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COVID-19 Outcomes and Persistent Symptoms in patients with Hypertrophic Cardiomyopathy: Association with pre-existing Cardiovascular Magnetic Resonance Phenotype

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Abstract

Background

The impact of COVID-19 in hypertrophic cardiomyopathy (HCM), particularly in the post-vaccine era, remains incompletely understood. We evaluated whether pre-existing cardiovascular magnetic resonance (CMR) phenotypes are associated with COVID-19 outcomes and recovery.

Methods

In 1,704 participants from the international HCM Registry (HCMR) with prior CMR phenotyping, COVID-19 infection and outcomes were assessed using patient-reported questionnaires. Associations between baseline CMR features and hospitalisation or impaired recovery (≥3 months) were evaluated using multivariable logistic regression.

Results

Among 767 participants with reported COVID-19 infection (mean age 49±11 years), 4% required hospitalisation, 19% reported impaired recovery at ≥3 months and 2 (0.26%) non-cardiac deaths occurred. Persistent symptoms were common, particularly fatigue (67%) and dyspnoea (33%). After adjustment, adverse CMR features, including hypertrophy, fibrosis (LGE), and extracellular volume, were not associated with hospitalisation or impaired recovery. Female sex and younger age were associated with persistent symptoms.

Conclusions

In this large HCM cohort, COVID-19 was associated with a substantial burden of persistent symptoms, but pre-existing CMR phenotype was not associated with adverse outcomes. These findings suggest that baseline structural disease severity may not identify patients at higher risk of post-COVID complications, although results should be interpreted in the context of self-reported outcomes and limited event rates.

Summary box

What is already known on this topic:

- Patients with hypertrophic cardiomyopathy (HCM) have increased cardiovascular risk, but the impact of COVID-19, particularly in the post-vaccine era, remains uncertain.

What this study adds:

- In a large international HCM cohort, COVID-19 was associated with a substantial burden of persistent symptoms (~1 in 5).

- Pre-existing CMR markers of disease severity (hypertrophy and fibrosis) were not associated with hospitalisation or impaired recovery.

How this study might affect research, practice or policy:

- Routine escalation of post-COVID surveillance based solely on baseline imaging phenotype in HCM may not be warranted.
- Management should instead focus on symptom-driven, multidisciplinary care, particularly for patients with persistent symptoms.

Introduction

The COVID-19 pandemic has disproportionately affected individuals with pre-existing cardiovascular disease, with multiple studies demonstrating their increased morbidity and mortality.[1,2] Patients with hypertrophic cardiomyopathy (HCM) represent a particularly vulnerable population due to their heightened baseline risk of arrhythmias, heart failure, and sudden cardiac death. However, the specific impact of COVID-19 on individuals with HCM remains poorly understood. Given that HCM is a heterogenous disease, with varying degrees of left ventricular hypertrophy, fibrosis, and microvascular dysfunction, it may be helpful to determine whether certain phenotypic features are associated with worse outcomes following COVID-19 infection.

While previous studies have shown that cardiovascular comorbidities, such as hypertension and coronary artery disease, are strong predictors of severe COVID-19 outcomes,[2] the effect of COVID-19 on patients with inherited cardiomyopathies, particularly HCM, has not been fully elucidated. These patients already experience an increased risk of cardiac decompensation, therefore viral infections, such as SARS-CoV-2, could exacerbate myocardial stress leading to worse acute outcomes and prolonged post-viral symptoms. Additionally, many HCM patients experience chronic cardiac symptoms such as fatigue, breathlessness, and chest discomfort, which overlap with symptoms of long COVID, making it essential to investigate whether this population is at an even greater risk of persistent post-viral morbidity.

