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Clinical spectrum of COVID-19 complications in young adults: combined analysis of the American Heart Association COVID-19 Cardiovascular Disease Registry and the Outcomes Registry for Cardiac Conditions in Athletes

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ABSTRACT

Background While young adults 18–24 years old bear a significant proportion of COVID-19 diagnoses, the risk factors for hospitalisation and severe COVID-19 complications in this population are poorly understood.

Objective The objective of this study was to identify risk factors for hospitalisation and other COVID-19 complications across the health spectrum of young adults diagnosed with COVID-19 infection.

Study design Retrospective cohort study.

Participants Young adults (aged 18–24) with confirmed COVID-19 infection from the American Heart Association (AHA) COVID-19 Cardiovascular Disease Registry of hospitalised patients and the Outcomes Registry for Cardiac Conditions in Athletes (ORCCA) study of collegiate athletes. The AHA registry included 636 young adults from 152 hospitals. The ORCCA registry consisted of 3653 competitive college athletes from 42 colleges and universities.

Intervention None (exposure to COVID-19).

Primary and secondary outcome measures Main outcomes included hospitalisation, death, major adverse cardiovascular events (MACE) and other severe clinical events.

Results In comparison to the ORCCA registry, patients in the AHA registry were more likely to be female (59% vs 33%); had higher average body mass index (BMI) (32.4 vs 25.6); and had increased prevalence of diabetes (10% vs 0.4%), hypertension (7% vs 0.6%), chronic kidney disease (2% vs 0%) and asthma (14% vs 8%), all with p<0.01. There were eight (2%) deaths in the AHA hospitalised registry compared with zero in the ORCCA cohort. BMI was a statistically significant predictor of death in the hospitalised cohort (OR 1.05, 95% CI 1.00, 1.10). No significant predictors of MACE or other severe clinical events were identified.

Conclusions The risk of cardiac events in young adults aged 18–24 diagnosed with COVID-19 infection is low. Patients who were hospitalised (AHA registry) were more likely to have pre-existing medical comorbidities and higher BMI than healthy collegiate athletes (ORCCA registry). Once hospitalised, elevated BMI is associated with increased mortality although other drivers of MACE and other severe clinical events remain unclear.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Through a comparison between two large independent cohorts, cardiac and other severe complications of COVID-19 in young adults between the ages of 18 and 24 were able to be identified.
⇒ Cross-comparisons between cohorts are limited as these are two independent cohorts with two different criteria for entry.
⇒ The low prevalence of basic cardiovascular testing in the American Heart Association cohort likely leads to underascertainment of major adverse cardiac events.

INTRODUCTION

COVID-19 infection has manifested in a wide array of clinical complications including but not limited to respiratory failure, systemic inflammation, thromboembolic events and cardiovascular events.[1–3] While older age and comorbidities including chronic kidney disease have been identified as significant risk factors for increased morbidity and mortality in patients infected with COVID-19, severe complications of COVID-19 have been

reported across all age groups including young adults aged 18–24.[4–6] Although these individuals bear a significant proportion of COVID-19 infections, the spectrum and risk of COVID-19 complications in this age group remain understudied.

The issue of cardiovascular complications and the necessity of screening following COVID-19 infection in young adults has been the source of significant debate.[7 8] While the vast majority of young adults recover with minor or no cardiovascular injury, several case reports and case series have demonstrated the potential cardiac impact of COVID-19 in healthy young adults.[9] Reported sequelae include myocardial infarction, myocarditis, sudden-onset biventricular heart failure requiring mechanical support and sudden cardiac death.[10–12] Multi-inflammatory response syndrome with multiorgan failure has also been noted in young adults.[13 14] The reasons why certain individuals have such devastating cardiovascular consequences of COVID-19 infection are not known.

Our study aims to better define the clinical spectrum of COVID-19 cardiac and non-cardiac complications in young adults by using two registries representing the 'bookends' of health: the American Heart Association COVID-19 Cardiovascular Disease Registry (AHA COVID-19 CVD Registry) of hospitalised patients and the Outcomes Registry for Cardiac Conditions in Athletes (ORCCA) study of previously healthy collegiate athletes. Through a combined analysis and comparison of these two registries, our primary aim is to evaluate both the prevalence of serious cardiac and non-cardiac complications and the risk factors for hospitalisation and severe complications in these young adults. Our secondary aim is to examine the utility of diagnostic testing for cardiac involvement along the health spectrum of young adults diagnosed with COVID-19.

