For this webinar, we are focusing on COVID-19 and how it relates to the heart.
Mended Hearts® mission is to inspire hope and improve the quality of life for heart patients and their families through ongoing peer-to-peer support, education and advocacy.

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Made possible through an educational grant from Bristol Myers Squibb
Before we begin

- All attendees are in listen-only mode
- If you cannot hear, check the audio button on your personal computer to assure the sound is on.
- Please type your questions into the Q&A box at any time during the presentation. Questions will be read and answered after the presentation.
  - Note: The presenter will not be able to answer questions about your child, specifically, or about you as a patient as he is not your treating physician.
- The PDF version of the slides, as well as the recording of this presentation, will be available on the Mended Hearts website following the event.
COVID and CVD

COVID and How It Relates to the Heart

Dr. Nelipovich,

• An Attending Cardiologist
• Director of the Women’s Heart Program at Maimonides Medical Center
• Dr. Nelipovich completed her cardiology fellowship at New York Presbyterian Hospital and New York Hospital Center Queens.
• She has been a teaching cardiology attending physician at Maimonides Medical Center since October 2011.
• Dr. Nelipovich’s special interests are non-invasive and minimally-invasive cardiology, as well as women’s heart issues

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COVID19 and Heart Disease

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Definitions

SARS-CoV-2, The Novel Coronavirus, named Severe Acute Respiratory Syndrome-Coronavirus-2

COVID-19, The Disease it causes, known as coronavirus disease 2019
Causes a range of symptoms from asymptomatic, to fever, dry cough, muscle pain, fatigue, loss of taste and smell, headaches, nausea, to sepsis, pneumonia, respiratory failure, multi-organ failure, and death

Direct effect of illness on the cardiovascular system
Severity of disease correlates with cardiovascular manifestations

Vulnerability of the patients with heart diseases to Covid-19 patients with CVD or risk factors for CVD may be prone to severe complications and increased mortality

Due to pandemic, significant implications for the cardiovascular care of patients
Impact: Cases, Deaths

COVID Data Tracker

United States at a Glance

**Cases**
- Total: 46,358,362
- Last: 30 Days

**Deaths**
- Total: 751,535
- Last: 30 Days

78.8% of People 12+ with At Least One Vaccination

Community Transmission
- High
This virus enters cells by binding to a surface protein of the host cell - ACE 2 which acts as a receptor.

Mechanisms of Injury

This virus enters cells by binding to a surface protein of the host cell - ACE 2 (angiotensin converting enzyme 2) which acts as a receptor. Using the spike-like protein on its surface, the SARS-CoV-2 virus binds to ACE2.

This protein, ACE-2 is present on many types of cells, especially in the lungs, heart, blood vessels, kidneys, liver and gastrointestinal tract. It is present in epithelial cells, cells lining organs. ACE-2 usually participates in the Renin Angiotensin System that regulates homeostatic functions such as blood pressure and electrolyte balance.

Usual function of ACE2 is to break down angiotensin II into molecules that counteract angiotensin II's harmful effects;

- Has anti-fibrosis, anti-inflammatory, vasodilation and anti-oxidant responses (and thus protects tissues)

When ACE 2 cannot perform its function, as there is less of it once cell is infected (downregulation), harmful effects are not counteracted,

- Increase in blood vessel constriction (vasoconstriction)
- Increased endothelial dysfunction (cells lining blood vessels)
- Increased retention/absorption of salt (sodium)
Impact of COVID19 on the Heart

CENTRAL ILLUSTRATION: Overview of the Mechanisms of Myocardial Injury in Patients With Coronavirus Disease 2019

Mechanisms of Myocardial Injury in Patients with COVID-19

SARS-CoV-2

Lung Injury

Direct Viral Myocardial Invasion

Stress cardiomyopathy

Microvascular thrombosis

Microvascular dysfunction

Coronary plaque rupture (Type 1 MI)

Inflammation-related Injury

Inflammation

Oxygen supply-demand imbalance (Type 2 MI)

IL-1, IL-6, TNF-α

Mechanisms of Injury To The Heart

Research is ongoing - Likely due to multiple factors

**Direct injury** to cardiac cells – causing cardiotoxicity/viral myocarditis
   In one study, 7% of patients ill with COVID-19 had myocardial injury from the infection
   22% of critically ill patients

