2 infection can induce cardiac damage. Therefore, in the absence of clear data, a cardiac evaluation was recommended for athletes before returning to play after recent SARS-CoV-2 infection.

Aim: To assess the proportion of anomalies detected by this cardiac screening.

Methods: We reviewed the medical files of elite athletes referred for cardiac evaluation before returning to play after a non-hospitalized SARS-CoV-2 infection (based on a positive polymerase chain reaction or antigen test) from March 2020 to July 2021 in 12 French centres.

Results: A total of 554 elite athletes (professional or national level) were included (median age 22 years, 72.0% male). An electrocardiogram (ECG), echocardiogram and exercise test were performed in 551 (99.5%), 497 (89.7%) and 293 (52.9%) athletes, respectively. We found anomalies with a potential link with SARS-CoV-2 infection in four ECGs (0.7%), three echocardiograms (0.6%) and three exercise tests (1.0%). Cardiac magnetic resonance imaging was performed in 34 athletes (6.1%), mostly due to abnormal first-line examinations, and was abnormal in one (2.9%). The rates of those abnormalities were not higher among athletes with cardiac symptoms or more severe forms of non-hospitalized SARS-CoV-2 infection. Only one athlete had a possible SARS-CoV-2 myocarditis and sport was temporally contraindicated. None had a major cardiac event declared during the follow-up.

Conclusion: The proportion of cardiac involvement after non-hospitalized forms of SARS-CoV-2 infection in athletes are very low. Systematic cardiac screening before returning to play seems to be unnecessary.

© 2022 Elsevier Masson SAS. All rights reserved.

Abbreviations: CI, confidence interval; CMR, cardiac magnetic resonance; ECG, electrocardiogram; LGE, late gadolinium enhancement; LVEF, left ventricular ejection fraction; LVNC, left ventricular non-compaction; RT-PCR, reverse transcriptase polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

* Corresponding author at: CHU Arnaud de Villeuneuve, 371, av. Doyen Gaston Giraud, 34090 Montpellier, France.

E-mail address: c-hedon@chu-montpellier.fr (C. Hédon).

<https://doi.org/10.1016/j.acvd.2022.06.005>

1875-2136/© 2022 Elsevier Masson SAS. All rights reserved.

1. Background

Myocardial injuries related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which have mainly been described in patients who were hospitalized for a severe form of SARS-CoV-2 infection, are associated with a poorer prognosis [1–3]. Whether myocardial damage in asymptomatic or moderately

symptomatic patients is possible has been less well established. Some studies have raised a concern regarding cardiac involvement, especially myocarditis [4] or pericarditis [5], even in asymptomatic athletes. Myocarditis due to SARS-CoV-2 infection is a key issue for sports cardiologists as this cardiac inflammation may be associated with an increased risk of sudden death during sport [6].

To limit SARS-CoV-2 propagation in a team or during a sporting event, regular screening for SARS-CoV-2 infection by reverse transcriptase polymerase chain reaction (RT-PCR) or antigen tests is often required by sports federations. Therefore, more frequent asymptomatic or pauci-symptomatic cases of SARS-CoV-2 infection are diagnosed in this specific population of athletes. After being released from the first lockdown in May 2020, in the absence of scientific data and on the basis of the precautionary principle, the French health ministry [7] and a number of sports federations proposed algorithms for carrying out systematic cardiac examinations before return-to-play (professional or high-level athletes) based on expert consensus [8–10]. These algorithms typically suggested a comprehensive cardiac assessment consisting of a clinical examination, a resting electrocardiogram (ECG), a resting echocardiography, a maximal exercise test, and a cardiac biomarker assay (especially troponin). Cardiac magnetic resonance (CMR) imaging is the best non-invasive examination for the diagnosis of myocarditis, but due to its limited availability, CMR remained at the discretion of the cardiologist, depending on the interpretation of the other examinations.

The aims of this study were to: (1) assess which examinations were performed in these athletes and (2) determine the proportion of abnormal cardiac findings among elite athletes who suffered from non-severe SARS-CoV-2 infection and were referred to a cardiologist before return-to-play.

2. Methods

2.1. Study population

We retrospectively reviewed the medical files of high-level athletes referred for cardiovascular evaluation before returning to play, from March 2020 to July 2021, in 12 French centres. High-level athletes were defined as professional players who were employed by their team and sportsmen/women playing at national level or higher who required annual medical supervision. SARS-CoV-2 infection was defined by a positive RT-PCR or antigen test. This test could have been performed because of a suspected infection (symptoms), in case of contact with an infected person or systematically (e.g. screening before a game). Athletes with a severe form of SARS-CoV-2 infection requiring hospitalization were excluded.

The study was approved by the Institutional Review Board (IRB-MTP_2020.11.202000647). All included athletes gave their informed consent to participate before data analysis.

2.2. Severity of SARS-CoV-2 infection symptoms

Athletes were classified into four groups according to the intensity of symptoms related to SARS-CoV-2 infection and the presence of cardiovascular symptoms, as proposed by Wilson et al. [11]. The first group included asymptomatic athletes. The second group was composed of patients with non-cardiovascular moderate symptoms (e.g. cough, fatigue, diarrhoea, headache, rhinorrhoea, myalgias) lasting < 14 days. The third group included patients with non-cardiovascular moderate symptoms lasting > 14 days. The last group was composed of patients with cardiovascular symptoms (i.e. chest pain, palpitations, dyspnoea) regardless of the severity of the extra-cardiovascular SARS-CoV-2 infection symptoms.

