COVID-19 pandemia: dilemmas and challenges for cardiologist in the ER

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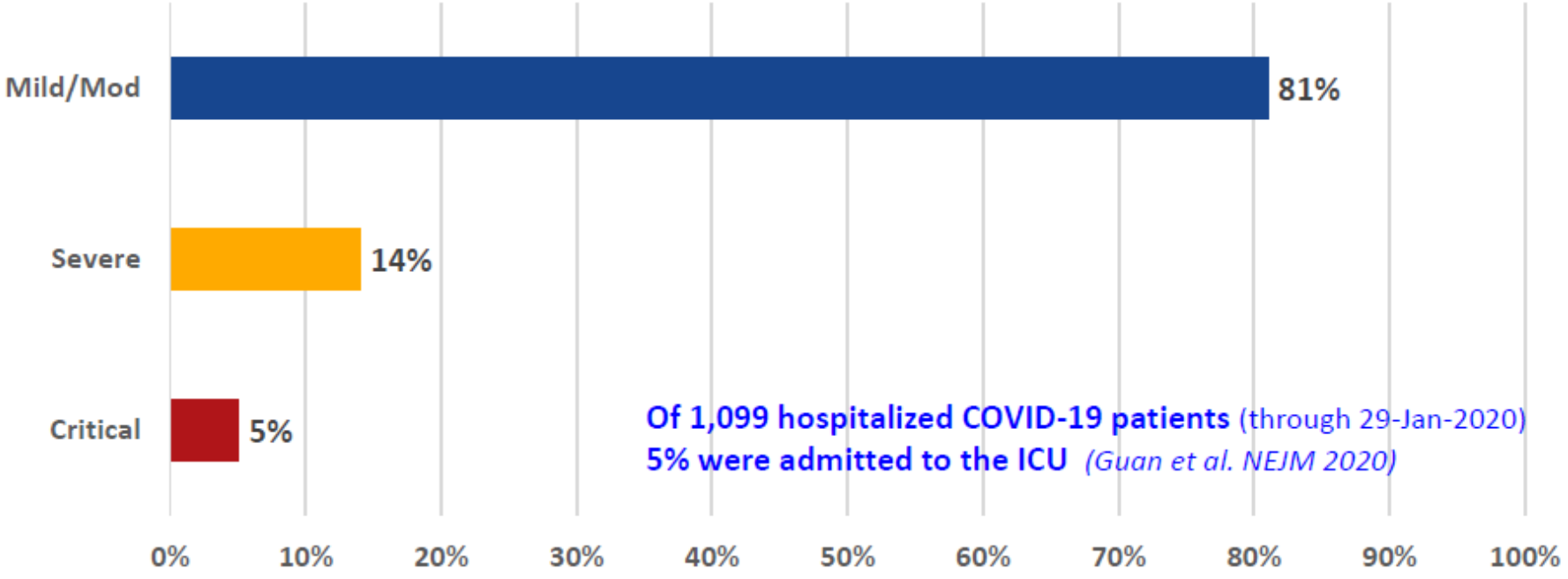
Most patients had mild to moderate disease, but nearly 20% had severe or critical illness

COVID-19 - China through 11-Feb-2020 (N=44,415)



Of 1,099 hospitalized COVID-19 patients (through 29-Jan-2020)
5% were admitted to the ICU *(Guan et al. NEJM 2020)*

