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Mid- to long-term cardiac magnetic resonance findings in elite athletes recovered from COVID-19: results from an ongoing observational COVID-19 study at a German Olympic medical centre

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Die Dissertationsschrift wurde von mir bisher weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

Die dieser Arbeit zugrunde liegenden Untersuchungen im Rahmen der Studie „Covid-19 im Hochleistungssport“ habe ich unter Aufsicht von Jonas Zacher und Hans Georg Predel am Institut für Kreislaufforschung und Sportmedizin der deutschen Sporthochschule Köln vorgenommen. Als Studienkoordinatorin fungierte ich als konstante Ansprechpartnerin für die Athleten und war für die vollständige Terminorganisation sowie die effiziente Durchführung aller organisatorischen Abläufe verantwortlich. Die Sammlung und Auswertung der demographischen und sportmedizinischen Daten insbesondere des klinischen Langzeitverlaufs sind durch mich erfolgt. Die Durchführung und Auswertung der MRT-Untersuchungen der Studienteilnehmer*innen wurden von Herrn Christopher Schneeweis und Herrn Robert Manka durchgeführt. Die Manuskripterstellung ist gleichermaßen durch mich und Herrn Christopher Schneeweis erfolgt, weshalb wir als gleichberechtigte Erstautoren aufgeführt sind.

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Köln, den 10.11.2024

Unterschrift: .....

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Inhaltsverzeichnis

Abkürzungsverzeichnis

ACC: American College of Cardiology

ARVC: Arrhythmogenic Right Ventricular Cardiomyopathy

BNP: Brain Natriuretic Peptide

CBT: Cognitive Behavioral Therapy

CFS: Chalder Fatigue Scale

CMR: Cardiac Magnetic Resonance

COVID-19: Coronavirus disease 2019

ECG: Electrocardiogram

GAD-7: Generalized Anxiety Disorder scale

GET: Graded Exercise Therapy

HST: High-Sensitivity Troponin

HRV: Heart Rate Variability

LGE: Late Gadolinium Enhancement

MBSR: Mindfulness-Based Stress Reduction

MI: Myocardial Infarction

POMS: Profile of Mood States

Rest-Q-Sport: Recovery Stress Questionnaire for Athletes

RTP: Return-to-play

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

VO2 max: Maximal Oxygen Uptake

1. Zusammenfassung

Einleitung

Die Coronavirus-Krankheit-2019 (COVID-19) - Pandemie, ausgelöst durch das schwere akute Respiratorisches Syndrom Coronavirus 2 (SARS-CoV-2)-Virus, hat weltweit erhebliche Auswirkungen auf das Gesundheitssystem und den Leistungssport. Neben den bekannten akuten respiratorischen Symptomen wie Husten, Atemnot und Fieber, können schwere kardiovaskuläre Komplikationen wie Myokarditis, Herzrhythmusstörungen und Myokardinfarkte auftreten, insbesondere bei Personen mit Vorerkrankungen wie Herz-Kreislauf-Erkrankungen, Diabetes oder Adipositas [1].

Nach der akuten Phase von COVID-19 berichteten viele Patienten von anhaltenden Symptomen, die als Post-COVID-Syndrom klassifiziert werden, wenn sie länger als 12 Wochen bestehen. Zu den häufigsten Langzeitsymptome zählen Fatigue, Atembeschwerden und kognitive Beeinträchtigungen, welche die Lebensqualität und die körperliche Leistungsfähigkeit erheblich einschränken können. Insbesondere die kardiovaskulären Langzeitfolgen stehen im Fokus der Forschung, da COVID-19 in vielen Fällen mit Myokarditis und anderen Herzerkrankungen in Verbindung gebracht wurde [6,7].

Kardiovaskuläre Auswirkungen bei SARS-CoV-2 positiven Eliteathleten

Obwohl die Mehrheit der Athleten milde Symptome zeigt und sich innerhalb von 10 Tagen erholt, berichten einige von anhaltenden Beschwerden wie Fatigue und Atemnot, die die sportliche Leistungsfähigkeit langfristig beeinträchtigen können. Diese Symptome können kardiovaskuläre Veränderungen hinweisen, die möglicherweise langfristige Auswirkungen auf die Herzgesundheit haben [10].

Trotz des überwiegend milden Krankheitsverlaufs bei Eliteathleten nehmen die Bedenken bezüglich subklinischer kardiovaskulärer Veränderungen zu. Studien zeigen, dass auch junge, gesunde und körperlich aktive Personen nach einer SARS-CoV-2-Infektion von solchen subklinischen Herzschäden betroffen sein können [4]. Bei Athleten können die hohen körperlichen Belastungen im Training und Wettkampf unentdeckte kardiovaskuläre Komplikationen wie Myokarditis oder Myokarditis oder Myokardfibrose, verstärken.

Rolle der kardialen Magnetresonanztomographie (CMR)

Die kardiale Magnetresonanztomographie (CMR) -Bildgebung gilt als Goldstandard zur Erkennung subklinischer Myokardveränderungen, wie Myokardödem, und Myokardfibrose, die auf entzündliche Prozesse oder Narbengewebe hinweisen können. Diese Veränderungen sind häufig asymptomatisch, können jedoch potenziell schwerwiegende Langzeitfolgen haben,

einschließlich chronischer Herzinsuffizienz oder eines erhöhten Risikos für plötzlichen Herztod [8].

Studien zur Prävalenz von Myokarditis bei Athleten nach COVID-19 zeigen eine erhebliche Variabilität. Während Petek et al. bei 0,6% der untersuchten Athleten Myokarditis feststellten, identifizierten Rajpal et al. Anzeichen von Myokarditis bei 15% der Athleten, auch bei asymptomatischen Verläufen [12,16]. Diese Diskrepanzen verdeutlichen, dass der Zeitpunkt der CMR-Bildgebung eine entscheidende Rolle spielt, da frühe entzündliche Veränderungen häufig vorübergehend sind [17].

Forschungsbedarf und Fragestellungen

Obwohl schwere kardiale Komplikationen bei Athleten selten auftreten, besteht ein erheblicher Forschungsbedarf zur langfristigen Relevanz subklinischer Befunde. Es bleibt unklar, inwieweit diese Veränderungen das Risiko für kardiovaskuläre Ereignisse erhöhen können. Zudem fehlen bisher standardisierte Leitlinien für den Einsatz von CMR bei asymptomatischen Athleten, was die Entwicklung und Implementierung einheitlicher, evidenzbasierter Return-to-Play (RTP)-Protokolle erschwert.

Ziele und Forschungsfragen

Das primäre Ziel dieser Studie besteht darin, die mittel- bis langfristigen kardialen Auswirkungen einer SARS-CoV-2-Infektion bei Eliteathleten zu untersuchen. Mittels hochauflösender CMR sollen das Vorhandensein und Ausmaß subklinischer Myokardveränderungen erfasst und mit einer gesunden Kontrollgruppe verglichen werden. Zusätzlich wird analysiert, ob ein Zusammenhang persistierenden Symptomen und den CMR-Befunden besteht.

Die zentralen Forschungsfragen lauten:

1. Wie häufig treten mittel- bis langfristige myokardiale Abnormalitäten wie Myokarditis, Myokardödem oder Fibrose, bei Eliteathleten nach einer SARS-CoV-2-Infektion im Vergleich zu einer gesunden Kontrollgruppe auf?

2. Gibt es eine Korrelation zwischen persistierenden Symptomen und mittels CMR nachgewiesenen myokardialen Veränderungen bei Eliteathleten nach überstandener COVID-19-Infektion?

3. Welche Faktoren sollten bei der Entwicklung individualisierter RTP-Protokolle berücksichtigt werden, um eine sichere und langfristige Rückkehr in den Leistungssport zu gewährleisten?

Methoden

Studiendesign und Teilnehmer

Diese Studie umfasste 27 Eliteathleten des deutschen Olympiastützpunkts NRW/ Rheinland, die zwischen Januar 2020 und Oktober 2021 eine laborbestätigte SARS-CoV-2-Infektion durchgemacht hatten. Die Athleten nahmen an einer fortlaufenden Beobachtungsstudie zum Thema „COVID-19 im Hochleistungssport“ am Institut für Kreislaufforschung und Sportmedizin der Deutschen Sporthochschule Köln (DSHS) teil. Als Kontrollgruppe dienten neun gesunde Nicht-Athleten ohne nachgewiesene COVID-19-Infektion dienten als Kontrollgruppe. Die kardiale Magnetresonanztomographie CMR wurde im Durchschnitt 182 Tage nach dem ersten positiven Testergebnis durchgeführt.

Ethik und Einwilligung

Die Studie wurde durch die Ethikkommission der Deutschen Sporthochschule Köln genehmigt (Nr. 087/2020) und gemäß den der Deklaration von Helsinki durchgeführt. Alle Teilnehmenden wurden umfassend über die Studie aufgeklärt und gaben ihr schriftliches Einverständnis zur Teilnahme.

Kontrollgruppe

Die Kontrollgruppe bestand aus neun gesunden Freiwilligen ohne dokumentierte SARS-CoV-2-Infektion und ohne bekannte kardiale Vorerkrankungen. Die CMR-Daten dieser Kontrollgruppe dienten unter anderem zur Definition spezifischer T1- und T2-Mapping-Referenzwerte zu definieren.

Rekrutierung und Studienkohorte

Die Studienkohorte umfasste Athleten des Bundes- und paralympischen Kaders, die routinemäßig an sportmedizinischen Untersuchungen am Institut für Kreislaufforschung und Sportmedizin teilnahmen. Einschlusskriterien waren ein nachgewiesener positiver SARS-CoV-2-Test (Polymerase-Kettenreaktion (PCR)- oder Antikörpertest), ein Mindestalter von 14 Jahren und das Fehlen akuter Erkrankungen. Die Rekrutierung erfolgte durch Antikörperscreening im Rahmen sportmedizinischer Untersuchungen oder durch direkte Kontaktaufnahme bei positivem Testergebnis. Die Erstuntersuchung fand nach einem negativen PCR-Test und einer mindestens zehntägigen symptomfreien Phase statt.

Kardiale Magnetresonanztomographie

Die CMR-Untersuchungen wurden mit einem Siemens Aera 1.5 Tesla Scanners durchgeführt und beinhalteten cine-Bildgebung sowie T1- und T2-Mapping zur Detektion von Myokardveränderungen. Late Gadolinium Enhancement (LGE) -Bildgebung wurde zur Identifikation von Myokardfibrose eingesetzt. Die Bildanalyse umfasste die Berechnung links- und rechtsventrikulärer Volumina, der Myokardmasse sowie der Ejektionsfraktionen. T1- und T2-Mapping-Werte wurden in sechs Segmenten der mittleren Kurzachse gemessen, um entzündliche Prozesse zu erkennen. Zwei erfahrene Kardiologen werteten die Bilddaten unabhängig voneinander aus.

