

SUPPLEMENTAL MATERIAL

OVERCOMING COVID-19 INVESTIGATORS

Alabama: Children's of Alabama, Birmingham. Michele Kong, MD.

Arizona: University of Arizona, Tucson. Mary Glas Gaspers, MD; Katri V. Typpo, MD.

Arkansas: Arkansas Children's Hospital, Little Rock. Ronald C. Sanders Jr., MD, MS; Katherine Irby, MD; Peter Mourani, MD.

California: Children's Hospital of Orange County, Orange County. Adam J. Schwarz, MD.

California: Miller Children's & Women's Hospital Long Beach, Long Beach. Christopher J. Babbitt, MD.

California: Rady Children's Hospital, San Diego. Helen Harvey, MD, MS.

California: UCSF Benioff Children's Hospital Oakland, Oakland. Natalie Z. Cvijanovich, MD.

California: UCSF Benioff Children's Hospital, San Francisco. Matt S. Zinter, MD.

Colorado: Children's Hospital Colorado, Aurora. Aline B. Maddux, MD, MSCS; Christina M. Osborne, MD; Sara Shankman, DNP, CPNC-AC.

Connecticut: Connecticut Children's, Hartford. Christopher L. Carroll, MD, MS.

Connecticut: Yale New-Haven Children's Hospital, New Haven. John S. Giuliano, Jr., MD.

Florida: Holtz Children's Hospital, Miami. Gwenn E. McLaughlin, MD, MSPH.

Florida: Nicklaus Children's Hospital, Miami. Paula S. Espinal, MD, MPH.

Georgia: Children's Healthcare of Atlanta at Egleston, Atlanta. Keiko M. Tarquinio, MD.

Illinois: Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago. Kelly N. Michelson, MD, MPH; Bria M. Coates, MD.

Indiana: Riley Hospital for Children, Indianapolis. Courtney M. Rowan, MD, MS.

Iowa: University of Iowa Stead Family Children's Hospital, Iowa City. Kari Wellnitz, MD; Guru Bhoojhwon MBBS, MD.

Kentucky: University of Louisville and Norton Children's Hospital, Louisville. Janice E. Sullivan, MD; Vicki L. Montgomery, MD; Kevin M. Havlin, MD.

Louisiana: Children's Hospital of New Orleans, New Orleans. Tamara T. Bradford, MD.

Maryland: Johns Hopkins Children's Hospital, Baltimore. Becky J. Riggs, MD; Melania M. Bembea, MD, MPH, PhD.

Maryland: University of Maryland Children's Hospital, Baltimore. Ana Lia Graciano, MD.

Maryland: Sinai Hospital of Baltimore, Baltimore. Susan V. Lipton, MD, MPH.

Massachusetts: Baystate Children's Hospital, Springfield. Kimberly L. Marohn, MD.

Massachusetts: Boston Children's Hospital, Boston. Adrienne G. Randolph, MD; Margaret M. Newhams, MPH; Audrey Dionne, MD; Jane W. Newburger, MD, MPH; Kevin G. Friedman, MD; Mary Beth F. Son, MD; Sabrina R. Chen; Cameron C. Young; Suden Kucukak, MD; Madyson FitzGerald; Julia Worden; Benjamin Boutselis.

Massachusetts: MassGeneral Hospital for Children, Boston. Ryan W. Carroll, MD, MPH; Phoebe H. Yager, MD; Neil D. Fernandes, MBBS.

Michigan: University of Michigan CS Mott Children's Hospital, Ann Arbor. Heidi R. Flori, MD, FAAP.

Michigan: Children's Hospital of Michigan, Detroit. Sabrina M. Heidemann, MD.

Minnesota: University of Minnesota Masonic Children's Hospital, Minneapolis. Janet R. Hume, MD, PhD.

Minnesota: Mayo Clinic, Rochester. Emily R. Levy, MD.

Mississippi: Children's Hospital of Mississippi, Jackson. Charlotte V. Hobbs, MD; Lora Martin MSN, FNP-C; Gurbaksh Singh, MSc; Urita Agana, BSc; Preeti Venula, MPH; Sarah McGraw MSN, FNP-C.