METHODS

Data sources

The AHA COVID-19 CVD Registry is a retrospective registry of consecutive patients collected by 152 hospitals and centres participating in this quality improvement registry. Eligible patients are all patients hospitalised with a diagnosis of COVID-19. All adults 18–24 years of age were included from the AHA registry between 1 March 2020 and 19 April 2021. The registry captures baseline demographics, testing, laboratory results and health outcomes.

The ORCCA study consists of National Collegiate Athletic Association (NCAA) athletes with confirmed COVID-19 infection from 1 September 2020 to 1 June 2021. Eligibility criteria and data collection methods have been described previously.[15] Patient demographics, COVID-19 symptoms, cardiac evaluations and cardiac outcomes were captured in the registry. Evaluations were performed per the discretion of local institutions and included a clinical assessment with or without cardiac testing such as a 12-lead ECG, cardiac troponin assay, transthoracic echocardiogram (TTE) and cardiac MRI (CMR). Results were communicated to the patients and if necessary were referred for further evaluation.

In both cohorts, individual participant consent was waived as only deidentified data were used.

Definition of primary outcomes

Primary outcomes included hospitalisation, death, major adverse cardiovascular events (MACE) and other severe clinical events. An MACE was defined as the occurrence of one or more of the following events: ischaemic stroke, myocardial infarction, sustained ventricular arrhythmias, cardiogenic shock, new-onset heart failure, myocarditis/myocardial involvement, requirement of permanent pacemaker or pulmonary embolism/deep vein thrombosis. Other severe clinical events included new haemodialysis or continuous renal replacement therapy (CRRT), requirement of mechanical ventilation or non-cardiogenic shock. COVID-19 myocardial involvement was defined in the current study as probable or definitive myocardial or myopericardial involvement per previous definitions.[15] Follow-up was requested from participating institutions periodically throughout the study period by the ORCCA investigators. There was no follow-up beyond the initial hospitalisation in the AHA COVID-19 Registry. The median duration of hospitalisation was 4 days. Because hospitalisation was an entry criterion for the AHA registry, hospitalisation rates were assessed only for ORCCA study participants.

Statistical analysis

Standard descriptive statistics were used to describe patient characteristics, symptoms, cardiac testing and incidence of MACE and other severe clinical complications in both cohorts. Asymptomatic patients, including female patients admitted for labour and delivery, were removed from the AHA cohort as COVID-19 likely was an incidental finding and not the cause of hospitalisation. Means and SD summarise continuous variables. Frequencies and percentages summarise categorical variables. Two-sample t-tests were used for continuous comparisons, while χ^2 tests or Fisher's exact tests were used for categorical comparisons, as appropriate. To account for the small number of observed events, univariable Firth logistic regression models were created to assess potential predictors of death, MACE and other severe clinical events. ORs and 95% CIs are provided for all models. We followed the Strengthening the Reporting of Observational Studies in Epidemiology checklist for reporting of cohort studies.[16] The AHA Precision Medicine Platform (https://precision.heart.org/) was used for data analysis. IQVIA (Parsippany, New Jersey) serves as the data collection and coordination centre. All statistical analyses were conducted in SAS V.9.4 (SAS Institute).

Patient and public involvement

No patient was involved.

