Cardiology in the Young

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Exercise testing in patients with multisystem inflammatory syndrome in children-related myocarditis versus idiopathic or viral myocarditis

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Original Article

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Abstract

Background: While most children with multisystem inflammatory syndrome in children have rapid recovery of cardiac dysfunction, little is known about the long-term outcomes regarding exercise capacity. We aimed to compare the exercise capacity among patients with multisystem inflammatory syndrome in children versus viral/idiopathic myocarditis at 3–6 months after initial diagnosis. *Methods:* We performed a retrospective cohort study among patients with multisystem inflammatory syndrome in children in June 2020 to May 2021 and patients with viral/idiopathic myocarditis in August 2014 to January 2020. Data from cardiopulmonary exercise test as well as echocardiographic and laboratory data were obtained. Inclusion criteria included diagnosis of multisystem inflammatory syndrome in children or viral/idiopathic myocarditis, exercise test performed within 3–6 months of hospital discharge, and maximal effort on cardiopulmonary exercise test as determined by respiratory exchange ratio >1.10. *Results:* Thirty-one patients with multisystem inflammatory syndrome in children and 25 with viral/idiopathic myocarditis were included. The mean percent predicted peak VO2 was 90.84% for multisystem inflammatory syndrome in children patients and 91.08% for those with viral/idiopathic myocarditis (p-value 0.955). There were no statistically significant differences between the groups with regard to percent predicted maximal heart rate, metabolic equivalents, percent predicted peak VO2, percent predicted anerobic threshold, or percent predicted O2 pulse. There was a statistically significant correlation between lowest ejection fraction during hospitalisation and peak VO2 among viral/idiopathic myocarditis patients (r: 0.62, p-value 0.01) but not multisystem inflammatory syndrome in children patients (r: 0.1, p-value 0.6). *Conclusions:* Patients with multisystem inflammatory syndrome in children and viral myocarditis appear to, on average, have normal exercise capacity around 3–6 months following hospital discharge. For patients with viral/idiopathic myocarditis, those with worse ejection fraction during hospitalisation had lower peak VO2 on cardiopulmonary exercise test.

An important established complication of COVID-19 is multisystem inflammatory syndrome in children, a condition which can result in myocardial injury manifested by myocarditis. This form of myocarditis appears to have a particularly rapid onset and can require vasoactive medicines and even extracorporeal membrane oxygenation.[1,2] Most patients have a favourable short-term recovery; however, prior studies have found persistence of diastolic and deformation abnormalities in some patients even after recovery of systolic function.[3,4]

In patients with classic idiopathic or viral myocarditis from the pre-COVID-19 era, there is a higher incidence of sudden cardiac death during exercise.[5–9] As a result, patients with myocarditis are recommended to refrain from competitive sports for 3–6 months after onset of illness.[10,11] Part of the assessment of heart recovery includes exercise electrocardiogram and in some instances cardiopulmonary exercise test, the gold standard for assessment of aerobic fitness and exercise safety. It is unclear whether these same restrictions and guidelines should apply to those with myocarditis from multisystem inflammatory syndrome in children.[12,13] There is some data to suggest reduced performance during 6-minute walk test following recovery from multisystem inflammatory syndrome in children; however, data regarding exercise performance assessed by cardiopulmonary exercise test is lacking.[14]

The purposes of this project were to 1) describe the functional capacity of patients with multisystem inflammatory syndrome in children myocarditis on cardiopulmonary exercise test at 3–6 months after hospital discharge and 2) compare these findings to those with viral/idiopathic myocarditis in the pre-COVID-19 era.

Materials and methods

Following approval by Children's Healthcare of Atlanta Institutional Review Board, we performed a retrospective cohort study of multisystem inflammatory syndrome in children patients diagnosed with myocarditis and viral/idiopathic myocarditis patients from the pre-COVID-19 era. Inclusion criteria included patients with a cardiopulmonary exercise test with maximal effort (respiratory exchange ratio >1.10 or peak heart rate >85% predicted for age) performed within 3–6 months of hospital discharge following either 1) diagnosis of multisystem inflammatory syndrome in children (as defined by CDC guidelines[15]) with myocarditis (elevated troponin, without evidence of another cause of troponin elevation) from June 2020 to May 2021 or 2) a diagnosis of viral/idiopathic myocarditis from August 2014 to January 2020 (MRI confirmed with Lake Louise criteria or elevated troponin, without evidence of another cause of troponin elevation).