The Hypertrophic Cardiomyopathy Registry (HCMR) is a large database of individuals with HCM and is diverse sampling participants from 44 sites across 6 countries.[3] The database incorporates extensive clinical, genetic, and advanced cardiovascular magnetic resonance (CMR) phenotyping[3]. This rich dataset provides a unique opportunity to explore the interplay between structural and functional myocardial abnormalities and clinical outcomes in a well-characterised population. In particular, the availability of detailed CMR parameters, such as left ventricular hypertrophy, fibrosis burden, myocardial shape, left ventricular outflow tract (LVOT) obstruction, and systolic function, allows for a nuanced evaluation of how these features may influence vulnerability to severe COVID-19 and its long-term sequelae. Leveraging the HCMR dataset, this study aimed to assess the impact of COVID-19 in individuals with HCM, with a specific focus on identifying phenotypic determinants of adverse outcomes and persistent post-viral symptoms.

Methods:

The full study design for HCMR, a prospective observational study, has been previously outlined, [3] with relevant methods summarised in the appendix. After obtaining written informed consent, participants underwent standard clinical evaluation blood sampling, genetic and biomarker analysis and CMR. CMR measures included cine imaging-derived left and right ventricular mass, regional wall thickness and hypertrophy pattern; left and right ventricular end diastolic and end systolic volumes; and systolic function assessed by ejection fraction and regional wall thickening. Focal myocardial fibrosis was assessed using late gadolinium enhancement, including presence, localisation, and scar pattern, while diffuse interstitial fibrosis was quantified using native and post contrast T1 mapping with extracellular volume estimation. [3] Longitudinal follow-up is ongoing to observe the incidence of cardiovascular events, as adjudicated by a clinical events committee.

Inclusion and Exclusion Criteria

Patients included were aged 18–65 years with a confirmed diagnosis of HCM defined as unexplained left ventricular (LV) hypertrophy (wall thickness >15 mm) without cavity dilation or identifiable causes such as uncontrolled hypertension or aortic stenosis.

Patients with known infiltrative or hypertrophic conditions (e.g., amyloidosis, sarcoidosis, Fabry disease, Danon disease, or Noonan syndrome) were excluded if diagnosed via HCMR genotyping or clinical evaluation. Other exclusion criteria included: 1) age >65 years due to increased competing mortality risks (e.g., coronary artery disease, cancer); 2) history of septal myectomy or alcohol septal ablation; 3) previous myocardial infarction or known coronary artery disease; 4) incessant ventricular arrhythmias; 5) inability to lie flat or contraindications to contrast-enhanced CMR (e.g., pacemakers, defibrillators, severe claustrophobia, stage IV/V chronic kidney disease); 6) diabetes mellitus with end-organ damage; 7) pregnancy; 8) inability to provide informed consent; 9) if they were not sent, or did not respond to, the COVID-19 questionnaire; 10) if they did not complete CMR or retracted consent.

Patient Enrolment

Enrolment occurred from April 2014 to April 2017 across 44 sites in the United States (18), Canada (4), United Kingdom (13), Italy (4), Germany (3), and the Netherlands (2).[4]

COVID-19 Assessment

A detailed history was taken from HCM patients to ascertain their COVID-19 status and clinical course. Key questions included: 1) Have you been diagnosed with COVID-19? 2) Was it confirmed by testing? 3) What was the date of the test confirmation, to the best of your knowledge 4) Did you experience breathlessness? 5) Did you experience palpitations? 6) Did you experience syncope? 7) Did you experience memory loss? 8) Did you experience fatigue? 9) Did you experience loss of sense of taste 10) Did you experience headache? 11) Were you admitted to the hospital? 12) Did you require oxygen? 13) Did you require mechanical ventilation? 14) Did you experience any heart complications? 15) Have your symptoms returned to baseline? The first questionnaires were sent in November 2021 and the last in November 2024 and sites retrospectively collected data related to COVID-19 infections as early as 2020.

Primary End Points

Data was analysed from the first instance of self-reported COVID-19 infection. Symptoms and hospitalisation were self-reported. Impaired recovery was defined as self-reported impaired recovery ≥3 months post COVID-19 infection. In addition to the questionnaire, patients were telephoned annually, and deaths were investigated by the respective centres.