Datenerhebung

Zusätzlich zu den CMR-Untersuchungen wurden kardiologische Untersuchungen bei allen Athleten durchgeführt, darunter Elektrokardiogramm (EKG) und Labortests, einschließlich hochsensitivem Troponin I. SARS-CoV-2-spezifische Symptome wurden mithilfe standardisierter Fragebögen erfasst. Die Datenerhebung erfolgte zu zwei Zeitpunkten: direkt unmittelbar nach der Genesung sowie etwa 16 Wochen später. Alle Daten wurden anonymisiert in einer studienspezifischen Datenbank dokumentiert.

Ergebnisse

Patienten und Kontrollgruppen

Die Studienkohorte bestand aus 16 männlichen (59%) und 11 weiblichen (41%) Eliteathleten sowie 5 weiblichen (55%) und 4 männlichen (45%) Kontrollpersonen. Der mediane Zeitraum zwischen der COVID-19-Diagnose und der ersten klinischen Untersuchung am Institut betrug 34 Tage. Die Mehrheit der Athleten (92%) berichtete von einem symptomatischen Verlauf, wobei 14 Athleten (54%) angaben, länger als 4 Wochen Symptome gehabt zu haben. Lediglich 3 Athleten (11%) klagten initial über Brustschmerzen. Keiner der Athleten mit länger als 4 Wochen andauernden Symptomen zeigte kardiale Beschwerden, wobei Fatigue das häufigste Symptom darstellte. Da keine schwerwiegenden Komplikationen auftraten, war keine spezifische Behandlung erforderlich. Die Athleten folgten zur sicheren Rückkehr zum Sport den RTP-Richtlinien von Elliot et al., die eine mindestens zehntägige Trainingspause nach einem positiven COVID-19-Test sowie eine symptomfreie Phase von mindestens 7 Tagen vor der Wiederaufnahme sportlicher vorschreiben [24] .

Troponin-Ergebnisse

Bei zwei Athleten wurde bei der Erstuntersuchung erhöhte Troponinwerte festgestellt. Einer dieser Athleten wurde aufgrund einer diagnostizierten arrhythmogenen rechtsventrikulären Kardiomyopathie (ARVC) von der Studie ausgeschlossen (siehe Ergebnisse der kardialen

Magnetresonanztomographie). Der zweite Athlet, der zu keinem Zeitpunkt kardiale Symptome zeigte, war zum Zeitpunkt der CMR-Untersuchung asymptomatisch. Sein initialer Troponinwert lag bei 108 ng/l und normalisierte sich innerhalb von 3 Tagen auf unter 80 ng/l. Es wurde festgestellt, dass dieser Athlet vor der Troponinbestimmung intensiv trainiert hatte. Der mediane Zeitraum zwischen dem positiven PCR-Test und der CMR-Untersuchung betrug 182 Tage.

Ergebnisse der kardialen Magnetresonanztomographie

Ein männlicher Schwimmer wurde aufgrund von CMR-Befunden, die auf eine ARVC hindeuteten, von der Studie ausgeschlossen. Bei einem weiteren männlichen Athleten wurde zufällig eine Masse an der freien lateralen Wand des rechten Ventrikels entdeckt, die als gutartiges Fibrom diagnostiziert wurde. Im Vergleich zur Kontrollgruppe zeigten die Athleten signifikant vergrößerte Volumina des linken (LVEDVi) und rechten Ventrikels (RVEDVi) sowie eine erhöhte linksventrikuläre Myokardmasse (LVMi) (LVEDVi: 103.4 vs 91.1 ml/m2, p = 0.031; RVEDVi: 104.1 vs.86.6 ml/m2, p = 0.007; LVMi: 59.0 vs. 46.2 g/m2, p = 0.002). Die Werte für den globalen longitudinalen Strain unterschieden sich nicht signifikant zwischen den Athleten und der Kontrollgruppe. Der globale zirrkumferentielle Strain war bei den Athleten zunächst signifikant niedriger, verlor jedoch nach der Bonferroni-Korrektur seine statistische Relevanz.

Es wurden keine signifikanten Unterschiede in der linksventrikulären Ejektionsfraktion (LVEF) festgestellt (LVEF: 56.5 vs. 58.9%, p = 0.072), wohingegen die rechtsventrikuläre Ejektionsfraktion (RVEF) der Athleten im Vergleich zur Kontrollgruppe signifikant reduziert war (RVEF: 51 vs. 54.8%, p = 0.008). Die T1- und T2-Mapping-Werte der Athleten zeigten keine Abweichungen im Vergleich zur Kontrollgruppe. In der LGE-Bildgebung konnten keine Myokardveränderungen nachgewiesen werden, die auf Myokardschäden hindeuten würden. Keiner der Athleten erfüllte die aktuellen Lake-Louise-Kriterien für eine akute Myokarditis. Nach Adjustierung auf Störfaktoren wie Alter und Geschlecht in der ANCOVA blieben keine signifikanten Unterschiede bestehen.

Diskussion

Langfristige kardiovaskuläre Auswirkungen einer SARS-CoV-2-Infektion bei Eliteathleten

Diese Dissertation untersucht die langfristigen kardiovaskulären Auswirkungen von COVID-19 bei Eliteathleten anhand der kardialen Magnetresonanztomographie. Sechs Monate nach der Infektion zeigten die untersuchten Athleten keine Hinweise auf Myokarditis oder signifikante myokardiale Schädigungen. Der fehlende Nachweis von LGE oder Fibrose deutet darauf hin,

dass subklinische Veränderungen, die in der Akutphase beschrieben wurden, im Langzeitverlauf nicht mehr nachweisbar sind. Dies legt nahe, dass dauerhafte myokardiale Schäden bei Eliteathleten nach COVID-19 selten auftreten und die kardiovaskuläre Prognose in dieser Population insgesamt günstig ist [17,18].

Während Studien zur Akutphase, wie die von Rajpal et al. eine Myokarditisrate von 15% bei Wettkampfathleten unmittelbar nach der Infektion berichteten [12], zeigte unsere Langzeitstudie, dass diese Befunde im Langzeitverlauf nicht bestehen bleiben. Dies unterstreicht die temporäre Natur myokardialer Veränderungen während der akuten Infektionsphase. Unterschiede in den LGE-Raten zwischen Studien lassen sich durch Variationen im Zeitpunkt der CMR-Untersuchungen, den untersuchten Populationen und den Kriterien zur Definition myokardialer Abnormalitäten erklären.

Differenzierte Anwendung der CMR-Bildgebung bei post-COVID-19-Athleten

Bedeutung des CMR-Zeitpunktes

Unsere Ergebnisse verdeutlichen, dass der Zeitpunkt der CMR-Untersuchung von entscheidend ist. Während in der Akutphase durchgeführte CMR-Untersuchungen häufig vorübergehende entzündliche Veränderungen erfassen, die später nicht mehr nachweisbar sind [17], bietet eine spätere CMR-Bildgebung, wie in unserer Studie etwa sechs Monate nach der Infektion, ein klareres Bild möglicher langfristiger kardialer Veränderungen und minimiert das Risiko einer Überdiagnose vorübergehender, klinisch nicht relevanter Befunde.

Zielgerichteter Einsatz der CMR-Bildgebung

Unsere Studie zeigt, dass eine routinemäßige CMR-Bildgebung bei asymptomatischen Athleten oder Athleten mit milden Symptomen nach COVID-19 nicht erforderlich ist. CMR sollte gezielt bei Athleten eingesetzt werden, die signifikante kardiovaskuläre Symptome wie Brustschmerzen oder Palpitation aufweisen oder einen schweren Krankheitsverlauf hatten, um eine myokardiale Beteiligung auszuschließen [20,21]. Athleten mit persistierenden LGE oder Fibrose in Langzeituntersuchungen benötigen eine fortlaufende Überwachung, da diese das Risiko für Arrhythmien und eine eingeschränkte Herzfunktion erhöht [15,22].

Differenzierung zwischen physiologischen und pathologischen CMR-Veränderungen

In unserer Kohorte zeigten mehrere Athleten vergrößerte links- und rechts ventrikuläre Volumina sowie eine erhöhte Myokardmasse, was typische physiologische Anpassungen an intensives Training darstellt, bekannt als „Athletenherz“ [21,24]. Diese physiologischen Anpassungen wurde auch in der Studie D´Ascenzi et al. beschrieben[25]. Es ist daher

essenziell, standardisierte Interpretationsrichtlinien zu entwickeln bzw. bestehende Referenzwerte [25] nochmals zu überprüfen, um physiologische von pathologischen Veränderungen im CMR zuverlässig zu unterscheiden.

Erholungsfähigkeit von Eliteathleten

Die geringe Prävalenz langfristiger myokardialer Komplikationen bei Eliteathleten könnte auf ihre hervorragende kardiovaskuläre Fitness und ein robustes Immunsystem zurückzuführen sein [26,27]. Untersuchungen zeigen, dass Eliteathleten eine gesteigerte Fähigkeit besitzen, vorübergehenden myokardialen Stress während der Akutphase zu bewältigen, wodurch das Risiko langfristiger Schäden minimiert wird [21,23]. Diese verbesserte Erholungsfähigkeit könnte ebenfalls zu den positiven Ergebnissen beigetragen haben, die in unserem Langzeit-Follow-up beobachtet wurden.

Die Rolle von hochsensitivem Troponin

Erhöhte Entzündungsmarker wie hochsensitives Troponin (HST), werden häufig als Indikatoren zur Risikoeinschätzung für das Auftreten von myokardialen Abnormalitäten nach COVID-19 genutzt [19,20]. Da in unserer Studie weder SARS-CoV-2-induzierte Troponin-Erhöhungen noch auffällige CMR-Befunde festgestellt wurden, können wir jedoch keine Aussage über einen möglichen Zusammenhang treffen.

Einfluss der Trainingsintensität auf die kardiale Erholung

Die Trainingsintensität spielt ebenfalls eine entscheidende Rolle bei der kardialen Erholung nach COVID-19. Studien haben gezeigt, dass hochintensives Training während der frühen Erholungsphase mit einer erhöhten Prävalenz subklinischer myokardialer Veränderungen assoziiert ist [29]. In unserer Studie fand sich jedoch keine solche Assoziationen, vermutlich aufgrund der strikten Einhaltung eines strukturierten RTP-Protokolls, das einen zu schnellen Wiedereinstieg in hochintensives Training zu vermeiden versucht [31].