Table 1 Baseline characteristics in the AHA and ORCCA cohorts of young adults with COVID-19

	ORCCA (N=3653)	AHA (N=636)	P value
Age, mean (SD)	19.91 (1.42)	21.43 (1.91)	<0.001
Female, N (%)	1209 (33)	376 (59)	<0.001
Race, N (%)			<0.001
Black	992 (28)	172 (27)	
Hispanic	112 (3)	205 (32)	
White non-Hispanic	2334 (65)	195 (31)	
Other*	166 (5)	64 (10)	
Medical history†			
Unremarkable medical history	2540 (70%)	397 (62%)	<0.001
BMI (kg/m^2), mean (SD)	25.64 (4.74)	32.40 (10.57)	<0.001
Atrial fibrillation	1 (0.03%)	3 (0.5%)	0.01
Stroke/transient ischaemic attack	0	8 (1%)	<0.001
Diabetes mellitus	12 (0.4%)	63 (10%)	<0.001
Dyslipidaemia	11 (0.3%)	9 (1%)	0.001
Heart failure		5 (0.8%)	
Hypertension	20 (0.6%)	47 (7%)	<0.001
Peripheral artery disease	0	1 (0.2%)	0.15
Chronic kidney disease	0	11 (2%)	<0.001
Deep vein thrombosis	0	5 (0.8%)	<0.001
Pulmonary embolism	1 (0.03%)	6 (1%)	<0.001
E-cigarette (vaping)		10 (2%)	
Smoking		48 (8%)	
Immune disorders	0	12 (2%)	<0.001
Congenital heart disease	18 (0.5%)	3 (0.5%)	0.99
Asthma	265 (8%)	90 (14%)	<0.001
Other pulmonary disease	0	5 (0.8%)	<0.001
Pulmonary arterial hypertension	0	3 (0.5%)	0.003

*Other race includes Mixed, Asian, American Indian, Native Hawaiian, Pacific Islander (ORCCA) and Asian/Pacific Islander, Unknown and Native American (AHA).
†Fisher's exact test used for all categorical comparisons due to small expected cell counts.
AHA, American Heart Association; BMI, body mass index; ORCCA, Outcomes Registry for Cardiac Conditions in Athletes.

RESULTS

Baseline characteristics

Baseline characteristics of participants in the AHA and ORCCA registries are shown in table 1.

A total of 3653 individuals were included in the ORCCA cohort with mean age of 19.9 (SD=1.42) years with 33% female, 65% white, 28% black and 3% Hispanic. 636 individuals were included in the AHA cohort with mean age of 21.4 (SD=1.91) years with 59% female, 31% white, 27% black and 32% Hispanic. Body mass index (BMI) was significantly higher in the hospitalised AHA registry (32.4 kg/m^2, SD=10.6) compared with the ORCCA registry (25.6 kg/m^2, SD=4.7), p<0.001. The frequencies of diabetes mellitus (10% vs 0.4%), hypertension (7% vs 0.6%), chronic kidney disease (2% vs 0.0%), obesity (51% vs 13%) and asthma (14% vs 8%) were greater in the AHA cohort compared with ORCCA cohort, all with p<0.01. Participants in the ORCCA cohort were more likely to have no significant medical history compared with the AHA cohort (70% vs 62%, p<0.01). In those participants with no medical history, participants in the ORCCA study were more likely to be non-obese (BMI<30 kg/m^2) compared with the AHA registry (87% vs 52%, p<0.01%).

Initial symptoms

The initial symptoms of both groups are shown in table 2.

The AHA cohort had greater proportions of fever/chills (43%), cough (41%), shortness of breath (38%), nausea/vomiting or diarrhoea (32%) and chest pain (7%) compared with the ORCCA cohort (19%, 17%, 6%, 5% and 3%, respectively), all p<0.01. In contrast, the ORCCA

Table 2 Initial symptoms and cardiac testing performed

	ORCCA (n=3653)	AHA (n=636)	P value
Initial symptoms* (%)			
Fever/chills	683 (19)	269 (43)	<0.001
Cough	612 (17)	258 (41)	<0.001
Shortness of breath	226 (6)	236 (38)	<0.001
Fatigue	553 (16)	90 (14)	0.55
Headache	853 (23)	75 (12)	<0.001
Myalgia	604 (17)	97 (15)	0.45
Sore throat	674 (18)	49 (8)	<0.001
Nasal congestion	644 (18)	34 (5)	<0.001
Nausea, vomiting or diarrhoea	182 (5)	198 (32)	<0.001
Loss of sense of smell/taste	834 (23)	36 (6)	<0.001
Chest pain (%)	121 (3)	44 (7)	<0.001
Not documented (%)	381 (11)	172 (27)	<0.001
Asymptomatic (%)	1078 (30)	N/A	
Cardiac testing (%)			
MRI	516 (14)	1 (0.33)	<0.001
ECG	3486 (95)	327 (52)	<0.001
Troponin	3166 (87)	232 (33)	<0.001
Echocardiogram	2999 (82)	47 (7)	<0.001
Myocardial injury (troponin elevation)	27 (0.9)	173 (77)	
Hospitalisation characteristics			
Hospitalised	4	731 (100%)	–
Ventilated	0	60 (9%)	–

