SUPPLEMENTAL MATERIAL

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Members of the ORCCA Study Group

Steering Committee:
Irfan M. Asif, MD, Aaron L. Baggish, MD, James Borchers, MD, Jonathan A. Drezner, MD, Katherine M. Edenfield, MD, Michael S. Emery, MD, MS, Kyle Goerl, MD, Brian Hainline, MD, Kimberly G. Harmon, MD, Jonathan H. Kim, MD, MSc, Stephanie Kliethermes, PhD, William E. Kraus, MD, Rachel Lampert, MD, Matthew Leiszler, MD, Benjamin D. Levine, MD, Matthew W. Martinez, MD, Nathaniel Moulson, MD, Francis G. O'Connor, MD, MPH, Manesh R. Patel, MD, Bradley J. Petek, MD, Dermot Phelan, MD, Lawrence D Rink, MD, Herman A Taylor, MD, MPH.

Investigators:
Carl Ade, PhD, Aryan Aiyer, MD, Jarrah Alfadhli, MD, Chloe Amaradio, Scott Anderson, ATC, Stephanie Arlis-Mayor, MD, Jonathan S. Aubry, MD, Andrea Austin, MSN, RN, Timothy Beaver, MD, Nicolas Benitez, Brant Berkstresser, Thomas M. Best, MD, PhD, Tiffany Bohon, MD, Jonathan P. Bonnet, MD, MPH, Elizabeth Boyington, James Bray, MD, Jenna Bryant, MD, Sean Carnahan, DO, Rachel Chamberlain, MD, Samantha Charters, ATC, Timothy W. Churchill, MD, Douglas Comeau, DO, Laura E Cook, MD, Deanna Corey, MD, Amy Costa, MD, Marshall Crowther, MD, Tarun Dalia, MD, Craig Davidson, MD, Kaitlin Davitt, MS, ATC, Annabelle De St. Maurice, MD, MPH, Peter N. Dean, MD, Katelyn DeZenzo, Courtney Dimitris, Jeanne Doperak, DO, Calvin Duffaut, MD, Craig Fafara, Katherine Fahy, MD, Jason Ferderber, MD, Megan Finn, Angelo Galante, MD, Todd Gerlt, ATC, Amy Gest, MPA, Carla Gilson, ATC, Jeffrey Goldberger, MD, Joshua Goldman, MD, MBA, Erich Groezinger, MS, Jonathan R. Guin, MD, Heather Halseth, Joshua Hare, MD, Beth Harness, ATC, Nicolas Hatamiya, DO, Julie Haylett, RN, MSN, Neal Hazen, MBA, PT, ATC, LAT, Yeun Hiroi, BS, Amy Hockenbrock, MD, Amanda Honsvall, MD, Jennifer Hopp, MD, Julia Howard, ATC, Samantha Huba, Mustafa Husaini, MD, Lindsay Huston, MD, Calvin Hwang, MD, Laura Irvin, DO, Val Gene Iven, MD, Robert Jones, MD, Donald Joyce, MD, Kristine Karlson, MD, Christian Klein, MD, Chris Klenck, MD, Michele Kirk, MD, Jordan Knight, Laura Knippa, RN, Madeleine Knutson, ATC, Louis E. Kovacs, MD, Yumi Kuscher, Andrea Kussman, MD, Chrissy Landreth, Amy Leu, DO, Dylan Lothian, Maureen Lowery, MD, Andrew Lukjanczuk, MS, ATC, LAT, John M. MacKnight, MD, Lawrence M. Magee, MD, Marja-Liisa Magnuson, DO, MS, Aaron V. Mares, MD, Anne Marquez, Grant McKinley, MD, Megan Meier, MD, Christopher Miles, MD, Emily Miller, MD, Hannah Miller, MSEd, ATC, LAT, Raul Mitrani, MD, Robert J Myerburg, MD, Greg Mytyk, ATC, Andrew Narver, DO, Aurelia Nattiv, MD, Laika Nur, MD, Brooke E. Organ, MD, Meredith Pendergast, ATC, Frank A. Pettrone, MD, Sourav K. Poddar, MD, Diana Priestman, Ian Quinn, DO, Fred Reifsteck, MD, Morgan Restivo, James B. Robinson, MD, Ryan Roe, PAC, Thomas Rosamond, MD, Carrie Rubertino Shearer, Miguel Rueda, Takamasa Sakamoto, MEd, ATC, Brock Schnebel, MD, Ankit B. Shah, MD, MPH, Alan Shahtaji, DO, Kevin Shannon, MD, Polly Sheridan-Young, PA-C, Siobhan M. Statuta, MD, Mark Stovak, MD, Andrei Tarsici, Kenneth S. Taylor, MD, Kim Terrell, Matt Thomason, ATC, Jason Tso, MD, Daniel Vigil, MD, Francis Wang, MD, Jennifer Winningham, MS, ATC, LAT, Susanna T. Zorn, MD.