2.3. Complementary investigations

We analysed which types of cardiac examinations were performed and whether they were considered normal or abnormal. The anomaly was not considered if the finding had already been described in a previous examination (when available) before the COVID-19 period.

Resting ECGs assessed the occurrence of repolarization anomalies (T-wave inversion), ventricular arrhythmias (at least one premature contraction) or any other abnormality using international criteria for ECG interpretation in athletes [12]. Resting echocardiography assessed global left ventricular ejection fraction (LVEF) alteration, occurrence of wall motion abnormality, pericardial effusion or any abnormal echocardiographic findings raising concern for potential acute cardiac injury. Maximal exercise tests looked for the occurrence of significant ventricular arrhythmia (more than 10 ventricular premature contractions during the test or doublets or triplets) or exercise-induced repolarization disorder. CMR imaging examined LVEF alteration, occurrence of late gadolinium enhancement (LGE) (especially non-ischemic), pericardial effusion or any abnormal CMR findings raising concern for potential acute cardiac injury. Ambulatory ECG monitoring assessed the occurrence of significant supraventricular or ventricular arrhythmias (more than 500 premature contraction over 24 hours or ventricular doublets or triplets). Blood tests assessed abnormal elevation of cardiac troponin greater than the 99th percentile of the reference laboratory value.

A potential link with recent SARS-CoV-2 infection was established if the anomalies had not previously been described (in case of previous cardiac evaluation) and/or if the anomaly was not linked with another obvious cause. Information regarding any temporary sport restrictions after the cardiac assessment was reported. Finally, medical contact was established in December 2021 with all the doctors in charge of the teams or training centres to find out whether there had been any clinical cardiac events that may be linked to the SARS-CoV-2 infection (sudden death, hospitalization for a cardiac symptom or any cardiac symptoms requiring a new cardiac assessment).

2.4. Statistical analysis

Quantitative variables are described as medians and interquartile ranges or means \pm standard deviations. Qualitative variables are described as numbers and percentages, with 95% confidence intervals (CIs) calculated by the Wilson/Brown method. The occurrence of any abnormality on complementary examinations were compared between the four groups of patients (in terms of SARS-CoV-2 infection symptom intensity). For qualitative variables, a Fisher's exact test was used to compare groups when at least one group had < 5 subjects; otherwise, a Pearson's chi-square test was used. The significance level was fixed at 0.05 for all comparisons. The analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC, USA).

3. Results

3.1. Study population

Overall, 554 athletes (399 men [72.0%]) aged 12–47 years (median [IQR] age 22 [18–26] years) were included. Sports practiced were mostly team sports (68%), including soccer (20%), rugby (18%), handball (12%) and basketball (8%). Individual sports including combat sports (12%), swimming (4%), cycling (4%), athletics (3%), triathlon (2%) and gymnastics (2%).

The four groups comprised 195 athletes (35.2%) with no symptoms related to SARS-CoV-2 infection, 253 (45.7%) with non-cardiac