Kardiovaskuläre Auswirkungen von Fatigue und psychischem Stress

Mehr als die Hälfte der Athleten berichtete von anhaltender Fatigue, was darauf hinweist, dass neben kardiovaskulären Faktoren auch nicht-kardiale Einflüsse, wie Fatigue, in die Bewertung der langfristigen Risiken einbezogen werden müssen. Obwohl Fatigue in der CMR keine unmittelbaren Befunde zeigte, sollte sie dennoch als Risikofaktor für längerfristige kardiovaskuläre Belastung berücksichtigt werden. Fatigue kann durch autonome Dysregulation, gemessen an einer verminderten Herzfrequenzvariabilität (HRV), zu erhöhter kardiovaskulärer Belastung führen, die die Anpassungsfähigkeit des kardiovaskulären

Systems an Belastungen beeinträchtigen und das Risiko für kardiovaskuläre Ereignisse erhöhen kann [32,33].

Psychischer Stress und anhaltende Fatigue können sich bei Athleten nach COVID-19 gegenseitig verstärken, was zu autonomer Dysfunktion und erhöhter kardiovaskulärer Belastung führt und die Erholung erschwert. Zusätzliche Faktoren wie Angst und Leistungsdruck können die Erholungsfähigkeit und die sportliche Leistung weiter beeinträchtigen [36–38]. Neben der HRV-Messung [33], sollten etablierte diagnostische Instrumente wie die Chalder Fatigue Scale (CFS) oder der Erholungs-Belastungs-Fragebogen für Sportler (RESTQ-SPORT) zur Bewertung von Fatigue und psychischen Stressoren in RTP-Protokolle integriert werden [34,41]. Interventionen wie Mindfulness-based Stress Reduction (MBSR) und kognitive Verhaltenstherapie (CBT) können gezielt eingesetzt werden, um sowohl Fatigue als auch psychischen Stress zu reduzieren und so die kardiovaskuläre Erholung zu fördern [42,43].

Optimierte RTP-Leitlinien

Auf Grundlage dieser Ergebnisse besteht die Notwendigkeit, RTP-Leitlinien weiterzuentwickeln, um die langfristige kardiovaskuläre Gesundheit und Leistungsfähigkeit von Athleten zu optimieren.

1. **Gezielter Einsatz der CMR-Bildgebung**: Unsere Studie zeigt, dass routinemäßige CMR-Untersuchungen bei asymptomatischen Athleten nicht erforderlich sind, da sie zu Überdiagnosen führen und unnötigen Trainingsrestriktionen führen können. Stattdessen sollte CMR gezielt bei Athleten mit signifikanten kardiovaskulären Symptomen oder schwerem Krankheitsverlauf eingesetzt werden, um myokardiale Beteiligungen auszuschließen. Standardisierte Interpretationsrichtlinien sind notwendig, um physiologische Anpassungen klar von pathologischen Veränderungen abzugrenzen.

2. **Systematische Fatigue- und psychologische Screeningverfahren**: Aufgrund der potenziellen Auswirkungen von Fatigue und psychischen Faktoren auf die autonome Regulation und Herzgesundheit sollten diese mit geeigneten Diagnosetools (z.B. HRV, CFS, REST-Q-Sport) systematisch erfasst und bei Bedarf durch gezielte Maßnahmen wie CBT oder MBSR behandelt werden.

3. **Individuell angepasste Trainingsintensität:** Die Trainingsgestaltung sollte auf Basis individueller Parameter erfolgen, um flexible Anpassungen an den Erholungsverlauf zu ermöglichen. Eine kontinuierliche Erhebung wichtiger Parameter wie HRV und mentaler

Status durch ein multidisziplinäres Team gewährleistet, dass das Training in Echtzeit an die klinischen Befunde angepasst werden kann.

Stärken und Limitationen

Eine wesentliche Stärke der Studie liegt im langen Nachbeobachtungszeitraum von 182 Tagen, der eine fundierte Beurteilung der langfristigen kardiovaskulären Gesundheit der Athleten ermöglichte. Die Anwendung der CMR als Goldstandard zur Erkennung von Myokardveränderungen erlaubte eine differenzierte Bewertung zwischen physiologischen Anpassungen und pathologischen Befunden inklusive subklinischer Befunde. Zudem wurden Symptome wie Fatigue erfasst, wodurch wertvolle Einblicke in subjektiv wahrgenommene Einschränkungen gewonnen wurden, die allein durch bildgebende Verfahren nicht erkennbar gewesen wären.

Zu den Limitationen der Studie zählt die kleine Stichprobengröße von 26 Athleten, was die statistische Aussagekraft einschränkt. Zusätzlich wurden psychologische und autonome Faktoren, die möglicherweise die langfristige kardiovaskuläre Erholung beeinflussen, nicht direkt gemessen. Die Fokussierung auf Eliteathleten könnte zudem zu einer Selektionsverzerrung führen, da diese aufgrund ihres hohen Fitnessniveau und besseren Zugangs zu medizinischer Versorgung möglicherweise andere Erholungsverläufe aufweisen als andere Bevölkerungsgruppen.

Zukünftige Forschungsansätze

Zukünftige Studien sollten größere Kohorten umfassen, um die geringe Prävalenz subklinischer myokardialer Veränderungen wie LGE zu validieren. Darüber hinaus ist eine Weiterentwicklung von Leitlinien für den gezielten Einsatz von CMR notwendig, insbesondere in Bezug auf den idealen Zeitpunkt und die klinischen Indikationen. Zudem sollte die Rolle psychologischer und autonomer Faktoren in der kardiovaskulären Risikobewertung stärker berücksichtigt werden, um ganzheitlichere und individuellere RTP-Protokolle zu entwickeln.

Fazit

Unsere Studie liefert wertvolle Erkenntnisse zur mittel- bis langfristigen kardiovaskulären Gesundheit von Eliteathleten nach einer SARS-CoV-2-Infektion und bestätigt eine insgesamt günstige Langzeitprognose. Sechs Monate nach der Infektion ergaben die CMR-Untersuchungen keine Hinweise auf persistierende Myokarditis oder andere signifikante myokardiale Schäden. Das Fehlen von LGE oder Fibrose deutet darauf hin, dass die im Akutstadium beschriebenen subklinischen Veränderungen transient sind. Mehrere Athleten

zeigten Zeichen eines „Sportlerherzens“ mit erhöhten ventrikulären Volumina und Myokardmasse, was eine physiologische Anpassung an intensives Training darstellt.

Der gezielte Einsatz der CMR unter Berücksichtigung des optimalen Zeitpunktes, spezifischer Indikationen sowie standardisierter Interpretationsrichtlinien zur Differenzierung zwischen physiologischen und pathologischen Befunden ist essenziell, um kardiale Komplikationen auszuschließen und Überdiagnosen zu vermeiden.

Ein erheblicher Anteil der Athleten berichtete von anhaltender Fatigue, die zwar nicht mit CMR-Befunden korrelierte, jedoch in Kombination mit psychischem Stress zu autonomer Dysregulation, Leistungsminderung und möglicherweise langfristig kardiovaskulären Komplikationen führen könnte. Dies verdeutlicht die Notwendigkeit, bei RTP-Entscheidungen nicht nur kardiovaskuläre Befunde, sondern auch nicht-kardiale Faktoren wie autonome Funktion, Fatigue, und mental Zustand des Athleten zu berücksichtigen.

Die Trainingsgestaltung sollte an individuelle Parameter wie HRV und anhaltender Symptome angepasst werden, um eine flexible Anpassung an den individuellen Erholungsverlauf in Echtzeit zu ermöglichen.

Wir empfehlen daher die Entwicklung ganzheitlicher RTP-Leitlinien, die sowohl physische als auch psychische Dimensionen integrieren. Individualisierte Trainingsprotokolle und standardisierte CMR-Kriterien sollten berücksichtigt werden, um die langfristige kardiovaskuläre Gesundheit und Leistungsfähigkeit von Eliteathleten nach einer SARS-CoV-2-Infektion optimal zu fördern.

2. Einleitung

2.1. Overview of COVID-19 and cardiovascular implications

The Coronavirus disease 2029 (COVID-19) pandemic, caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), has exerted a profound impact on healthcare systems globally, presenting a diverse spectrum of clinical manifestations from mild respiratory issues to severe complications, leading to substantial morbidity and mortality [1,2]. Common symptoms include cough, dyspnea, fever, and loss of taste and smell, while individuals with pre-existing conditions such as cardiovascular disease, obesity, and diabetes are at an elevated risk of severe outcomes like pneumonia and myocarditis [3].

After the resolution of the acute phase of COVID-19, many patients continue to experience persistent symptoms. When these symptoms extend beyond 12 weeks, they are classified as post-COVID syndrome [4,5]. Common long-term effects include fatigue, dyspnea, and cognitive impairment, which significantly diminish quality of life and physical capacity [4].

COVID-19 has also been linked to a spectrum of cardiovascular complications, including myocarditis, arrhythmias, and myocardial infarction (MI) [6,7]. Studies utilizing cardiovascular magnetic resonance (CMR) imaging have revealed high rates of myocardial involvement in COVID-19 patients, with 78% showing cardiac abnormalities, 60% exhibiting signs of active myocarditis, and 18% showing late gadolinium enhancement (LGE), which indicated myocardial fibrosis and potential long-term cardiac complications [8].

Although these complications are predominantly observed in older adults and individuals with comorbidities, recent evidence indicates that even young, healthy, and physically active individuals may experience significant cardiovascular effects following COVID-19 [4]. This is particularly concerning for elite athletes, as the demands of high intensity may increase their risk of undetected cardiac complications [9], necessitating further investigations into their long-term cardiovascular health.

2.2. Cardiovascular effects of COVID-19 in elite athletes

Although elite athletes tend to experience a milder course of COVID-19, concerns about potential subclinical cardiac involvement have emerged, especially as they resume high-intensity training. A comprehensive review of athletes indicates that cardiovascular complications are relatively rare in this population, underscoring their generally lower risk profile [9]. Schwellnus et al. reported that most athletes experienced mild symptoms, with a median recovery time of 10 days [10], while Schumacher et al. noted comparable recovery

patterns [11]. Common symptoms among athletes include fatigue, headaches, fever, muscle pain, sore throat, and disturbances in taste and smell [10,11]. While these symptoms generally resolve during the acute phase, some athletes continue to experience persistent fatigue and respiratory difficulties, which may impair their athletic performance [10] and raise concerns about potential underlying cardiovascular complications [4].