Initially, at our institution, all patients >8 years of age with evidence of cardiac involvement during an acute episode of multisystem inflammatory syndrome in children were referred for cardiopulmonary exercise test for exercise clearance. After our initial early experience, this guideline was updated to include only patients with ejection fraction less than 50% during their acute episode of multisystem inflammatory syndrome in children. This study population represents patients prior to when this guideline was enacted and therefore represents a broad range of disease severity.

Cardiopulmonary exercise tests were performed on a treadmill using modified Bruce ramping protocol. The Bruce ramping protocol is a maximal exercise testing protocol consisting of 1-minute stages that increase in speed and/or grade. There are three different starting points for the Bruce ramping protocol depending on self-reported fitness level, age, and body surface area – Low, Medium, High/Athletic. A facemask is used to measure breath-by-breath gas analysis to obtain metabolic variables. A running 12-lead electrocardiogram monitors heart rate and rhythm throughout exercise and recovery. Blood pressure and oxygen saturation are obtained at 2-minute intervals throughout exercise and recovery. This protocol was performed identically for both cohorts in this study. Those undergoing testing during the COVID-19 pandemic were required to have a negative COVID-19 polymerase chain reaction test prior to performing the cardiopulmonary exercise test.

The primary outcome of interest was percent predicted peak VO2 as measured via cardiopulmonary exercise test, with values less than 80% predicted for age and sex considered abnormal. The predicted values were calculated using the James equation for those 15 years and younger and the Wasserman equation for those 16 years and older. Secondary outcomes of interest included other exercise testing parameters, including exercise duration, metabolic equivalents, maximum heart rate, heart rate response, maximum blood pressure, respiratory exchange ratio, VO2 at anerobic threshold, peak VO2, O2 pulse, and breathing reserve.

Demographics and clinical variables (initial ejection fraction on admission, lowest ejection fraction during hospitalisation, and peak troponin-I during hospitalisation) were summarised using mean and standard deviation or median and interquartile ranges for continuous variables as appropriate, and count and percentage for categorical variables. Comparisons between groups were conducted using two-sample t-tests or Wilcoxon rank-sum tests for continuous variables and chi-squared tests or Fisher's exact tests for categorical variables. The association between lowest ejection fraction during hospitalisation, peak troponin-I levels, and exercise data were analysed using Pearson's correlation. Correlation coefficients (r) and corresponding p-values were reported.

All analyses were performed using R (R version 4.0.2). Significance was defined as a p-value of less than 0.05.

Results

In total, 31 patients with multisystem inflammatory syndrome in children and 25 patients with viral myocarditis were included in this study. Patients with multisystem inflammatory syndrome in children were younger than those with viral myocarditis (13.10 years versus 15.77 years, p-value <0.001). A higher proportion of males were found among the viral myocarditis population (95.8% versus 67.7%, p-value = 0.015). The median time from discharge to cardiopulmonary exercise test was 94.5 days for those with multisystem inflammatory syndrome in children and 105 days for this with viral myocarditis (p-value = 0.179). No multisystem inflammatory syndrome in children patients required extracorporeal membrane oxygenation compared to two in the viral/idiopathic myocarditis group.

On the in-patient cardiac evaluation during the acute illness, multisystem inflammatory syndrome in children patients had statistically significant worst ejection fraction (45% versus 52%, p-value = 0.019) and lower peak troponin-I levels (0.7 ng/ml versus 27.6 ng/ml, p-value = 0.001) than those with viral myocarditis (Table 1). All patients had normal ejection fraction (>55%) prior to cardiopulmonary exercise test.