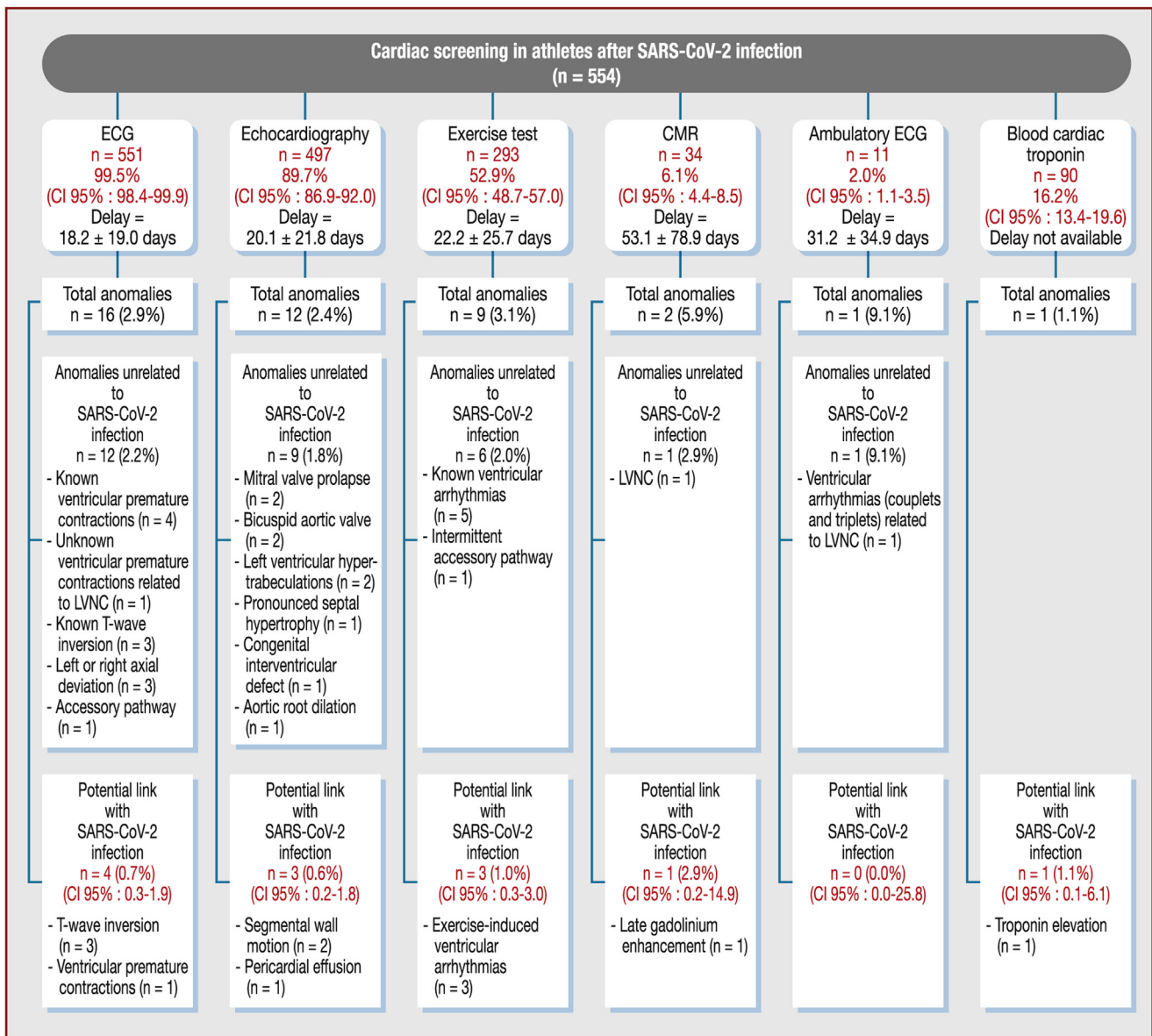


Fig. 1. Cardiac examinations performed and the proportions of anomalies found after recent SARS-CoV-2 infection. CMR: cardiac magnetic resonance; ECG: electrocardiogram; LVNC: left ventricular non-compaction; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

moderate symptoms lasting < 14 days; 84 (15.2%) with moderate non-cardiac symptoms lasting > 14 days; and 22 (4.0%) with cardiac symptoms (intermittent or not) during or after the SARS-CoV-2 infection.

3.2. Electrocardiogram

An ECG was performed in 551 athletes (99.5%) (Fig. 1) and the three athletes in whom an ECG was not performed were all asymptomatic (Table 1). The ECG was abnormal in 16/551 athletes (2.9%) and four anomalies (0.7%, 95% CI 0.3–1.9) had a possible link with recent SARS-CoV-2 infection. A new repolarization abnormality (pathological T-wave inversion) was described in three athletes (0.5%) (athletes 1–3 in Table 2). All three had normal echocardiography and exercise test and CMR was normal in two, but in one, sub-epicardial LGE was reported (athlete 3). A 3-month sport restriction was advised for this athlete. Two other athletes had two ventricular premature contractions on resting ECG (one possibly related and one finally unrelated to SARS-CoV-2 infection). The first one (athlete 4; possibly related) had normal

echocardiography and exercise test and could return to sport. The other one (unrelated) had significant ventricular arrhythmias on ambulatory ECG, and CMR finally diagnosed a left ventricular non-compaction (LVNC) cardiomyopathy. According to the recent guidelines, he was advised to stop competitive sport participation. There was no difference in the occurrence of possible SARS-CoV-2 infection-related ECG changes between the four groups of patients with different SARS-CoV-2 infection symptom severity.

3.3. Echocardiography

Resting echocardiography was performed in 497 athletes (89.7%) (Fig. 1), with similar rates in the different groups of patients (Table 1). Echocardiographic anomalies were noticed in 12 athletes (2.4%) and three (0.6%, 95% CI 0.2–1.8) had a possible link with recent SARS-CoV-2 infection. None had a significant LVEF decrease (LVEF < 50%). There was possible segmental hypokinesia in two athletes that was not confirmed by CMR (athletes 5 and 6; Table 2). One athlete had a small pericardial effusion on echocardiography (athlete 7), with no other element for pericarditis and normal CMR,

Table 1
Results of the cardiac examinations, overall and according to the severity of symptoms.