2.3. Cardiac magnetic resonance (CMR) findings in SARS-CoV-2-positive athletes

Research has increasingly focused on the cardiovascular risks faced by athletes, with particular attention to subclinical myocardial changes that often remain undetected. CMR imaging is regarded as the gold standard for evaluating myocardial structure characteristics, function, and inflammation. It is particularly valuable for detecting critical indicators of myocardial involvement, such as myocarditis, myocardial edema, and LGE. Myocardial edema reflects acute inflammatory processes, whereas LGE reveals regions of fibrosis or scar tissue. These findings are often asymptomatic and serve as essential markers for determining the extent of myocardial injury and assessing the risk of long-term cardiac complications, including chronic dysfunction and increased risk of future cardiovascular events [8]. The optimal use of CMR in athletes post-COVID-19 remains a topic of ongoing debate, with studies presenting differing recommendations. While some advocate for routine CMR screening in asymptomatic athletes [12,13], others propose a more targeted approach, reserving CMR for cases with specific clinical indications [14–16].

The prevalence of acute myocarditis in athletes appears to be low. Petek et al. reported a rate of 0.6% among 3,564 asymptomatic or mildly symptomatic collegiate athletes [16]. Similarly, Moulson et al. found myocardial abnormalities in 0.7% of athletes, while Clark et al. observed a slightly higher prevalence of 3%, suggesting that myocarditis may often go undetected without CMR [15]. In contrast, Rajpal et al. identified myocarditis in 15% of competitive athletes during the acute phase of COVID-19, including those who had symptoms [12].

Emerging evidence indicates that while most athletes recover fully from COVID-19, a subset may be at risk of subclinical myocardial injury and potential long-term cardiovascular implications. Malek et al. identified no cases of myocarditis but found that 19% of athletes exhibited myocardial edema and fibrosis two months post-infection, despite being asymptomatic[14]. In a related study, Wroblewski et al. found myocardial inflammation in 32% of athletes shortly after infection, which resolved within 6 to 8 weeks without adverse cardiac

events over a two-year follow-up [17]. Similarly, van Hattum et al. observed transient LGE in 4% of athletes shortly after infection, which also resolved without long-term consequences [18].

2.4. Conclusion and research gaps

Overall, while severe cardiac complications such as myocarditis are relatively uncommon in elite athletes following COVID-19, growing evidence suggests a notable prevalence of subclinical myocardial changes, including myocardial edema and fibrosis. These findings, frequently identified through CMR imaging, raise concerns about the potential long-term impact on athletes´ cardiovascular health. Given these changes often occur without symptoms, their implications for future cardiovascular events remain uncertain.

2.4.1. Research gaps

Despite valuable insights from recent studies, several critical research gaps persist. The long-term clinical significance of subclinical findings, such as myocardial edema and fibrosis, remains incompletely understood, particularly regarding their potential to affect future cardiac outcomes and contribute to chronic cardiovascular conditions. The lack of standardized guidelines for CMR imaging in post-COVID-19 athletes further complicates the situation, with no consensus on optimal timing, frequency, or indications, especially for asymptomatic or mildly symptomatic athletes. These uncertainties limit the ability to implement uniform screening protocols and may lead to suboptimal monitoring and management of athletes at risk for subclinical myocardial damage. Addressing these gaps is essential to gain a comprehensive understanding of long-term cardiovascular risks in elite athletes post-COVID-19 and to develop evidence-based return-to-play (RTP) protocols.

2.5. Aims and research questions

This study aims to systematically examine the mid-to long-term cardiac effects of COVID-19 in elite athletes, utilizing advanced CMR imaging techniques. Specifically, it will assess the presence and extent of myocardial abnormalities, including subclinical fibrosis, edema, and other structural changes, comparing these findings with those in a healthy control group. Furthermore, the study will investigate potential correlations between persistent symptoms and myocardial abnormalities in elite athletes. The overarching objective is to provide data that support the development of tailored, evidence-based RTP protocols, ensuring a safe and sustainable reintegration into competitive sports.

2.5.1. Research questions

1. **Characterization of mid- to long-term myocardial health in elite athletes post-COVID-19:**

- What is the prevalence of myocardial abnormalities, such as edema and fibrosis, in elite athletes post-COVID-19 compared to a healthy control group in the mid-to long-term?
- How frequently do severe cardiac events occur in elite athletes during a follow-up period several months post-SARS-CoV-2 infection compared to a healthy control group?

2. **Association between persistent symptoms and myocardial involvement:**

- Is there a correlation between persistent symptoms and CMR-detected myocardial abnormalities in elite athletes recovering from COVID-19, and how can these findings inform future monitoring strategies?
- What other factors observed during the investigation are associated with myocardial involvement?

3. **Development of safe and sustainable RTP protocols:**

- How can CMR findings be utilized to inform and refine current RTP protocols for elite athletes post-COVID-19?
- What are the key considerations for developing individualized RTP protocols to ensure a safe and sustainable return to high-performance sports for athletes?

3. Publikation

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Mid- to long-term cardiac magnetic resonance findings in elite athletes recovered from COVID-19: results from an ongoing observational COVID-19 study at a German Olympic medical centre

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Summary

INTRODUCTION: The cardiac magnetic resonance (CMR) data on mid- to long-term myocardial damage due to COVID-19 infections in elite athletes are scarce. Therefore, this study investigated the mid -to long-term consequences of myocardial involvement after a COVID-19 infection in elite athletes.

MATERIALS AND METHODS: This study included 27 athletes at the German Olympic Centre North Rhine-Westphalia (NRW)/Rhineland with a confirmed previous COVID-19 infection between January 2020 and October 2021. The athletes were part of an ongoing observational COVID-19 study at the Institute of Cardiology and Sports Medicine Cologne at the German Sport University (DSHS).Nine healthy non-athletes with no prior COVID-19 illness served as controls. CMR was performed within a mean of 182 days (standard deviation [SD] 99) of the initial positive test result.

RESULTS: CMR did not reveal any signs of acute myocarditis (according to the current Lake Louise criteria) or myocardial damage in any of the 26 elite athletes with previous COVID-19 infection. Of these athletes, 92% experienced a symptomatic course, and 54% reported symptoms lasting for more than 4 weeks. One male athlete was excluded from the analysis because CMR revealed an arrhythmogenic right ventricular cardiomyopathy (ARVC). Athletes had significantly enlarged left and right ventricle volumes and increased left ventricular myocardial mass in comparison to the healthy control group (LVEDVi 103.4 vs 91.1 ml/m^2, p = 0.031; RVEDVi 104.1 vs 86.6 ml/m^2, p = 0.007; LVMi 59.0 vs 46.2 g/m^2, p = 0.002). Only two cases of elevated high-sensitivity-Troponin were documented; in one, the participant had previously engaged in high-intensity training, and in the other, CMR revealed a diagnosis of an arrhythmogenic cardiomyopathy.

CONCLUSION: Our findings suggest that the risk for mid- to long-term myocardial damage is very low to negligible in elite athletes. Our results do not allow conclusions to be drawn regarding myocardial injury in the acute phase of infection nor about possible long-term myocardial effects in the general population.

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Introduction

The global pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), is still ongoing despite the rapid progress of vaccination and other containment efforts. Since the early report [1] of myocardial involvement in COVID-19 detected by cardiovascular magnetic resonance (CMR), extensive research has raised concerns about myocardial damage due to COVID-19 infection. A study by Puntmann et al. [2] reported cardiac involvement in an alarming 78% of patients, with signs of ongoing myocarditis in 60%. These data were collected from random middle-aged patients in need of hospital care. A multicentre study revealed myocarditis-like injury patterns in 28% of troponin-positive hospitalised patients with COVID-19 infection [3], prompting many follow-up studies. Myocarditis and myocarditis-like patterns are serious myocar-

dial injuries and can cause cardiac complications, such as heart failure, arrhythmia, and cardiogenic shock [4]. Cardiac magnetic resonance offers a unique combination of high-resolution functional imaging, parametric mapping, and late gadolinium enhancement (LGE) imaging and thereby provides detailed insight into myocardial texture. Thus, cardiac magnetic resonance is the imaging modality of choice and serves as the gold standard for detecting myocardial injury in suspected myocarditis [5, 6]. Because myocarditis is one of the leading causes of sudden cardiac death in athletes [7], early detection of myocardial damage is essential. The current Graduated Return to Play Protocol highlights the crucial role of cardiac magnetic resonance in athletes [8], especially in athletes with prolonged symptoms [9].

Studies on athletes with COVID-19 infection have presented inconsistent results. The COMPETE-CMR study observed myocarditis-like injury in 3% of the athletes [10], and a study by Rajpal et al. [11] found myocarditis-like injury in 15%; by contrast, Malek et al. [12] found no signs of acute myocarditis but observed other cardiac magnetic resonance abnormalities in 19% of athletes. These heterogeneous trials are limited in several regards: some did not include control patients, some were not focused on elite athletes, and some were not cardiac magnetic resonance-only studies. So far, only two cardiac magnetic resonance-only studies involving elite athletes have been conducted; these studies included 12 and 26 athletes [12, 13] and investigated myocardial damage shortly after infection. Furthermore, no data are available on mid- to longer-term myocardial damage due to COVID-19. At the time our study was initiated, an expert analysis by Sharma et al. [14] provided a thorough overview of the existing data and studies. Thus, our study investigated the potential mid- to long-term myocardial effects of prior COVID-19 infection in elite athletes.

Material and methods

Ethics approval and consent to participate

The project was approved by the ethics committee of the German Sport University, Cologne, on June 22, 2020 (no. 087/2020) and was carried out in accordance with the Declaration of Helsinki. Written informed consent was obtained from all athletes and controls.

Study cohort and recruitment

This study utilised data from an observational COVID-19 study titled "COVID-19 in High-Performance Sports" involving 65 elite athletes from the Olympic Centre of North Rhine-Westphalia (NRW)/Rhineland participating in different sports. The study was conducted from January 2020 to October 2021 at the Institute of Cardiology and Sports Medicine, which is licensed by the German Olympic Sports Confederation (DOSB) and located at the German Sport University. Among the study participants were two Olympic gold medalists, four world championship gold medalists, two world championship silver medalists, three world championship bronze medalists, three European champions, and seven national champions.

Inclusion criteria were (1.) a proven infection with SARS-CoV-2 assessed by polymerase chain reaction (PCR) or positive serum SARS-CoV-2 IgG, (2.) registration as a member of the German Federal Squad or Paralympic Federal Squad and regular annual routine sports medical examination at our DOSB-licensed institute, (3.) an age of 14 years or older, and (4.) no acute illness (e.g., febrile disease). Recruitment was conducted either through an antibody screening during the sports medical examination or a request for athletes with positive PCR test results. Written informed consent was required for inclusion and was obtained from all athletes. Prior to enrollment, all participants were informed about the objectives, procedure, and design of the study; subsequent data saving; and anonymity regarding the data. If study participants were under 18 years old, their written consent also had to be signed by a parent or guardian. Participants could withdraw from the study at any time without providing a reason.