Virus causes **systemic inflammation** – inflammatory cytokine release
   immune cell activation causing “cytokine storm”
   direct injury to organs and organ failure, direct injury to vasculature

Vascular inflammation – coronary plaque instability and rupture

Cytokine injury – myocardial inflammation

Cytokine injury – increased clotting risk (hyper-coagulable state)

**Altered cardio-metabolic demand** on the body – OXYGEN supply and demand
   due to systemic infection and Sepsis
   extra demands on the heart (to pump faster and harder)
   coupled with hypoxia (not enough oxygen supply)

Coronary plaque rupture and thrombosis (increased shear stress, increased blood flow)

Electrolyte imbalances (hypokalemia – low potassium levels)
   due to interaction of SARS-CoV-2 with renin-angiotensin-aldosterone system
   vulnerability to various arrhythmias.
Impact of COVID19 on the Heart

Possible Mechanisms of Cardiovascular Injury Due to Covid-19

Pathophysiological Effects

- Direct cardiotoxicity
- Hypoxaemia-mediated
- Supply-demand mismatch
- Cytokine storm
- DIC

Cardiovascular Manifestations

- Acute coronary syndrome
- Arrhythmia
- Myocarditis
- Venous thromboembolism
- Heart failure/Cardiogenic shock

Complications of COVID19 on the Heart

Arrhythmias:
- few studies available
- hypoxia mediated, scar mediated
- reports of 5.9% occurrence (ventricular tachycardia)
- with other cardiac injury up to 17.3% \( (\text{Guo}\uparrow) \)
- hospital arrest 5.9% due to shockable rhythm
- tachycardia (fast heart rate), atrial fibrillation (irregular heart rate)
- worse by electrolyte imbalance (low potassium – hypokalemia)
- Effect on QT prolongation by hydroxychloroquine (not FDA approved)
- Effect on QT prolongation by azithromycin (antibiotic treating co-infection, often secondary pneumonia)

Acute coronary syndrome:
- inflammation mediated plaque destabilization and rupture
- due to pro-thrombotic state
- symptoms + evidence (EKG changes q waves, Loss of myocardium on new motion changes on Echo, thrombus on angiography
- not enough oxygen supply for cardio-metabolic demand
- increased risk with viral infections by 3-10 fold
- careful approach (triage prior to cath lab/angiography versus fibrinolytics)

Impact of COVID-19 on the Heart

Myocarditis:
- true prevalence not known
- due to direct cell injury (virus entry)
- or Inflammatory infiltration of the muscle (T cell mediated immune response)
- role of biomarkers, ECG, Echocardiographic evidence,
- evidence from MRI and biopsy in diagnosis (last two may not be feasible)
- Acute injury due determined by biomarkers (small studies report)
  - troponin elevation in 28% of pt hospitalized for COVID-19 who have known CVD associated with much higher mortality rate

Heart failure:
- due to combination of above – hypoxia, ischemia, inflammation of heart
  “stress cardiomyopathy”
- part of multi organ failure
- Heart failure had occurred in 52% of the patients who subsequently died in 12% of the patients who were discharged from the hospital.

Risk Factors

Association between risk factors for Cardiovascular disease and severity of COVID-19

Hypertension
- present in up to 49% of pt ill/hospitalized with COVID19 (severe disease) range: 35-57%

Pre-existing Coronary Artery Disease (CAD) or Heart Disease (CHD)
- per CDC 28 % on pt with COVID19
  other studies up to 30-35% of severely ill range 10-17%
  specific predisposition has not been studied

Diabetes Mellitus
- 10.9% ill, of severely ill 19% of COVID-19

Obesity
- 48% of ill (source: CDC COVID-Net)

Increasing Age
- 14.8% for patients older than 80 years of age

Severely ill patients appear to have most CVD risk factors present
The presence of diabetes, cardio-cerebrovascular disease and hypertension was associated with a 2-fold, 3-fold and 2-fold greater risk of severe disease or requiring intensive care unit (ICU) admission (Kang, COVID-19Heart 2020;106:1132-1141 and China, CDC weekly 2020:2: 113-122)
Death Rate by Risk Factors

