South Bay Cardiovascular Center
Accredited Echocardiography and Nuclear Cardiology Facility

COVID-19 AND CARDIAC INVOLVEMENT

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RISK STRATIFICATION:

Cardiovascular patients with COVID-19 are categorized into the 3 main risk groups:

1. **Risk**: Patients with CAD including prior stents and CABG
   Recs: stay at home and refrain from attending essential needs like grocery shopping, outdoor exercise and pharmacy pickups.
2. **Particularly high risk**: More than 70 years and who have heart disease, or heart disease along with lung disease or chronic kidney disease, (heart disease is identified as congestive heart failure, valvular disease, cardiomyopathy and congenital heart disease)
   Recs: stay at home and no essential outings.
3. **Extremely high risk**: Patients with heart transplant and pregnant woman with significant heart disease
   Recs: stay at home at all times and minimize contact with people for 12 weeks.

PREVALENCE

Cardiovascular comorbidities are common in older patients who also have a lower immunity and hence more susceptible to Covid 19.

1. Hypertension: There is increased prevalence of hypertension, amounting to 17.1%
2. Cardiac and cerebrovascular disease: prevalence is 16.4%
3. Diabetics make up about 9.7%.

Why is this important because those patients with pre-existing cardiac disease have increased risk of severe disease and death. Overall case fatality rate is 2.3%.

Fatality rate, in hypertensive patients is 6%, Cardiac and cerebrovascular disease is 10.5%, Diabetes is 7.3%.

SYMPTOMS

USUAL: Fever, cough, dyspnea, myalgias and fatigue, diarrhea, loss of smell and taste.

CARDIOVASCULAR CLINICAL PRESENTATIONS:

1. Chest pain with ST elevation MI without fever or cough and usually with normal coronary arteries on angiogram.
2. Cardiogenic shock with acute respiratory distress or hypoxemia, therefore have low threshold to assess for cardiogenic shock patients with acute heart failure related to Covid 19.

3. Underlying cardiac disease patient's present with profound decompensation with related COVID-19 infection leading to decompensation of heart failure and cardiogenic shock.

TESTING

1. BLOOD TESTS: Troponin testing is routinely performed a hospitalized patient as it may have a prognostic value and be useful as a baseline. Checked on admission and follow-up in 24-48 hours.
   Mild elevation in troponin is most common and is often associated with no cardiac symptoms.

   Currently moderate troponin elevation is seen with clinically suspected myocarditis or stress cardiomyopathy.
   Progressive moderate troponin elevation is seen in patients with respiratory failure and accelerated rise after the second week leading to cytokine storm and death.
   BNP level, NT-proBNP levels are obtained in patients with suspected heart failure.
   In addition C-reactive protein, ferritin, d-dimer, IL-6 and LDH are markedly elevated in patients with profound systemic inflammatory response and associated with poor prognosis.

2. ECG, needed baseline and ongoing for QT interval management. ECG abnormalities include ST elevations, ST depressions, T-wave inversions and Q waves. PVC's

3. ECHOCARDIOGRAM: This is an important tool but also important to minimize sonographer time with COVID-19 patient's to reduce the risk of spread. Therefore the use of POCUS (point-of-care ultrasound), can provide useful information on cardiac function while limiting the number of people that are exposed to any infected patient.

   The presence of reduced LV function and poor myocardial edema could influence the use of inotropic agents, mechanical support or help risk stratify for more aggressive anti-inflammatory therapies.

   Minimal role for TEE and cardiac MRI.

4. PULMONARY ARTERY CATHETER ASSESSMENT: Provide useful information about hemodynamic status and cardiac filling pressures. May have a role in selected cases where a patient is in refractory shock and responding poorly to empiric vasopressor/inotropic therapy and mechanical support/ECMO is being contemplated.

   In most patients however hemodynamic monitoring can consists of mean arterial pressure measurements via an arterial line and CVP assessments from a central venous catheter and monitoring of central mixed venous oxygen saturations.

5. ENDOMYOCARDIAL BIOPSY: There is currently no evidence to support the use of this procedure especially the information would not change management. Only used in the rare younger patient in whom the decision to employ aggressive anti-inflammatory or other investigational therapies requires biopsy evidence of myocarditis.

MECHANISM OF CARDIAC INVOLVEMENT:

1. Direct myocardial involvement VIA ACE2
2. Cytokine storm,
3. Hypotension

CARDIOVASCULAR SEQUALAE

1. **MYOCARDIAL INJURY** which encompasses all conditions causing cardiomyocyte death. Prevalence (as reflected by increased troponin levels in hospitalized patients) is 7-28%.

   Presumed causes of myocardial injury in patients with COVID-19 include:
   - Myocarditis
   - Hypoxic injury
   - Stress Cardiomyopathy
   - Ischemic injury caused by cardiac microvascular damage or thromboses due to hypercoagulability
   - Epicardial CAD with plaque rupture or demand ischemia
   - SIRS systemic inflammatory response syndrome called cytokine storm.