Because of the initial reports of a high risk of myocardial injury from COVID-19 infection, 27 of the 65 athletes were randomly selected for cardiac magnetic resonance, with special regard to upcoming competitions or high-stress events (e.g., training camps). A negative PCR result and a symptom-free period of at least 10 days were required before enrollment. As part of the larger study, additional tests (electrocardiogram [ECG] and laboratory tests, including high-sensitivity [hs] troponin I) were performed on all athletes, and a standardised questionnaire was distributed to record the clinical manifestations of COVID-19 and the infection mechanisms and to assess the subjective performance at the clinical visits. The symptoms assessed included fever, cough, loss of taste or smell, runny nose, sore throat, shortness of breath at rest and during exertion, diarrhoea, headache, palpitations, dizziness, chest pain, syncope, muscle pain, joint pain, performance reduction, sleep disturbance, mood swings, concentrations disorders, and skin changes. The normal range of hs troponin-I was below the 99th percentile upper cutoff value (<80 ng/l).

Controls

The control group comprised nine healthy volunteers (five female and four male) with no relevant medical history or regular medication and no prior COVID-19 infection or clinical signs of infection within the past 6 months. The volunteers did not have any cardiac conditions, and the cardiac magnetic resonance examinations were assessed to establish new cardiac magnetic resonance protocols and scanner-specific T1 and T2 mapping values. All participants provided written informed consent for the use of their data.

Data collection

Data were collected by administering COVID-19-specific paper-based questionnaires, implementing SARS-CoV-2 antibody testing, and conducting study-specific diagnostics (e.g., venous blood sampling and resting ECG) along with functional analyses (e.g., spiroergometric and echocardiography including strain analysis). Study-specific diagnostics and data collection were performed at two time points: t0 and t1. Baseline diagnostics at t0 were scheduled after complying with the quarantine guidelines recommended by the Robert Koch Institute (quarantine period of seven

days, symptom-free period of 48 hours, and a negative PCR test), and a follow-up visit at t1 was conducted 16 weeks after t0. Data were documented in a study-specific patient chart for which each participant was assigned a unique eight-digit code. To ensure the accuracy and validity of the data, well-established tools, internal monitoring, and quality checks were implemented in addition to external random visits to our study centre. If any data were not available, they were marked as N/A, and a comment was included if needed.

Cardiac magnetic resonance

Cardiac magnetic resonance was performed in the follow-up after recovery from COVID-19 on a Siemens Aera 1.5 Tesla scanner (Erlangen, Germany). The study followed a standard protocol including scout images and cine-balanced steady-state free precession (bSSFP) breath-hold sequences in the long axis (two-, three-, and four-chamber) and short axis (SAX) orientations. SAX images were acquired as a stack of images including the ventricles from their valvular plane to their apex. Additionally, parametric mapping was performed in three SAX slices (basal, medial, and apical). T1-mapping utilised a conventional modified look-locker inversion recovery (MOLLI) sequence, and T2-mapping was performed with a T2-prepared SSFP sequence. Dark-blood T2-weighted images with fat suppression were performed in the SAX stack orientation. For late gadolinium enhancement (LGE) imaging, a gadolinium contrast agent (gadoteric acid, DotaVision©, b-e-imaging GmbH) was administered at 0.15 mmol/kg followed by a flush of 30 ml of isotonic saline. Late gadolinium enhancement images were obtained with a breath-hold technique using a phase-sensitive inversion recovering sequence (PSIR) in combination with a conventional bSSFP LGE sequence. Late gadolinium enhancement images were acquired 10 minutes after contrast agent administration. The correct inversion time was determined by a time of inversion finder (TI finder) sequence. Late gadolinium enhancement images were acquired in all three long-axis orientations and as a stack of SAX ccine images covering the full ventricle length.

Image analysis was performed with cardiac magnetic resonance-dedicated software (Circle cvi42 version 5.13.5). Both end-diastolic and end-systolic endocardial and epicardial contours were drawn automatically for the left ventricle (LV) and right ventricle (RV) in the SAX stack of bSSFP cine images. Manual correction was conducted when needed. For the quantification of left ventricular end-diastolic volume (LVEDV), right ventricular end-diastolic volume (RVEDV), left ventricular systolic volume (LVSV), right ventricular systolic volume (RVSV), left and right stroke volumes (LSV and RSV), LV and RV ejection fractions (LVEF/RVEF), and LV mass (LVM), the delineated contours were used, and the assessed volumes were indexed to the body surface area (LVEDVi; RVEDVi, LVSVi, RVSVi, LSVi, and RSVi). T1 and T2 relaxation times were calculated with a T1 and T2 map with motion correction (MOCO) in the midventricular SAX orientation. For this purpose, the slice was divided into six segments following the American Heart Association (AHA) segmentation. Epicardial and endocardial contours were drawn by hand. An offset of 10% was used to avoid including blood pools or extracardiac tissue. The presence of late gadolinium enhancement was assessed visually. Strain analysis was performed with the Circle Cardiovascular Imaging (CVI)-dedicated plug-in for strain analysis. The global longitudinal strain (GLS) was evaluated by using the two-, three-, and four-chamber cine images and the global circumferential strain (GCS) of the SAX cine stack. Images were analysed by two cardiologists (CS and RM) with more than 12 years of experience in cardiac magnetic resonance and a cardiac magnetic resonance level III certification from the European Society of Cardiology (ESC) and the Society of Cardiac Magnetic Resonance (SCMR).

Statistical methods

The Shapiro-Wilk test was used to assess the normality of the data distribution. All variables were normally distributed except for LVEDVi and RVEF. The inspection of boxplots revealed no extreme outliers in the data, except for one athlete with a value of +3 SD in LVM and one control with a value of −3 SD in LVEDVi. Levene's test for equality of variance revealed homogeneity in the variances for the T1 mapping values but not for the T2 mapping values or LVEF. Accordingly, depending on the normal distribution and variance homogeneity, t-tests, Welch's t-tests, or Mann-Whitney tests for independent samples were used to assess the significance of between-group differences (athletes vs control group). A p-value of less than 0.05 was considered indicative of a statistically significant difference. Given the 16 multiple comparisons conducted in the analysis, a Bonferroni correction was applied, resulting in significance thresholds of $p < 0.003$ for two-sided tests and $p < 0.006$ for one-sided tests. All values are presented with the standard deviation (SD). Statistical analysis was performed with SPSS V.28 (IBM).

Results

Patients and control subjects

The study group consisted of 16 male (59%) and 11 female (41%) elite athletes as well as 5 female (55%) and 4 male (45%) controls. Further details are presented in table 1. The median (interquartile range [IQR]) time interval between COVID-19 diagnosis and the first clinical examination at the Olympic medical centre was 34 (23–54 days) days. Most athletes (92%) experienced a symptomatic course, and 14 athletes (54%) reported having symptoms for more than 4 weeks. Only three athletes (11%) mentioned chest pain at the initial presentation. Of the 14 athletes with symptoms persisting for >4 weeks, none had cardiac symptoms, and fatigue was the predominant complaint amongst this subgroup. Since none of the athletes experienced major complications, no specific treatment was required beyond symptomatic therapy with anti-inflammatory and anti-rheumatic drugs, such as ibuprofen. To ensure the safe resumption of sports, we followed the return-to-play guidelines outlined by Elliott et al. for SARS-CoV-2-positive athletes. At the time of the study, this included a minimum training break of 10 days after testing positive for COVID-19 and a symptom-free period of at least 7 days before returning to activity.

In two athletes, elevated troponin values were observed at the initial clinical visit, one of whom was the excluded ath-

lete (see "Cardiac magnetic resonance findings"). The other athlete experienced no cardiac symptoms at any time and was asymptomatic at the time of cardiac magnetic resonance; troponin was 108 ng/l and had normalised to <80 ng/l 3 days later. The athlete had trained intensely prior to the initial troponin elevation. The median time interval between the positive PCR test and the cardiac magnetic resonance study was 182 days (SD 99).

The ECG was normal in all athletes (bradycardia is a physiological feature in trained athletes). None of the athletes were treated with any specific pharmacological agent for COVID-19.

Cardiac magnetic resonance findings

One male athlete (a swimmer) was excluded from the study because of cardiac magnetic resonance findings indicating arrhythmogenic right ventricular cardiomyopathy (ARVC). In another male athlete, an incidental mass of the right ventricle at the free lateral wall was found and diagnosed as a benign fibroma. Athletes had significantly enlarged left and right ventricle volumes and an increased left ventricular myocardial mass in comparison with the healthy control group (LVEDVi: 103.4 vs 91.1 ml/m^2, p = 0.031; RVEDVi: 104.1 vs 86.6 ml/m^2, p = 0.007; LVMi: 59.0 vs 46.2 g/m^2, p = 0.002). Global longitudinal strain values did not differ between the athlete and the control cohort (global longitudinal strain –16.6 vs –17.8 % with p = 0.066). Global circumferential strain values were significantly lower in athletes compared with controls (global circumferential strain −16.7 vs −18.7 %, p = 0.029), but this difference was reduced to a tendency after applying the Bonferroni correction for multiple comparisons. No differences were observed in left ventricular ejection fraction (LVEF: 56.5 vs 58.9%, p = 0.072), whereas the right ventricular ejection fraction of athletes was reduced in comparison with the control group (RVEF: 51 vs 54.8%, p = 0.008). The T1 and T2 mapping values of the athletes did not differ from those of the control group (T1 values: 992.5 vs 1015.4 ms; T2 values: 47.8 vs 48.7 ms; p = 0.530 and p = 0.313); see figure 1.

LGE imaging did not reveal any abnormalities in myocardial tissue characterisation indicating myocardial damage. None of the athletes met the current Lake Louise criteria for acute myocarditis [15]. To account for the potential confounding effects of age, weight, height, and BMI, we also performed analysis of covariance (ANCOVA). After this adjustment, no differences retained statistical significance. However, the inclusion of control variables in the ANCOVA model was constrained by the sample size; our small sample size may have limited statistical power, and the introduction of multiple control variables warrants careful consideration given the potential complications in interpretation. The full details of the cardiac magnetic resonance findings are presented in table 2; figure 2 shows exemplary cardiac magnetic resonance images and strain analyses of a control (A–D) and an athlete (E–I).

Discussion

It is well-documented that COVID-19 infection can cause myocardial involvement with a myocarditis-like pattern in the cardiac magnetic resonance diagnostic assessment [1, 3]. The present study examined the mid- to long-term effects of COVID-19 infection on the hearts of elite athletes as assessed by cardiac magnetic resonance. The main findings of the study were as follows: (a) no signs of myocarditis or myocardial damage were documented in 26 elite athletes with previous COVID-19 infection; (b) the hearts of the athletes demonstrated elevated left and right ventricular volumes and left ventricular mass as well as slightly lower RVEF values in comparison with the control group; and (c) the ejection fractions and strain values were within the normal range for athletes.