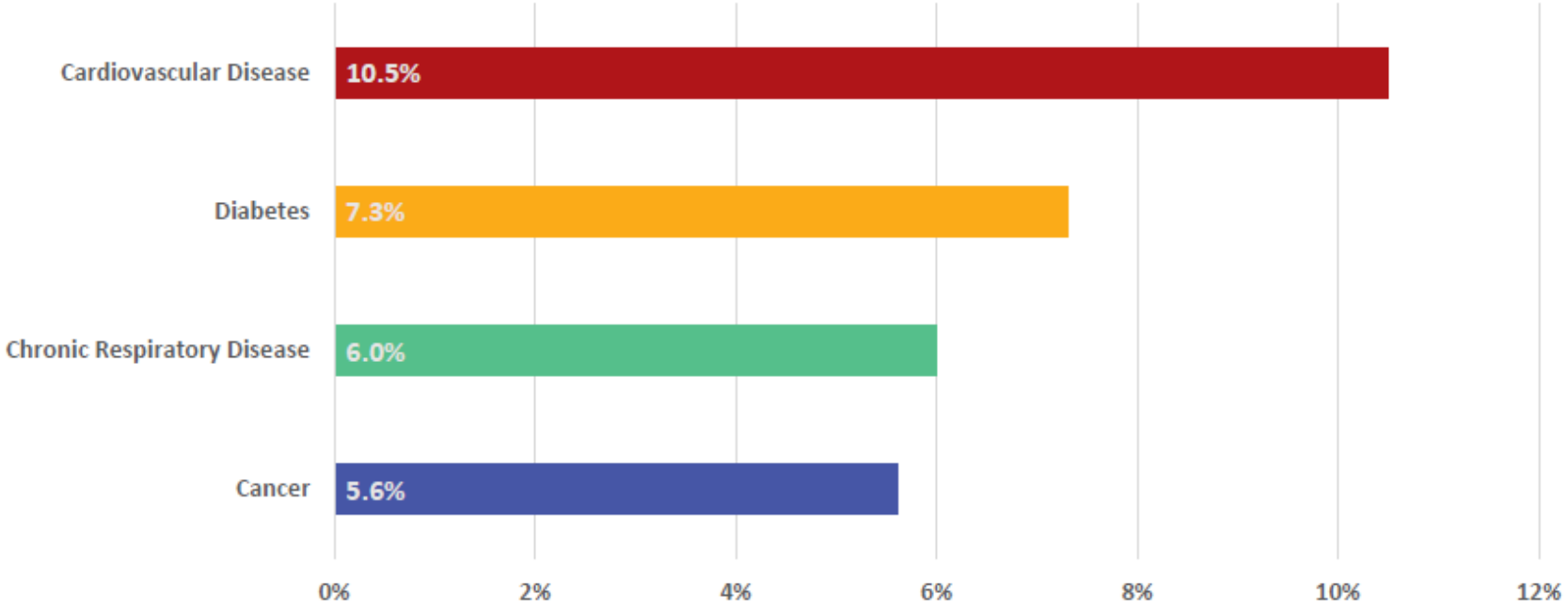
Links: *Wu JAMA 2020*

Early Cardiac Implications From Case Reports on COVID-19

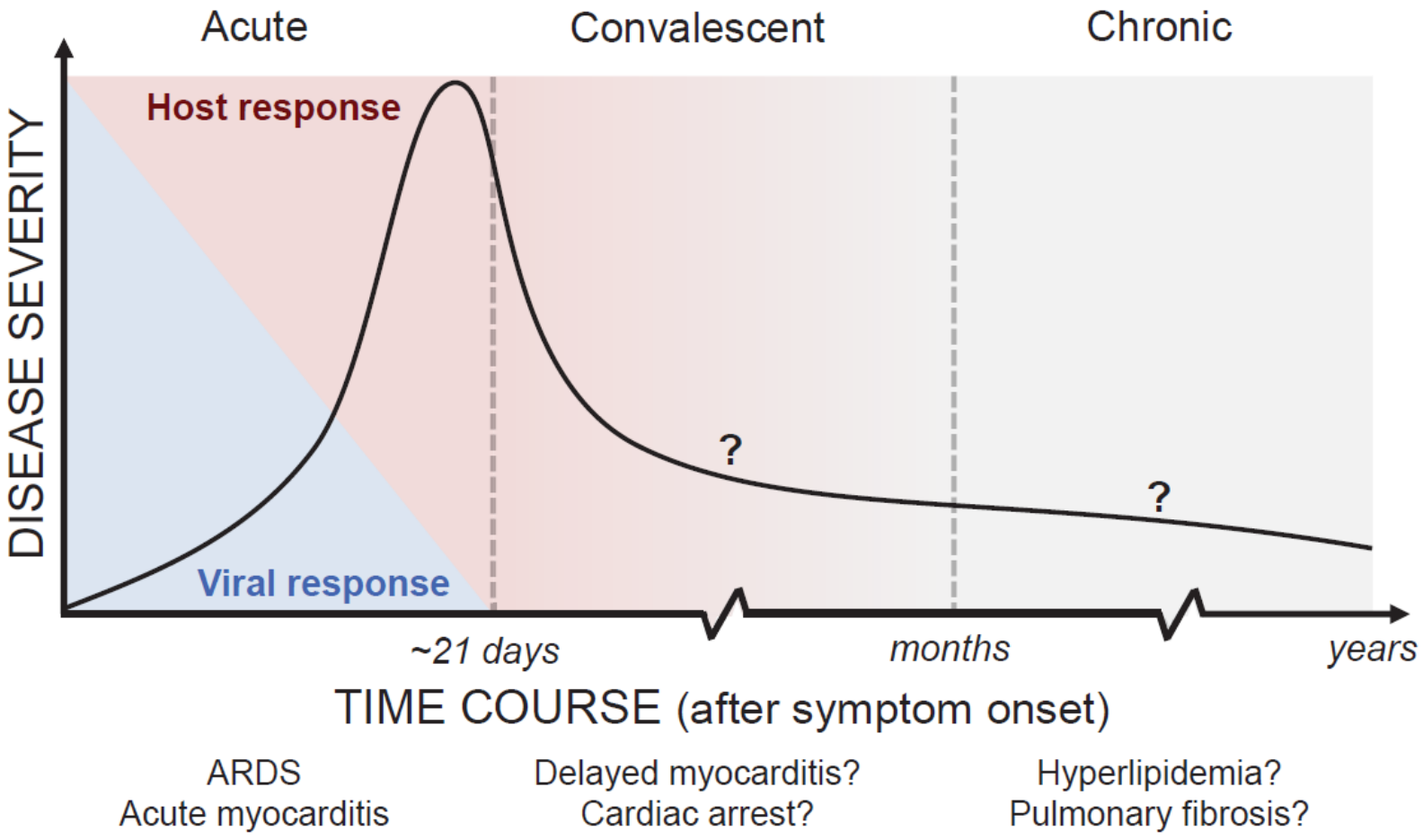
- In the most recent large-scale reporting from China CDC, 25% of patients with complete medical histories have comorbidities, the majority of which are cardiovascular- or diabetes-related; while lower than initial reports, 53% of all COVID-19 confirmed patients in the study were missing documentation of underlying conditions[xii]
- Overall the case mortality rate remains low at 2.3%; however, the mortality rate jumps to 6% in hypertensives, 7.3% in diabetics, 10.5% in patients with cardiovascular disease, and 14.8% for patients ≥ 80 years of age[xii]
- Notably, the case mortality rate for underlying cardiovascular disease (10.5%) is greater than in patients with underlying chronic respiratory disease (6.3%)

Mortality from COVID-19 is highest among persons with underlying medical conditions