Missouri: Children's Mercy Hospital, Kansas City. Jennifer E. Schuster, MD.

Missouri: Washington University in St. Louis. Philip C. Spinella MD.

Nebraska: Children's Hospital & Medical Center, Omaha. Melissa L. Cullimore, MD, PhD; Russell J. McCulloh, MD.

New Jersey: Hackensack University Medical Center, Hackensack. Katharine N. Clouser, MD.

New Jersey: Newark Beth Israel Medical Center, Newark. Rowan F. Walsh, MD

New Jersey: St. Barnabas Medical Center, Livingston. Shira J. Gertz, MD.

New Jersey: Bristol-Myers Squibb Children's Hospital, New Brunswick. Lawrence C. Kleinman, MD, MPH, FAAP; Simon Li, MD, MPH; Steven M. Horwitz, MD.

New York: Golisano Children's Hospital, Rochester. Kate G. Ackerman, MD; Jill M. Cholette, MD, Joseph D. Kuebler MD MBA.

New York: Hassenfeld Children's Hospital at NYU Langone, New York. Adam J. Ratner, MD, MPH; Heda Dapul, MD; Vijaya L. Soma, MD.

New York: Kings County Hospital, Brooklyn. Michael A. Keenaghan, MD.

New York: Maria Fareri Children's Hospital, Valhalla. Aalok R. Singh, MD.

New York: The Mount Sinai Hospital, New York City. Sheemon P. Zackai, MD; Jennifer K. Gillen, MD.

New York: Stony Brook University Hospital, Stony Brook. Ilana Harwayne-Gidansky, MD; Saul R. Hymes, MD.

New York: SUNY Downstate Medical Center University Hospital, Brooklyn. Sule Doymaz, MD.

North Carolina: University of North Carolina at Chapel Hill, Chapel Hill. Stephanie P. Schwartz, MD; Tracie C. Walker, MD.

Ohio: Nationwide Children's Hospital, Columbus. Mark W. Hall MD, FCCM.

Ohio: University Hospitals Rainbow Babies and Children's Hospital, Cleveland. Steven L. Shein, MD; Amanda N. Lansell, MD.

Ohio: Akron Children's Hospital, Akron. Ryan A. Nofziger, MD.

Ohio: Cincinnati Children's Hospital, Cincinnati. Mary A. Staat, MD, MPH.

Pennsylvania: Children's Hospital of Philadelphia, Philadelphia. Julie C. Fitzgerald, MD, PhD, MSCE; Ryan Burnett, BS; Jenny L. Bush, RNC, BSN.

Pennsylvania: Penn State Children's Hospital, Hershey. Neal J. Thomas, MD, MSc.

Pennsylvania: St. Christopher's Hospital for Children, Philadelphia. Monica L. Koncicki, MD, Andrew D. Butler MD.

Pennsylvania: UPMC Children's Hospital of Pittsburgh. Ericka L. Fink, MD, MS; Joseph A. Carcillo, MD.

South Carolina: MUSC Children's Health, Charleston. Elizabeth H. Mack, MD, MS; Laura S. Smallcomb MD.

Tennessee: Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville. Natasha B. Halasa, MD, MPH.

Tennessee: Le Bonheur Children's Hospital, Memphis. Dai Kimura, MD.

Texas: Texas Children's Hospital, Houston. Laura L. Loftis, MD.

Texas: University of Texas Health Science Center, Houston. Alvaro Coronado Munoz, MD.

Texas: University of Texas Southwestern, Children's Medical Center Dallas, Dallas. Cindy Bowens, MD, MSCS; Mia Maamari, MD.

Utah: Primary Children's Hospital, Salt Lake City. Hillary Crandall, MD, PhD.

Washington: Seattle Children's Hospital, Seattle. Lincoln S. Smith, MD; John K. McGuire, MD.

Wisconsin: University of Wisconsin-Madison, Madison. Pelin Cengiz, MD.