Athletes are considered a low-risk population for severe COVID-19 because of their young age and good general health. However, because of the persistence of the pandemic and the rising number of athletes with acute and prior infections (some repeatedly), research into the potential cardiac effects is highly relevant, especially considering that myocarditis is one of the leading causes of sudden cardiac death in athletes [16]. As return-to-play guidelines continue to evolve, [17] the data of the present study support

Table 1:
Characteristics of athletes and controls.

		Athletes (n = 27)	Control group (n = 9)
Age (years)		Mean = 23.69 (SD = 5.05)	Mean = 41.11 (SD = 6.27)
Body mass index (kg/m^2)		Mean = 23.30 (SD = 2.82)	Mean = 23.18 (SD = 3.59)
Gender		11 female, 16 male	5 female, 4 male
Sporting disciplines, n (%)	Fencing	9 (34.62%)	
	Judo	4 (15.38%)	
	Boxing	3 (11.54%)	
	Athletics	2 (7.69%)	
	Swimming	2 (7.69%; 1 excluded because of ARVC)	
	Taekwondo	2 (7.69%)	
	Wrestling	2 (7.69%)	
	Basketball	1 (3.85%)	
	Hockey	1 (3.85%)	
	Rowing	1 (3.85%)	
Symptoms, n (%)	Initially	24 (92.31%)	
	After 4 weeks	14 (53.80%)	
Elevated high-sensitivity troponin I, n (%)		2 (7.69%)	

ARVC: arrhythmogenic right ventricular cardiomyopathy

the key insight that mid- to long-term myocardial damage seems to be very rare in athletes. As recently demonstrated by Wroblewsi et al. [18], a differentiation between acute and sub-acute to mid- and long-term effects must be differentiated; using cardiac magnetic resonance, the authors found that 38 out of 117 (32%) college athletes had signs of cardiac inflammation, but all of these signs had resolved by the follow-up cardiac magnetic resonance 6–8 weeks later [19].

Interestingly, this study did not reveal any signs of myocardial inflammation even though 54% of athletes still reported symptoms at the time of data collection. However, these were unspecific symptoms, with most athletes reporting lingering fatigue (no chest pain or dyspnea).

Generally, the results of the present study are in line with a growing body of evidence indicating a very low incidence of myocarditis in athletes [14]. So far, the largest COVID-19 study in professional athletes by Martinez et al. [19] showed a low incidence of abnormal cardiac screening results (3.8%) during standard return-to-play examinations. Additional indication-based cardiac magnetic resonance in 30 of >800 college athletes found signs of myocarditis in only 0.6% of athletes. Another cardiac magnetic resonance-only study in 12 professional athletes showed no signs of cardiac involvement [13]. In almost all studies to date, cardiac magnetic resonance examinations have been performed in the acute or early phase after infection. Insights from a longitudinal study involving patients without COVID-19 with cardiac magnetic resonance-established myocarditis showed that the amount of LGE increased in up to 20% of the patients in the 3 months following initial diagnosis, despite the normalisation of cardiac enzymes [20]. In the present study, cardiac magnetic resonance was performed 182 days after the positive COVID-19 PCR result; therefore, this study elucidates the cardiac effects during long follow-up periods after infection. Our data suggest that the risk for mid to long-term myocardial damage is low to negligible in elite athletes after COVID-19 infection. These findings are in line with the results of a recently published study reporting that initial cardiac magnetic resonance signs of myocardial damage (elevated T1-mapping values and signs of LGE) were not observed in non-athletic patients after 6 months, despite symptom persistence in 52% of cases [18]. Although cardiac magnetic resonance is the most sensitive imaging test and the gold standard for diagnosis of myocardial inflammation, cardiac magnetic resonance should not be used as direct screening, as summarised in the current guidelines [21]. According to our data and the results of recent trials, cardiac magnetic resonance should primarily be conducted in athletes if it is indicated by symptoms or pathological findings via ECG, echocardiogram [19], or elevated relevant cardiac enzymes (e.g., hs troponin).

The current recommendations [21] are based on published data and the experience of the past three years. In summary, our results indicate that despite the initial awareness and results of the signs of myocardial inflammation at the beginning of the pandemic, the true incidence of myocardial damage in elite athletes is very low.

It should be noted that the observed cardiac magnetic resonance values for ventricle volumes and ejection fractions are typical physiological adaptations of elite athletes commonly described as “athlete’s heart” [22, 23].

Hence, future research should focus on when a safe return to sports is possible when cardiac magnetic resonance indicates signs of myocardial damage without active oedema. Is there a safe way – especially for elite athletes – to return to full sports activity despite cardiac magnetic resonance signs of previous myocarditis? So far there are no existing data on that. The current guidelines recommend at least 3 to 6 months of rest after a diagnosis of myocarditis

Figure 1: Bar graph illustrating the comparison of T1 and T2 mapping values in athletes and controls, with p = 0.530 for T1 mapping and p = 0.313 for T2 mapping.

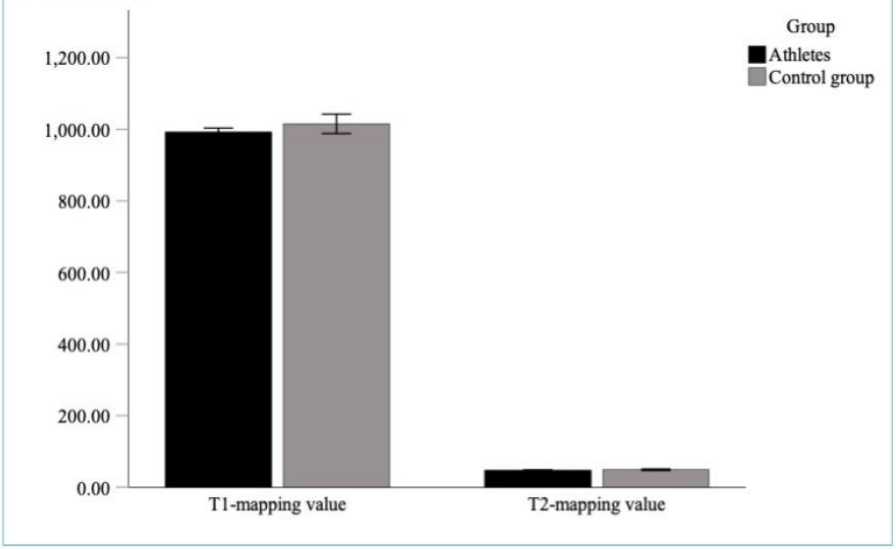
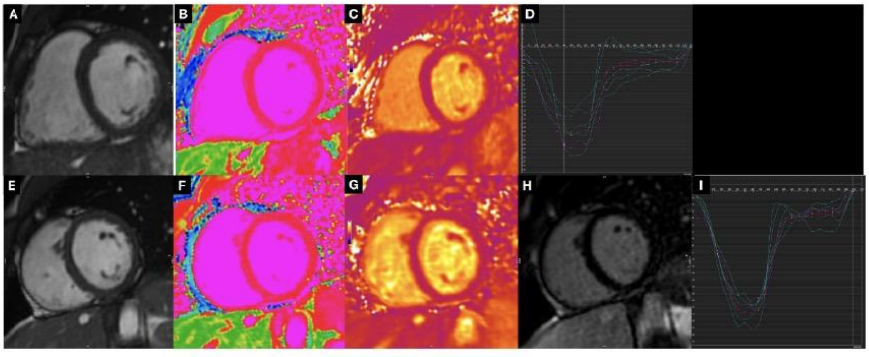


Table 2:
Details of cardiac magnetic resonance values and comparison between athletes and control subjects. The between-group comparisons show p-values, mean differences (non-standardised) and 95% CI. All comparisons between athletes and controls were made using independent t-tests. Levene's test for quality of variance showed no homogeneity of variances. Accordingly, Welch's t-test was used to assess the between-group significance. Because the data were not normally distributed, comparisons for LVEDVi (ml/m^2) and RVEF were conducted with Mann-Whitney tests; distributions did not differ between groups, Kolmogorov-Smirnov p = 0.118 and p = 0.059.

	Athletes (n = 26)				Control group (n = 9)				Group difference	
	Mean	SD	Median	IQR	Mean	SD	Median	IQR	p-value (two-sided)	Mean difference (95% CI)
LVEDD basal (mm)	52.47	4.62	51.70	4.62	50.81	5.17	51.50	7.30	0.374	1.7 (−2.1 to 5.4)
Left ventricle mass (g)	112.77	30.45	103.50	30.45	87.44	32.55	69.00	61.50	0.099	21.1 (−4.7 to 47.0)
Left ventricle mass / body surface area (g/m^2)	59.00	9.83	56.90	9.83	46.16	10.41	41.10	19.10	0.002	12.8 (5.0 to 20.7)
LVEDV (ml)	196.54	42.87	182.50	42.87	162.78	41.61	155.00	65.00	0.048	33.8 (0.3 to 67.3)
LVEDVi (ml/m^2)	103.39	15.62	99.70	99.70	84.77	20.96	91.00	17.00	0.031	12.3 (0.35 to 24.2)
LVESV (ml)	89.65	21.27	84.50	21.27	67.89	19.21	66.00	30.00	0.011	21.8 (5.4 to 38.1)
LVEF (%)	56.50	2.00	56.00	2.00	58.89	3.37	59.00	6.50	0.072	−2.4 (−5.0 to 0.3)
RVEDV (ml)	197.96	44.64	183.50	44.64	158.22	42.22	148.00	70.50	0.026	39.7 (5.1 to 74.4)
RVEDVi (ml/m^2)	104.06	16.52	101.15	16.52	86.64	12.69	84.90	15.15	0.007	17.4 (5.1 to 29.8)
RVESV (ml)	98.08	25.99	88.50	25.99	73.89	20.20	66.00	31.00	0.016	24.2 (4.7 to 43.6)
RVESVi (ml/m^2)	51.43	10.33	50.10	10.33	39.69	6.13	40.30	3.40	0.003	11.7 (4.2 to 19.2)
RVEF (%)	51.04	2.86	51.00	2.86	54.78	3.80	56.00	30.00	0.008	−3.7 (−6.2 to −1.3)
Native T1 (ms)	992.54	27.27	991.43	41.61	1015.36	35.31	1009.72	62.27	0.530	−22.8 (−46.0 to 0.3)
Native T2 (ms)	47.75	1.45	47.77	2.03	48.74	2.64	49.57	4.08	0.313	−1.0 (−3.1 to 1.1)
Global longitudinal strain (%)	16.59	1.45	16.50	1.45	17.84	2.32	18.20	4.45	0.066	−1.3 (−2.6 to 0.1)
Global circumferential strain (%)	16.73	1.07	16.85	1.07	18.69	2.20	17.80	4.30	0.029	−1.9 (−3.1 to 0.8)
Late gadolinium enhancement	0				n.a.					

LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; LVEDV: left ventricular end-diastolic volume; RVEDV: right ventricular end-diastolic volume; RVESVi: right ventricle end-systolic volume indexed to the body surface area.

Figure 2: Panels A–D show example images from a participant in the control group: (**A**) still frame of a medial short-axis cine image, (**B**) the corresponding T1 map, (**C**) the related T2 map, and (**D**) the associated strain analysis with image A. Panels E–I show examples from an athlete: (**E**) still frame of a medial short axis cine image, (**F**) the corresponding T1 map, (**G**) the related T2 map, (**H**) the late gadolinium enhancement image, and (**I**) the circumferential strain curve associated with image E.



in athletes. Future studies should focus on whether cardiac magnetic resonance is a valuable tool to guide a safe early return to play.

Strengths and limitations

The main strength of this study is the elite status of the included athletes. All were part of the German Olympic team at the time of inclusion, and many were international and national medalists. The cardiologists in charge of magnetic resonance imaging (MRI) had extensive experience in the field of cardiac MRI and sports medicine, reducing the margin for error in the assessment.

The sample was limited by its size (26 athletes) and the non-athletic random control group. Normally, athletes are only referred to cardiac magnetic resonance because of specific findings in baseline tests or cardiac-related symptoms. During the first pandemic wave, healthy athletes were advised to strictly avoid unnecessary contact. Therefore, no cardiac magnetic resonance data are available for healthy elite athletes during this period. Because COVID-19 has now affected such a large portion of the population, it seems impossible to find a control group that has not been infected since this study was conducted. The time points of data collection do not allow for acute and long-term conclusions, but the explicit aim of this study was to assess the midrange period after infection. Since the study population consisted of elite athletes only, the results cannot be generalised to the general population.

Conclusion

The findings of this study add to the growing body of evidence that the risk for mid- to long-term myocardial damage following COVID-19- is very low in elite athletes.

Acknowledgments

Author contributions: JZ, TS and H-GP conceived the study design ('Covid-19 in high-performance sport'), recruited funding and obtained ethics approval. KD, JZ and CS participated in coordination and data collection. KD, JZ, TS and H-GP examined the athletes as part of study and the return to play protocol. CS performed and evaluated, together with RM, the CMR exams and collected the CMR-specific data. CSy was responsible for the statistical analysis. CS and KD contributed equally to the manuscript and drafted the manuscript; therefore, both will serve as joint first authors. As JZ and RM contributed equally with their expertise and mentorship in their fields, there was the consensus of all authors that both should be stated as joint last authors. HGP, TS, JZ and RM revised and edited the manuscript and participated in data interpretation. All authors have read and approved the final manuscript and take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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4. Diskussion

4.1. Long-term cardiac MRI findings in elite athletes post-COVID-19

Our study assessed 26 elite athletes approximately 182 days post-COVID-19 infection and found no evidence of myocarditis or significant myocardial damage. The absence of LGE or fibrosis in our cohort reinforces the conclusion that subclinical changes described in earlier studies during the acute phase are no longer detectable after several months. This suggests that persistent myocardial damage is uncommon in elite athletes post-COVID-19, supporting a generally favorable cardiac prognostic in this population. These findings align with long-term investigations that consistently report a low prevalence of myocarditis and adverse cardiac events in athletes during extended follow-up periods [17,18].

In contrast, studies focusing on the acute phase, such as Rajpal et al., reported myocarditis in 15% of competitive athletes shortly after an infection, with 46% demonstrating LGE despite being asymptomatic [12]. This marked contrast highlights the transient nature of myocardial involvement during the acute phase, where early abnormalities detected through CMR frequently reflect temporary inflammatory responses that resolve over time and may not persist [17,18]. This observation underscores the importance of timing in CMR imaging, as early-phase imaging may capture temporary alterations that spontaneously resolve, while delayed imaging provides a more accurate assessment of persistent cardiac changes. Variability in LGE prevalence reported across studies [12,15,17] likely reflects differences in study populations, timing of CMR assessments, and criteria used to define myocardial abnormalities, highlighting the need for standardized CMR protocols.

4.2. Tailored CMR use in post-COVID-19 athletes

Building on our findings that elite athletes several months post-COVID-19 did not show significant myocardial damage or persistent subclinical abnormalities, it is crucial to explore the appropriate use of CMR imaging in this population.

4.2.1. Timing considerations for CMR imaging

CMR imaging is instrumental in detecting myocardial inflammation and other structural abnormalities. However, the timing of CMR imaging is critical for distinguishing between transient changes during the acute phase of infection and persistent, clinically significant abnormalities. To reduce the likelihood of capturing transient alterations and to provide a clearer assessment of lasting cardiac abnormalities, CMR was conducted approximately six

months post-infection in this study. This aligns with the recommendations of Wroblewski et al. who advocate for MRI imaging several months after recovery [17]. Our findings affirm that performing CMR in the chronic phase offers a more precise and reliable evaluation of long-term myocardial health, particularly in asymptomatic athletes.

4.2.2. Indications for CMR use

Our findings suggest that routine CMR screening is not necessary for asymptomatic athletes or those with mild symptoms post-COVID-19, as no cardiac abnormalities were detected, even in athletes reporting persistent non-cardiac symptoms. However, CMR should be prioritized for athletes presenting with significant cardiovascular symptoms such as chest pain, palpitations, or unexplained dyspnoea and for those who experienced severe COVID-19 infection [13,19–21]. In these cases, CMR is essential to exclude serious myocardial involvement before returning to high-intensity training. Athletes with persistent LGE or fibrosis should undergo ongoing monitoring due to their elevated risk of arrhythmias and impaired cardiac function [15,22].

4.2.3. Differentiating physiological from pathological CMR changes

In our cohort, some athletes displayed increased left and right ventricular volumes and mass, findings consistent with physiological adaptations commonly known as the “athlete´s heart” phenomenon. These benign changes reflect normal cardiac remodeling due to prolonged intensive training [21,23,24]. This observation aligns with the findings of D´Ascenzi, who also reported enlarged ventricular volumes in certain athletes[25]. Differentiating between physiological remodeling and true pathological changes is essential to avoid misdiagnosis and prevent unnecessary restrictions on athletic performance [21,25].

To address this, standardized CMR interpretation criteria for post-COVID-19 athletes should be established by reevaluating pre-existing reference values [25]. Such guidelines would improve diagnostic accuracy and consistency, allowing a clearer differentiation between the physiological adaptations typical of athletes and true pathological findings.

4.3. Protective factors for long-term cardiac health

The low prevalence of long-term myocardial complications in elite athletes may be attributed to superior cardiovascular conditioning and robust immune response. High levels of physical fitness are associated with enhanced immune function and increased infection resilience, likely contributing to the reduced prevalence of severe outcomes in this population [26,27]. Research indicates that elite athletes demonstrate an improved capacity to cope with and recover from transient myocardial stress during the acute phase of infection, especially when adhering

structured RTP protocols, thereby reducing the risk of sustained myocardial damage [21,23]. This enhanced recovery ability may explain the favorable outcome observed in our long-term follow-up.

4.4. The role of high-sensitive troponin and cardiac symptoms

Elevated inflammatory markers have been linked with an increased risk of myocardial abnormalities following COVID-19. Biomarkers such as high-sensitivity troponin (HST) are recommended as potential early indicators of myocardial involvement, as they may identify athletes who could benefit from further CMR evaluation and an extended rest period post-COVID-19 [19,20]. In our study, two athletes showed elevated troponin levels during their initial clinical assessment, approximately 34 days after their COVID-19 diagnosis. One athlete was subsequently diagnosed with Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), while the other had engaged in intense training before the assessment. These results show that none of the troponin elevations in our cohort were attributable to COVID-19 infection. Although elevated cardiac biomarkers have been reported during the acute phase in other studies, they generally resolve without resulting in lasting myocardial injury [17,25]. While we cannot entirely exclude the possibility that COVID-19-induced troponin elevation could lead to long-term myocardial damage, it is plausible that the transient nature of troponin elevations aligns with that of subclinical changes.

Although three athletes in our cohort initially reported cardiac symptoms, such as chest pain, these resolved within four weeks and were not associated with any detectable cardiac abnormalities on CMR. This suggests that initial cardiac symptoms may not reliably predict long-term myocardial complications. Nevertheless, given the potential risks associated with prolonged cardiovascular symptoms, it remains essential to monitor athletes with persistent symptoms closely, as they may still be at risk for underlying issues not captured in initial evaluations [19,28].

4.5. Impact of training intensity on cardiac recovery

Exercise intensity is a critical factor influencing cardiac recovery in athletes post-COVID-19. Modica et al. demonstrated that high-intensity training during early recovery is associated with an increased prevalence of subclinical myocardial changes such as LGE and myocardial edema, potentially predisposing athletes to long-term complications. In contrast, moderate-intensity exercise appears to have a protective effect, highlighting the importance of carefully managing training loads [29].

The notion that high-intensity training or an early return to such exercise may adversely affect cardiac health may also explain the variable prevalence of subclinical changes observed between elite and recreational athletes. For example, Rajpal et al. reported a higher prevalence of subclinical findings in elite athletes compared to collegiate athletes, potentially due to increased training intensity and a more rapid reintegration into competitive sports [12,15]. Similarly, Petek et al. suggested that a rapid escalation to peak training loads in elite athletes may elevate myocardial stress, exacerbating transient changes detectable by CMR [16].

In our study, this association was not observed, likely due to the strict adherence to a structured RTP protocol that emphasizes gradual reintegration into high-performance sports. Similar studies support this finding, highlighting that standardized RTP protocols reduce long-term cardiac complications by preventing premature training and allowing adequate time for myocardial recovery [30,31].

4.6. The role of fatigue and mental health

Despite the absence of myocardial damage detected by CMR in our cohort, the high prevalence of persistent fatigue - reported by over half of the athletes for more than four weeks - underscores the need to consider factors beyond immediate cardiac findings. Although fatigue may not correlate with immediate CMR-detectable abnormalities, it remains a critical component in risk assessments due to its potential impact on long-term cardiovascular health and athletic performance.

4.6.1. Effects of fatigue on cardiovascular health and performance

Fatigue is a complex, multifactorial condition characterized by persistent, overwhelming exhaustion that can impair both physical and mental performance [32]. Prolonged fatigue has been shown to impair cardiovascular function by disrupting autonomic regulation, as reflected in reduced heart rate variability (HRV) and heightened cardiovascular strain. This autonomic dysfunction can impair the cardiovascular system´s ability to adapt to physical demands, potentially increasing the risks of adverse effects [28,32,33].

