AHA Rapid Response COVID-19 Research – What’s Hot?

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Disclosures: Research funding: AHA, NIH
COVID-19

Funding for COVID-19 Initiatives

• AHA responded rapidly to COVID-19
• Over 750 Applications
• Over 150 AHA volunteer reviewers
• 16 individual awards
• 4 Health Tech and Innovation SFRN supplemental awards
• Coordinating Center
• June 1-July 1 start dates

COVID-19 Infection, African American Women and Cardiovascular Health
Michelle A. Albert, MD, MPH; Co-PI, Yvette C. Cozier ScD
University of California, San Francisco

Health care disparities amplify the spread of COVID-19 to populations experiencing ...

- Greater economic deprivation
- Dense, low-resource community environments
- Less access to quality health care despite a higher burden of underlying health conditions

Compared to women of other races/ethnicities, black women ...

- Have the highest levels of cardiovascular disease
- Reside in lower socioeconomic status households
- More likely serve as caregivers for children and elderly relatives
- More frequently experience bias at all levels of society

Sample size = ~ 11,000 women
Age Range: 21–69
Mean Age: 59.4 years

STUDY AIMS

1. To document the experiences and perceptions of black women related to the COVID-19 pandemic in relation to infection risk, diagnostic testing accessibility, and perceived barriers to care
2. To examine the relation of COVID-19 infection and illness-related severity to cardiovascular health
3. To assess the relation of use of certain medications to COVID-19 infection and cardiovascular complications
Harnessing Glycomics to Understand Myocardial Injury in COVID-19

Rebekah L. Gundry, PhD, FAHA

• Identify the glycan signatures that predict patients with susceptibility versus those with protection to COVID-19 infection and post-viral myocardial injury.

• Provide targets for precision medicine evaluation and new mechanistic understanding of how COVID-19 induces myocardial injury.

Analysis of Blood Glycans by Mass Spectrometry
Repurposing Drugs for COVID–19

Joseph Loscalzo, MD, PhD
Brigham and Women’s Hospital
Harvard Medical School

The COVIDOME

SARS-CoV2 targets in cardiomyocytes: 230 proteins and 319 interactions
Integrin $\alpha_5\beta_1$ facilitates CoV-2 binding and cell entry

Bristow MR et al, JBTS Sept 2020. DOI: 10.1016/j.jacbts.2020.06.007
Published online June 25, 2020

The Integrin Binding Peptide, ATN-161, as a Novel Therapy for SARS-CoV-2 Infection (in review, Greg Bix laboratory & BSL3 Core, Tulane SoM)

Gregory Bix, MD, PhD, FAHA gbix@tulane.edu
Director, Clinical Neuroscience Research Center, Tulane

ATN-161
(non RGD peptide derived from fibronectin, binds to $\alpha_5\beta_1$ at an $\alpha_5$ ITG binding site). In VeroE6 cells:
- CoV-2 binds to $\alpha_5\beta_1$
- ATN-161 prevents CoV-2 binding to $\alpha_5\beta_1$, (nM affinity), and $\alpha_5$ binding to ACE2 ($\mu$M)
- ATN-161 prevents CoV-2 cell infection (3.16 $\mu$M IC$_{50}$)

https://doi.org/10.1101/2020.06.15.153387doi: bioRxiv preprint

Myocardial Virus and Gene Expression in SARS CoV-2 Positive Patients with Clinically Important Myocardial Dysfunction
Michael Bristow, University of Colorado AMC
A Comprehensive Assessment of Arterial and Venous Thrombotic Complications in Patients with COVID-19
Sanjum Sethi, MD, MPH, Columbia University Irving Medical Center

The Relationship of D-Dimer and Deep Venous Thrombosis in COVID-19
Mahesh V. Madhavan, MD

Median peak D-Dimer levels were similar in patients with (N=186) and without (N=328) diagnosis of DVT (18.5 mg/dL [IQR: 6.4, 20.0] vs. 12.2 mg/dL [IQR: 3.7, 20], p = 0.83)

Intermediate or Prophylactic-Dose Anticoagulation for Venous or Arterial Thromboembolism in Severe COVID-19: A Cluster Based Randomized Selection Trial

NCT04367831

From the Frontlines of the Pandemic: Best of COVID-19 Clinical Research
Friday, November 13, 2020, 9:00 am - 10:00 am
Pathogenesis of Cardiac Inflammation During COVID-19
Daniela Cihakova, Department of Pathology, Johns Hopkins University, Baltimore

Objective: We will determine changes of cardiac stroma cells and infiltrating immune cells phenotypes induced by COVID-19 infection by comparing heart autopsy samples of COVID-19 and non-CIVID-19 patients by immunohistochemistry, multiparameter flow cytometry, and scRNA sequencing.

ACE2 expression in endothelial cells as seen via IHC

Dr. Daniela Cihakova (PI) Dr. Taejoon Won

Monica Talor Megan Wood David Hughes

OPEN TO COLLABORATION!