CDC COVID-19 Response Team on Overcoming COVID-19: Manish M. Patel, MD, MPH; Leora R. Feldstein, PhD, MSc; Mark W. Tenforde, MD PhD; Ashley M. Jackson MPH; Laura D. Zambrano, PhD; Angela P. Campbell, MD.

Data S1.

Supplemental Methods

Case-Definition for Severe Acute COVID-19 ^a

- Admitted to the hospital intensive care unit or high-acuity stepdown unit with symptoms suspected to be related to COVID-19
- Evidence of infection with SARS-CoV-2 based on a positive RT-PCR test result during current illness
- Severe organ system involvement including at least 1 of the following:
 - **Respiratory**
 - Receipt of mechanical ventilation or any type of supplemental oxygen (or increased support for patients receiving respiratory support at baseline)
 - Severe bronchospasm requiring continuous bronchodilators
 - Pulmonary infiltrates on chest radiograph
 - Lower respiratory infection
 - Pleural effusion
 - Pneumothorax or other signs of barotrauma
 - Pulmonary hemorrhage
 - Chest tube or drainage required
 - **Cardiovascular**
 - Cardiac dysrhythmia or arrhythmia
 - Ejection fraction <55%
 - Pulmonary edema due to left heart failure
 - Coronary artery aneurysm (LAD or RCA z score ≥ 2.5)
 - B-type natriuretic peptide ≥ 1000 pg/mL
 - Elevated troponin-based on the upper limit of normal for the site laboratory
 - Receipt of vasopressor or vasoactive support
 - Receipt of cardiopulmonary resuscitation or ECMO support
 - **Kidney**

- Receipt of dialysis (for patients without chronic kidney failure)
- Acute kidney injury^b (in patients without prior kidney disease)
- **Neurologic**
 - Stroke or acute intracranial hemorrhage
 - Seizures
 - Coma
 - Encephalitis, aseptic meningitis, or demyelinating disorder (eg, acute disseminated encephalomyelitis) diagnosed by a neurologist
 - Decreased hearing or vision
 - Iritis or uveitis
- **Gastrointestinal**
 - Appendicitis
 - Pancreatitis
 - Hepatitis or hepatomegaly
 - Gallbladder hydrops or edema
 - Other complications as determined by site clinicians included ileitis, colitis, or mesenteric adenitis
- **Hematologic**
 - Absolute lymphocyte count $<1 \times 10^3$ cells/ μ L
 - Absolute neutrophil count $<0.5 \times 10^3$ cells/ μ L excluding chemotherapy patients³
 - Severe anemia^c
 - Platelet count $<50\,000/\mu$ L
 - Deep vein thrombosis
 - Pulmonary embolism
 - Hemolysis
 - Bleeding
 - Ischemia of an extremity
 - Other complications as determined by site clinicians included hemolytic uremic syndrome, anemia requiring transfusion, and pancytopenia

Abbreviations: COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; LAD, left anterior descending; MIS-C, multisystem inflammatory syndrome in children; RCA, right coronary artery; RT-PCR, reverse transcriptase–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^a Case definition was created by clinical consensus among the Overcoming COVID-19 steering committee principal investigators.

^b Acute kidney injury was defined as a creatinine level equal to or above the following values by age: less than 4 weeks: 1.59 mg/dL; 4 weeks to less than 1 year: 0.62 mg/dL; 1 to 10 years: 1.13 mg/dL; and ≥ 11 years: >1.59 mg/dL.

^c Severe anemia was defined as hemoglobin level less than 7 g/dL among children younger than 59 months of age, otherwise hemoglobin level less than 8 g/dL.

Centers for Disease Control and Prevention Case-Definition for MIS-C^a

- Age <21 y
- Fever ≥ 38.0 °C for ≥ 24 h or report of subjective fever lasting ≥ 24 h
- Laboratory evidence of inflammation^b
- Evidence of clinically severe illness requiring hospitalization with multisystem (≥ 2) organ involvement (cardiac, kidney, respiratory, hematologic, gastrointestinal, dermatologic, or neurological)
- No alternative plausible diagnoses
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, antibody, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 wk prior to the onset of symptoms^c

Abbreviations: COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children; RT-PCR, reverse transcriptase–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^a Must meet all criteria after adjudication by site and coordinating center principal investigators.