Methods Supplement

Recruitment

Eligible NCAA institutions were invited to participate during conference-based team physician meetings, emails addressed to individual institutions, and by local conference physician leaders and consultants who helped to recruit new institutions. Invitation letters were sent to each institution accompanied by the following: 1) Study Overview, 2) Frequently Asked Questions (FAQ) primer, 3) Full IRB Application, 4) IRB Approval Letter, 5) Standardized Data Capture Tool, and 6) Data Use Agreement (DUA) template. Upon receipt of this information, eligible institutions were asked to declare their interest in participation. All aspects of this study were approved by the Massachusetts General Brigham IRB (Protocol #2020P002667) which determined that transmission and storage of de-identified data did not require participating institutions to secure individual IRB approval. However, sites were encouraged to explore the need for local IRB approval or a DUA with their institution regulatory office. For a site to be officially enrolled in the study, they were required to submit a 1) completed letter of agreement from the site PI agreeing to the study protocols and parameters, 2) site IRB approval (if necessary), and 3) local site DUA (if necessary). Any site that fulfilled the above criteria was allowed to contribute data to this registry.

Data Collection

All cardiovascular testing reports (ECG, troponin, echocardiography, cardiac MRI) that were considered abnormal by local institutions and all testing reports in athletes diagnosed to have myocardial or pericardial involvement of SARS-CoV-2 infection were evaluated by 3 separate reviewers who were blinded to outcomes (BJP, NM, ALB). For each cardiovascular testing

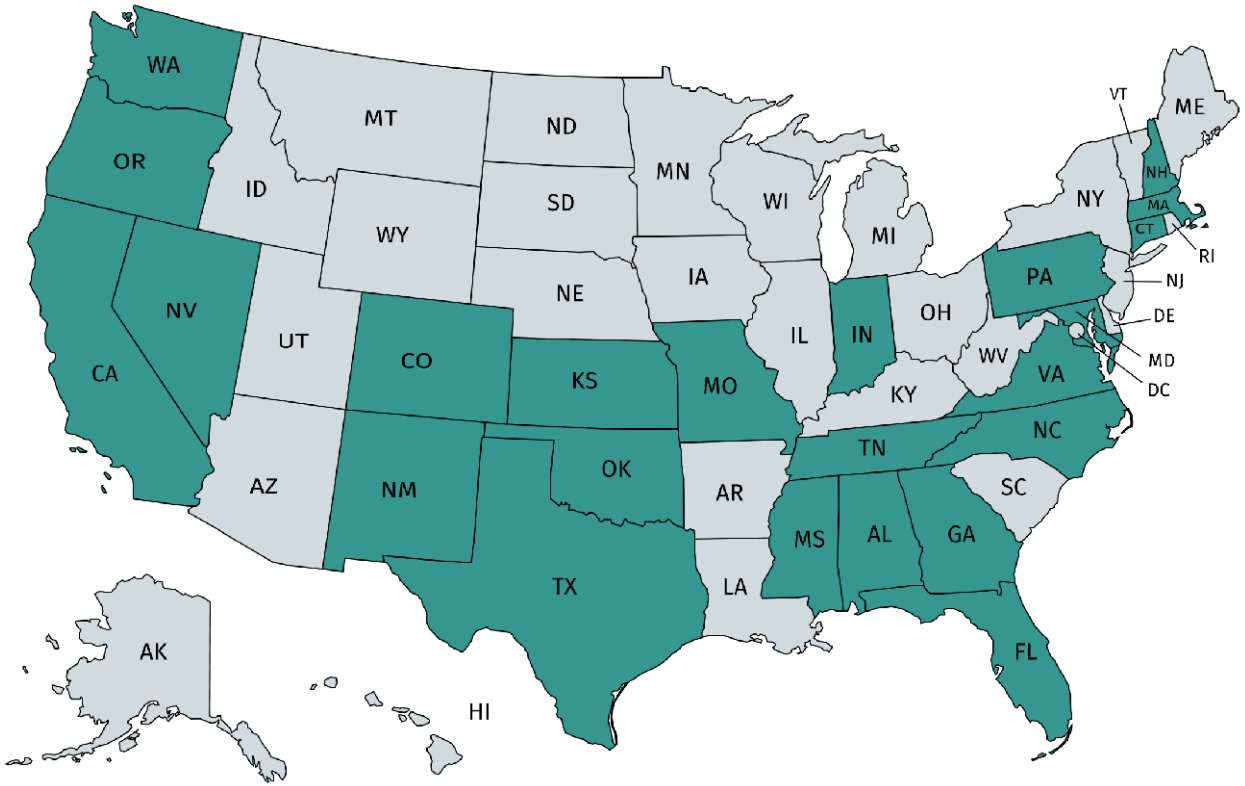
strategy, the reviewers adjudicated the findings as one of the following: 1) Normal, 2) Abnormal- possibly related to SARS-CoV-2 infection, or 3) Abnormal- likely unrelated to SARS-CoV-2 infection. Precise definitions for normal and abnormal cardiovascular testing reports are outlined below and were generated using recommendations for the diagnosis of myocarditis.[10] Participating institutions were regularly contacted to provide updates to their standardized data capture tool for potential new cases and to update follow-up outcomes measures for existing cases while maintaining de-identification.