   Myocardial injury patients are an older population and have more comorbidities and greater lab abnormalities including higher CRP level, pro-calcitonin and aspartate aminotransferase, more lung radiographic abnormalities and more complications.
   This is associated with severe disease and worse prognosis with a mortality rate of 51%.

COVID and CAD

With Covid 19 infection the majority of MI's are Type II (consequent to a mismatch between oxygen supply and demand) and related to primary infection, hemodynamic and respiratory derangement. Therefore the primary disorder should be treated and most cases the patient can be treated conservatively.
If Type I myocardial infarction (possible acute atherothrombotic CAD and usually precipitated by atherosclerotic plaque disruption) is thought to be the primary etiology then standard therapies including PCI can be considered.

STEMI

Patients have CP and ECG changes of ST elevation. However ECG criteria are not specific for coronary artery thrombosis as ST elevations may also occur with stress cardiomyopathy or possibly myocarditis and therefore this has to be ruled out prior to reperfusion therapy.
In critically ill patients PCI should be considered. If Myocarditis seems more likely than STEMI a conservative approach with aspirin and heparin is used under the diagnosis becomes clear.
Not critically ill patients, either PCI or consider Fibrinolytic therapy in lower risk patients. Factors such as significant associated comorbidities including pneumonia with respiratory failure and hospital resource limitations should be taken into account when deciding between primary PCI and fibrinolytic therapy.

NSTEMI

Require urgent management but generally do not require cardiac catheterization emergently. Therefore urgent catheterization is reserved for patients with ongoing evidence of myocardial ischemia related to repetitive episodes of angina, dynamic EKG changes, ventricular arrhythmias or heart failure.

CARDIOMYOPATHY.

SARS-CoV2 can cause cardiomyopathy in severe Covid 19 patient's by at least three distinct mechanisms. Firstly the latter phase of Covid 19 disease is associated with profound systemic inflammatory response. The cytokine storm has the potential to trigger cardiomyocyte dysfunction and cardiac depression. Secondly the virus can directly infect the heart leading to

immune cell recruitment and myocarditis. Thirdly the infection could impact the microvasculature which could trigger microvascular dysfunction and tissue ischemia. Cardiomyopathy is defined as decreased global left ventricular ejection fraction on echo Doppler exam in association with either elevated cardiac biomarkers, decreased SVO2 or clinical signs of shock.

Stress cardiomyopathy in based on identification of 4 features: transient left ventricular systolic dysfunction, absence of angiographic evidence of obstructive coronary artery disease or plaque rupture, presence of new ECG abnormalities (either ST segment elevations and/or T-wave inversions) or modest elevation in cardiac troponin.

MYOCARDITIS:

Myocarditis results in focal or global myocardial inflammation, necrosis and eventually ventricular dysfunction.

Focal myocarditis is often suspected and patient presenting with chest pain after an influenza-like syndrome with clinical evidence suggesting acute coronary syndrome on EKG or lab testing or with evidence of wall motion abnormalities and without evidence of obstructive coronary artery disease by coronary angiogram.

Pathogenesis may be related to dissemination of the virus through the blood or lymphatic system and/or exaggerated inflammatory response may be triggered. Cardiac MRI shows diffuse edema and slow gadolinium washout.

Myocarditis may be acute and fulminant myocarditis and is associated with adverse outcomes. Myocarditis can lead to QT prolongation and make a patient more susceptible to ventricular arrhythmias. Frequent EKG monitoring is needed which may pose a risk to a healthcare workers and therefore suggest telemetry monitoring. 7% of the deaths is due to myocarditis.

There is no established therapy for clinically suspected myocarditis, routine evaluation for myocarditis is not recommended with cardiovascular magnetic resonance imaging (CMR) or myocardial biopsy. Management involves supportive care including management of heart failure, and therapy for arrhythmias and avoidance of cardiac toxins.

PERICARDITIS has also been reported with COVID- 19 infection. Patient with ST elevations and marked hemodynamic instability and normal coronaries, think Peri-Myocarditis. No anticoagulation is needed.

2. **HEART FAILURE** was identified as a complication in 49% of patients who died and 3% of patients who recovered. It is identified by elevations in BNP and NT proBNP levels. Patient with known history of heart failure also suffered an acute decompensation due to COVID-19 disease.

3. **CARDIAC ARRHYTHMIAS AND CARDIAC ARREST.** Prevalence is 16.7%. Most common cardiac arrhythmia sinus tachycardia with atrial fibrillation, atrial flutter or ventricular tachycardia may also. Increased prevalence is due to hypoxemia and neurohormonal or inflammatory stress

4. **Venous thromboembolic disease.**

Presents with increased d-dimer, DIC in critically ill patients with prolonged immobilization and vascular inflammation preferred treatment is low molecular weight heparin or heparin due to interaction of the new oral anticoagulant agents with the antiviral agents.