| | Total population (n = 554) | Asymptomatic (n = 195) | Moderate non-cardiac symptoms (< 14 days) (n = 253) | Moderate non-cardiac symptoms (> 14 days) (n = 84) | Cardiac symptoms (n = 22) | P* |
|--|-------------------------------|---------------------------|---|--|---------------------------------|---------|
| ECG | 551 (99.5) | 192 (98.5) | 253 (100) | 84 (100) | 22 (100) | 0.22 |
| Normal | 535 (97.1) | 186 (96.9) | 247 (97.6) | 82 (97.6) | 20 (90.9) | 0.22 |
| Anomalies unrelated to SARS-CoV-2 | 12 (2.2) | 5 (2.6) | 4 (1.6) | 2 (2.4) | 1 (4.5) | – |
| Pathological T-wave inversion | 3 (0.5) | 1 (0.5) | 1 (0.4) | 0 | 1 (4.5) | 0.17 |
| Ventricular premature contractions | 1 (0.2) | 0 | 1 (0.4) | 0 | 0 | 1.00 |
| Echocardiography | 497 (89.7) | 175 (89.7) | 227 (89.7) | 74 (88.1) | 21 (95.5) | 0.86 |
| Normal | 485 (97.6) | 172 (98.3) | 220 (96.9) | 73 (98.6) | 20 (95.2) | 0.54 |
| Anomalies unrelated to SARS-CoV-2 | 9 (1.8) | 3 (1.7) | 5 (2.2) | 0 | 1 (4.8) | – |
| Segmental wall motion anomalies | 2 (0.4) | 0 | 1 (0.4) | 1 (1.4) | 0 | 0.47 |
| Pericardial effusion | 1 (0.2) | 0 | 1 (0.4) | 0 | 0 | 1.00 |
| Exercise test | 293 (52.9) | 98 (50.2) | 146 (57.7) | 31 (36.9) | 18 (81.8) | <0.0001 |
| Normal | 284 (96.9) | 95 (96.9) | 140 (95.9) | 31 (100) | 18 (100) | 0.84 |
| Anomalies unrelated to SARS-CoV-2 | 6 (2.0) | 1 (1.0) | 5 (3.4) | 0 | 0 | – |
| Exercise-induced ventricular arrhythmias | 3 (1.0) | 2 (2.0) | 1 (0.7) | 0 | 0 | 0.75 |
| CMR | 34 (6.1) | 12 (6.2) | 13 (5.1) | 5 (6.0) | 4 (18.2) | 0.14 |
| Normal | 32 (94.1) | 12 (100) | 11 (84.6) | 5 (100) | 4 (100) | 0.72 |
| Anomalies unrelated to SARS-CoV-2 | 1 (2.9) | 0 | 1 (7.7) | 0 | 0 | – |
| Late gadolinium enhancement | 1 (2.9) | 0 | 1 (7.7) | 0 | 0 | 1.00 |
| Ambulatory ECG | 11 (2.0) | 4 (2.1) | 6 (2.4) | 0 | 1 (4.5) | 0.35 |
| Normal | 10 (90.9) | 4 (100) | 5 (83.3) | 0 | 1 (100) | 1.00 |
| Anomalies unrelated to SARS-CoV-2 | 1 (9.1) | 0 | 1 (16.7) | 0 | 0 | – |
| Blood cardiac troponin | 90 (16.2) | 39 (20.0) | 42 (16.6) | 4 (4.8) | 5 (22.7) | 0.005 |
| Normal | 89 (98.9) | 38 (97.4) | 42 (100) | 4 (100) | 5 (100) | 0.53 |
| Elevated | 1 (1.1) | 1 (2.6) | 0 | 0 | 0 | 0.53 |

Data are expressed as number (% of total) for each type of test or number (% of those who underwent the test) for test results. CMR: cardiac magnetic resonance imaging; ECG: electrocardiogram; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

* P values for statistical comparison between the four groups.

therefore this was also judged as physiological. There were no differences in echocardiography anomalies between the four groups by symptom intensity.

3.4. Maximal exercise test

Maximal exercise test was performed in 293 athletes (52.9%) (Fig. 1). This was mainly performed in athletes with cardiac symptoms (81.8% vs 36.9–57.7% in the other three groups; $P < 0.0001$; Table 1). Nine exercise tests (3.1%) were considered abnormal and a potential link with recent SARS-CoV-2 infection was considered in three athletes (1.0%, 95% CI 0.3–3.0; athletes 8, 9 and 10). In all these three athletes, isolated ventricular premature contractions were observed during exercise. All had normal resting ECG and echocardiography (and athlete 10 had a normal CMR), therefore all were cleared for return-to-play. There were no differences in exercise test anomalies between groups by symptom intensity.

3.5. Cardiac magnetic resonance imaging

Only 34 athletes (6.1%) underwent CMR imaging (Fig. 1). This was done systematically in one centre (12 athletes) and was always normal in these cases. However, 22 CMR were performed because of abnormal first-line examinations and two CMR (5.9%) were considered abnormal (Table 1). In one athlete, who had significant ventricular arrhythmias on ECG and ambulatory ECG, CMR demonstrated pronounced left ventricular hypertrabeculations with a definite diagnosis of LVNC cardiomyopathy which was, therefore, not related to SARS-CoV-2 infection. One other athlete had localized subepicardial LGE, and the diagnosis of SARS-CoV-2 myocarditis was retained (athlete 3). There were no differences in the rates of CMR anomalies between groups by symptom intensity.

3.6. Ambulatory electrocardiogram monitoring

Only 11 athletes (2.0%) had an ambulatory ECG monitoring (Fig. 1), with slightly more among athletes with cardiac symptoms

(4.5% vs 0–2.4% in the other three groups; $P = 0.35$; Table 1). One ECG monitoring (9.1%) was considered abnormal, with significant premature ventricular contractions and concerned the athlete with a diagnosis of LVNC cardiomyopathy. There were no differences in ambulatory ECG anomalies between groups by symptom intensity.