Statistical Analysis

Normality was assessed visually. Continuous variables were analysed using two tail Mann-Whitney U test or independent t-test and were presented as median [IQR] or mean ± standard deviation, for non-parametric and parametric data respectively. Binary categorical variables were analysed using the Fisher's exact test and non-binary categorical variables were analysed with the Chi squared test. Ordinal variables, such as the New York Heart Association (NYHA) functional class, were assessed using the Cochran–Armitage trend test. The NYHA classification was used to evaluate the extent of physical activity limitation. The thresholds used for abnormal CMR values follow established CMR reference and guideline sources.[5]

The frequency of COVID-19 outcomes was expressed as a percent of the total number of HCM patients infected with COVID-19 that responded to the question. Multivariable logistic regression was used to assess how CMR and echo features relate to hospitalisation and impaired recovery post-COVID-19. For each covariate, the odds ratio was calculated adjusting for common COVID-19 risk factors (age, sex and BMI) and reported using 95% confidence intervals. Most variables had < 3% missingness and clinical relevance guided covariate inclusion. All statistical analyses were performed using open-source software (Python and R). The analysis being largely exploratory, multiple comparison corrections were not applied.

Patient and Public Involvement

We participated in a patient priority setting exercise in collaboration with the James Lind Alliance. The top 10 questions prioritized - based on importance to patients, carers and the public - were published in Thorax[6]. Of these, three directly speak to the need to evaluate the long-term effects of COVID-19 and the impact of comorbid cardiac diseases and our research helps to address this unmet need.

Results

Baseline Demographics

Figure 1 shows the flow chart demonstrating how data for this ancillary study were obtained. Subtracting those who withdrew consent, did not complete CMR or those who were not sent the questionnaire, the proportion of participants who were sent the questionnaire and responded was (1704/2046 =) 83.2%. In the appendix, table 1 compares the baseline characteristics of participants in the registry who were included in the present study compared to those that were not.

Of those who responded to the questionnaire, 767 (45%) reported a COVID-19 infection (mean age: 49 ±11 years; 73% male, 87% white), with 96% of cases confirmed through laboratory testing. Recurrent infections were reported in 3% of cases. Infections per year can be found in Appendix Table 2, with the majority of infections occurring in 2022 (54.8%, likely Omicron-related), followed by 21.4% in 2021 and 14.9% in 2023.

Figure 1: Flow chart outlining the recruitment of patients.

Table 1 demonstrates a descriptive comparison of baseline characteristics of HCM patients with and without reported COVID-19 infection. The baseline characteristics between these groups were largely similar, although, patients with reported infection were more likely to be slightly younger, white ethnicity, have a lower prevalence of heart failure (and severe heart failure), hypertension and dyspnoea. Patients with and without reported COVID-19 also had similar CMR characteristics.

Table 1: A table comparing the baseline characteristics in HCM patients that reported COVID-19 compared to those that did not.

