COVID-19: CARDIAC MANIFESTATIONS IN ADULTS

Kaveh Oraii Yazdani. Interventional cardiologist. Zaums.

INTRODUCTION

- Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
- Patients with COVID-19 typically present with symptoms and signs of respiratory tract infection.
- Cardiac manifestations, including signs of myocardial injury, are common.

ETIOLOGY

- Myocarditis.
- Hypoxic injury.
- Stress (takotsubo) cardiomyopathy.
- Ischemic injury caused by cardiac microvascular dysfunction, small vessel cardiac vasculitis, endotheliitis, or epicardial coronary artery disease (with plaque rupture or demand ischemia).
- Right heart strain (acute cor pulmonale, with causes including pulmonary embolism, adult respiratory distress syndrome, and pneumonia).
- Systemic inflammatory response syndrome (cytokine storm).

SPECTRUM OF CLINICAL PRESENTATIONS

- Some patients manifest no clinical evidence of heart disease.
- Some have no symptoms of heart disease but have cardiac test abnormalities (such as serum cardiac troponin elevation, asymptomatic cardiac arrhythmias, or abnormalities on cardiac imaging).
- Some have symptomatic heart disease.
- Cardiac complications include myocardial injury, heart failure (HF), cardiogenic shock, and cardiac arrhythmias including sudden cardiac arrest.

STRESS CARDIOMYOPATHY

- In a review of 12 cases of stress cardiomyopathy associated with COVID-19:
  - The mean age was 70.8
  - The majority of patients were female
  - An elevated troponin level was identified in 11 of the cases
  - Complications included HF, cardiogenic shock, cardiac tamponade, and hypertensive crisis.
- A study identified increased incidence of stress cardiomyopathy in patients without COVID-19 during the COVID-19 pandemic compared with prepandemic periods.

STRESS CARDIOMYOPATHY

- A diagnosis of stress cardiomyopathy is based on presence of **all** of the following four features:
  - Transient left ventricular (LV) systolic dysfunction (typically not in a single coronary distribution).
  - Absence of angiographic evidence of obstructive coronary disease or acute plaque rupture.
  - New ECG abnormalities (ST-segment elevation and/or T-wave inversion) **or** modest elevation in cardiac troponin.
  - Absence of pheochromocytoma or myocarditis.
- Those who survive the acute episode typically recover ventricular function within one to four weeks.

HEART FAILURE

- A study of 6439 patients hospitalized with COVID-19 at a hospital in New York:
  - A history of HF was associated with adverse outcomes
    - longer length of stay (eight versus six days)
    - Increased risk of mechanical ventilation (22.8 versus 11.9 percent; adjusted odds ratio [OR] 3.64, 95% CI 2.56-5.16)
    - Mortality (40.0 versus 24.9 percent; adjusted OR 1.88, 95% CI 1.27-2.78)
  - Outcomes among patients with different types of HF were similar, regardless of LV ejection fraction (LVEF).

HEART FAILURE

- Right heart failure:
  - Acute cor pulmonale (right HF due to acute pulmonary hypertension) precipitated by acute pulmonary embolism or adult respiratory distress syndrome (ARDS) has been described in patients with COVID-19.
  - Venous thromboembolism (including extensive deep vein thrombosis and pulmonary embolism) is common in acutely ill patients with COVID-19.

CARDIAC TEST FINDINGS (TROPONIN)

- In a study from New York of 2736 hospitalized patients (mean age 66.4 years), 36 percent of patients had elevated hs-cTnI levels. Troponin elevation was more prevalent among patients with known cardiovascular disease or cardiovascular risk factors. The mortality rate during hospitalization was 18.5 percent.
- The frequency of troponin elevation appears to be lower among patients with mildly symptomatic COVID-19.
- Studies have identified greater frequency and magnitude of troponin elevations in hospitalized patients with more severe disease and worse outcomes

CARDIAC TEST FINDINGS (NATRIURETIC PEPTIDES)

- Natriuretic peptide elevation is associated with mortality risk.
- Natriuretic peptide elevation is commonly associated with cardiac troponin elevation.
- NT-proBNP levels were significantly higher in patients with elevated troponin levels than in patients without troponin elevation.