Overall death rate (range by country 0.3% to 5.7% based on reported statistics):
  USA: 1.6%, Russia 2.8%, China 2.3% (4.4% As per Johns Hopkins coronavirus resource center)

Death rate by risk factors:
One of frequently cited study from China reported mean death rate of 2.3%
  increases to 5% in patients with cardiovascular disease (CHD)
  increased to 7.3% in those with diabetes mellitus (DM)
another study reported history of CAD in 4.2% of all cases but in 22.7% of fatal cases in China

Another study case fatality rate of persons ill with coronavirus and having risk factors:
  10.5% for CAD/CHD presence,
  7.3% for DM presence,
  6% for HTN presence
Risk Factors: Obesity

Defined as BMI of >30 kg/m²
Prevalence remains high – above 30-40% of population in 38 states

Leads to metabolic syndrome which increases risk of damage to organs
Increased inflammation due to higher cytokines associated with obesity
  higher inflammatory response
Increased expression of ACE2 on surface cells – the protein receptor that viral S protein
  binds (overexpressed in lungs and heart) making patient more vulnerable
  Increased risk of lung injury on molecular level

Negative effects on pulmonary system/lung mechanics
  – predisposition to more severe respiratory distress/failure
  – limited chest expansion and movement (expiratory reserve volume, functional
capacity and respiratory system compliance) Increased risk of thromboembolism

If a person is obese and becomes ill with COVID19
  More at risk for Hospitalization - 113% higher hospitalization rate
  ICU admissions 74%, higher rates of mechanical ventilation
  Mortality (death) 48% increase
Impact of COVID19 on CHD

• those ill with COVID-19 and pre-existing cardiovascular disease have an increased risk of severe disease and death.
• infection has been associated with cardiovascular complications including acute myocardial injury, myocarditis, arrhythmias, and venous thromboembolism.
• therapies under investigation for COVID-19 may have cardiovascular side effects.
• response to COVID-19 can compromise the rapid triage of patients with cardiovascular conditions.
• patients with chest pain avoid seeking medical help due to fear of contagion or, have no possibility to access overcrowded emergency services.
Potential Treatments of COVID19

Remdesivir (Veklury) – Gilead - in hospitalized patients (IV)- speeds up recovery– FDA approved
Regen-COV - Regeneron monoclonal antibody (IV) – casirivimab and imdevimab – has emergency use authorization from FDA
Dexamethasone – steroid – decreases inflammatory response – but not officially approved by FDA – widely used for sickest patients

Not approved by FDA but has potential for near future (studies pending):
Paxlovid – Pfizer oral pill - protease inhibitor (affects virus replication) + ritonavir per press release, decreased hospitalization or death in 89% vs placebo (Pfizer press release 11/7/2021)
Lavgevrio – molnupiravir, oral, manufactured by Merck lowered death by 50% (press release 10/8/21 nature.com), not approved by FDA

NOT APPROVED BY FDA:
FDA emergency use was revoked for Hydroxycholorquine - no benefit and high risk of CV events (adverse effects: Cardiomyopathy, arrhythmia due to QT prolongation, ventricular arrhythmia, torsade de pontes) 6/15/2020
Ivermectin NOT FDA approved (adverse effects: hypotension, tachycardia, asthma, hepatitis)
Prevention

- Vaccination is effective.
- Reduces mortality and hospitalizations in high risk patients.
- Topic of Vaccination is too large for today’s discussion
- Prevention of cardiovascular risk factors always appropriate.
Citations

CDC.Gov


Megan Scudellari How the coronavirus infects cells — and why Delta is so dangerous https://www.nature.com/articles/d41586-021-02039-y.
Thank you!
For additional questions, please email: Andrea.baer@mendedhearts.org

Join us for the next session of the series:
COVID and CVD Moderated Patient Panel

November 16th, 2021
8:00 PM ET

Presenter: Dr. Jason Robin
Moderator: Andrea Baer, MS, BCPA

Register at mendedhearts.org

Made possible through an educational grant from Bristol Myers Squibb