Baseline feature	Total (n = 1704)	Reported COVID-19 (n = 767)	No reported COVID-19 (n = 937)
Age (yrs)	50 ± 11	49 ± 11	50 ± 11
Male	1208 (70.9)	555 (72.4)	653 (69.7)
BMI (kg/m²)	28.4 [25.3 - 32.2]	28.1 [25.4 - 31.8]	28.6 [25.2 - 32.6]
Minority	256 (15.0)	99 (12.9)	157 (16.8)
History of syncope	219 (12.9)	90 (11.8)	129 (13.8)
History of heart failure	81 (4.8)	26 (3.4)	55 (5.9)
History of hypertension	618 (36.4)	251 (32.9)	367 (39.3)
History of stroke	35 (2.1)	15 (2.0)	20 (2.1)
History of chest pain	542 (31.9)	230 (30.1)	312 (33.4)
Type 1 diabetes mellitus	9 (0.5)	3 (0.4)	6 (0.6)
Type 2 diabetes mellitus	119 (7.0)	42 (5.5)	77 (8.2)
Dyspnoea	728 (42.9)	298 (39.1)	430 (46.0)
Systolic blood pressure (mmHg)	130 ± 17	130 ± 17	129 ± 18
Diastolic blood pressure (mmHg)	76 ± 12	77 ± 12	76 ± 12
NYHA functional class			
I	1134 (67.5)	524 (69.5)	610 (65.9)
II	443 (26.4)	198 (26.3)	245 (26.5)
III	98 (5.8)	32 (4.2)	66 (7.1)
IV	4 (0.2)	0 (0.0)	4 (0.4)
Current smoker	205 (12.1)	79 (10.4)	126 (13.5)
ESC SCD risk score	2.3 [1.6 - 3.5]	2.2 [1.6 - 3.4]	2.3 [1.7 - 3.6]
Genetics			
Sarcomere mutation (+)	578 (35.3)	260 (35.1)	318 (35.5)
Study Measurements			
Resting LVOT Obstruction	297 (24.0)	114 (21.0)	183 (26.3)
NTproBNP	242 [105 - 596]	230 [91 - 573]	253 [111 - 621]
TnTStat	11 [7 - 16]	10 [7 - 15]	11 [8 - 16]
CMR			
LV mass indexed (g/m²)	80 [66 - 97]	80 [66 - 97]	81 [66 - 97]
LV max. wall thickness (mm)	19.8 [17.1 - 23.1]	19.7 [17.1 - 23.1]	19.8 [17.1 - 23.1]
LV EF (%)	65 [59 - 70]	64 [59 - 70]	65 [59 - 70]
RV EF (%)	68.3 [61.0 - 76.0]	68.1 [60.6 - 75.8]	68.5 [61.3 - 76.5]
LGE (% of LV mass)	0.08 [0.00 - 1.60]	0.05 [0.00 - 1.61]	0.12 [0.00 - 1.60]

LV global longitudinal strain (%)	-10.91 ± 2.59	-11.03 ± 2.59	-10.82 ± 2.59

Data is displayed as count (proportion as a percentage of the total in that category), mean ± SD (for normally distributed variables), median [IQR] (for non-normally distributed variables). ESC SCD risk = European Society of Cardiology sudden cardiac death risk. LVOT= left ventricular outflow tract. LV EF= left ventricular ejection fraction. EF = right ventricle ejection fraction. LGE= late gadolinium enhancement.

Clinical Course during Acute Infection (patient survey)

The prevalence of symptoms among those reporting COVID-19 infections stratified by sex is shown in

Figure 2. Fatigue was the most reported COVID-19 symptom (63%), followed by headache (44%), dyspnoea (31%), loss of taste/smell (25%), palpitations (11%), and memory loss (5%).

Table 2 shows how COVID-19 acute infection symptoms associated with baseline demographic and CMR characteristics. HCM patients reporting headache were more likely to be younger, have a history of syncope, lower blood pressure, and a history of smoking. Those reporting palpitations were more likely to have a prior history of syncope, chest pain, dyspnoea, and a higher LGE burden. Patients experiencing loss of smell tended to be younger, had pre-existing dyspnoea, and a slightly elevated ESC-predicted 5-year risk of sudden cardiac death. In contrast, those reporting syncope during COVID-19 were more likely to have a history of stroke.

In Table 2, the sample size varies owing to participants not always answering all the questions in the questionnaire.

Table 2: Reported COVID-19 Symptoms Associated with Baseline Demographic and CMR Characteristics.

Reported Symptom	Sample size and response rate	Baseline Demographic Detail Associated with Increased Risk	Symptom Declared	Symptom Not Declared	P-value
Fatigue	719 (93.7%)	Female Sex	30.6%	20.3%	0.004
Headache	721(94.0%)	Smoking	15.1%	6.8%	<0.001
		Lower SBP	128±17	133±17	<0.001
		Younger Age	48±11	51±11	0.001
		Lower DBP	75±12	78± 11	0.003
		History of Syncope	15.1%	8.6%	0.007
Breathlessness	724(94.4%)	Female Sex	33.9%	24.2%	0.008
		History of chest pain	35.5%	27.2%	0.024
		Pre-existing dyspnoea	46.2%	35%	0.004
Loss of sense of smell	714 (93.1%)	Younger Age	47±11	50±11	0.005
		Higher ESC SCD Risk Score	2.6	2.1	0.011
		Pre-Existing Dyspnoea	46%	36.3%	0.023
Palpitations	718 (93.6%)	Pre-Existing Dyspnoea	59.3%	35.7%	<0.0001
		Chest Pain	44.2%	28.3%,	0.004
		Previous History of Syncope	20.9%	10%,	0.006
		Presence of LGE	59.3%	47.2%,	0.039
Memory loss	715 (93.2%)	RV EF (%)	75	68	0.002
Syncope	718 (93.6)	Previous history of stroke	14.3%	1.7%	0.028