^b Including, but not limited to, 1 or more of the following: an elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, D-dimer, ferritin, lactate dehydrogenase, interleukin 6, elevated neutrophils, reduced lymphocytes, and low albumin level.

^c Patients without a positive SARS-CoV-2 test result were excluded after May 31, 2020, when site RT-PCR and antibody testing was more available.

Arrhythmia Case Report Form

Dear Overcoming COVID-19 Investigators,

You have identified _____ as having an arrhythmia during hospitalization for COVID-19 / MIS-C. We are working on the spectrum of tachyarrhythmias in this disease and hoping you can provide us with additional information on the arrhythmia.

1. Please confirm all observed tachyarrhythmia during hospitalization (please select all that apply).
 - a. Supraventricular tachycardia (narrow- or usual-complex tachycardia more than 3 beats with $\geq 1:1$ atrial-ventricular association)
Please specify type if known
 1. Atrial fibrillation
 2. Atrial flutter
 3. Ectopic atrial tachycardia
 4. Reentrant supraventricular tachycardia
 - b. Accelerated junctional rhythm / Junctional ectopic tachycardia (narrow- or usual- complex tachycardia with $\geq 1:1$ ventricular-atrial association and rates > 100 bpm)
 - c. Non-sustained ventricular tachycardia (3 consecutive ventricular beats at a rate of 120 bpm and < 30 seconds duration)
 - d. Sustained ventricular tachycardia (> 30 seconds or requiring intervention for termination)
 - e. Ventricular fibrillation
2. Where did the diagnosis of arrhythmia come from (select all that apply)?
 - a. Non-cardiac ICU progress note
 - b. Cardiac ICU progress note
 - c. Non-cardiology inpatient progress note
 - d. Cardiology inpatient progress note
 - e. Cardiology consultation
 - f. 12-lead ECG
3. What date was an arrhythmia first observed?
Date:
4. What date was an arrhythmia last observed?
Date:
5. Were any interventions required for treatment of tachyarrhythmias (please select all that apply)?
 - a) No treatment
 - b) Antiarrhythmic medication
If yes, please specify:
Medication:
Route administration (oral vs IV):
Dose:

- c) DC cardioversion
- d) CPR
- e) ECMO

6. Was the patient discharged home on antiarrhythmic medication?

- a) Yes

If yes, please specify:

Medication:

Dose:

- b) No

Please provide any available de-identified ECG or rhythm strips either embedded within this document or as an additional attachment to the email response.

Thank you

Table S1: Characteristics of patients hospitalized with acute COVID-19 and MIS-C with a reported tachyarrhythmia in 63 U.S. hospitals participating in the ‘Overcoming COVID-19’ public health registry, March 15—December 31, 2021.

	MIS-C (n=41)	Acute COVID-19 (n=22)	P value
Age (years)	14.5 [10.2, 16.9]	16.6 [11.2, 18.2]	0.18
Male Sex	26 (63)	13 (59)	0.95
At least one underlying condition	18 (44)	18 (82)	0.007
Cardiovascular	1 (2)	5 (23)	0.02
Congenital Heart Disease	1 (2)	3 (14)	0.12
Cardiomyopathy	0 (0)	2 (9)	0.12
Arrhythmia	0 (0)	2 (9)	0.12
Acquired Heart Disease	0 (0)	0 (0)	1.00
Other	0 (0)	0 (0)	1.00
Obesity	23/41 (56)	12/19 (63)	0.82
Presentation Conditions			
Duration of Symptoms Pre-Hospitalization (days)	4 [3, 6]	3 [1, 4.5]	0.048
Organ systems involved	5 [5, 6]	4 [2.25, 5]	0.001
Initial Laboratory Values			
Neutrophil to Lymphocyte Ratio	12.17 [5.74, 17.82]	5.90 [2.77, 12.57]	0.02
ALT (U/L)	60.5 [36.0, 90.5]	28.5 [18.0, 79.0]	0.06
CRP (mg/dL)	18.0 [13.4, 28.7]	1.1 [0.7, 2.7]	<0.001
Troponin (ng/mL), median [Q1,Q3]	0.50 [0.11, 6.75]	0.08 [0.02, 0.56]	0.77
Cardiac Complications			
Cardiovascular Involvement*	38 (93)	13 (59)	0.002
BNP or NT-proBNP >1,000 pg/mL	29/31 (94)	4/9 (44)	0.003
Elevated Troponin	33/38 (87)	9/13 (69)	0.21
Echocardiogram performed	41 (100)	21 (95)	0.35
Normal ventricular systolic function	9 (22)	11 (52)	0.03
Mild-moderate ventricular dysfunction	18 (44)	4 (19)	0.09
Severe ventricular dysfunction	13 (32)	6 (29)	1.00
Unknown ventricular function	1 (2)	0	1.00
CAA (RCA or LAD z-score ≥ 2.5)	15 (37)	0	0.001
Pericarditis or Pericardial Effusion	18 (44)	7 (33)	0.560
Critical Care Interventions			