ROUTINE EVALUATION

- **Troponin:**
  - Is commonly performed in hospitalized patients with COVID-19.
  - Some experts also perform troponin testing in selected outpatients with uncertain level of risk.
- **ECG**
  - A baseline ECG is generally performed in patients presenting for acute care with suspected symptomatic COVID-19.
  - QTc will need to be monitored if QT-prolonging therapies are initiated (azithromycin, chloroquine) to reduce the risk of acquired long QT syndrome.

TARGETED CARDIAC EVALUATION

- **Indications:**
  - New-onset HF (including left HF and acute cor pulmonale)
  - Unexplained cardiac arrhythmias
  - ECG changes (particularly ST elevation)
- If the clinical presentation is suggestive of acute coronary syndrome based upon the presence of chest pain, new HF, sudden cardiac arrest, and/or new ischemic ECG changes, timely evaluation is required to determine if urgent coronary angiography and intervention are indicated.
- Most patients with mild troponin elevation without symptoms and signs of acute HF can be clinically monitored without cardiac imaging.

MANAGEMENT

- The management of patients with myocardial injury, including clinically suspected myocarditis, involves supportive care (including management of HF, therapy for arrhythmias, and avoidance of cardiotoxins).
- Patients with COVID-19 and HF or asymptomatic LV systolic dysfunction should receive standard therapy for these conditions including pharmacologic therapy, careful management of fluid balance.
  - There is no evidence that treatment ACEI/ARB worsens the clinical course of SARS-CoV-2 infection.

MYOCARDIAL INFARCTION AND OTHER CORONARY ARTERY ISSUES

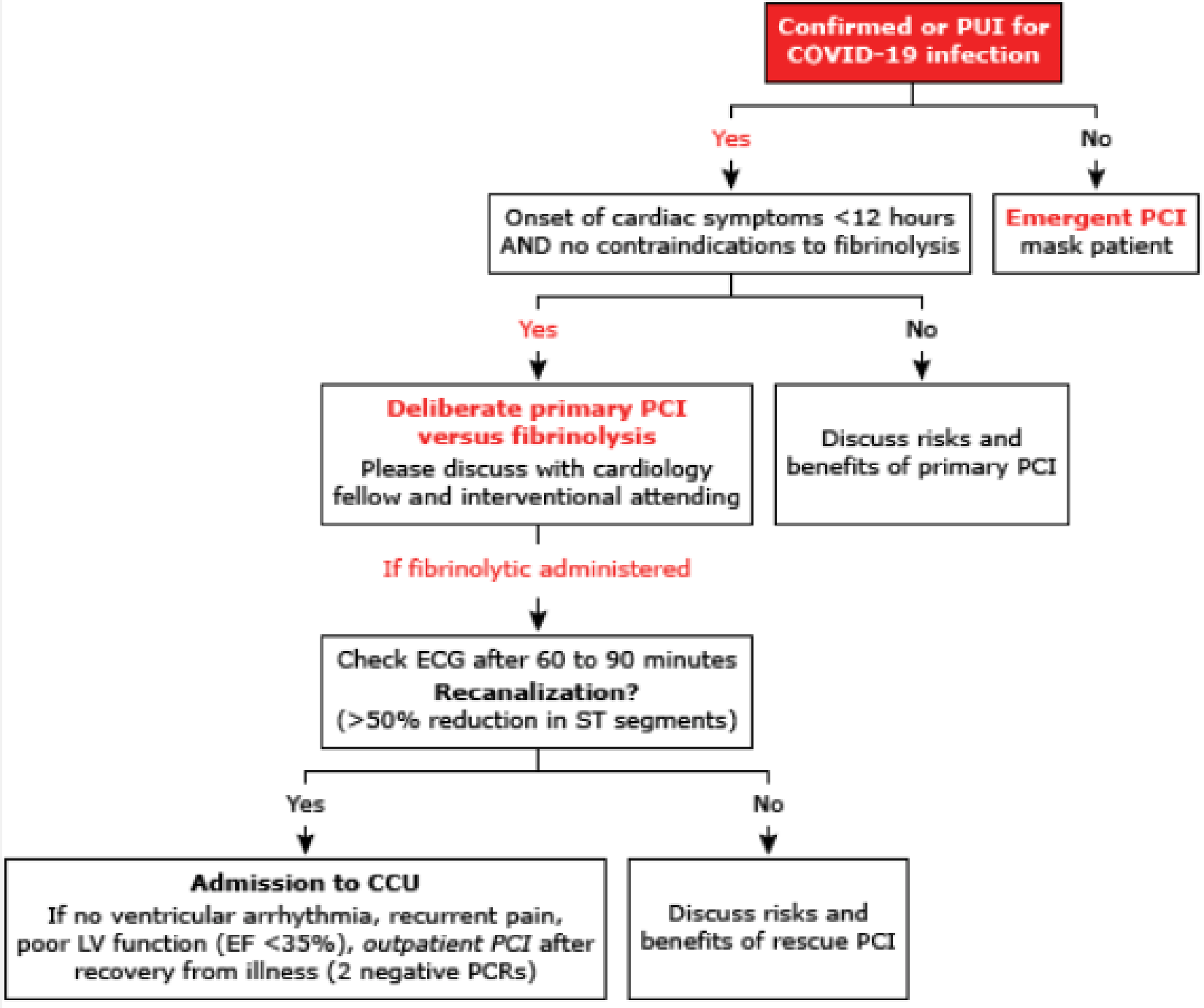
- Pneumonia and influenza infections have been associated with sixfold increased risk of acute MI.
- There is some evidence that COVID-19 increases the risk of acute MI.
- There is substantial evidence of an association between cardiovascular disease risk factors of hypertension, diabetes, prior CAD, and the risk and severity of COVID-19 infection.