Continuous variables were analysed using the Mann-Whitney U test. Binary categorical variables were analysed using the Fisher's exact test and non-binary categorical variables were analysed with the Chi squared test. SBP = systolic blood pressure, LGE = late gadolinium enhancement, ESC SCD risk = European Society of Cardiology sudden cardiac death risk. RV EF = right ventricle ejection fraction.

Among those with reported infections, 30 patients (4%) required hospitalisation. Advancing age (56±8 vs 49±11, p=0.001), non-white ethnicity (26.7% vs 12.3%, p=0.044), higher systolic blood pressure (137±19 vs 130 ± 17, p=0.021) and baseline type 2 diabetes (16.7% vs 5.0%, p=0.019) was associated with increased risk of hospitalisation.

18 (2%) needed oxygen therapy, with advancing age increasing this risk (57±7 vs 49±11, p=0.002). 9 (1%) experienced cardiac complications, and 2 (0.3%) required mechanical ventilation. Two patients had non-cardiac deaths: 65-year-old female, with diabetes (BMI 34.4 kg/m², NYHA class III, LVEF 60%, RVEF 69%, no significant late gadolinium enhancement (LGE) or LVOT obstruction) and 71-year-old male with no diabetes (BMI 26.7 kg/m², NYHA class I, LEVF 60%, RVEF 52%, no significant LGE, or LVOT obstruction).

Figure 2: Symptom Burden During COVID-19 Infection

Self-reported symptoms post-COVID-19

At follow-up, 31% (232/753) of patients reported incomplete recovery. However, when only including patients asked 3 months after initial infection, 19% (124/668) reported no return to baseline.

Younger and female patients reported more post COVID-19 symptoms. On comparing individual clinical characteristics based on presence or absence of specific symptoms, we found that patients with pre-existing dyspnoea, chest pain and female gender were more likely to report post-COVID dyspnoea.

Adverse CMR Phenotypes

After adjusting for age, sex and BMI, adverse CMR phenotypes were not detected to be associated with increased risk of hospitalisation, symptom burden and impaired recovery, as shown in Figure 3.

Figure 3: Adjusted odds ratio for hospitalisation and impaired recovery.

Discussion

Given the conflicting evidence regarding the cardiovascular impact of COVID-19 on HCM, our study aimed to assess the relationship between adverse CMR features and clinical outcomes of COVID-19. In this large, well-phenotyped HCM cohort, we observed two key findings: (1) a substantial burden of persistent post-COVID symptoms, and (2) no detectable association between pre-existing CMR phenotype and adverse outcomes.

Our surveyed HCM population had a higher hospitalisation rate with COVID-19, compared to the general infected population in the US and UK.[7,8] 19% of patients demonstrated impaired recovery at 3 months, a rate higher than the long COVID prevalence in the US.[9] Despite this, adverse CMR phenotypes were not correlated with increased risk of hospitalisation or impaired recovery.