HRV assessment provides a sensitive, noninvasive measure for evaluating autonomic dysfunction and the body´s stress response [33]. To complement HRV monitoring, established diagnostic fatigue screening like the Chalder Fatigue Scale (CFS), which evaluates both physical and mental dimensions of fatigue, should be integrated into RTP protocols [34]. This approach will allow for tailored training adjustments, optimizing recovery strategies for affected athletes.

Chronic fatigue in athletes has also been associated with reductions in peak oxygen uptake (VO2 max), a key marker of cardiovascular fitness and endurance capacity [31]. Although VO2 max was not directly measured in our study, the persistence of fatigue could still have impacted exercise capacity in our study cohort. Gradual exercise progression, such as graded exercise therapy (GET), has been shown to improve VO2 max and overall functional capacity in cases of post-viral fatigue syndromes [35]. This strategy could be adapted for post-COVID-19 athletes to address fatigue while supporting HRV and VO2 max retention.

4.6.2. Interaction between fatigue and psychological stress

Fatigue was the most frequently reported symptom in our cohort, with qualitative data indicating that many athletes also experienced significant mental stress, such as performance pressure and uncertainty about returning to pre-COVID-19 fitness levels. Psychological stress and fatigue are closely interlinked, with prolonged fatigue contributing to increased psychological stress in athletes post-COVID-19, which can exacerbate autonomic dysfunction and cardiovascular strain, further complicating recovery [36]. Additionally, psychological factors such as anxiety, performance pressure, and depressive symptoms can disrupt HRV and amplify the psychological impact of fatigue [37,38]. These combined stressors may lead to chronic autonomic imbalance, further hindering cardiovascular recovery and athletic performance. Therefore, mental health screening should be integrated into post-COVID-19 evaluations to complement fatigue assessment and guide training adjustments.

Validated tools, such as the Generalized Anxiety Disorder scale (GAD-7) for anxiety, the Recovery Stress Questionnaire for Athletes (REST-Q-Sport) for stress and recovery, and the Profile of Mood States (POMS) for mood disturbances, are essential for identifying athletes who need psychological support [39–41]. Evidence-based interventions, including cognitive behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR), have shown efficacy in reducing psychological stress and alleviating fatigue, especially in athletes recovering from prolonged illness [42,43]. Incorporating resilience-building strategies into recovery protocols ensures a more comprehensive and holistic approach to rehabilitation, addressing the physical and psychological aspects of recovery in elite athletes [36,37].

4.7. Recommendations for the refinement of RTP guidelines

Given the risks of myocarditis and other cardiovascular complications in athletes post-COVID-19, current RTP protocols emphasize early cardiovascular assessments to ensure a safe return to sport. Protocols, such as those by Elliot et al. and the American College of Cardiology

(ACC) prioritize diagnostic tools like electrocardiogram (ECG) to detect arrhythmias, echocardiography to assess cardiac function, and blood tests for biomarkers such as high-sensitivity troponin (HST) and brain natriuretic peptide (BNP) to evaluate cardiac stress. CMR imaging is recommended when a detailed assessment is necessary. Gradual increases in training intensity are also integral, allowing athletes to safely regain peak performance [24,29].

However, our findings indicate a need for more holistic and individualized RTP guidelines, encompassing physical and psychological dimensions, to support the long-term recovery and performance of elite athletes post-COVID-19.

4.7.1. Targeted CMR use

Our study found that long-term myocardial damage is rare, although transient subclinical changes may occur in early recovery. Therefore, we recommend a more selective CMR approach to avoid unnecessary interventions:

- **Symptom-based application:** CMR should be prioritized for athletes with significant cardiovascular symptoms (e.g., chest pain, palpitations, or dyspnea) or severe COVID-19, as they are at higher risk for myocardial complications.

- **Indicated follow-up:** Persistent LGE or fibrosis, associated with adverse outcomes like arrhythmias, warrants ongoing CMR monitoring in athletes at risk.

- **Avoidance of routine early screening:** Routine CMR screening in asymptomatic athletes during early recovery is unnecessary and may lead to overdiagnosis of transient non-pathological changes.

- **Establishing interpretation guidelines:** Standardized interpretation criteria are essential to distinguish between physiological changes (e.g., the “athlete´s heart”) from pathology, supporting evidence-based decision-making.

4.7.2. Routine fatigue and mental health screening

The prevalence of persistent fatigue in our study cohort underscores the need to expand RTP protocols beyond cardiovascular health to address autonomic regulation and psychological stress:

- **Systematic fatigue assessment**: Standardized tools like the Chalder Fatigue Scale (CFS) should assess fatigue severity and impact on performance.

- **Continuous HRV monitoring:** Given fatigue´s link to autonomic dysfunction, HRV monitoring can track autonomic regulation and recovery status, informing tailored RTP strategies.

- **Psychological assessment**: Tools such as the Generalized Anxiety Disorder Scale (GAD-7) and the Recovery Stress Questionnaire for Athletes (REST-Q-Sport) can identify mental health issues closely linked to fatigue.

- **Resilience-building strategies:** Interventions such as cognitive behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR) can enhance mental resilience, supporting holistic recovery.

4.7.3. Adaptive and flexible training protocols based on individualized criteria

Gradual reintegration into training, guided by individual health metrics, is crucial to minimize the long-term complications:

- **Continuous multidisciplinary monitoring**: Ongoing assessment by a team of cardiologists, sport scientists, and psychologists is necessary to manage the complex interplay of persistent symptoms, mental health issues, cardiovascular function, and performance.

- **Flexible, gradual reintegration:** Training protocols should be tailored to the athlete´s individual parameters, allowing for gradual increases in intensity and flexibility to adjust as needed. This included options to revert to a previous intensity level or to incorporate recovery periods to prevent overtraining and its associated consequences.

4.8. Strengths and limitations

Strengths

- **Comprehensive long-term follow-up:** The 182-day follow-up provided a reliable basis for assessing long-term cardiac health in elite athletes post-COVID-19, minimizing the risk of overdiagnosing transient myocardial changes, and enabling a more accurate evaluation of persistent cardiac effects.

- **High diagnostic accuracy with advanced CMR imaging:** using CMR as the gold standard in cardiac imaging allowed for a sensitive assessment of structural and myocardial changes, distinguishing physiological adaptations from pathological changes. Expert interpretation further enhanced diagnostic accuracy reliability.

- **Combined objective diagnostics and subjective assessment:** Integrating CMR findings with subjective reports of symptoms provided valuable insights into objective cardiac findings but also perceived limitations that may not appear on imaging.

- **Targeted focus on elite athletes**: The exclusive focus on elite athletes avoided the confounding factors associated with mixing data from recreational athletes, allowing for a more precise understanding of the cardiovascular recovery process unique to elite athletes and ensuring tailored recommendations to their specific demands.

- **Adherence to structured RTP protocols**: Strict adherence to RTP protocols, including appropriate rest periods and gradual training increases, minimized variability, and enhanced comparability, setting this study apart from others including various athlete cohorts where protocol adherence may vary.

Limitations

- **Limited sample size and generalizability:** The small cohort of 26 elite athletes provided focused insights but limited statistical power and generalizability to broader athletic populations. A larger cohort would strengthen these findings.

- **Lack of direct psychological and autonomic assessment:** While the study identified persistent symptoms like fatigue, it did not include direct measures of psychological stress or autonomic function (e.g., HRV), factors known to influence cardiovascular health.

- **Selection bias in elite athlete focus:** Focusing on elite athletes with access to specialized healthcare and high fitness levels introduces potential selection bias, limiting the applicability of findings on diverse fitness levels and healthcare access.

4.9. Future research

To address current gaps and improve long-term cardiovascular management in elite athletes post-COVID-19, future research should prioritize the following areas:

1. **Validation of subclinical myocardial changes in larger cohorts:** Although our findings suggest a low prevalence of persistent myocardial damage, larger multi-centre studies are needed to confirm these results and assess the clinical significance of subclinical changes, such as LGE, with greater statistical power.

2. **Refinement of CMR recommendation:** The targeted use of CMR is essential for identifying subclinical myocardial abnormalities. Future research should refine CMR guidelines by determining optimal timing and clinical indications, balancing sensitivity for detecting significant abnormalities to minimize overdiagnosis. This approach will support evidence-based RTP guidelines that ensure safe and individualized decisions without unnecessary restrictions for athletes.

3. **Incorporating psychological and autonomic factors in cardiovascular recovery:** Given the high prevalence of persistent fatigue, future studies should explore the interactions between mental health, autonomic function, and cardiovascular recovery in elite athletes. Integrating psychological stress assessments with autonomic markers (e.g., HRV) may provide insights into recovery trajectories and facilitate early detection of cardiovascular strain, enhancing interventions that address performance limitations and mental well-being in post-COVID athletes.

4. **Investigating the impact of training intensity on cardiac recovery:** While our study did not observe a direct correlation between high training intensity and long-term myocardial damage, likely due to the strict adherence to RTP protocols, controlled studies are needed to systematically vary training intensities during recovery. These studies could monitor key physiological markers, such as HRV and VO2 max, to establish clearer guidelines on safe training progression, further informing RTP protocols.

4.10. Fazit

Our study provides valuable insights into the mid-to long-term cardiovascular health of elite athletes post-COVID-19, reinforcing that persistent myocardial damage is uncommon and supporting a generally favorable prognosis. Six months after infection, CMR examinations revealed no evidence of myocarditis or significant myocardial damage. The absence of LGE or fibrosis suggests that subclinical myocardial changes observed in the acute phase are transient and typically resolve over time. Several athletes exhibited signs of “athlete´s heart”, characterized by increased ventricular volumes and myocardial mass, representing normal physiological adaptations to intensive training.

The targeted use of CMR, considering optimal timing, indications, and standardized interpretation guidelines to differentiate between physiological and pathological findings, is essential to prevent complications and avoid overdiagnosis.

Persistent fatigue affected over half of the athletes in our cohort. Although not directly linked to CMR abnormalities, when combined with mental stress, it can present a significant barrier to athletic performance and may contribute to long-term cardiovascular strain. This highlights the importance of incorporating non-cardiac screenings, such as fatigue and psychological assessments, in RTP decision-making.

Moreover, training programs should be flexibly adjusted based on individualized parameters (e.g., HRV) through continuous monitoring by a multidisciplinary team to meet individual recovery trajectories and overtraining.

This holistic, individualized approach, which integrates physical and psychological dimensions with standardized CMR use, addresses the unique recovery trajectories of each athlete, ensuring a safe and sustainable return to high-performance sports.

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