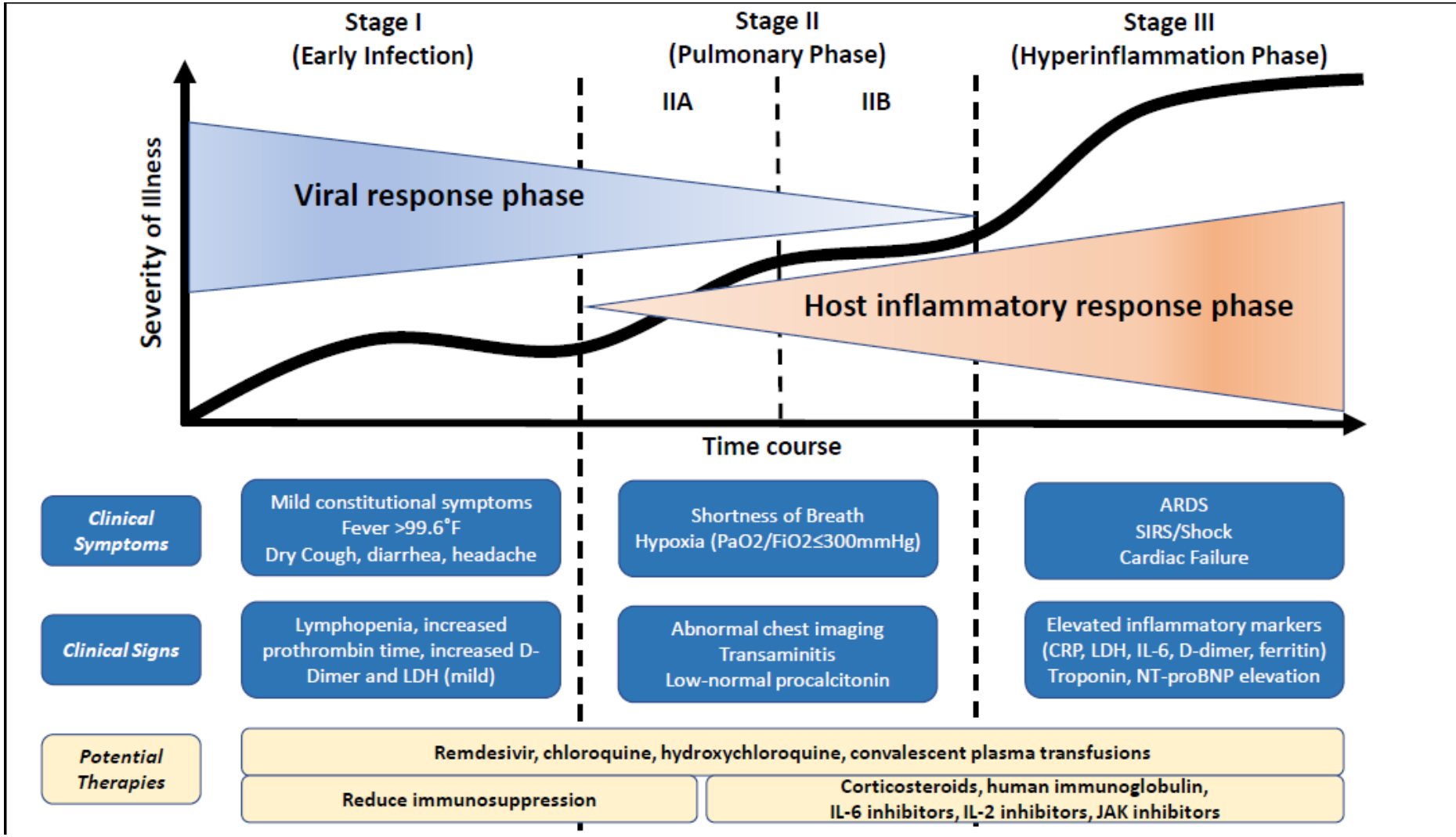
COVID-19 - China through 11-Feb-2020



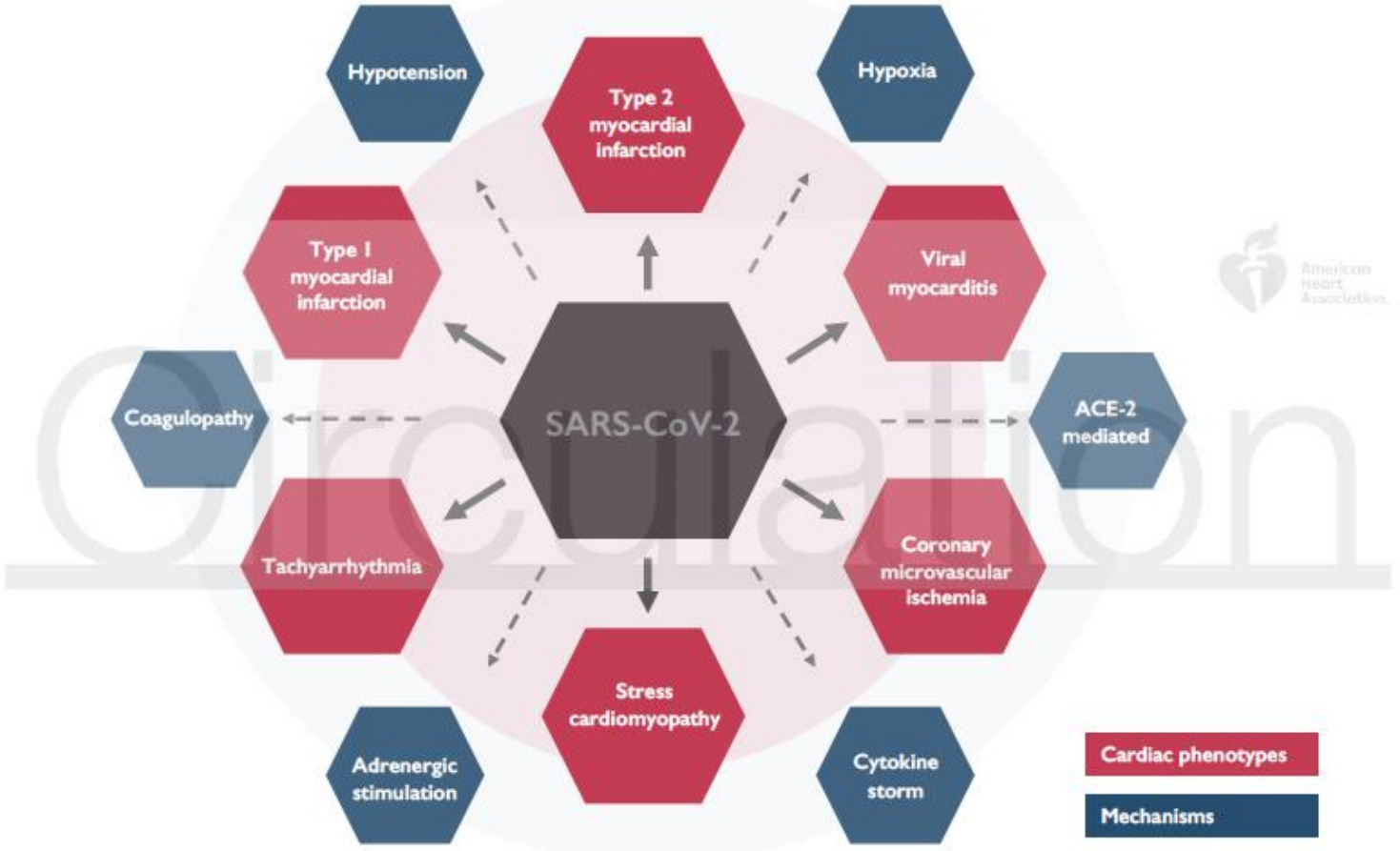
Link: China COVID-19 Epi Team 2020


Acute
Convalescent
Chronic
DISEASE SEVERITY
Host response
Viral response
?
?
~21 days
months
years
TIME COURSE (after symptom onset)
ARDS
Acute myocarditis
Delayed myocarditis?
Cardiac arrest?
Hyperlipidemia?
Pulmonary fibrosis?