The primary outcome of percent predicted peak VO2 at 3–6 months after hospital discharge was similar between the two groups. The mean percent predicted peak VO2 was 90.84% for multisystem inflammatory syndrome in children patients and 91.08% for those with viral myocarditis (p-value = 0.955). Six of 31 patients (19.4%) with multisystem inflammatory syndrome in children compared to 6 of 25 patients (24.0%) with viral myocarditis had a percent predicted peak VO2 less than 80% (p-value = 0.750). For the multisystem inflammatory syndrome in children and viral/idiopathic myocarditis patients with peak VO2 less than 80% predicted, the mean O2 pulse was 76.6% predicted and 80.3% predicted, respectively. All patients with peak VO2 less than 80% predicted had a breathing reserve greater than 15%.

There were no statistically significant differences in: percent predicted maximal heart rate, heart rate response, metabolic equivalents, percent predicted VO2 at anerobic threshold, or percent predicted O2 pulse between the groups (Table 2).

Five patients with multisystem inflammatory syndrome in children compared to one patient with viral/idiopathic myocarditis had ventricular ectopy during testing; two patients with viral/idiopathic myocarditis had atrial ectopy. These instances of ectopy were single monomorphic beats which resolved with peak exercise. No patients had clinically relevant arrhythmias such as frequent or complex repetitive forms of ventricular or supraventricular ectopy.

Among multisystem inflammatory syndrome in children patients, the data showed no statistically significant positive correlation between lowest ejection fraction during hospitalisation or peak troponin and peak VO2 (r: 0.1, p-value: 0.60 and r: −0.09, p-value: 0.16) (Fig 1). For those with viral/idiopathic myocarditis, there was a statistically significant positive correlation between lowest ejection fraction during hospitalisation and peak VO2 and O2 pulse on cardiopulmonary exercise test (r: 0.62, p-value: 0.01; r: 0.43, p-value: 0.03). There also was a negative correlation between peak troponin levels and peak VO2 (r: −0.44, p-value: 0.03) (Fig 1). For both patient groups, there was a strong

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Table 1. Demographic and clinical data among those with MIS-C and viral/idiopathic myocarditis

	Overall	MIS-C myocarditis	Viral/idiopathic myocarditis	p
Age (years, SD)	14.29 (2.95)	13.10 (2.73)	15.77 (2.55)	<**0.001**
Sex (%)				**0.015**
Female	11 (20.0%)	10 (32.3%)	1 (4.2%)	
Male	44 (80.0%)	21 (67.7%)	23 (95.8%)	
Race/ethnicity (%)				0.847
African American*	35 (62.5%)	18 (58.1%)	17 (68.0%)	
Asian*	1 (1.8%)	1 (3.2%)	0 (0.0%)	
Caucasian*	15 (26.8%)	8 (25.8%)	7 (28.0%)	
Hispanic	2 (3.6%)	1 (3.2%)	1 (4.0%)	
Other*	2 (3.6%)	2 (6.5%)	0 (0.0%)	
Unspecified*	1 (1.8%)	1 (3.2%)	0 (0.0%)	
Height (cm, SD)	166.84 (14.23)	161.65 (13.12)	173.28 (13.07)	**0.002**
Weight (kg, SD)	69.01 (22.22)	64.93 (23.15)	74.07 (20.33)	0.127
Initial EF at admission (%, mean (SD))	53 (11)	50 (11)	56 (9)	0.054
Lowest EF during hospitalisation (%, mean ((SD; range))	48 (11)	45 (10; 31–64)	52 (12; 6–67)	**0.019**
Peak troponin-I during hospitalisation (ng/L, median [IQR])	4.71 [0.63, 26.95]	0.70 [0.16, 1.93]	27.60 [14.40, 42.70]	<**0.001**
Time from discharge to exercise test (days [median, IQR])	102.00 [90.00, 131.00]	94.50 [90.00, 106.25]	105.00 [95.00, 143.00	0.179

MIS-C = multisystem inflammatory syndrome in children; EF = ejection fraction.