ACUTE CORONARY SYNDROME PATIENTS

- The Fourth Universal Definition of MI includes a clinical classification according to the assumed proximate cause of the myocardial ischemia:
  - **Type 1:** MI caused by acute atherothrombotic CAD and usually precipitated by atherosclerotic plaque disruption (rupture or erosion).
  - **Type 2:** MI consequent to a mismatch between oxygen supply and demand.
- With COVID-19 infection, the majority of MIs are type 2 and related to the primary infection, hemodynamic, and respiratory derangement.
- **Assessment of COVID-19 status:**
  - Testing for COVID-19 is recommended for NSTEMI patients who are stable prior to transfer for catheterization.

ACUTE CORONARY SYNDROME PATIENTS (STEMI)

- There have been reports of increased coronary artery thrombus burden in patients with STEMI.
  - This is consistent with an increased frequency of thrombotic strokes, particularly in young people, during the pandemic.
- **Approach to ST-elevation myocardial infarction:**
  - In patients who are **critically ill**, the decision to reperfuse (with either primary PCI or fibrinolysis) or not should be managed on a case-by-case basis.
  - If the patient is **not critically ill**, primary PCI rather than fibrinolysis in most cases, similar to patients without COVID-19.
  - Some centers have chosen to administer fibrinolytic therapy in eligible patients.


Confirmed or PUI for COVID-19 infection
Yes
No
Onset of cardiac symptoms <12 hours AND no contraindications to fibrinolysis
Emergent PCI mask patient
Yes
No
Deliberate primary PCI versus fibrinolysis
Please discuss with cardiology fellow and interventional attending
Discuss risks and benefits of primary PCI
If fibrinolytic administered
Check ECG after 60 to 90 minutes
Recanalization?
(>50% reduction in ST segments)
Yes
No
Admission to CCU
If no ventricular arrhythmia, recurrent pain, poor LV function (EF <35%), outpatient PCI after recovery from illness (2 negative PCRs)
Discuss risks and benefits of rescue PCI

ACUTE CORONARY SYNDROME PATIENTS (STEMI)

- **Diagnosis and differential diagnosis:**
  - Alternative causes of myocardial injury (such as stress cardiomyopathy or myocarditis) are important to consider.
  - STEMI usually requires that the patient have chest pain or anginal equivalent symptomatology and ECG characteristics that include ST-segment elevation in at least two contiguous leads:
    - New ST-segment elevation at the J-point in two contiguous leads with the cut-points: ≥0.1 mV in all leads other than leads V2 to V3.
    - For leads V2 to V3: ≥2 mm in men ≥40 years of age, ≥2.5 mm in men <40 years of age, or ≥1.5 mm in women regardless of age.
    - In the absence of ST elevation on ECG, new left bundle branch block with anginal symptoms is considered to be a STEMI equivalent.

ACUTE CORONARY SYNDROME PATIENTS (STEMI)

- **Management:**
  - If myocarditis seems more likely than STEMI, a conservative approach with aspirin and heparin administration until the diagnosis becomes clearer.
  - There are two important early management questions:
    - Does the patient have a life-threatening illness, such as respiratory failure from COVID-19, that makes them a less-than-ideal candidate for reperfusion?
    - During the pandemic, should fibrinolytic therapy be used more liberally as the choice for early reperfusion?
  - Irrespective of the initial reperfusion strategy, treat all STEMI patients with early aspirin, $P2Y_{12}$ inhibitor, and anticoagulation. High-dose statin is started as soon as possible after the diagnosis.