COVID-19 Illness in Native and Immunosuppressed States:



Potential mechanisms of acute myocardial injury in COVID-19 and related cardiac phenotypes



10.1161/CIRCULATIONAHA.120.047008

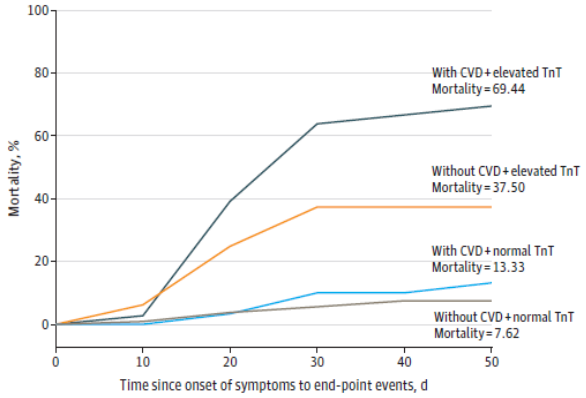
Cardiovascular complications in coronavirus disease

Manifestation	Incidence	Remarks
Acute cardiac injury* (most commonly defined as elevation of cardiac troponin I above 99th percentile upper reference limit)	8–12% on average [10]	• Most commonly reported cardiovascular abnormality • Can result from any of the following mechanisms- •Direct myocardial injury •Systemic inflammation •Myocardial oxygen demand supply mismatch •Acute coronary event •Iatrogenic • Strong adverse prognostic value
Acute coronary event	Not reported, but appears to be low	Potential mechanisms- • Plaque rupture due to inflammation/increased shear stress • Aggravation of pre-existing coronary artery disease
Left ventricular systolic dysfunction	Not reported	Any of the causes of myocardial dysfunction mentioned above can lead to acute left ventricular systolic dysfunction
Heart failure	Reported in one study- 52% in those who died, 12% in those who recovered and were discharged [5]	• Any of the causes of myocardial dysfunction mentioned above can lead to acute heart failure • Increased metabolic demand of a systemic disease can cause acute decompensation of pre-existing stable heart failure
Arrhythmia	16.7% overall; 44.4 in severe illness, 8.9% in mild cases [8]	Both tachyarrhythmia and bradyarrhythmia can occur but exact nature not described
Potential long-term consequences	Too early to assess	Too early to ascertain for coronavirus disease 2019. However, patients recovering from a similar earlier illness- Severe Acute Respiratory Syndrome- continued to have long-term abnormalities of lipid and glucose metabolism and of cardiovascular homeostasis [12]

Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 247–250

Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19)

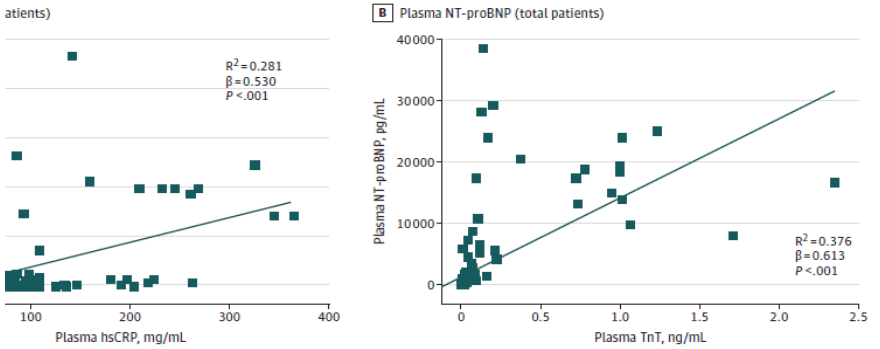
Figure 2. Mortality of Patients With Coronavirus Disease 2019 (COVID-19) With/Without Cardiovascular Disease (CVD) and With/Without Elevated Troponin T (TnT) Levels



No. at risk

Without CVD + normal TnT (n = 105)	102	86	41	10	0
Without CVD + elevated TnT (n = 16)	15	12	7	1	0
With CVD + normal TnT (n = 30)	29	25	10	4	0
With CVD + elevated TnT (n = 36)	34	20	8	2	0