Table 2. Comparison of resting and exercise data among those with MIS-C and viral/idiopathic myocarditis

	Overall	MIS-C myocarditis	Viral/idiopathic myocarditis	p
Resting vitals:				
Supine HR (bpm)	75.23 (12.85)	78.32 (12.29)	71.40 (12.72)	**0.044**
Supine systolic blood pressure (mmHg)	118.29 (14.71)	113.55 (13.04)	124.16 (14.78)	**0.006**
Supine diastolic blood pressure (mmHg)	59.66 (11.55)	55.71 (8.45)	64.56 (13.08)	**0.003**
Exercise data:				
Maximal heart rate (% predicted, mean (SD))	94.83 (5.73)	95.06 (5.16)	94.54 (6.45)	0.739
Heart rate response (bpm, mean (SD)	120.00 (16.03)	117.40 (15.61)	123.2 (16.28)	0.175
Max METs (METs, mean (SD))	10.99 (2.35)	10.54 (2.21)	11.69 (2.44)	0.086
Peak VO2 (% predicted, mean (SD))	90.95 (15.71)	90.84 (13.81)	91.08 (18.10)	0.955
Anaerobic threshold (% of predicted peak VO2, mean (SD))	46.85 (8.38)	47.61 (8.18)	45.88 (8.70)	0.451
O2 pulse (% predicted, mean (SD))	97.91 (18.76)	98.26 (20.77)	97.48 (16.35)	0.879
Peak systolic blood pressure (mmHg, mean (SD))	187.00 [167.00, 209.50]	181.00 [164.00, 195.00]	205.00 [183.00, 218.00]	**0.022**
RER	1.21 [1.15, 1.30]	1.21 [1.16, 1.29]	1.23 [1.13, 1.31]	0.915
Speed max value (mph, mean (SD))	3.80 (0.46)	3.73 (0.52)	3.95 (0.27)	0.178
Grade max value (%, mean (SD))	14.53 (1.12)	14.36 (1.16)	14.87 (0.99)	0.158

MIS-C = multisystem inflammatory syndrome in children; HR = heart rate; METs = metabolic equivalents; RER = respiratory exchange ratio; SD = standard deviation; IQR = interquartile range [1st Quartile, 3rd Quartile].

positive correlation between peak VO2 and O2 pulse (r: 0.91, p-value: <0.001 for patients with viral/idiopathic myocarditis; r: 0.89, p-value: <0.001 for multisystem inflammatory syndrome in children patients; Fig 1). There was no significant difference between timing of cardiopulmonary exercise test between the two groups (Table 1).

Discussion

In this study, we assessed exercise capacity with cardiopulmonary exercise test in patients with multisystem inflammatory syndrome in children, and we found 1) that most patients with multisystem inflammatory syndrome in children had normal exercise performance at

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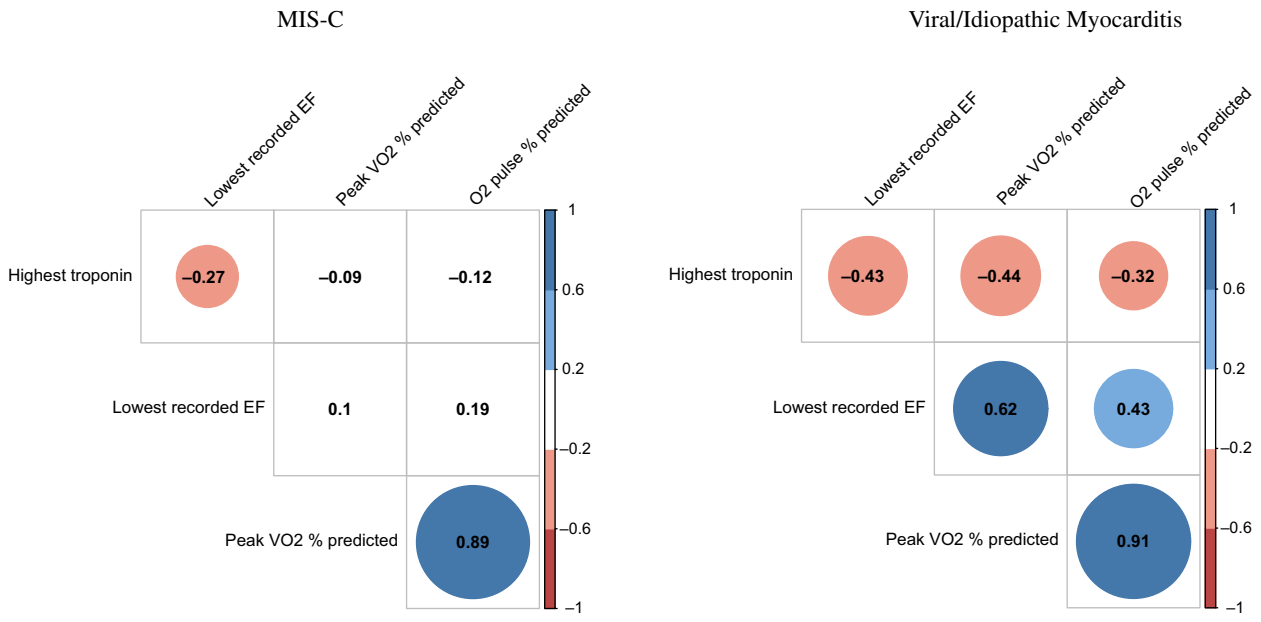

