COVID-19 AND CARDIOVASCULAR MANIFESTATIONS

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Disclosures

- None
Goals of Talk

- Quick overview of COVID-19
- Review Myocardial injury
- Review heart failure
- Review arrhythmias
CORONAVIRUS
DISEASE OF 2019
In 2020, COVID-19 was the 3rd leading cause of death in the U.S.

Heart disease still the number one cause of death in the U.S.
SARS COV-2

- Sudden Acute Respiratory Syndrome Coronavirus 2
- Targets the angiotension-converting enzyme 2 (ACE2) receptor
  - Heart
  - Lungs
  - Vessels
SARS COV-2

- Cases of viral entry in the endothelial cells of blood vessels including those in the heart and vascular beds
  - Thought to cause the deregulation of the renin-angiotension-aldosterone system
    - Regulate BP and activation of proinflammatory response – including cytokines and clotting factors

- Autopsy samples with myocytes with high viral load
  - Inversely no viral load detected in the heart from autopsy samples
Renin-angiotensin system

- **Drop in blood pressure**
  - **Drop in fluid volume**

- **Renin release from kidney**
- **Renin acts on angiotensinogen to form angiotensin I.**

- **ACE (angiotensin-converting enzyme) release from lungs**
- **ACE acts on angiotensin I to form angiotensin II.**

- **Angiotensin II acts on the adrenal gland to stimulate release of aldosterone.**

- **Angiotensin II also acts directly on blood vessels, stimulating vasoconstriction (narrowing).**

- **NaCl H₂O**
- **Aldosterone acts on the kidneys to stimulate reabsorption of salt (NaCl) and water (H₂O).**
COVID-19 Symptoms per CDC

- Shortness of breath or difficulty breathing
- Nausea or vomiting or diarrhea
- Fatigue
- Fever or chills
- Cough
- Headache
- Muscle or body aches
- Congestion or runny nose
- Sore throat
- New loss of taste or smell
Unofficial Symptoms

- Chest Pain
- Palpitations
COVID-19

Disease transmission
- direct contact
- respiratory droplets or aerosols
- ingestion of viral particles

Fever
- due to alveolar vasodilation and permeability of cytokine (IL-6)

Cardiovascular complications
- due to increased sympathetic stimulation, hypercoagulability and inflammation

Gastrointestinal manifestations
- abdominal pain, nausea, vomiting, diarrhea, anorexia, and impaired liver function

Systemic pathogenesis
- shortness of breath or difficulty breathing
- due to intense inflammatory response and lung edema
Comorbidities the CDC Classifies for Severe COVID-19

- Established risk factors:
  - Serious cardiovascular disease (heart failure, CAD, cardiomyopathies)
  - Obesity
  - Smoking
  - Type 2 diabetes
  - CKD
  - Down syndrome
  - Immunocompromised
  - Pregnancy
  - Obesity

- Possible risk factors:
  - HTN
  - Overweight (BMI 25-30)
  - Type 1 diabetes
  - Pulmonary fibrosis
  - Asthma (moderate to severe)
• Reported nearly 1/3 of COVID-19 patients are reported to present with:
  • Acute cardiac injury
  • Myocarditis
  • Heart failure
  • Cardiogenic shock
  • Significant dysrhythmias

• Associated with high rates of thromboembolic and disseminated intravascular coagulation complications
  • Concern for pulmonary embolism
Assumed Manifestations of Heart Disease

- Myocarditis
- Hypoxic Injury
- Stress (Takotsubo) Cardiomyopathy
- Ischemic Injury
  - Cardiac Microvascular Dysfunction
- Small Vessel Cardiac Vasculitis
- Right Heart Failure (Acute Cor Pulmonale)
- Adult Respiratory Distress Syndrome (ARDS)
- Systemic Inflammatory Response Syndrome (Cytokine Storm)
COVID-19

- Myocardial Injury
- Heart Failure
- Dysrhythmias
MYOCARDIAL INJURY
Prevalence

- Broad range for prevalent coronary artery disease (CAD)
- Case reports of frequencies vary from 7 to 28%

- Pre-existing risk factors have associated risk and severity of COVID-19
  - Hypertension
  - Diabetes
  - Prior CAD
  - Older age
  - Hx of heart failure
Troponin

- Elevated Troponin
  - About 1 in 5 hospitalized patients with more than half of those with known cardiac conditions
  - Likely not indicative of acute coronary syndrome in absence of cardiac signs/symptoms, ECG findings

- Increased troponin levels likely associated with increased inflammation
  - C-Reactive protein, ferritin, lactate dehydrogenase, neutrophil count

- Theory: Troponin level correlates with risk of mortality
  - Even mildly elevation was associated with risk of death
Types of Myocardial Injury