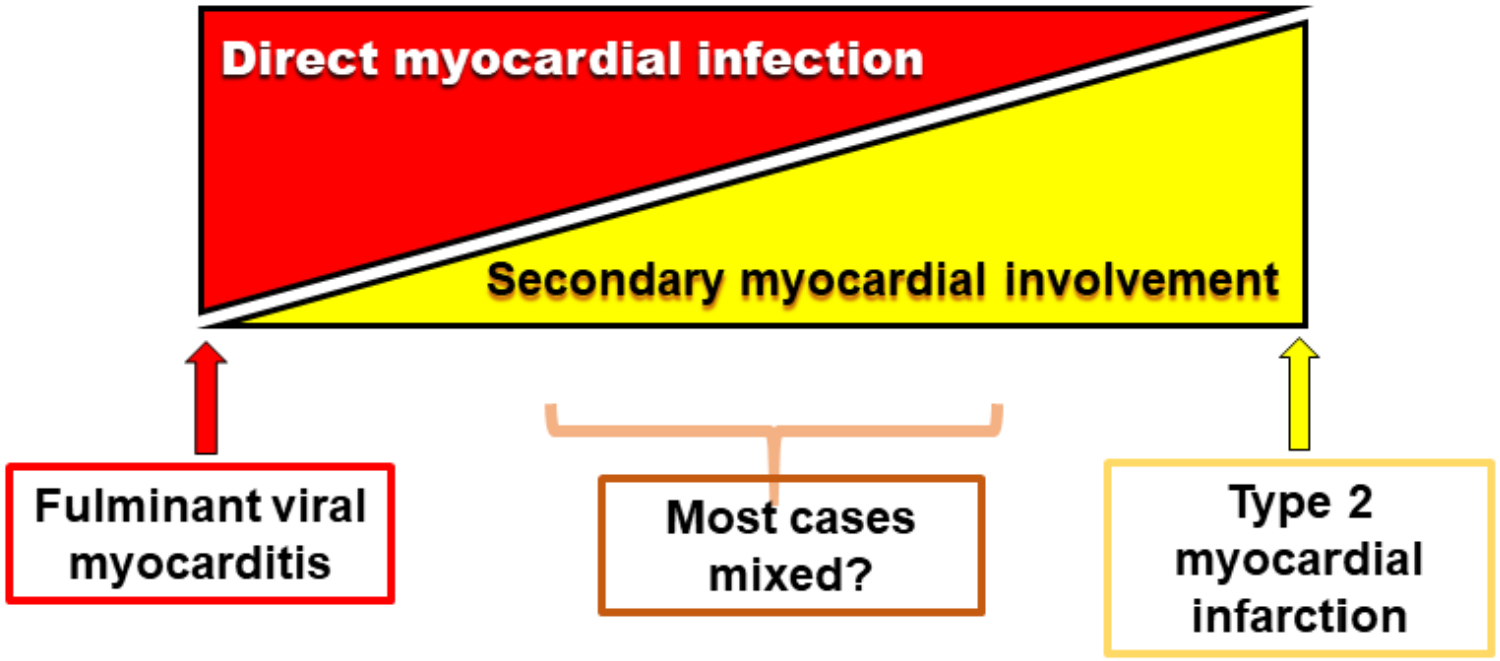
tween Plasma TnT and NT-proBNP With hsCRP



high-sensitivity C-reactive protein levels (hsCRP), and N-terminal pro–brain natriuretic peptide (NT-pro BNP) collected on admission.