*Initial symptoms for ORCCA and symptoms at the time of admission for AHA.
AHA, American Heart Association; ORCCA, Outcomes Registry for Cardiac Conditions in Athletes.

cohort had greater proportions of headache (23%), loss of sense of smell/taste (23%), sore throat (18%) and nasal congestion (18%) compared with the AHA cohort (12%, 6%, 8% and 5%, respectively) (all p<0.01).

Cardiac testing

Cardiac testing for the AHA and ORCCA cohorts is depicted in table 2 and figure 1. There was significantly more cardiac testing including CMR (14% vs 0.3%), ECG (95% vs 52%), troponin assay (87% vs 33%) and TTE (82% vs 7%) in the ORCCA cohort compared with the AHA cohort (all p<0.001).

Death, MACE and other severe clinical events

Clinical outcomes

Table 3 depicts the incidence of death, MACE and secondary clinical events in the ORCCA cohort and AHA cohort.

There were 12 (2%) deaths in the AHA cohort compared with 0 death in the ORCCA cohort.

With respect to MACE, there were 22 (0.6%) overall events in the ORCCA cohort, with 1 (0.03%) case of pulmonary embolism and 21 (0.6%) cases of COVID-19 myocardial involvement. The range of the events occurred from August 2020 to February 2021. In the AHA cohort, 22 (3.5%) patients experienced an MACE. There were 6 (1%) cases of ischaemic stroke, 4 (0.6%) cases of pulmonary embolism, 5 (0.8%) cases of new-onset heart failure, 3 (0.5%) events of sustained ventricular arrhythmias, 3 (0.5%) cases of myocarditis and 1 (0.2%) myocardial infarction. There were no other severe clinical events in the ORCCA group. There were 104 (16.4%) other severe clinical events in the AHA registry with 60 (9%) young adults requiring ventilation, 19 (3%) meeting criteria for shock and 4 (0.6%) requiring haemodialysis or CRRT.

There were four (0.1%) hospitalisations for COVID-19 in the ORCCA cohort, while all patients in the AHA cohort by definition were hospitalised. The median follow-up for the ORCCA cohort was 411 (IQR: 387, 447) days; given the cross-sectional design of the AHA registry, no follow-up was conducted on those patients.