Summary: No statistically significant correlation between peak VO2 or O2 pulse and highest troponin and lowest ejection fraction for MIS-C patients. For those with Idiopathic/Viral myocarditis, negative correlation between highest troponin and peak VO2 as well as positive correlation between lowest recorded EF and peak VO2 and O2 pulse.

Fig. 1. Correlation Between Clinical Metrics and Exercise Data.

3–6 months after hospitalisation and 2) that patients with multisystem inflammatory syndrome in children had exercise tolerance comparable to those with viral/idiopathic myocarditis in the pre-COVID-19 era. These findings suggest that patients with multisystem inflammatory syndrome in children, even those with severe ventricular dysfunction, can have normal exercise capacity following a brief period of activity restriction and recovery.

The mean peak VO2 for both groups were in the normal range (>80% predicted) for age and sex. That being said, 19% of patients with multisystem inflammatory syndrome in children and 24% with viral myocarditis had predicted peak VO2 less than 80% suggesting diminished aerobic capacity. All patients with low peak VO2 had a normal breathing reserve suggesting the absence of pulmonary limitation. There appears to be a strong correlation between O2 pulse and peak VO2, suggesting an inability to augment stroke volume at peak activity in patients with low predicted peak VO2. This is most likely related to deconditioning, especially given that these patients were activity restricted for months prior to this test. Of the patients with low percent predicted peak VO2, only one had a percent predicted peak VO2 <70% which would indicate a significant cardiac limitation. This patient had viral myocarditis requiring extracorporeal membrane oxygenation and had a peak VO2 of 41% predicted. While this patient clearly had a cardiac limitation, the others with low peak VO2 were not as significantly limited.

While there was no correlation between lowest ejection fraction or peak troponin-I and percent predicted peak VO2 for those with multisystem inflammatory syndrome in children, there does appear to be a correlation for those with viral/idiopathic myocarditis in the pre-COVID-19 era. The lack of correlation between lowest ejection fraction and peak VO2 in those with multisystem inflammatory syndrome in children seems to fit with data suggesting a rapid cardiac recovery with this syndrome.[16,17] Several studies have looked at cMRI findings in both multisystem inflammatory syndrome in children and other forms of myocarditis, finding different pattens of inflammation, which may suggest different pathological mechanisms.[18,19] Still others have shown that the degree of troponin leak does not correlate with myocardial involvement on cMRI suggesting a non-specific role of troponin in this cohort.[20] Our data add further evidence that the degree of troponin leak or ventricular dysfunction during hospitalisation does not appear to impact functional capacity following recovery.

Those with severe forms of classic viral/idiopathic myocarditis in our study, as evidenced by lower ejection fraction and higher troponin, appear to have lower peak VO2 and O2 pulse suggesting a delay in return of aerobic capacity. These data are useful for providers and may suggest closer follow-up and exercise testing with metabolic analysis for activity clearance in those patients with viral/idiopathic myocarditis, especially in those with significant cardiac involvement.