Supplemental Figure Legends

Figure I. Map of Participating Institutions in the Study and Flow Diagram for Study Inclusion

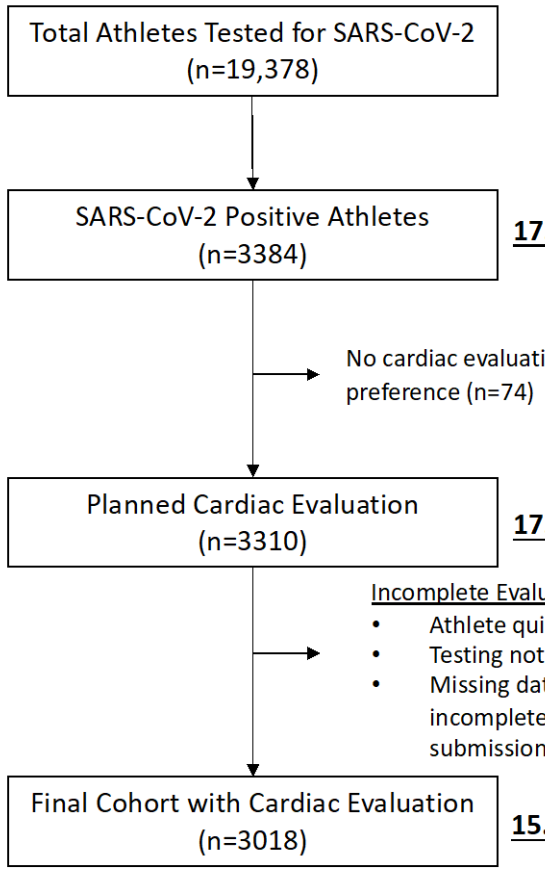
Definition of abbreviations: IQR= interquartile range

42 Colleges/Universities • 23 States • 14 Athletic Conferences



Created with mapchart.net

Median Length of Follow-up = 113 days IQR [90,146]



Supplemental Tables

Supplemental Table I. Definitions for Abnormal Cardiovascular Studies Possibly Related to SARS-CoV-2 vs. Likely Unrelated to SARS-CoV-2 Infection