Any respiratory support	35 (85)	16 (73)	0.38
Invasive Mechanical Ventilation	22 (54)	11 (50)	0.99
Non-Invasive Mechanical Ventilation Only	5 (12)	3 (14)	1.00
Vasopressor Requirement	38 (93)	14 (64)	0.01
ECMO†	7 (17)	8 (36)	0.16
Severity Scores 1st 24 Hours			
pSOFA, median [Q1,Q3]	4 (3, 7)	3.5 (1, 4.75)	0.04
Outcomes			
ICU Admission	40 (98)	21 (95)	1.00
ICU Length of Stay, median [Q1,Q3], days	8 [5, 12]	18 [6, 28]	0.04
Hospital Length of Stay, median [Q1,Q3], days	12 [9, 18]	8 [5, 37]	0.73
Death	2 (5)	7 (32)	0.006

n (%) or median [Q1,Q3]

* defined as BNP \geq 1,000 pg/mL, elevated troponin, systolic ventricular dysfunction or coronary artery aneurysm

†Includes ECMO (veno-venous and veno-arterial) at any point during hospitalization, irrespective of indication

ALT: alanine transaminase, CRP: C-reactive protein, BNP: B-type natriuretic peptide, CAA: coronary artery aneurysm, RCA: right coronary artery, LAD: left anterior descending coronary artery, ECMO: extracorporeal membrane oxygenation, ICU: intensive care unit, MIS-C: multisystem inflammatory syndrome in children. NT-proBNP: N-terminal pro B-type natriuretic peptide, pSOFA: pediatric sequential organ failure assessment

Table S2: Characteristics of patients hospitalized with acute COVID-19 and MIS-C and ventricular tachycardia in 63 U.S. hospitals participating in the ‘Overcoming COVID-19’ public health registry, March 15—December 31, 2021.

	Sustained VT (n=13)	Non-sustained VT (n=25)
Age (years)	14.3 [6.9, 15.7]	15.6 [9.1, 17.4]
Male Sex	6 (46)	15 (60)
MIS-C diagnosis	7 (54)	20 (80)
Underlying Conditions		
At least one underlying condition	8 (62)	9 (16)
Cardiovascular	2 (15)	2 (8)
Obesity	8/12 (67)	14/25 (56)
Presentation Conditions		
Duration of Symptoms Pre-Hospitalization (days)	4 [3, 5]	4 [2, 6]
Number Organ Systems Involved	6 [4, 6]	5 [5, 6]
Initial Laboratory Values		
Neutrophil to Lymphocyte Ratio	6.95 [5.07, 14.5]	12.25 [5.72, 15.93]
ALT (U/L)	49 [28.32, 92.75]	48 [24.5, 71.5]
CRP (mg/dL)	26.4 [7.63, 44.38]	17.33 [8.77, 29.23]
Troponin (ng/mL), median [Q1,Q3]	2.66 [0.73, 4.58]	0.78 [0.1, 13]
Cardiac Complications		
Cardiovascular Involvement *	12 (92)	21 (84)
BNP or NT-proBNP >1,000 pg/mL	6/6 (100)	16/17 (94)
Elevated Troponin	9/10 (90)	18 (86)
Echocardiogram performed	13 (100)	24 (96)
Normal ventricular systolic function	3 (23)	9 (38)
Mild-moderate ventricular dysfunction	4 (31)	10 (42)
Severe ventricular dysfunction	6 (46)	5 (21)
CAA (RCA or LAD z-score ≥ 2.5)	3 (23)	6 (25)
Pericarditis or Pericardial Effusion	4 (31)	11 (46)
Critical Care Interventions		
Any respiratory support	12 (92)	20 (80)
Invasive Mechanical Ventilation	11 (85)	12 (48)