Hospitalisation and mortality

Overall, our cohort (mean age 49; 76% infected between 2021 and 2022) demonstrated marginally higher rates of hospitalisation (4%) and mortality (0.26%) than estimates for the general COVID-19-infected population. For comparison, in the United States the infection-related hospitalisation rate between December 2021 and February 2022 for individuals aged 50-69 was 2.38%.[7] In England, the infection-related hospitalisation risk was approximately 0.25% and infection fatality risk was 0.025% between March 2022 and March 2023 for individuals aged 45-54 years reported an infection.[8] Our findings are consistent with prior studies suggesting worse COVID-19 outcomes in patients with HCM; for example Gimeno et al reported a 30% hospitalisation rate among COVID-19 infected HCM patients, notably their cohort had a higher mean age and level of co-morbidities.[10]

Although hospitalisation rates were higher in our cohort, direct comparisons with other population studies may be limited due to possible differences in SARS-CoV-2 variants, ascertainment, age distributions, vaccination status and baseline health characteristics. Additionally, our study is confounded by outcomes being self-reported and self-selected. When considered in this context, the matched hospitalisation rate may not be markedly different from that of the general population.

Adverse CMR phenotype

It was previously hypothesized that adverse phenotypes may correlate with worse outcomes in HCM patients. This was thought to be due to infection-induced systemic stress may lead to a hyperdynamic state, worsening LVOT obstruction, exacerbating myocardial abnormalities which in turn may precipitate arrhythmias, and lead to decompensated heart failure.

Contrary to expectations, our study found no significant association of LVOT obstruction with reported COVID-19 infection. One possible explanation for the lack of association might be that these patients likely adopted stricter protective behaviours, such as self-isolation. Additionally, individuals with more advanced disease and poorer baseline health may have been less inclined to recognise or report subtle deteriorations in their condition. In contrast, a study by Gimeno et al that used a HCM cohort reported a 5.6-fold increase in COVID-related mortality among patients with LVOT obstruction.[10]

Here, we also found no other significant associations between CMR features and reported COVID-19 infection, likely due to lower incidence of severe infections in this cohort. Pezel et al retrospectively analysed CMR data from patients hospitalised with COVID-19 and found that LVEF and LGE significantly associated with all-cause death.[11] In our study, given the low in-hospital mortality among those with COVID-19, we were unable to validate this relationship. Another key difference from the prior studies is the sex distribution of participants. In our cohort, 73.5% were men, whereas previous studies have shown that women with HCM are at greater risk of adverse outcomes from COVID-19 infections, including higher mortality.[12] Future studies may consider larger gender-balanced cohorts to examine such associations.

Symptom burden and long-COVID

Nearly 1 in 5 of the HCM patients who had COVID-19 had incomplete recovery in our cohort (mean age 49). This contrasts to nearly 1 in 10 people age 35-49 year olds in the US getting long COVID.[9] The increased prevalence on long COVID in patients with HCM suggests there may be an interplay between HCM and persistent symptoms after COVID-19 infections.

Our result is concordant with the prevalence of persistent symptoms of long COVID among individuals with other cardiac pathologies. Ioannou et al reported a 34% higher risk of physician-documented long COVID in congestive heart failure patients compared to those without pre-established heart failure.[13] Furthermore, a 2023 meta-analysis, involving 201,906 patients, reported a 28% times higher risk of long COVID in patients with ischaemic heart disease.[14] The similarity in prevalence across these cardiac conditions could suggest common pathophysiological processes underpin the increased susceptibility to long COVID. Our study also found that female sex was associated with prolonged symptoms following COVID-19, in line with previous findings. In the general population, women are more likely to report long COVID, which may partly account for this observation. In the context of HCM, standard diagnostic thresholds for wall thickness (15 mm for probands, 13 mm for familial cases) may also underestimate disease severity in women, and this may also contribute to a greater symptom burden among women.[15]

Clinical Implications

Several studies have underscored the importance of holistic assessment in the general long COVID population to support timely referral to services such as cardiopulmonary rehabilitation, mental health support, and occupational or social therapy.[16,17]

Limitations

The data in this HCM registry is geographically diverse, having sampled from 44 sites across 6 countries. However, the majority of our cohort is young and white (87%), thus limiting applicability to diverse populations across ages. Furthermore, the registry is susceptible to selection bias because it excludes those with severe HCM (i.e., those with ICDs and MRI contraindication) and those with significant comorbidities.[3]