Cardiovascular Testing	Abnormal- possibly related to SARS-CoV-2 infection	Abnormal- likely unrelated to SARS-CoV-2 infection
ECG	Abnormal by one of the following*: 1) Abnormal TWI 2) Pathologic Q waves 3) Abnormal ST-depressions 4) ≥2 PVCs 5) Complete LBBB 6) QRS≥140ms 7) 3rd degree AV block 8) Atrial tachyarrhythmias 9) Ventricular tachyarrhythmias 10) Complete RBBB combined with axis deviation or atrial enlargement 11) Diffuse ST elevations or PR depressions	1) Abnormal by International Criteria not meeting criteria for possibly related SARS-CoV-2 infection (i.e. prolonged QTc, ventricular pre-excitation) 2) Abnormal by International Criteria and meeting criteria for possibly related to SARS-CoV-2 infection, but the local institution designated that the abnormal findings were documented on a previous baseline ECG
TTE	1) LVEF <50% 2) Regional wall motion abnormality 3) Small or greater pericardial effusion 4) Focal thickening suggestive of edema 5) Intracavitary thrombi 6) Diastolic dysfunction† 7) Global longitudinal strain < -16%	1) Moderate or greater valvular regurgitation or stenosis 2) Atrial structural abnormality (i.e. PFO, ASD, intra-atrial aneurysm) 3) Ventricular structural abnormality (i.e. VSD, LVH, HCM, LV non-compaction) 4) Valvular structural abnormality (i.e., bicuspid aortic valve, mitral valve prolapse, mitral annular disjunction, valvular mass) 5) Aortopathy (i.e. aortic dilation or aneurysm) 6) Non-cardiac finding
Cardiac MRI	1) LVEF <45%‡ 2) Regional wall motion abnormality‡ 3) Small or greater pericardial effusion‡ 4) Non-ischemic Myocardial Injury (Abnormal T1, ECV, or LGE)^ 5) Hyperemia, capillary leak or myocardial edema (T2-mapping or T2W imaging abnormality)^ 7) Intracavitary thrombi 8) Diastolic dysfunction	1) Moderate or greater valvular regurgitation or stenosis 2) Atrial structural abnormality (i.e. PFO, ASD, intra-atrial aneurysm) 3) Ventricular structural abnormality (i.e. VSD, LVH, HCM, LV non-compaction) 4) Valvular structural abnormality (i.e bicuspid aortic valve) 5) Aortopathy (i.e. aortic dilation or aneurysm) 6) Non-cardiac finding

Definitions of abbreviations: AV= atrioventricular, ASD= atrial septal defect, ECV= extracellular volume, HCM= hypertrophic cardiomyopathy, LBBB= left bundle branch block, LGE= late gadolinium enhancement, LVEF= left ventricular ejection fraction, LVH= left ventricular hypertrophy, PFO= patent foramen ovale, PVC=pre-ventricular contraction RBBB= right bundle branch block, TWI= T-wave inversion, VSD= ventricular septal defect

*Adapted per the International Criteria[15]

†Diastolic dysfunction defined as peak trans-mitral E-wave velocity < peak trans-mitral A-wave velocity and/or lateral mitral annular pulse-wave peak tissue velocity of <10 cm/s

^Updated Lake Louise Imaging Criteria Main Criteria[16]
‡Updated Lake Louise Imaging Criteria Supportive[16]

Supplemental Table II. Sporting Discipline for SARS-CoV-2 Positive Athletes

Sport (n=3018)	**n (%)**
Football	1072 (36)
Baseball	269 (9)
Track and Field/Cross Country	249 (8)
Lacrosse	190 (6)
Basketball	187 (6)
Swimming/Diving	149 (5)
Soccer	146 (5)
Cheerleading/Dance	123 (4)
Volleyball	121 (4)
Softball	90 (3)
Golf	82 (3)
Wrestling	59 (2)
Tennis	56 (2)
Crew	54 (2)
Gymnastics	36 (1)
Ice Hockey	36 (1)
Equestrian	22 (0.7)
Field Hockey	13 (0.4)
Rugby	13 (0.4)
Fencing	11 (0.4)
Water Polo	11 (0.4)
Sailing	10 (0.3)
Squash	10 (0.3)
Skiing	7 (0.2)
Synchronized Swimming	2 (0.1)

Supplemental Table III. Indications for Cardiac Magnetic Resonance Imaging Performed in the Cohort as Reported by Local Institutions

Cardiac MRI Indication (n=317)	**n (%)**
Primary Screening Protocol	198 (62)
Clinical Indication	119 (38)
- Abnormal TTE	43 (14)
- Symptoms*	32 (10)
- Abnormal ECG	21 (7)
- Elevated Troponin	10 (3)
- Multiple Abnormal CV Tests	5 (2)
- Unknown	4 (1)
- Abnormal CV Test + Symptoms	2 (0.6)
- Other†	2 (0.6)

Definition of abbreviations: CV= cardiovascular, ECG= electrocardiogram, MRI= magnetic resonance imaging, TTE= transthoracic echocardiogram

*All symptomatic athletes had moderate or cardiopulmonary symptoms, there were 4 athletes who also had abnormal CV studies in this group (abnormal ECG n=1, abnormal TTE n=3)