3.7. Blood cardiac troponin

A blood test with cardiac troponin measurement was performed in 90 athletes (16.2%) (Fig. 1). It was performed more often in athletes with cardiac symptoms (22.7% vs 4.8–20.0% in the other three groups; $P = 0.005$; Table 1). One athlete (1.1%) had a slight cardiac troponin elevation (high-sensitivity cardiac troponin T 46 and 48 ng/L on consecutive days, compared to a normal value < 34 ng/L) (athlete 11). He was asymptomatic, had a normal ECG, echocardiography and exercise test, and was therefore cleared for return-to-play. There were no differences in troponin anomalies between groups by symptom intensity.

3.8. Overall results, clinical implication and follow-up

In the entire population of athletes in this study and the global result of cardiac evaluations, 12 anomalies with a potential relationship with recent SARS-CoV-2 infection were found (0.8% of all examinations performed, 95% CI 0.4–1.3). These concerned 11 different athletes (2.0% of overall athlete population, 95% CI 1.1–3.5). One athlete had a temporary sport restriction (athlete 3). He had only mild SARS-CoV-2 symptoms (fatigue, fever and myalgias during 4 days), a normal echocardiography and exercise test, no troponin elevation, but had unknown ECG repolarization anomalies motivating CMR imaging. The latter found significant inferolateral LGE indicating previous myocarditis. No relevant clinical event was reported during the follow-up of this athlete. Another athlete had an initial suspicion of SARS-CoV-2-related cardiac anomalies with ventricular premature contractions on resting and ambulatory ECG. However, additional examinations (particularly CMR) diagnosed LVNC cardiomyopathy and, therefore, no link with SARS-CoV-2

Table 2
Characteristics of athletes with potential cardiac anomalies related to recent SARS-CoV-2 infection.

| Athlete # | Sex, age, sport | SARS-CoV-2 symptoms | Cardiac symptoms | ECG | Echocardiography | Exercise test | CMR | Ambulatory ECG | Cardiac troponin | Sport participation status |
|-----------|---------------------|----------------------|-----------------------|--------------------------------------|-----------------------------|---|---|----------------|------------------|----------------------------|
| 1 | Male, 23, rugby | Moderate (> 14 days) | Chest pain, dyspnoea) | D3, aVF, V1-V2-V3 T-wave inversion | Normal | Normal | Normal | Not performed | Not performed | Return-to-play |
| 2 | Male, 32, football | None | None | Anterior T-wave inversion | Normal | Normal | Normal | Not performed | Not performed | Return-to-play |
| 3 | Male, 21, handball | Moderate (< 14 days) | None | Inferolateral T-wave inversion | Normal | Normal | Inferolateral subepicardial LGE | Normal | Normal | 3-month contraindication |
| 4 | Male, 21, rugby | Moderate (< 14 days) | None | 2 ventricular premature contractions | Normal | Normal | Not performed | Not performed | Not performed | Return-to-play |
| 5 | Female, 20, tennis | Moderate (> 14 days) | None | Normal | Segmental hypokinesia? | Normal | Normal global and segmental LV kinetics. Small physiological pericardiac effusion | Not performed | Not performed | Return-to-play |
| 6 | Female, 24, tennis | Moderate (< 14 days) | None | Normal | Segmental hypokinesia? | Normal | Normal global and segmental LV kinetics. Small physiological pericardiac effusion | Not performed | Not performed | Return-to-play |
| 7 | Male, 22, rugby | Moderate (< 14 days) | None | Normal | Small pericardiac effusion? | Normal | Normal | Not performed | Normal | Return-to-play |
| 8 | Male, 15, football | None | None | Normal | Normal | Ventricular premature contractions decreasing during effort | Not performed | Not performed | Not performed | Return-to-play |
| 9 | Male, 18, football | None | None | Normal | Normal | Ventricular premature contractions decreasing during effort | Not performed | Not performed | Not performed | Return-to-play |
| 10 | Male, 40, athletics | Moderate (< 14 days) | None | Normal | Normal | Ventricular and supraventricular premature contractions | Normal | Normal | Not performed | Return-to-play |
| 11 | Male, 24, football | None | None | Normal | Normal | Normal | Not performed | Not performed | Slight elevation | Return-to-play |

CMR: cardiovascular magnetic resonance imaging; ECG: electrocardiogram; LGE: late gadolinium enhancement; LV: left ventricular.

infection. During the follow-up (mean \pm standard deviation duration 376 ± 125 days), no major cardiac event that could have been linked to SARS-CoV-2 infection occurred in the overall population (sudden death, hospitalization for a cardiac symptom or any cardiac symptoms requiring a new cardiac assessment).

4. Discussion

We report the data from cardiac evaluations after non-hospitalized forms of SARS-CoV-2 infection in 554 athletes, performed in 12 French cardiac centres before return-to-play. This study allows us to highlight several key findings. Firstly, ECG and echocardiography were frequently performed, in accordance with initial French and international recommendations for the first-line cardiac evaluation in athletes after SARS-CoV-2 infection [7,10,13]. Additional evaluations—by CMR, exercise test and ambulatory ECG—were mainly guided by the initial assessment. Secondly, most abnormalities found during screening were not related to SARS-CoV-2 infection. Indeed, among a total of 41 anomalies, only 12 were potentially related to recent SARS-CoV-2 infection, concerning 11 different athletes (2.0% of the overall population). However, the screening enabled the diagnosis of anomalies that posed a potential risk during sporting activities, such as a structural cardiomyopathy (LVNC cardiomyopathy) and one case of accessory pathway, which were not known before. Finally, the number of athletes with SARS-CoV-2 infection-related cardiac involvement requiring a restriction of competitive sport practice was low, with the screening only allowing the detection of one probable SARS-CoV-2 infection-related myocarditis. No adverse events were declared in the follow-up in the overall population.