- Type I: “Caused by acute atherothrombotic CAD and usually precipitated by atherosclerotic plaque disruption (rupture or erosion)”
- Type II: “Consequent to a mismatch between oxygen supply and demand”
- With COVID-19, majority of cases are Type II
Type II Myocardial Injury

- Severe Hypoxia
- Sepsis
- Systemic Inflammation
- Stress Cardiomyopathy
- Myocarditis
Possible Causes with COVID-19

- Increased sympathetic stimulation leading to increased myocardial oxygen demand
- Direct vascular infection causing inflammation
- Plaque rupture from
  - Cytokine storm
  - Hypercoagulability
Sympathetic System
Testing

- ECG
  - New ST elevation in two contiguous leads
  - New left bundle branch block with anginal symptoms
- Not required but helpful is Echocardiogram:
  - No wall motion abnormalities (WMA) with chest pain
  - No regional WMAs in area suggested by ECG
Management

- STEMI - cath lab as primary percutaneous intervention is preferred to improve outcomes irrespective of COVID-19 status
  - Aspirin, P2Y12 inhibitor, statin, nitrate
  - No standard CAD medication associated with worse outcomes in setting of COVID-19

- Fibrinolysis only when needed
  - Resource utilization and/or risk of viral exposure

- However, it is case by case basis
  - Comorbidities
  - Hemodynamic stability
  - Delay in presentation
MANAGEMENT

◦ NSTE MI – still require urgent management
◦ Consider:
  ◦ Repetitive episodes of angina
  ◦ Ventricular arrhythmias
  ◦ Dynamic ECG changes
HEART FAILURE
Prevalence

- Pts with known HF were associated with adverse outcomes:
  - Longer hospitalization
  - Increased risk of mechanical ventilation
  - Mortality

- Elevated B-type natriuretic peptide (BNP) and N-terminal pro-BNP are common along with troponin
Causes of Heart Failure

- Ischemia / Myocardial infarction
- Increased sympathetic stimulation leading to increased myocardial oxygen demand
- Direct infection leading to myocarditis (Myocyte necrosis) – Limited evidence
- Myocardial depression from proinflammatory effects
- Acute Respiratory Distress Syndrome leading to hypoxia resulting in
  - Decreased oxygen supply for myocytes (Ischemia)
  - Pulmonary hypertension -> Right heart failure
Myocarditis

- Inflammatory disease of cardiac muscle caused by many infectious and noninfectious conditions accompanied by cardiac dysfunction

- Not all inclusive list:

<table>
<thead>
<tr>
<th>Infectious</th>
<th>Noninfectious</th>
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<tbody>
<tr>
<td>Viral</td>
<td>EtOH, Cocaine</td>
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<tr>
<td>Bacterial</td>
<td>Hypersensitivity reactions (insect bites, antibiotics, diuretics)</td>
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<tr>
<td>Spirochetal (Lyme disease, Syphilis)</td>
<td>Systemic Disorders (Celiac disease, IBS, sarcoidosis, thyrotoxicosis)</td>
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Myocarditis

Myocarditis is commonly clinically suspected, but few histologically confirmed cases

Usually resolves on its own as the infection wanes
Right heart failure

- Acute cor pulmonale due to
  - Acute pulmonary embolism – hypercoagulability
  - Acute Respiratory Distress Syndrome (ARDS)
Stress Cardiomyopathy

- Diagnosis based on presence of **all** of the following four features:
  - Transient left ventricular dysfunction (not in a single coronary distribution)
  - Absence of angiographic evidence of obstructive CAD
  - New ECG abnormalities (ST elevation and/or T-wave inversion) or modest troponin elevation
  - Absence of myocarditis

- Those who survive the acute episode typically recover
Testing

- Echocardiogram:
  - Right ventricular dilation and dysfunction (39% of pts)
  - Left ventricular diastolic dysfunction (16% of pts)
  - Left ventricular dysfunction (10% of pts)
Management

- COVID Clinics
  - Long haul COVID-19 symptoms

- Consult Heart Failure Cardiologist
  - Help management of Heart Failure
  - Early recognition of advanced surgical options
 Athletes

- More than ½ of pts who recovered from uncomplicated COVID-19 had abnormal echo or cardiovascular magnetic resonance (CMR)
  - Meaning subclinical myocardial and pericardial disease
- Consequences could be fatal during physical activity
- American College of Cardiology COVID-19 return-to-play guidelines
COVID-19 negativea and asymptomatic

- No limitations to exercise
- Follow social distancing guidelines
- Close monitoring for development of symptomsb

Asymptomatic (considered in setting of screening with known exposure or team-/school-/league-based mandatory screening)

- Rest/no exercise for 2 wk from positive test result
- Close monitoring for symptom onset or late deteriorationb
- Slow resumption of activity after 2 wk from positive test result under guidance of health care team

COVID-19 positivea

Mild symptoms; not hospitalized

During symptomatic period:
- Rest/recovery with no exercise
- Reasses for clinical deterioration and consider further cardiac testing and/or hospitalization if development of cardiac symptoms