†Includes family history as indication (n=1) and known history of hypertrophic cardiomyopathy (n=1)

Supplemental Table IV. Clinical Characteristics for Athletes with Abnormal Cardiac Testing but without Cardiac Magnetic Resonance Imaging

Athlete No.	Sex	Symptom Severity/Duration - Initial Symptoms/Duration - Exertional Symptoms	ECG	Troponin (normal ng/ml)	TTE	Other Work-up/ Follow-up
22	M	-Unknown	Normal	**Troponin I 0.11 (<0.04)**	Normal	Repeat Troponin 0.06
23	F	-None	Normal	**Troponin I 0.05 (<0.04)**	Normal	Repeat Troponin 0.05
24	M	-None	Normal	**Troponin I 0.06 (<0.04)**	Normal	Repeat Troponin <0.01
25	F	-None	Normal	**Troponin I 0.12 (<0.04)**	Normal	Repeat Troponin 0.04
26	M	-Cough	**Abnormal TWI V5-V6**	Undetectable	Normal	n/a
27	M	-SOB, loss of taste/smell, headache	Normal	**Troponin I 0.08 (<0.04)**	N/A	Repeat Troponin 0.04
28	M	-Cough, SOB, sore throat, myalgias, chest pain -None	Normal	Undetectable	**Abnormal GLS -14%**	
29	M	-Fever, SOB, loss of taste/smell, fatigue -None	Normal	Undetectable	**Abnormal GLS -13%**	
30	M	-Rhinorrhea, headache (2 days) -None	Normal	Undetectable	**Abnormal Mildly reduced GLS**	
31	M	-Cough, myalgias, nausea, rhinorrhea, headache, fatigue (2 days) -None	Normal	Undetectable	**Abnormal Mildly reduced GLS**	
32	F	-Sore throat, rhinorrhea, loss of taste/smell, headache (6 days) -None	Normal	Undetectable	**Abnormal -Possible subtle WMA -GLS -15.7%**	
33	M	-Unknown (10 days) -None	Normal	**Troponin I 0.07 (<0.04)**	Normal	

34	M	-Unknown (7 days) -None	**Abnormal** **New inferior TWI**	Undetectable	Normal	
35	F	-Unknown (14 days) -None	Normal	**Troponin I HS** **20 (<15)**	Normal	
36	M	-Unknown -None	**Abnormal** **>2 PVCs**	Troponin I HS 8 (<15)	Normal	
37	M	-Unknown	**Abnormal** **2 PVCs**	Undetectable	Normal	
38	M	-Unknown (15 days); **Hospitalized for bilateral PE** -Not returned to sport	Normal	**Troponin I HS** **36 (<15)**	Normal	-Restricted from sport -On anticoagulation
39	M	-Unknown -None	Normal	**Troponin I HS** **30 (<15)**	Normal	
40	M	-Unknown (7 days)	Normal	**Troponin I HS** **26 (<15)**	Normal	
41	M	-Fever, cough, headache (1 day) -None	**Abnormal** **inferolateral TW abnormality**	Undetectable	N/A	
42	F	-Rhinorrhea, loss of taste/smell (9 days) -SOB with return to exercise	Normal	Undetectable	**Abnormal** **large pleural effusion** **Normal cardiac parameters**	
43	F	-Fever, SOB, sore throat, myalgias, fatigue, chest pain (6 days) -None	**Abnormal** **TWI V1-V3**	Undetectable	Normal	
44	M	-Fever, myalgias, loss of taste/smell -None	Normal	**Troponin I** **0.05 (<0.04)**	Normal	
45	M	-Loss of taste/smell, headache (3 days) -None	Normal	**Troponin T** **0.034 (<0.027)**	Normal	

46	M	-Headache (1 day) -None	Normal	Undetectable	**Abnormal septal WMA**	
47	M	-Fever, loss of taste/smell, headache (8 days) -SOB on return to exercise	**Abnormal diffuse TWI**	Undetectable	Normal	CT-PE and ETT normal
48	M	-Unknown (1 day) -None	Normal	**Troponin T 0.15 (<0.10)**	Normal	
49	M	-None -None	**Abnormal V5-V6 TWI**	N/A	Normal	
50	M	-Cough, sore throat, muscle pain, headache, nasal congestion, chills (7 days) -None	**Abnormal TWI V1-V3**	Undetectable	Normal	
51	M	-SOB, headache (5 days) -Not returned to exercise	Normal	Undetectable	**Abnormal LVEF 47%**	CMR Pending