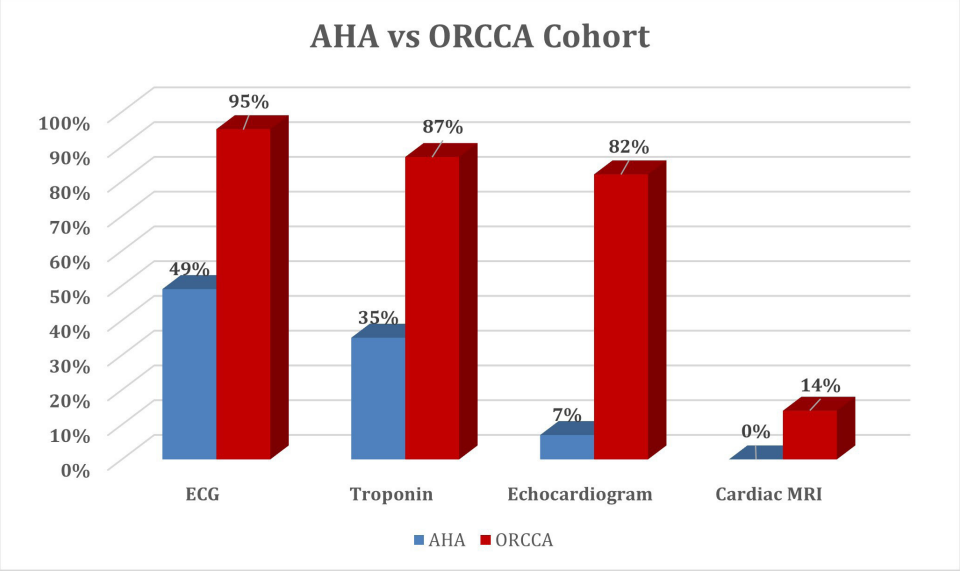

Figure 1 Comparision of cardiac testing in the AHA and ORCCA Cohorts. AHA, American Heart Association; ORCCA, Outcomes Registry for Cardiac Conditions in Athletes.

Table 3 Incidence of major adverse cardiovascular events and other severe clinical events in young adults with COVID-19

	ORCCA	AHA
Death, n (%)	0	12 (2)
Major adverse cardiovascular events (MACE)		
Total events	22 (0.6%)	22 (3.5%)
Ischaemic stroke/intracranial haemorrhage, n (%)	0	6 (1)
Pulmonary embolism, n (%)	1 (0.03)	4 (0.6)
New-onset heart failure, n (%)	0	5 (0.8)
Sustained ventricular arrhythmias, n (%)	0	3 (0.5)
Requirement of PPM, n (%)	0	0
Acute myocardial infarction, n (%)	0	1 (0.2)
Myocarditis, n (%)	21 (0.6)	3 (0.5)
Cardiogenic shock, n (%)	0	0
Other severe clinical events		
Total events	0 (0.0%)	104 (16.4%)
New haemodialysis or CRRT, n (%)	0	4 (0.6)
Ventilation, n (%)	–	60 (9)
In-hospital shock, n (%)	0	19 (3)
Requirement of mechanical support, n (%)	–	2 (0.4)
Requirement of pressor support, n (%)	–	19 (3)

AHA, American Heart Association; CRRT, continuous renal replacement therapy; ORCCA, Outcomes Registry for Cardiac Conditions in Athletes; PPM, permanent pacemaker.

Univariable analysis

Results of univariable analyses to identify predictors for death, MACE and other severe clinical events in the AHA cohort are provided in table 4.

A higher BMI was associated with death (OR 1.05, 95% CI 1.00, 1.10; p=0.04). No significant predictors of MACE or other severe clinical events were identified.

DISCUSSION

The purpose of this study was to define the clinical spectrum of disease and identify cardiac and other severe complications of COVID-19 in young adults between the ages of 18 and 24 from two established registries on potentially opposite sides of the disease severity continuum. The patients in the AHA registry were more likely to have medical comorbidities including diabetes mellitus, hypertension, chronic kidney disease and asthma compared with patients in the ORCCA study. Importantly, there were racial disparities in the two cohorts with the ORCCA cohort being 65% white and only 3% Hispanic, while the AHA cohort was 31% white and 32% Hispanic. There were also sex differences which may have a role in COVID-19 outcomes, with 59% of patients in the AHA cohort being female versus 35% in the ORCCA cohort.[17] Initial symptoms differed between the groups, with more severe symptom presentations in hospitalised patients from the AHA cohort such as shortness of breath, fever and vomiting compared with symptoms in the ORCCA registry, perhaps indicating an eventual more severe illness course. It should be noted that the ORCCA study does not represent the general population aged 18–24 years but rather a young, athletic population. This is the first analysis of health outcomes in young adults hospitalised with COVID-19 from the AHA COVID-19 CVD Registry. Importantly, we observed: (1) more pre-existing

Table 4 Univariable predictors of death, MACE and other severe clinical events in AHA cohort