Non-Invasive Mechanical Ventilation Only	0 (0)	3 (12)
Vasopressor Requirement	13 (100)	22 (88)
ECMO †	7 (54)	5 (20)
Severity Scores 1st 24 Hours		
pSOFA, median [Q1,Q3]	3 [2, 5]	3 [1, 5]
Outcomes		
ICU Admission	13 (100)	25 (100)
ICU Length of Stay, median [Q1,Q3], days	16 [7, 28]	9 [6, 12]
Hospital Length of Stay, median [Q1,Q3], days	19 [14 , 75]	12 [9, 19]
Death	6 (46)	2 (8)

n (%) or median [Q1,Q3]

* defined as BNP \geq 1,000 pg/mL, elevated troponin, systolic ventricular dysfunction or coronary artery aneurysm

† Includes ECMO (veno-venous and veno-arterial) at any point during hospitalization, irrespective of indication

ALT: alanine transaminase, CRP: C-reactive protein, BNP: B-type natriuretic peptide, CAA: coronary artery aneurysm, RCA: right coronary artery, LAD: left anterior descending coronary artery, ECMO: extracorporeal membrane oxygenation, ICU: intensive care unit, MIS-C: multisystem inflammatory syndrome in children. NT-proBNP: N-terminal pro B-type natriuretic peptide, pSOFA: pediatric sequential organ failure assessment

Table S3: Characteristics of patients with adjudicated and not-adjudicated tachyarrhythmia in 63 U.S. hospitals participating in the ‘Overcoming COVID-19’ public health registry, March 15—December 31, 2021.

	Adjudicated Arrhythmia (n=23)	No available tracing for review (n=40)	P- value
Age (years)	15.68 [10.74, 17.22]	15.1 [9.9, 17.51]	0.92
Male sex	15 (65)	24 (60)	0.89
MIS-C diagnosis	14 (61)	27 (68)	0.80
Arrhythmia			
SVT	12 (52)	16 (40)	0.50
Accelerated junctional rhythm	6 (26)	3 (8)	0.06
Ventricular tachycardia	11 (48)	27 (68)	0.20
Cardiovascular involvement			
Cardiovascular involvement*	18 (23)	33 (83)	0.94
BNP or NT-proBNP >1,000 pg/mL	13/16	20/24	1.00
Elevated troponin	14/18	28/33	0.70
Echocardiogram performed	23 (100)	39 (98)	1.00
Normal ventricular systolic function	7 (30)	13 (33)	
Mild-moderate ventricular dysfunction	8 (35)	14 (36)	0.93
Severe ventricular dysfunction	8 (35)	11 (28)	
Unknown	0	1 (3)	
CAA (RCA or LAD s-score \geq 2.5)	5 (22)	10 (26)	0.97
Pericarditis or Pericardial Effusion	4 (17)	21 (54)	0.007
Arrhythmia intervention			
None	8 (35)	18 (45)	0.60
Antiarrhythmic medication	15 (65)	16 (40)	0.10
Electrical cardioversion	6 (26)	5 (13)	0.31
CPR	4 (17)	4 (10)	0.45
ECMO for arrhythmia	5 (22)	4 (10)	0.27
Critical Care Interventions			
Any respiratory support	18 (73)	33 (83)	0.94
Invasive mechanical ventilation	13 (57)	20 (50)	0.81
Non-invasive mechanical ventilation only	4 (17)	4 (10)	0.45
Vasopressor Requirement	19 (83)	33 (83)	1.00
ECMO†	6 (26)	9 (23)	0.99
Outcomes			