ACUTE CORONARY SYNDROME PATIENTS (NON-ST-ELEVATION MYOCARDIAL INFARCTION)

- NSTEMI patients require urgent management but generally do not require a catheterization laboratory emergently.
- Any decision to proceed with an invasive strategy should take into account current health care resources.
- Perform urgent catheterization on NSTEMI patients for reasons such as ongoing evidence of myocardial ischemia (eg, repetitive episodes of angina or dynamic ECG changes, ventricular arrhythmias, or heart failure).

ACUTE CORONARY SYNDROME PATIENTS

- **Echocardiography:**
  - Among patients with COVID-19 with suspected ACS, the role of echocardiography in altering the pretest probability of CAD is limited to low- or intermediate-risk patients.
  - Findings on an echocardiogram that favor a condition other than ACS (eg, stress cardiomyopathy, myocarditis, pericarditis, or noncardiac cause of chest pain) include:
    - No wall motion abnormalities during chest pain
    - Wall motion abnormalities not supportive of regional injury suggested by the ECG
    - Wall motion abnormalities in a noncoronary distribution
    - Less specific findings, such as small pericardial effusion

STABLE CORONARY ARTERY DISEASE PATIENTS

- Attempt to delay elective revascularization procedures in patients for whom the indication is relief of symptoms.
- For patients who must have revascularization for reasons such as extremely poor quality of life or prolongation of life, as with significant left main CAD, test the patient for COVID-19 infection.
- Decisions regarding the type of revascularization (CABG Vs PCI]) in these patients may be altered during the pandemic, favoring PCI as a method to shorten the duration of exposure of the patient to the hospital environment.

ARRHYTHMIAS AND CONDUCTION SYSTEM DISEASES

- In a study from Italy, there was a nearly 60 percent increase in the rate of out-of-hospital cardiac arrest during the peak of the 2020 COVID-19 pandemic (when compared with the same time frame from 2019).
- In a study from France, there was a 52 percent increase in the cumulative incidence of out-of-hospital cardiac arrest during a two-month period between February and April 2020 compared with 2019.
- This observation could be related to COVID-19 infections, stress related to the pandemic, or delays in seeking medical attention by those with cardiac symptoms.

ARRHYTHMIAS AND CONDUCTION SYSTEM DISEASES

- **Potential risk factors:**
  - Patients who present with other cardiovascular complications in the setting of COVID-19 infection, such as myocardial injury or myocardial ischemia.
  - Patients with hypoxia, shock (septic or cardiogenic), or evidence of widespread systemic inflammation.
  - Patients with electrolyte disturbances (eg, hypokalemia).
  - Patients who are receiving therapies that prolong the QT interval, which may increase the risk of polymorphic VT.
  - Patients taking remdesivir, as cases of sinus bradycardia attributable to remdesivir have been reported. Several large randomized trials of remdesivir did not report bradycardia as an adverse event.
  - Patients with fever, which can unmask cases of cardiac channelopathies such as Brugada syndrome and long QT syndrome.

PATIENTS RECEIVING THERAPIES THAT PROLONG THE QT INTERVAL

- The patient's baseline QTc value should be obtained prior to administering any drugs with the potential to prolong the QT interval.
- A systematic review of 14 studies showed that about 10 percent of patients developed a QTc interval ≥500 ms or change of >60 ms while taking hydroxychloroquine or chloroquine.
- Patients with baseline QTc interval ≥500 milliseconds (with a QRS ≤120 milliseconds) are at increased risk for significant QT prolongation and polymorphic VT.
  - In such patients, efforts should be made to correct any contributing electrolyte abnormalities (eg, hypocalcemia, hypokalemia, and/or hypomagnesemia), with a goal potassium of close to 5 mEq/L.