Both cohorts had a normal mean resting heart rate for age, similar precent predicted peak heart rate, and similar heart rate response during exercise (Table 2). The viral myocarditis group did have a higher mean resting and peak systolic blood pressure compared to those with multisystem inflammatory syndrome in children. While the difference may be partially reflective of age differences between the groups, those with viral/idiopathic myocarditis had a mean peak systolic blood pressure of 205 mmHg at peak exercise. This is on the high end of normal for a children undergoing a treadmill exercise test.[21] These patients may have some degree of increased vascular tone and afterload, which may provide some insight as to why those with severe

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involvement had lower percent predicted peak VO2. In addition, these data suggest that monitoring the blood pressure response during activity for these patients may be beneficial in clearing them for activity.

The current guidelines for return to activity for myocarditis in the pre-COVID-19 era suggest activity restriction until echocardiogram, 24-hour Holter and exercise electrocardiogram 3 to 6 months after initial illness show no abnormalities.[11] No patients in our cohort had pathologic arrhythmias that would result in activity restriction. Based on the lack of significant abnormalities found among our multisystem inflammatory syndrome in children cohort, as well as prior studies showing lack of myocardial scaring on MRI,[17] these return-to-play guidelines may not be necessary for those with multisystem inflammatory syndrome in children. We believe the metabolic data obtained with cardiopulmonary exercise test is useful for those with viral/idiopathic myocarditis and severe cardiac involvement to ensure no significant aerobic limitations and may also be helpful to provide guidance for those who could benefit from a medically supervised exercise programme given that one-quarter of these patients have decreased aerobic capacity.

Limitations

These data do have several limitations. First, there were notable demographic differences between the two patient groups. Those with prior viral myocarditis were older, taller, and more likely to be male. That being said, all metabolic markers were normalised to patient's age and sex, and therefore we do believe the percent predicted values are comparable. Second, while our group's practice is typically to obtain cardiopulmonary exercise test for all age-eligible patients with idiopathic/viral myocarditis, only those with significant cardiac involvement during their multisystem inflammatory syndrome in children course were referred for cardiopulmonary exercise test, potentially introducing a selection bias into the comparisons. However, given that those with multisystem inflammatory syndrome in children did quite well on cardiopulmonary exercise test, we do not feel that this bias is significant. Finally, most patients with viral myocarditis had an MRI performed during the acute myocarditis episode to confirm diagnosis, while those with multisystem inflammatory syndrome in children did not; therefore, we cannot compare the extent of myocardial scaring during the acute illness between the groups.

Conclusion

Most children and adolescents with multisystem inflammatory syndrome in children myocarditis and viral myocarditis had normal exercise testing 3–6 months after discharge. For those with viral/idiopathic myocarditis, lower ejection fraction and higher troponin at time of acute illness are associated with lower percent predicted peak VO2 on cardiopulmonary exercise test at 3–6 months following discharge.

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Conflicts of interest. None.