2 wk of Convalescence without resumption of exercise after symptom resolution

Evaluation by a medical professional for consideration of return to activity:
- hsTn
- 12-lead electrocardiogram
- 2-Dimensional echocardiogram
- Consider additional symptom-guided testing

Normal

hsTn >99 percentile and/or abnormal cardiac study

• Rest/recovery with no exercise while symptomatic
• Evaluation by medical professional after minimum of 2 wk of convalescence without resumption of exercise after symptom resolution
• Consider convalescent cardiac testing if not performed while hospitalized
• Slow resumption of activity under guidance of health care team
• Close monitoring for clinical deterioration

Follow myocarditis RTP guidelinesc

Normal

hsTn >99 percentile and/or abnormal cardiac study

- Slow resumption of activity under guidance of health care team
- Close monitoring for clinical deterioration

Follow myocarditis RTP guidelinesc

NOTE: If symptoms concerning for COVID-19 develop and testing is negative or not obtained, consider following pathway as if COVID-19 positive.
ARRHYTHMIAS
Arrhythmias

- Most common arrhythmia is sinus tachycardia
- Current evidence unclear of prevalence of arrhythmia or conduction disease
- Systemic Illness is likely cause, not direct COVID-19 infection
  - Hypoxia and electrolytes derangements – known to cause acute arrhythmias

- Vast majority of patients with COVID-19 will not have signs or symptoms of arrhythmias or conduction disease

- Fevers can unmask some preexisting diseased pathways such as Brugada syndrome or prolonged QT syndrome
Arrhythmias

- Other arrhythmias include:
  - Atrial fibrillation
  - Atrial flutter
  - Monomorphic or polymorphic ventricular tachycardia

- Right Bundle Branch Block (7.8% of pts)
- Left Bundle Branch Block (1.5% of pts)
Causes of Arrhythmias due to COVID-19

- Increased sympathetic stimulation
- Myocarditis
- Proinflammatory effects
Cardiovascular testing

- ECG:
  - Rate
  - Bradyarrhythmia (including pauses or high grade AVB are not typically seen)
  - Regularity
  - QRS width
  - QTc (average ~350 to 440 milliseconds) -> polymorphic VT
- CMP (hyper/hypokalemia, hypocalcemia, hypomagnesemia)
- Echocardiogram
Management

- Unstable patients (hemodynamically unstable, severely symptomatic, pulseless)
  - ACLS
  - Cardioversion
  - IV magnesium for torsades de pointes
  - Correcting electrolytes
Management

- Stable patients:
  - Correcting electrolytes / metabolic derangements
  - Oxygen
  - Anti-arrhythmic medications
    - Beta blockers, calcium channel blockers, amiodarone
  - Electrophysiology consult
QT prolonging medications

- Hydroxychloroquine and chloroquine are not recommended for treatment of COVID-19
  - June 2020, FDA revoked emergency use authorization
  - About 10% of pts developed prolonged QT

- Long list of QT prolonging medications and pharmacy consult
- Discussion of benefit vs risk to continue any known QT prolonging meds
IMPORTANT DISEASE STATES TO MENTION
Hypercoagulability

- Pathogenesis not completely understood in setting of COVID-19

- Virchow’s Triad – all 3 apply to severe COVID-19 infection
  - Endothelial injury – evidence of direct infection
  - Stasis – immobilization can cause blood flow stasis
  - Hypercoagulable state:
    - Elevated factor VIII, fibrinogen, prothrombotic microparticles, etc.
Hypercoagulability

- Stroke
- Pulmonary Embolism
- Limb ischemia
Thromboprophylaxis

- Inpatient:
  - LMW heparin preferred
  - Treatment generally not continued at discharge
Management

- Full dose anticoagulation for documented VTE
  - Treatment for 3 months

- Reserve fibrinolytic agents (i.e., tPA) for limb-threatening DVT, massive pulmonary PE, stroke
  - Discussion with each specialist prior to administration
Pericardial Effusion and Pericarditis

- There is limited data or published cases at this time
WRAP UP
Management

- No optimal management treatment course has been determined
- Continue supportive care for each suspected diagnosis
ACE Inhibitors / ARB Use

- Angiotensin converting enzyme inhibitor or angiotensin receptor blocker are used in treatment of heart failure and coronary artery disease

- Theory: elevated ACE2 levels caused by the inhibitors might impact susceptibility of SARS COV-2 but there is no evidence use worsens the clinical course of COVID-19
Robust evidence of pts delaying care resulting in decreased hospitalizations and less percutaneous interventions

Important Note

◦ This information is likely to change as more studies are performed and further data is collected
References

- Scientific America, Jan 13, 2021
- Imazio, Massimo. “COVID-19 as a Possible Cause of Myocarditis and Pericarditis.” American College of Cardiology. Feb 5, 2021