4.1. Results of the different complementary examinations

Regarding ECG, four athletes (0.7% of ECGs performed) demonstrated new ECG abnormalities with a potential link with recent SARS-CoV-2 infection. Martinez et al. reported similar data, with six abnormal ECGs among 789 professional athletes (0.8%) who tested positive for SARS-CoV-2 and underwent systematic return-to-play cardiac screening [14]. Of note, all six athletes had a normal CMR. Another study demonstrated that ECG was useful to detect anomalies linked to recent SARS-CoV-2 infection in hospitalized patients [15]. The only athlete with known possible SARS-CoV-2 infection-related myocarditis had unknown inferolateral T wave inversion, justifying the realization of a CMR and a final diagnosis of myocarditis.

Regarding echocardiography, only three anomalies (0.6% of echocardiographies) had a potential link with recent SARS-CoV-2 infection. Two athletes had a suspicion of segmental hypokinesia and one athlete had a small pericardial effusion; ECG and CMR were normal in these three cases. Even if echocardiography could be necessary in patients with severe SARS-CoV-2 infection [16], our finding adds weight to other studies to support that systematic echocardiography is not cost-effective to detect SARS-CoV-2 infection-related cardiac involvement [17].

Exercise testing was only performed in 52.9% of our population. The indication was most often guided by a clinical approach, as 81.8% of athletes with cardiac symptoms underwent exercise tests. We found three abnormal exercise tests with premature ventricular arrhythmias. However, these three athletes had normal resting ECG and echocardiography. In the absence of severe premature ventricular contractions (e.g. increase on exertion, repetitive or polymorph premature ventricular contractions), no additional CMR was requested in this situation and no restriction to play sport was formulated. The actual link with recent SARS-CoV-2 infection

is uncertain and the proportion of these abnormalities is similar to the prevalence of ventricular arrhythmias usually encountered during routine exercise tests of athletes [18].

In our study, CMR imaging was mainly performed because of a suspicion of a cardiac anomaly on first-line ECG or echocardiography, with 35.3% performed systematically. Only one athlete (2.9%) had LGE indicating a potential myocarditis related to recent SARS-CoV-2 infection. In this case, CMR was performed because of pathological T-wave inversion on resting ECG. CMR is the best non-invasive examination to assess myocarditis, as this diagnosis can be missed by ECG or echocardiography [19]. Previous studies have evaluated the interest of systematic CMR in athletes after a SARS-CoV-2 infection. Daniels et al. reported that 2.3% of athletes were diagnosed with clinical or subclinical myocarditis [20]. Nevertheless, this systematic approach is difficult in clinical practice given the limited accessibility and cost of this examination. Additionally, as mentioned by Udelson et al. in an editorial, it is unclear whether CMR abnormalities after SARS-CoV-2 infection represent an increased risk marker of sudden death in athletes [21]. Similarly, in our study, we did not find abnormal left ventricular function or arrhythmias in the athlete with myocarditis on CMR.

Only 11 ambulatory ECG (2.0% of global population) were performed in our study, mostly motivated by an abnormal first-line finding. We describe one athlete with significant ventricular arrhythmias (including couplets and triplets) but concerned an athlete with a definite diagnosis of LVNC cardiomyopathy on CMR, obviously unrelated to the recent SARS-CoV-2 infection. Although an arrhythmic risk has been described in relation to SARS-CoV-2 inflammation [22], previous studies have demonstrated that the systematic use of ambulatory ECG is not cost-effective [23].

Blood cardiac troponin was tested in 90 of our athletes (16.2%). This was done systematically in some athletes, as it was required by the French Federations of Football and Handball. Only one athlete (1.1%) had a mild cardiac troponin elevation, but in the absence of cardiac or general symptoms and normal ECG and echocardiography, no more examinations (especially CMR) were proposed. Although the interest in screening for troponin elevation has been described in subjects hospitalized for severe SARS-CoV-2 infection [24], its interest is still uncertain in athletes without cardiovascular symptoms [25]. Furthermore, the only athlete with myocarditis in our study had a normal troponin level, but he had no cardiovascular symptoms and troponin testing was probably performed after the acute phase of the myocarditis (12 days after a SARS-CoV-2 positive RT-PCR).

4.2. General interpretation

A comprehensive cardiac evaluation in athletes after SARS-CoV-2 infection before return-to-play was proposed following the first phase of the epidemic, when we were faced with the emergence of a new virus whose consequences were then little known. The main point was the fear of a potential myocarditis, described in post-mortem SARS-CoV-2 infection autopsies [26] or severe forms of infection [27]. These findings were extrapolated to athletes with a positive SARS-CoV-2 RT-PCR or antigen test, even in asymptomatic athletes. The aim of this study was to judge the benefits of such a systematic evaluation.