Direct data on the thromboembolic risk with Covid 19 is limited. Elevating the risk of DVT in this population is the presence of critical illness, comorbidities and advanced age.

MANAGEMENT

The optimal management myocardial injury associated with COVID-19 has not been determined. Mainstay of management involves supportive care including management of heart failure, therapy for arrhythmias and avoidance of cardiac toxins. Some general principles include:

1. Avoid aggressive fluid resuscitation given challenges with oxygenation. Target CVP 6-8 millimeters of mercury.

   Higher preload (CVPs 12-15) may be desirable with significant RV dysfunction and/or high PEEP states are present.
2. Target a mean arterial pressure MAP of 60-65 mm HG and preferably start with norepinephrine infusion for hypotension.
3. Consider dobutamine in the setting of worsening hypotension with cardiac dysfunction.
4. Epinephrine and vasopressin should be considered for refractory hypotension
5. Ace inhibitors and ARBs, standard indications of these drugs for management of heart failure with reduced ejection fraction still applied to patient's with COVID-19. Although there has been some speculation that elevated ACE2 levels caused by Renin-angiotensin-aldosterone system inhibitors may impact susceptibility to SARS-CoV-2 because ACE2 is a receptor for this virus, however there is no evidence that treatment with these drugs worsens the clinical course of SARS-CoV-2 infection.

MECHANICAL SUPPORT/ECMO (EXTRA CORPOREAL MEMBRANE OXYGENATION)
ECMO is a limited resource and should be reserved for those with the greatest chance of recovery. It is currently being considered for patients with refractory hypoxemia and respiratory acidosis despite advanced ventilator management or in patients with significant cardiomyopathy and cardiogenic shock.

DRUG THERAPY

1. ANTIVIRAL agents---RIBAVIRIN, REMDESIVIR

   LOPINAVIR AND RITONAVIR--and specifically cause increased QT prolongation and PR interval prolongation especially in patients with baseline abnormalities who have long QT syndrome and conduction abnormalities or taking other QT prolonging drugs.
   We need to also Avoid new oral anticoagulants agents like Xarelto or eliquis due to interaction. These agents also increased the levels of P2Y12 inhibitors. By increasing the levels of ticagrelor and with decreasing the levels of clopidogrel and prasugrel. Prasugrel inhibition may be less and therefore may be the drug of choice.
   STATINS myopathy with lovastatin and simvastatin therefore try to use atorvastatin or rosuvastatin with the lowest possible dose.

2. HYDROXYCHLOROQUININE, has being increasingly prescribed

   Side effects:
   Myocardial toxicity, maybe restrictive or dilated cardiomyopathy related with increased exposure, higher weight-based dose, pre-existing cardiac disease or and renal insufficiency.
   Altered cardiac conduction including AV block, bundle branch block, torsade, V. tach/V. fib
   Torsade increased risk with patient's with electrolyte abnormalities and other QT prolonging agents.
   Increased concentration of beta blockers especially metoprolol, carvedilol, labetalol therefore carefully monitor heart rate and blood pressures

Hydroxychloroquine and azithromycin have been used for potential prophylaxis with treatment with COVID 19 and both drugs are listed as definite causes of torsade due to increase in QT interval prolongation and thereby increase in the risk of other arrhythmias and sudden death by the AHA, ACC and heart rhythm Society.
They recommended holding the medications with baseline QT prolongation more than 500 ms, known congenital long QT syndrome, correcting hyperkalemia to levels >4 and hypomagnesemia levels > 2 and avoiding other QTC prolonging agents.
(Ideally before medication administration QT interval has to be monitored and be less than 470 ms in narrow QRS or less than 500 ms in QRS more than 120 ms). Monitor the QT for 3-5 hours after the first dose of hydroxychloroquine and then every 12 hours for the first 3 days. Monitor for increase in PVCs or episodes of nonsustained ventricular tachycardia.
Use Risk score for prediction of drug associated QT prolongation in hospitalized patients.

3. ANTI-INFLAMMATORY THERAPIES -- METHYLPREDNISONE, IVIG, INTERLEUKIN-6 INHIBITORS

4. CARDIAC INTERVENTIONS

   Coronary angiogram--many cardiac catheterization laboratories are positive pressure but infection control requiring is negative pressure room's for Covid 19 patient's.

   STEMI-to reduce the risk of spreading infection, some centers are considering fibrinolytic therapy for hemodynamically stable STEMI patients and with no suspected COVID-19.

   For NSTEMI patient's intensifying medical treatment and with treating culprit lesion prior to appropriate discharge. PCI certainly preferable to CABG.

   CHF patient's recommended early discharge with IV diuretics monitoring with devices and pacemakers.