ICU length of stay, median [Q1,Q3], days	7 [5, 10.75]	9 [5.5, 17.5]	0.30
Hospital Length of Stay, median [Q1,Q3], days	12 [6, 16]	10 [8, 19]	0.56
Death	4 (17)	5 (13)	0.71

n (%) or median [Q1,Q3]

* defined as BNP \geq 1,000 pg/mL, elevated troponin, systolic ventricular dysfunction or coronary artery aneurysm

†Includes ECMO (veno-venous and veno-arterial) at any point during hospitalization, irrespective of indication

BNP: B-type natriuretic peptide, CAA: coronary artery aneurysm, RCA: right coronary artery, LAD: left anterior descending coronary artery, ECMO: extracorporeal membrane oxygenation, ICU: intensive care unit, MIS-C: multisystem inflammatory syndrome in children, NT-proBNP: N-terminal pro B-type natriuretic peptide, pSOFA: pediatric sequential organ failure assessment, SVT: supraventricular tachycardia

Table S4: ECG findings in patients with tachyarrhythmias hospitalized with MIS-C and acute COVID-19 in 63 U.S. hospitals participating in the ‘Overcoming COVID-19’ public health registry, March 15—December 31, 2021.

	All patients (n=22)	SVT (n=10)	Accelerated junctional rhythm (n=2)	Ventricular tachycardia (n=15)	Underlying cardiac disease (n=3)
ST segment changes	15 (68)	10 (100)	1 (50)	8 (53)	2 (67)
ST segment elevation	2 (9)	0 (0)	1 (50)	2 (13)	0 (0)
ST segment depression	1 (5)	1 (10)	0 (0)	1 (7)	1 (33)
T-wave inversion	5 (23)	3 (30)	0 (0)	2 (13)	0 (0)
Non-specific	7 (32)	6 (60)	0 (0)	3 (20)	1 (33)
Prolonged QTc interval	8 (36)	3 (30)	1 (50)	5 (33)	2 (67)
Right bundle branch block	3 (14)	0 (0)	1 (50)	2 (20)	1 (33)
Incomplete right bundle branch block	3 (14)	3 (30)	0 (0)	1 (7)	0 (0)
Axis deviation					
Right axis	2 (9)	1 (10)	0 (0)	1 (7)	0 (0)
Left axis	2 (9)	1 (10)	0 (0)	1 (7)	1 (33)
Ventricular hypertrophy					
Right	2 (9)	1 (10)	1 (50)	1 (7)	1 (33)
Left	1 (5)	0 (0)	0 (0)	1 (7)	1 (33)
Atrial enlargement	1 (5)	0 (0)	0 (0)	1 (7)	1 (33)
1st degree atrioventricular block	1 (5)	0 (0)	0 (0)	1 (7)	0 (0)
Premature atrial beat	1 (5)	1 (10)	0 (0)	0 (0)	0 (0)

n (%)

SVT: supraventricular tachycardia

Table S5: Characteristics of patients treated and not treated for tachyarrhythmia in 63 U.S. hospitals participating in the ‘Overcoming COVID-19’ public health registry, March 15—December 31, 2021.