Most anomalies detected during check-ups were related to known anomalies or without an obvious link to recent SARS-CoV-2 infection. The interest of screening outside the SARS-CoV-2 pandemic is therefore not discussed here. Overall, 11 athletes (2.0% of global population screened) had cardiac anomalies with a potential link with recent SARS-CoV-2 infection. In a similar but more exhaustive study, 3018 young athletes who had tested positive for SARS-CoV-2 infection underwent a cardiac evaluation and 2820

had at least an ECG, troponin test or transthoracic echocardiography followed by CMR if clinically indicated [28]. They also detected few anomalies related to recent SARS-CoV-2 infection, with 0.7% abnormal findings by ECG, 0.9% by cardiac troponin and 0.9% by echocardiography. Definite, probable or possible SARS-CoV-2 cardiac involvement was identified in 0.7% [28]. The diagnostic yield of a CMR with clinical indication was 4.2 times that of systematic screening. They reported only one (0.03%) adverse cardiac event during a median follow-up of 113 days. Hence, the authors of this study concluded that CMR is most useful in athletes with a high pretest probability for SARS-CoV-2 cardiac involvement, as defined by the presence of cardiopulmonary symptoms and/or abnormalities on cardiac testing (ECG, troponin, echocardiography) [28]. However, the significance of CMR findings in the absence of symptoms remains unknown. Only one athlete in our study had a suspicion of myocarditis and had a sport restriction for 3 months. In his case, ECG was also initially abnormal (T-wave inversion). Other anomalies detected by the cardiac screening in our population did not lead to a sport restriction. No athletes diagnosed with possible cardiac involvement had an adverse cardiac event through the 1-year follow-up period, which is also very reassuring. Despite the increase in out-of-hospital cardiac arrests described during the first phase of the SARS-CoV-2 epidemic in the Paris region [29], no alert signal was evoked concerning cardiac arrests related to sport. It is necessary to distinguish the data concerning the general population from that of the athlete population, which is mostly free of pathology and cardiovascular risk factors.

Finally, it is important to remember the limitations of medical explorations for the detection of possible cardiac anomalies. Education of athletes, for example with the help of the 10 golden rules of the French sports cardiologists' club [30], is also an effective element of prevention based on the good practices of physical activity. In the context of SARS-CoV-2 infection, physical activities should be stopped for 1 week during the active phase of infection and physicians must insist on the need to consult in case of new cardiac symptoms when returning to sport.

4.3. Limitations

Some limitations of this study should be noted. This was a retrospective study, hence, data might not be exhaustive and could have generated a selection bias. No review of the examinations was done and the interpretation of the normality or not of a cardiac examination was left to the free interpretation of the cardiologist in charge of the athlete. The indication of a complementary examination was also at the discretion of the cardiologist, influenced during the study by the repeated modifications of the sport federation protocols and by the advance in scientific data. Nonetheless, this register allows a real-life appreciation.

5. Conclusions

In this multicentre cross-sectional study, the proportion of cardiac involvement after non-hospitalized forms of SARS-CoV-2 infection in athletes was very low. Systematic cardiac screening before return-to-play seems not be mandatory in the majority of athletes.

Acknowledgements

This study was possible thanks to the collaboration between cardiologists who are members of the French "club des cardiologues du sport".