Definition of abbreviations: CMR= cardiac magnetic resonance imaging, CT-PE= computed tomography pulmonary embolism protocol, ECG= electrocardiogram, ETT= exercise treadmill test, F=female, HS= high sensitivity, GLS= global longitudinal strain, IUD= intrauterine device, LVEF=left ventricular ejection fraction, M=male, OCP= oral contraceptive pill, PCR=polymerase chain reaction, PE= pulmonary embolism, PVC= pre-ventricular contraction, SCT= sickle cell trait, SOB= shortness of breath, TTE=transthoracic echocardiography, TW= T-wave, TWI= T-wave inversion, WMA= wall motion abnormality. Mean age 20.3±0.2 years (range 18-22).

Supplemental Table V. Univariable Firth Logistic Regression Models for Associations with SARS-CoV-2 related Definite, Probable or Possible Myocardial/Pericardial Involvement (n=2988)

Patient Characteristics	OR (95% CI)	p-value
Female*	1.96 (0.85, 4.55)	0.12
Age (n=2975)	0.99 (0.74, 1.33)	0.93
BMI (n=2591)	0.96 (0.87, 1.07)	0.48
Race (n=2950)		**0.01**
White- Non-Hispanic	REF	REF
Black	1.90 (0.77, 4.72)	0.17
White-Hispanic	7.58 (2.20, 26.06)	0.001
Other[†]	0.64 (0.04, 11.07)	0.76
Sport		**0.005**
Basketball	5.09 (1.79, 14.48)	0.002
Football	1.02 (0.38, 2.72)	0.97
Other	REF	REF
Prescription Med Use (n=2766)	0.62 (0.22, 1.75)	0.37
Pre-Existing Conditions (n=2773) [‡]	1.53 (0.48, 4.82)	0.47
Symptoms		
Symptom Severity (n=2655)		**0.01**
Asymptomatic	REF	REF
Mild	0.93 (0.27, 3.24)	0.90
Moderate	1.10 (0.32, 3.85)	0.88
Cardiopulmonary	4.21 (1.43, 12.40)	0.009
Cardiac Testing^		
Abnormal ECG (n=2969)	17.19 (2.81, 105.09)	**0.002**
Abnormal TTE (n=2528)	81.44 (25.47, 260.40)	**<0.001**
Abnormal Troponin (n=2690)	18.54 (2.95, 116.58)	**0.002**
Abnormal ECG, TTE or Troponin	48.22 (18.51, 125.64)	**<0.001**

*****n=1 non-binary athlete removed from analyses

[†]Other category includes Mixed, Asian, American-Indian, Native Hawaiian, Pacific Islander and self-selected other

[‡]Pre-existing conditions include: sickle cell trait, diabetes, hypertension, hyperlipidemia, asthma (mild-intermittent or mild-persistent or greater), immunosuppressive agent, structural/valvular cardiac disease, electrical cardiac disease

^All abnormal tests were adjudicated by study team to be possibly related to SARS-CoV-2 Infection

REF indicates comparator levels for Odds Ratio (OR) estimates of categorical variables

Supplemental Table VI. Multivariable Firth Logistic Regression Model for Associations with SARS-CoV-2 related Definite, Probable or Possible Myocardial/Pericardial Involvement (n=2620)

Patient Characteristics	OR (95% CI)	p-value
Female Sex*	2.43 (0.97, 6.11)	0.06
Race		0.054
White – Non Hispanic	REF	REF
Black	1.94 (0.73, 5.16)	0.19
White -Hispanic	6.34 (1.61, 24.93)	0.008
Other[†]	0.78 (0.05, 13.00)	0.86
Presence of Cardiopulmonary Symptoms[‡]	3.08 (1.24, 7.67)	**0.02**
Abnormal ECG, TTE or Troponin	37.38 (13.27, 105.30)	**<0.001**

*N=1 non-binary athlete removed from analyses

[†]Other category includes Mixed, Asian, American-Indian, Native Hawaiian, Pacific Islander and self-selected other

[‡]Symptom severity was modeled as presence of cardiopulmonary symptoms versus all other categories (e.g. asymptomatic, mild or moderate) in multivariable analyses due to lack of significance identified in univariable analyses