Come see our website: http://labs.pathology.jhu.edu/cihakova/about/lab-members/
**Cardiovascular Outcomes and Biomarker Titrated Corticosteroid Dosing for SARS COV-2 (COVID-19): A Randomized Controlled Trial**

**SMART-COVID Trial**

Yewande Odeyemi, MD; Ognjen Gajic, MD, MS, Jacob C Jentzer, MD, Hemang Yadav, MD. Mayo Clinic

- **Feasibility** of individualized-dosing (based on CRP) for adjuvant steroids
- **Comparison of individualized-dosing** to:
  - Fixed dose / one-size-fits-all (dexamethasone 6mg for 10 days)
  - No steroids
- **Secondary CV Outcomes**: arrhythmias, pressor requirement, evidence of myocardial injury (daily troponin)

![Diagram showing CRP guidelines for steroid dosing](image-url)
Human iPSCs and Organ Chips Model SARS-CoV-2-Induced Viral Myocarditis
Clive Svendsen and Arun Sharma, Cedars-Sinai Medical Center
Rapid COVID-19-on-A-Chip to Screen Competitive Targets for SARS-CoV-2 Spike Binding Sites

Tzung Hsiai, MD, PhD, University of California, Los Angeles


Tzung Hsiai, MD, PhD

Angela Lai, PhD

Sandro Satta, PhD

Susana Cavallero, PhD

Cayden Williamson, PhD student
Testing of SARS-CoV-2 Infectivity and Antiviral Drug Effects in Engineered Heart Tissue, Microglial Cell Models, and COVID-19 Patient Registries

Mina Chung, MD; Mitali Das, PhD, Cleveland Clinic

A new way to study COVID-19 and test drugs

iPSCs ⇒ Cardiomyocytes ⇒ Engineered Heart Tissues
COVID-19 (C19) Health Tech SFRN supplements

Andrea Beaton, Cincinnati Children's Hospital
- Ejection Fraction as Sixth Vital Sign in C19 Patients: Improved triage using point-of-care echo

David Newman-Toker, Johns Hopkins University
- In-Home Diagnostic Triage via Smartphone Video Virtual Check-In for Potential Stroke Symptoms During Pandemic: Novel Approach to Improving CV Health Equity & Long-Term Prevention

Paul Wang, Stanford University
- Digital C19 Patient Tracking & Reporting Tool Kit Focused on CV Complications & Disease

Brahmajee Nallamothu, University of Michigan
- C19 Health Eval & CV Complications Study: Using mHealth to Track Physiological & CV Consequences

Ejection Fraction as the Sixth Vital Sign for Patients with COVID: Improved triage using point-of-care echocardiography

Andrea Beaton, Cincinnati Children's Hospital

- Access to echo is limited in many situations
- Rapid scale up of non-expert echo has challenges
- Navigational guidance provides a technology solution
- Conserves resources, improves access to diagnosis, change outcomes
- Prediction tool will be built to include LVEF

Real time feedback given on probe position and diagnostic quality
Possible Barriers to Data Entry:

• Add to stress to providers and health care system
• May prevent low resource centers from participating, undermining attempts to get data from diverse populations
• May result in incomplete data entry
• May result in selective non-consecutive entry of patients
Hypothesis
COVID 19 pandemic has resulted in an adverse change of activity measures, such as step count and exercise; physiologic measures, such as blood pressure and heart rate; and other health measures, such as stress and mood levels.

Vision
To develop interventions to maintain activity, control BP, and modulate stress and mood levels.

Our Approach
Use Apple Watch to understand changes in activity as well as heart rate
Use Omron blood pressure cuff to measure changes in blood pressure over time
Distribute COVID survey, with questions on COVID related symptoms, diagnosis, testing, exposures, and treatment
Baseline, weekly and quarterly distribution intervals

Next Steps
Complete analysis on step count, HR, mood, stress
Recruit small cohort of participants in UM community with documented COVID 19 to understand recovery trajectory using wearable device
Step counts of participants by week across COVID pandemic
AHA COVID–19 Coordinating Center

- Website
  
  https://professional.heart.org/en/research-programs/aha-rapid-response-grant-covid19
Thank You.
AHA Rapid Response Grants
COVID-19 and Its Cardiovascular Impact

Michelle Albert, University of California, San Francisco
• COVID-19 Infection, African American Women and Cardiovascular Health

Anand Prasad, University of Texas Health Science Center at San Antonio
• SARS-CoV-2 Infection and the Development of Cardiac Dysfunction

Jaejin An, Kaiser Permanente Southern California
• Risk of Severe Morbidity and Mortality of Coronavirus Disease 2019 (COVID-19) Among Patients Taking Antihypertensive Medications

Paul Heidenreich, Stanford University
• Outcomes for Patients with Hypertension, Diabetes and Heart Disease in the Coronavirus Pandemic: Impact of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers Treatment

Michael Lu, Massachusetts General Hospital
• Deep learning using chest radiographs to predict COVID-19 cardiopulmonary risk
AHA Rapid Response Grants
COVID-19 and Its Cardiovascular Impact

Rebekah Gundry, University of Nebraska Medical Center
• Harnessing Glycomics to Understand Myocardial Injury in COVID-19

Michael Bristow, University of Colorado AMC
• Myocardial Virus and Gene Expression in SARS CoV-2 Positive Patients with Clinically Important Myocardial Dysfunction

Joseph Loscalzo, Brigham and Women’s Hospital and Harvard Medical School
• Repurposing Drugs for Treatment of Cardiomyopathy Caused by SARS-CoV-2
AHA Rapid Response Grants
COVID-19 and Its Cardiovascular Impact

Sanjum Sethi, Columbia University Irving Medical Center
• A Comprehensive Assessment of Arterial and Venous Thrombotic Complications in Patients with COVID-19

Jane Freedman, University of Massachusetts Medical School
• The Role of the Platelet in Mediating Cardiovascular Disease in SARS-CoV-2 Infection

Emily Tsai, Columbia University Vagelos College of Physicians & Surgeons
• Elucidating the Pathogenesis of COVID-19 Cardiac Disease: Histopathological and snRNA-Seq Analyses of Human Myocardium

Daniela Cihakova, Johns Hopkins
• Pathogenesis of Cardiac Inflammation During COVID-19
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• Rapid COVID-19-on-A-Chip to Screen Competitive Targets for SARS-CoV-2 Spike Binding Sites

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