	Death (n=12)		Major adverse cardiovascular event (MACE)* (n=22)		Other severe clinical events† (n=63)	
Variable	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.02 (0.76, 1.36)	0.92	0.93 (0.75, 1.16)	0.53	0.98 (0.85, 1.12)	0.72
Female	0.50 (0.16, 1.52)	0.22	0.47 (0.20, 1.11)	0.08	0.64 (0.38, 1.08)	0.09
Race/ethnicity		0.75		0.60		0.77
Black	0.62 (0.13, 2.98)	0.37	0.65 (0.22, 1.89)	0.59	0.87 (0.45, 1.68)	0.92
Hispanic	0.95 (0.25, 3.58)	0.90	0.54 (0.18, 1.57)	0.31	0.72 (0.37, 1.38)	0.34
White non-Hispanic	Ref		Ref		Ref	Ref
Other	1.70 (0.35, 8.28)	0.33	1.12 (0.32, 3.97)	0.44	1.01 (0.42, 2.44)	0.69
BMI (kg/m^2)	1.05 (1.00, 1.10)	0.04	0.98 (0.93, 1.02)	0.31	1.01 (0.98, 1.03)	0.50
Diabetes	1.17 (0.21, 6.65)	0.86	1.10 (0.29, 4.23)	0.89	1.43 (0.66, 3.12)	0.37
Hypertension	0.49 (0.03, 8.59)	0.62	1.53 (0.39, 5.95)	0.54	1.45 (0.60, 3.49)	0.41
Asthma	0.78 (0.14, 4.38)	0.78	0.41 (0.08, 2.20)	0.30	1.05 (0.51, 2.19)	0.89
Smoking	0.48 (0.03, 8.39)	0.61	1.49 (0.38, 5.80)	0.56	0.67 (0.22, 2.08)	0.49

*MACE: ischaemic stroke, myocardial infarction, sustained ventricular arrhythmias, cardiogenic shock, new-onset heart failure, myocarditis, requirement of permanent pacemaker (PPM) and pulmonary embolism/deep vein thrombosis.
†Other severe clinical events were new haemodialysis or continuous renal replacement therapy (CRRT), requirement of ventilation or non-cardiogenic shock.
AHA, American Heart Association; BMI, body mass index.

comorbidities in hospitalised patients, (2) a mortality rate of 2% and (3) a higher risk of death with higher BMI. This study also highlights the low rate of cardiac testing in the AHA hospitalised patient cohort, in contrast with frequent cardiac testing and high-resource utilisation in the ORCCA study collegiate athlete cohort. Unlike initial studies of older adults hospitalised with COVID-19, this study did not find a similarly high rate of myocardial injury or MACE.[18–20]

Prior studies of young adults demonstrate low mortality rates for patients hospitalised with COVID-19, though point estimates range from 0.2% for 18–29 year-olds in a large academic health system to 2.7% in a large series of 18–34 year-olds derived from insurance data.[21 22] Our findings confirm that obesity is a risk factor for COVID-19-related mortality in young adults.[21] While heterogeneity exists for mortality in younger individuals hospitalised with COVID-19, the mortality rate in the young is strikingly lower than that of elderly individuals, estimated by Nguyen *et al* to be 26.6% in individuals aged 80 and older.[23]

Comparison to data from the National Health and Nutrition Examination Survey (NHANES) puts the prevalence of comorbidities found in the AHA hospitalised COVID-19 cohort in context.[24] While prevalence of asthma (14%) in young adults hospitalised with COVID-19 seems high, this is similar to the 18% prevalence seen in the overall population of 18–24 year-olds.[24] In contrast, the incidences of diabetes mellitus (10%) and hypertension (7%) are higher than those seen in the overall population according to NHANES data (0.5% and 4%, respectively).[24] Despite the high comorbidity burden compared with non-hospitalised collegiate athletes, 62% of patients in the AHA hospitalised cohort still had no remarkable medical history, highlighting that COVID-19 adverse outcomes can affect any patient and that risk factors are hard to predict and incompletely understood.

Our analysis juxtaposing an athletic young adult cohort with a hospitalised young adult cohort highlights the heterogenous nature of BMI as a risk predictor. BMI has been identified as a risk factor for hospitalisation and mortality following hospitalisation across all age groups.[25–27] However, in the ORCCA data set involving collegiate athletes, BMI was not found to be associated with COVID-19 myocardial involvement.[15] Notably, however, the elevated BMI of an elite athlete is different from the elevated BMI of a non-athlete as the traditional BMI metric does not take into account muscle mass, body composition and bone density.[28] Therefore, the limitations of using BMI should be considered before extrapolating the risks of elevated BMI in the general population to athletes with COVID-19. A more detailed assessment of adiposity in conjunction with BMI is an important area of future study.