PATIENTS RECEIVING THERAPIES THAT PROLONG THE QT INTERVAL

- In general, patients with the following QTc intervals are at low risk for significant QT prolongation and polymorphic VT:
  - QTc <460 milliseconds in prepubertal males/females
  - QTc <470 milliseconds in postpubertal males
  - QTc <480 milliseconds in postpubertal females

PATIENTS RECEIVING THERAPIES THAT PROLONG THE QT INTERVAL

- An ongoing dynamic assessment of the QT interval and benefits and risks of treatment is mandatory:
  - An ECG at baseline and again at four hours after administration of QT-prolonging medication if:
    - There is congenital or acquired long QT syndrome
    - Patients are already taking other QT-prolonging medications
    - Patients have structural heart disease or bradycardia
  - Another ECG can be completed one to three days later.
  - For most others, an ECG or other QTc interval-monitoring method can be done 24 hours after starting the medication.
  - If the QTc increases to ≥500 milliseconds, if the change in QT interval is ≥60 milliseconds, or if ventricular ectopy develops, this protocol recommends cardiology consultation.

HYPERCOAGULABILITY (PATHOGENESIS)

- Hypercoagulability can be thought of in terms of Virchow's triad.
- All three of the major contributions to clot formation apply to severe COVID-19 infection:
  - Endothelial injury
  - Stasis
  - Hypercoagulable state
- Very elevated levels of D-dimer have been observed that correlate with illness severity.
- Antiphospholipid antibodies, which can prolong the activated partial thromboplastin time (aPTT), are common in viral infections.
  - They are often transient and do not always imply an increased risk of thrombosis.

HYPERCOAGULABILITY (COAGULATION ABNORMALITIES)

- Prothrombin time (PT) and aPTT normal or slightly prolonged
- Platelet counts normal or increased (mean, 348,000/microL)
- Fibrinogen increased (mean, 680 mg/dL; range 234 to 1344)
- D-dimer increased (mean, 4877 ng/mL; range, 1197 to 16,954)
- Factor VIII activity increased (mean, 297 units/dL)
- VWF antigen greatly increased (mean, 529; range 210 to 863), consistent with endothelial injury or perturbation
- Minor changes in natural anticoagulants
  - Small decreases in antithrombin and free protein S
  - Small increase in protein C

HYPERCOAGULABILITY (DISTINCTION FROM DIC)

- The major clinical finding in COVID-19 is thrombosis, whereas the major finding in acute decompensated DIC is bleeding.
- COVID-19 has some similar laboratory findings to DIC, including a marked increase in D-dimer and in some cases, mild thrombocytopenia.
- In COVID-19, the typical findings include high fibrinogen and high factor VIII activity, suggesting that major consumption of coagulation factors is not occurring.

HYPERCOAGULABILITY (EVALUATION)

- **Routine testing:**
  - Complete blood count (CBC) including platelet count
  - Coagulation studies (prothrombin time [PT] and activated partial thromboplastin time [aPTT])
  - Fibrinogen
  - D-dimer
- Repeat testing is reasonable on a daily basis or less frequently, depending on the acuity of the patient's illness, the initial result.
- For outpatients, routine coagulation testing is not required.

HYPERCOAGULABILITY (MANAGEMENT)

- Venous thromboembolism prophylaxis is appropriate in all hospitalized medical, surgical, and obstetric patients with COVID-19, unless there is a contraindication to anticoagulation (eg, active bleeding or serious bleeding in the prior 24 to 48 hours) or to the use of heparin.
- **Dosing:**
  - Enoxaparin:
    - For patients with creatinine clearance (CrCl) >30 mL/min, 40 mg once daily.
    - For CrCl 15 to 30 mL/min, 30 mg once daily.
    - For individuals with a weight >120 kg or body mass index (BMI) >35 kg/m^2, prophylactic dosing of enoxaparin 40 mg twice daily can be used.
  - For patients with CrCl <15 mL/min or renal replacement therapy, we use unfractionated heparin.

HYPERCOAGULABILITY (MANAGEMENT)

- **Outpatient thromboprophylaxis**
  - **Patients discharged from the hospital**
    - Do not use routine post-discharge thromboprophylaxis.
    - Individuals with documented VTE require a minimum of three months of anticoagulation.
    - Do not monitor laboratory tests such as D-dimer.
  - **Patients not admitted to the hospital**
    - Anticoagulation is generally not used in outpatients.
    - May be appropriate in selected individuals with COVID-19 who are not admitted to the hospital, especially those with other thrombotic risk factors such as prior VTE or recent surgery, trauma, or immobilization.
      - Rivaroxaban 10 mg daily for 31 to 39 days.

THANK YOU FOR YOUR ATTENTION