COVID-19 infection and symptoms were captured through a questionnaire, therefore open to variations in subjectivity and recall bias. Patients also have natural variations in symptom thresholds, and patients with HCM may be hyperaware of symptoms due to preconceived risk, thus at risk of over-reporting. Information on duration of hospitalisation, and intensity of treatment was not systematically collected as part of the COVID-19 questionnaire and therefore could not be analysed. We attributed changes from baseline 3 months after acute COVID-19 infection to long COVID, however, alternative pathologies may have contributed to the symptom change potentially leading to an over-estimation in long COVID prevalence. Furthermore, we do not have vaccination or variant data, including number and type of vaccinations, thus we are unable to interpret the impact of immunity. Whilst this study possesses a longer follow up period than previous reports, we cannot accurately conclude on the long-term impact of COVID-19 on HCM. Longitudinal studies are required to assess whether COVID-19 leads to increased cardiovascular dysfunction, and whether adverse CMR phenotypes predict this risk. Another limitation

of this work is that we did not have a control cohort to compare risk of recovery and other manifestations with.

Future Work'

Prospective studies incorporating contemporaneous imaging and objective outcome measures are needed to determine whether dynamic changes in cardiac phenotype influence susceptibility to post-viral morbidity.

Conclusion

Our study provides new insights into the impact of COVID-19 on HCM patients, particularly in the post-vaccine era, demonstrating higher hospitalisation and significant burden of impaired recovery. Contrary to expectations, adverse CMR phenotypes were not observed to be associated with worse outcomes, highlighting the need for further research into the interplay between COVID-19 and long-term cardiovascular risk in HCM populations.

Declarations

Competing Interests

Dr Desai holds consultant and research contracts with BMS, Viz AI, Edgewise, Tenaya, and Cytokinetics. Dr Kramer has received research support from Cytokinetics and BMS. Dr Raman holds a research contract with Cytokinetics and is a consultant for Imbria. Dr Ho has received consulting fees and unrestricted research funding from Bristol Myers-Squibb (MyoKardia), Pfizer, Cytokinetics, Biomarin, Tenaya, Lexicon, and vizAI.

Authors' contributions

KM and SN conceived and designed the HCMR study. BR contributed to the conception and development of the COVID-19 substudy. All co-investigators participated in study conduct, patient recruitment, and critical revision of the manuscript. BR, AS, EA, and OA performed data analysis and interpretation related to COVID-19 outcomes in HCM patients and their association with adverse CMR phenotypes. They were also the primary contributors to the writing of the manuscript. All authors reviewed and approved the final version.

AS and EA contributed equally to this work.

BR is the overall guarantor.

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Ethical Approval

Health Authority Research and University of Oxford Research Ethics Committee (REC: 14/SC/0190) and National Heart Lung Blood Institute U01HL117006-01A1, National Institute of General Medical Sciences U54-GM10494

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Patient and Public Involvement

We participated in a patient priority setting exercise in collaboration with the James Lind Alliance. The top 10 questions prioritized - based on importance to patients, carers and the public - were published in Thorax[6]. Of these, three directly speak to the need to evaluate the long-term effects of COVID-19 and the impact of comorbid cardiac diseases and our research helps to address this unmet need.

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Figure Legends /Titles

Figure 1: Flow chart outlining the recruitment of patients

Figure 2: Symptom Burden During COVID-19 Infection by Gender.

N (people that were COVID-19 positive) =767, of which 555 were male.

Figure 3: Adjusted odds ratio for hospitalisation and impaired recovery.

N (people that were COVID-19 positive) =767. Odds ratios were determined using logistic regression adjusted for age, sex, and BMI. 1 or more CMR Abnormalities was defined as the presence of any of the following: reduced LVEF (<55%), reduced RVEF (<48%), significant LV LGE (>15% of myocardium), or LVOT obstruction. SCD risk = sudden cardiac death risk; LVOTO = left ventricular outflow tract obstruction; RVEF= right ventricular ejection fraction; LGE % 6SD = late gadolinium enhancement, LVEF = left ventricular ejection fraction.