References

1. Belhadjer Z, Méot M, Bajolle F, et al. Acute heart failure in multisystem inflammatory syndrome in children in the context of global SARS-CoV-2 pandemic. Circulation. 2020; 142: 429–436. DOI 10.1161/circulationaha.120.048360.
2. Kaushik S, Aydin SI, Derespina KR, et al. Multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2 infection (MIS-C): a multi-institutional study from New York City. J Pediatrics. 2020; 224: 24–29. DOI 10.1016/j.jpeds.2020.06.045.
3. Matsubara D, Kauffman HL, Wang Y, et al. Echocardiographic findings in pediatric multisystem inflammatory syndrome associated with COVID-19 in the United States. J Am Coll Cardiol. 2020; 76: 1947–1961. DOI 10.1016/j.jacc.2020.08.056.
4. Gaitonde M, Ziebell D, Kelleman MS, et al. COVID-19-related multisystem inflammatory syndrome in children affects left ventricular function and global strain compared with Kawasaki Disease. J Am Soc Echocardiogr. 2020; 33: 1285–1287. DOI 10.1016/j.echo.2020.07.019.
5. Maron BJ. Sudden death in young athletes. Lessons from the Hank Gathers affair. N Engl J Med. 1993; 329: 55–57. DOI 10.1056/NEJM199307013290113.
6. Maron BJ. Sudden death in young athletes. N Engl J Med. 2003; 349: 1064–1075. DOI 10.1056/NEJMra022783.
7. Larsson E, Wesslen L, Lindquist O, et al. Sudden unexpected cardiac deaths among young Swedish orienteers – morphological changes in hearts and other organs. APMIS. 1999; 107: 325–336. DOI 10.1111/j.1699-0463.1999.tb01561.x.
8. Eckart RE, Scoville SL, Campbell CL, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. Ann Intern Med. 2004; 141: 829–834. DOI 10.7326/0003-4819-141-11-200412070-00005.
9. Drory Y, Turetz Y, Hiss Y, et al. Sudden unexpected death in persons less than 40 years of age. Am J Cardiol 1991; 68: 1388–1392. DOI 10.1016/0002-9149(91)90251-f.
10. Pelliccia A, Corrado D, Bjørnstad HH, et al. Recommendations for participation in competitive sport and leisure-time physical activity in individuals with cardiomyopathies, myocarditis and pericarditis. Eur J Cardiovasc Prev Rehabil. 2006; 13: 876–885. DOI 10.1097/01.hjr.0000238393.96975.32.
11. Maron BJ, Udelson JE, Bonow RO, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 3: hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies, and myocarditis. Circulation 2015; 132: e273–e280. DOI 10.1161/cir.0000000000000239.
12. Arena R, Myers J, Williams MA, et al. Assessment of functional capacity in clinical and research settings. Circulation. 2007; 116: 329–343. DOI 10.1161/circulationaha.106.184461.
13. Lee KJ, McCrindle BW, Bohn DJ, et al. Clinical outcomes of acute myocarditis in childhood. Heart. 1999; 82: 226–233. DOI 10.1136/hrt.82.2.226.
14. Penner J, Abdel-Mannan O, Grant K, et al. 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: a retrospective cohort study. Lancet Child Adolesc Health. 2021; 5: 473–482. DOI 10.1016/s2352-4642(21)00138-3.
15. CDC, Information for Healthcare Providers about Multisystem Inflammatory Syndrome in Children (MIS-C), 2021, CDC, Accessed September 21, 2021, 2021. https://www.cdc.gov/mis-c/hcp/,
16. Patel T, Kelleman M, West Z, et al. Comparison of multisystem inflammatory syndrome in children-related myocarditis, classic viral myocarditis, and COVID-19 vaccine-related myocarditis in children. J Am Heart Assoc 2022; 11, 10.1161/jaha.121.024393.
17. Dove ML, Oster ME, Hashemi S, Slesnick TC. Cardiac magnetic resonance findings after multisystem inflammatory syndrome in children. J Pediatr 2022; 245: 95–101. DOI 10.1016/j.jpeds.2022.02.049.
18. Li DL, Davogustto G, Soslow JH, et al. Characteristics of COVID-19 myocarditis with and without multisystem inflammatory syndrome. Am J Cardiol. 2022; 168: 135–141. DOI 10.1016/j.amjcard.2021.12.031.
19. Dove ML, Slesnick TC, Oster ME, Hashemi S, Patel T, Wilson HC. Cardiac Magnetic Resonance Findings of COVID-19 Vaccine Associated

Myocarditis at Intermediate Follow Up: a Comparison to Classic Myocarditis and MIS-C Related Myocarditis. Cold Spring Harbor Laboratory, 2022.
20. Aeschlimann FA, Misra N, Hussein T, et al. Myocardial involvement in children with post-COVID multisystem inflammatory syndrome: a cardiovascular magnetic resonance based multicenter international study-the CARDOVID registry. J Cardiovasc Magn Reson 2021; 23: 140. DOI 10.1186/s12968-021-00841-1.
21. Sasaki T, Kawasaki Y, Takajo D, Sriram C, Ross RD, Kobayashi D. Blood pressure response to treadmill cardiopulmonary exercise test in children with normal cardiac anatomy and function. J Pediatr 2021; 233: 169–174 e1. DOI 10.1016/j.jpeds.2021.02.043.

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