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Toloui A, Moshrefiaraghi D, Madani Neishaboori A, Youseffard M, Haji Aghajani M. Cardiac complications and pertaining mortality rate in COVID-19 patients; a systematic review and meta-analysis. *Arch Acad Emerg Med* 2021;9:e18.
- [2] Lu JQ, Lu JY, Wang W, Liu Y, Buczek A, Fleysler R, et al. Clinical predictors of acute cardiac injury and normalization of troponin after hospital discharge from COVID-19. *EBioMedicine* 2022;76:103821.
- [3] Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. *Nat Med* 2022;28:583–90.
- [4] Rajpal S, Tong MS, Borchers J, Zareba KM, Obarski TP, Simonetti OP, et al. Cardiovascular magnetic resonance findings in competitive athletes recovering from COVID-19 infection. *JAMA Cardiol* 2021;6:116–8.
- [5] Brito D, Meester S, Yanamala N, Patel HB, Balcik BJ, Casaclang-Verzosa G, et al. High prevalence of pericardial involvement in college student athletes recovering from COVID-19. *JACC Cardiovasc Imaging* 2021;14:541–55.
- [6] Finocchiaro G, Papadakis M, Robertus JL, Dhutia H, Steriotis AK, Tome M, et al. Etiology of sudden death in sports: insights from a United Kingdom regional registry. *J Am Coll Cardiol* 2016;67:2108–15.
- [7] Ministère des Sports et des Jeux Olympiques et Paralympiques. Des guides pratiques post-confinement liés à la reprise des activités physiques et sportives. Available at: <https://www.sports.gouv.fr/accueil-du-site/actualites/article/des-guides-pratiques-post-confinement-lies-a-la-reprise-des-activites-physiques> [accessed date: 20 Jun 2022].
- [8] Phelan D, Kim JH, Chung EH. A Game plan for the resumption of sport and exercise after Coronavirus Disease 2019 (COVID-19) infection. *JAMA Cardiol* 2020;5:1085–6.
- [9] Baggish A, Drezner JA, Kim J, Martinez M, Prutkin JM. Resurgence of sport in the wake of COVID-19: cardiac considerations in competitive athletes. *Br J Sports Med* 2020;54:1130–1.
- [10] Kim JH, Levine BD, Phelan D, Emery MS, Martinez MW, Chung EH, et al. Coronavirus Disease 2019 and the athletic heart: emerging perspectives on pathology, risks, and return to play. *JAMA Cardiol* 2021;6:219–27.
- [11] Wilson MG, Hull JH, Rogers J, Pollock N, Dodd M, Haines J, et al. Cardiorespiratory considerations for return-to-play in elite athletes after COVID-19 infection: a practical guide for sport and exercise medicine physicians. *Br J Sports Med* 2020;54:1157–61.
- [12] Drezner JA, Sharma S, Baggish A, Papadakis M, Wilson MG, Prutkin JM, et al. International criteria for electrocardiographic interpretation in athletes: consensus statement. *Br J Sports Med* 2017;51:704–31.
- [13] Bhatia RT, Marwaha S, Malhotra A, Iqbal Z, Hughes C, Borjesson M, et al. Exercise in the severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) era: A Question and Answer session with the experts Endorsed by the section of Sports Cardiology & Exercise of the European Association of Preventive Cardiology (EAPC). *Eur J Prev Cardiol* 2020;27:1242–51.
- [14] Martinez MW, Tucker AM, Bloom OJ, Green G, DiFiore JP, Solomon G, et al. Prevalence of inflammatory heart disease among professional athletes with prior COVID-19 infection who received systematic return-to-play cardiac screening. *JAMA Cardiol* 2021;6:745–52.
- [15] McCullough SA, Goyal P, Krishnan U, Choi JJ, Safford MM, Okin PM. Electrocardiographic findings in Coronavirus disease-19: insights on mortality and underlying myocardial processes. *J Card Fail* 2020;26:626–32.
- [16] Giustino G, Croft LB, Stefanini GG, Bragato R, Silbiger JJ, Vicenzi M, et al. Characterization of myocardial injury in patients with COVID-19. *J Am Coll Cardiol* 2020;76:2043–55.
- [17] Catena C, Colussi G, Bulfone L, Da Porto A, Tascini C, Sechi LA. Echocardiographic comparison of COVID-19 patients with or without prior biochemical evidence of cardiac injury after recovery. *J Am Soc Echocardiogr* 2021;34:193–5.
- [18] Verdile L, Maron BJ, Pelliccia A, Spataro A, Santini M, Biffi A. Clinical significance of exercise-induced ventricular tachyarrhythmias in trained athletes without cardiovascular abnormalities. *Heart Rhythm* 2015;12:78–85.
- [19] Clark DE, Parikh A, Dendy JM, Diamond AB, George-Durrett K, Fish FA, et al. COVID-19 Myocardial Pathology Evaluated Through scREning Cardiac Magnetic Resonance (COMPETE CMR). medRxiv 2020:[Preprint].
- [20] Daniels CJ, Rajpal S, Greenshields JT, Rosenthal GL, Chung EH, Terrin M, et al. Prevalence of clinical and subclinical myocarditis in competitive athletes with recent SARS-CoV-2 infection: results from the big ten COVID-19 cardiac registry. *JAMA Cardiol* 2021;6:1078–87.
- [21] Udelson JE, Rowin EJ, Maron BJ. Return to play for athletes after COVID-19 infection: the fog begins to clear. *JAMA Cardiol* 2021;6:997–9.
- [22] Lazzarini PE, Boutjdir M, Capecechi PL. COVID-19, arrhythmic risk, and inflammation: mind the gap! *Circulation* 2020;142:7–9.
- [23] Jiménez-Jáimez J, Macías-Ruiz R, Bermúdez-Jiménez F, Rubini-Costa R, Ramírez-Taboada J, Flores PIG, et al. Absence of relevant QT interval prolongation in not critically ill COVID-19 patients. *Sci Rep* 2020;10:21417.
- [24] Sandoval Y, Januzzi Jr JL, Jaffe AS. Cardiac Troponin for Assessment of Myocardial Injury in COVID-19: JACC Review Topic of the Week. *J Am Coll Cardiol* 2020;76:1244–58.
- [25] Gervasi SF, Pengue L, Damato L, Monti R, Pradella S, Pirroni T, et al. Is extensive cardiopulmonary screening useful in athletes with previous asymptomatic or mild SARS-CoV-2 infection? *Br J Sports Med* 2021;55:54–61.

- [26] Halushka MK, Vander Heide RS. Myocarditis is rare in COVID-19 autopsies: cardiovascular findings across 277 postmortem examinations. *Cardiovasc Pathol* 2021;50:107300.
- [27] Jaffe AS, Cleland JGF, Katus HA. Myocardial injury in severe COVID-19 infection. *Eur Heart J* 2020;41:2080–2.
- [28] Moulson N, Petek BJ, Drezner JA, Harmon KG, Kliethermes SA, Patel MR, *et al.* SARS-CoV-2 cardiac involvement in young competitive athletes. *Circulation* 2021;144:256–66.
- [29] Marijon E, Karam N, Jost D, Perrot D, Frattini B, Derkenne C, *et al.* Out-of-hospital cardiac arrest during the COVID-19 pandemic in Paris, France: a population-based, observational study. *Lancet Public Health* 2020;5:e437–43.
- [30] Club de Cardiologues du Sport. Les 10 règles d'or. Available at: <https://www.clubcardiosport.com/10-regles-or> [accessed date: 20 Jun 2022].