The utilisation of cardiac testing was starkly different between the ORCCA cohort and the AHA cohort. Initial concerns for myocardial inflammation from COVID-19 infection and an elevated risk of sudden death in competitive athletes drove initial consensus recommendations to err on the side of early detection with the potential for overdiagnosis.[29] Thus, institutions participating in the ORCCA study used protocols aimed at sensitivity, with

93.4% of athletes receiving at least one of troponin, ECG or TTE, and 6.6% of participants receiving mandatory CMR screening.[15] In the AHA cohort, cardiac diagnostic testing was likely to be more specific, driven by clinical suspicion and the need to minimise healthcare worker exposure or the transport of critically ill patients. For hospitalised patients, there was a lower than expected rate of cardiac testing with only 49% of patients receiving ECG, 35% troponin testing, 7% TTE and 0.2% CMR. With over 42% of patients in the AHA cohort experiencing shortness of breath or chest pain, the use of TTE in only 7% of patients is significantly lower than in previous studies of hospitalised patients with similar symptoms.[30 31] Similarly, an ECG in less than 50% of patients is much lower than previously described in hospitalised patients given patient comorbidities, symptom description, early concerns around myocarditis and the frequency with which QT_C prolonging medications were used for the treatment of COVID-19.[32–34] A desire to minimise patient contact and the scarcity of personal protective equipment early in the pandemic likely limited cardiac testing in the hospital. These lower rates of cardiac testing also may have been due to an underappreciation of the cardiac manifestations of COVID-19, or errors and discrepancies in reporting cardiac testing in the AHA registry. Our findings raise the possibility that underutilisation of cardiac testing in hospitalised patients may have led to underdiagnosis of cardiac involvement, while overutilisation of cardiac testing in competitive athletes may have led to overdiagnosis.

There are several important limitations to this study. First, this is a comparison of two independent cohorts with two different criteria for entry: participation in NCAA athletics for the ORCCA cohort versus hospitalisation for COVID-19 in the AHA cohort. These differences limit cross-comparisons between cohorts. Second, the AHA cohort relies on registry abstraction and may be overweighted towards hospitals and hospital systems with resources sufficient to populate these registries. Thus, outcomes in the AHA cohort may not fully reflect the outcomes experienced for young adult patients hospitalised with COVID-19 across all hospitals in the USA. Third, in contrast to the ORCCA study with greater than 1 year of follow-up, there is no follow-up beyond the initial hospitalisation in the AHA COVID-19 CVD Registry. This limits the accurate assessment of the true incidence of severe events, MACE and mortality related to COVID-19 hospitalisation. The rates of CT scanning were not included in the AHA registry which may affect the rates of pulmonary embolism diagnosis. Fourth, registry capture in the AHA cohort was incomplete, with 27% of patients not having documented presenting symptoms. Fifth, the low prevalence of basic cardiovascular testing in the AHA cohort likely leads to underascertainment of MACE. Another important consideration is that data were collected in these registries before widespread availability of the COVID-19 vaccination, which has shown to be effective in reducing severe complications and hospitalisation from COVID-19 infection. Last, with the relatively low prevalence of mortality, MACE and severe COVID-related adverse events, and the relatively small sample size of patients aged 18–24 years hospitalised for COVID-19, our study is underpowered for detailed modelling of risk factors associated with poorer outcomes in the setting of COVID-19 illness.

In conclusion, this study compared clinical outcomes in young adult patients across the health spectrum with COVID-19 infection. We found a significantly higher burden of comorbidities and lower rates of cardiac testing in hospitalised patients as compared with competitive athletes with COVID-19. Nine per cent of hospitalised young adults with COVID-19 required mechanical ventilation, 3.5% suffered an MACE and 2% died. Importantly, elevated BMI predicted mortality in hospitalised patients. Additional research is needed to better elucidate risk factors for severe health outcomes in young adults afflicted with COVID-19.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Massachusetts General Hospital Review Board (Reference ID: 2020P002667). Participants gave informed consent to participate in the study before taking part.

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