	Intervention for tachyarrhythmia (n=37)	No intervention for tachyarrhythmia (n=26)	P value
Age (years)	15.62 [10.62, 17.63]	14.74 [10.6, 16.79]	0.64
Male Sex	21 (57)	18 (69)	0.46
Underlying Conditions			
At least one underlying condition	22 (59)	14 (54)	0.85
Cardiovascular	5 (14)	1 (4)	0.39
Cardiac Complications			
Cardiovascular Involvement *	28 (76)	23 (88)	0.33
BNP or NT-proBNP >1,000 pg/mL	19/20 (95)	14/20 (70)	0.09
Elevated Troponin	23/30 (77)	19/21 (90)	0.28
Echocardiogram performed	37 (100)	25 (96)	0.41
Normal ventricular systolic function	14 (38)	6 (24)	
Mild-moderate ventricular dysfunction	11 (30)	11 (44)	0.49
Severe ventricular dysfunction	11 (30)	8 (32)	
Unknown ventricular function	1 (3)	0 (0)	
CAA (RCA or LAD z-score ≥ 2.5)	10 (27)	5 (20)	0.74
Pericarditis or Pericardial Effusion	11 (30)	14 (56)	0.07
Critical Care Interventions			
Any respiratory support	30 (81)	21 (81)	1.00
Invasive Mechanical Ventilation	23 (62)	10 (38)	0.11
Non-Invasive Mechanical Ventilation Only	2 (5)	6 (23)	0.06
Vasopressor Requirement	30 (81)	22 (85)	1.00
ECMO†	12 (32)	3 (12)	0.07
Severity Scores 1st 24 Hours			
pSOFA, median [Q1,Q3]	4 [2, 6]	4 [2.25, 5.75]	0.78
Outcomes			
ICU Admission	37 (100)	24 (92)	0.17

ICU Length of Stay, median [Q1,Q3], days	11 [5, 20]	7.5 [5, 10.25]	0.23
Hospital Length of Stay, median [Q1,Q3], days	15 [7, 22]	10 [8, 15]	0.42
Death	8 (22)	1 (4)	0.07

n (%) or median [Q1,Q3]

* defined as BNP \geq 1,000 pg/mL, elevated troponin, systolic ventricular dysfunction or coronary artery aneurysm

^aIncludes ECMO (veno-venous and veno-arterial) at any point during hospitalization, irrespective of indication

BNP: B-type natriuretic peptide, CAA: coronary artery aneurysm, RCA: right coronary artery, LAD: left anterior descending coronary artery, ECMO: extracorporeal membrane oxygenation, ICU: intensive care unit, MIS-C: multisystem inflammatory syndrome in children, NT-proBNP: N-terminal pro B-type natriuretic peptide, pSOFA: pediatric sequential organ failure assessment

Table S6: Clinical characteristics of patients with tachyarrhythmias who died during hospitalization in 63 U.S. hospitals participating in the ‘Overcoming COVID-19’ public health registry, March 15—December 31, 2021.

Patient	Age	MIS-C	Organ systems involved	Ventricular dysfunction	Tachyarrhythmia	ECMO	Cause of death
1	18–<21	No	Respiratory Cardiac Neurologic Hematologic	Mild	Supraventricular tachycardia (atrial flutter)	No	Primary respiratory
2	<1	No	Respiratory Cardiac Neurologic Hematologic	Severe	Supraventricular tachycardia (ectopic atrial tachycardia), Sustained ventricular tachycardia, and ventricular fibrillation	Yes	Primary respiratory
3	13–<18	Yes	Respiratory Cardiac Neurologic Gastrointestinal Hematologic Renal	None	Accelerated junctional rhythm, Non-sustained ventricular tachycardia, and Ventricular fibrillation	Yes	Primary cardiac
4	18–<21	No	Respiratory Cardiac Neurologic Gastrointestinal Hematologic Renal	None	Non-sustained ventricular tachycardia	Yes	Multiorgan failure
5	13–<18	No	Respiratory Cardiac Neurologic Hematologic Renal	ECHO Not Performed	Non-sustained ventricular tachycardia	No	Multiorgan failure
6	18–<21	No	Respiratory Cardiac Neurologic Gastrointestinal Hematologic Renal	Severe	Non-sustained ventricular tachycardia, Sustained ventricular tachycardia, and ventricular fibrillation	Yes	Multiorgan failure
7	6–<13	No	Respiratory Cardiac Renal	Severe	Sustained ventricular tachycardia	No	Primary cardiac
8	13–<18	Yes	Respiratory Cardiac Neurologic	None	Sustained ventricular tachycardia and ventricular fibrillation	No	Multiorgan failure

9	13-<18	No	Respiratory Cardiac Neurologic Gastrointestinal Hematologic Renal	Mild	Ventricular fibrillation	Yes	Multiorgan failure
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MIS-C: multisystem inflammatory syndrome in children