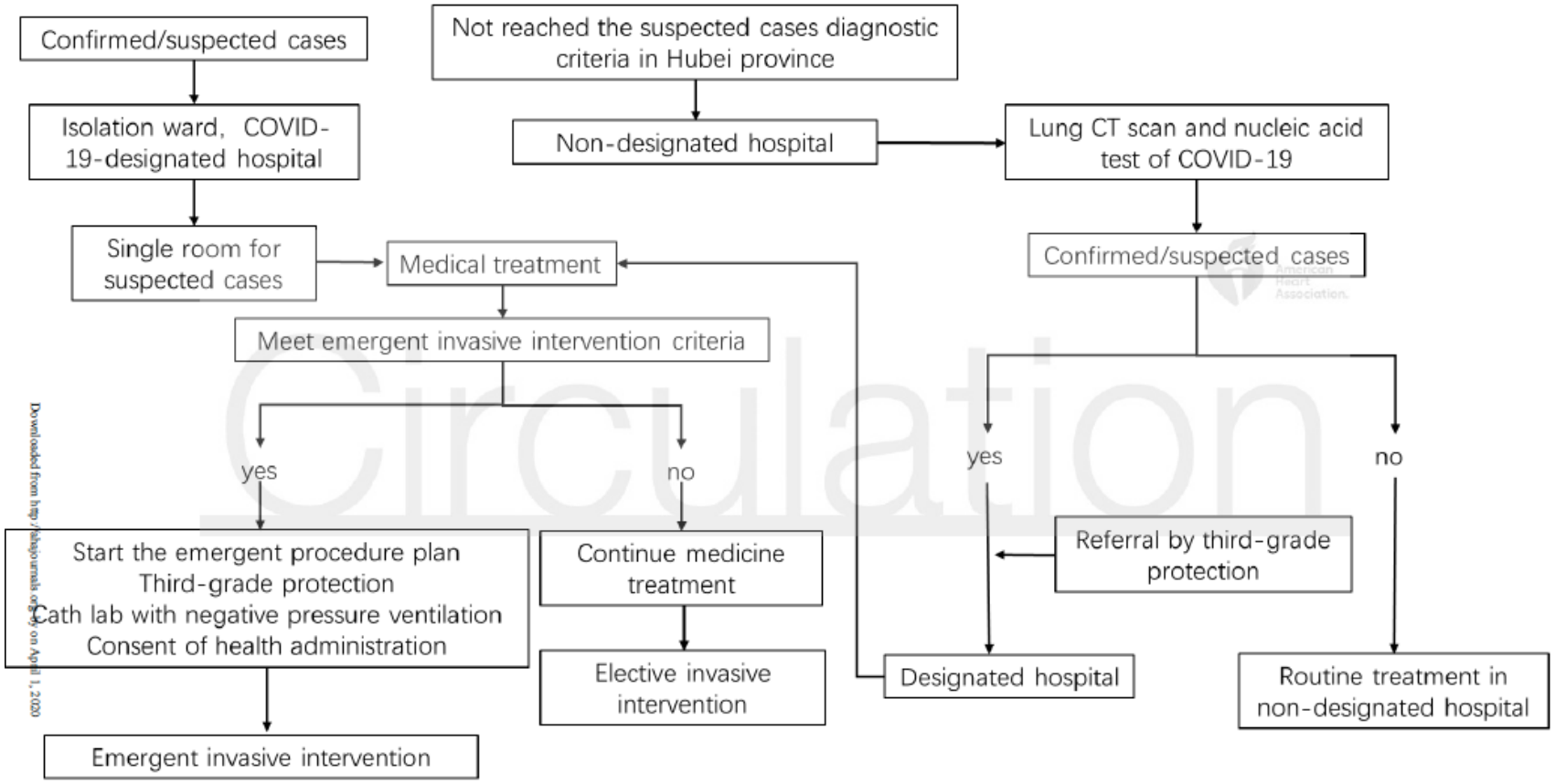
JAMA Cardiology Published online March 27, 2020

The Heart in COVID19: Primary Target or Secondary Bystander?



JACC: Basic to Translational Science 2020

CSC Expert Consensus on Principles of Clinical Management of Patients with Severe Emergent Cardiovascular Diseases during the COVID-19 Epidemic



10.1161/CIRCULATIONAHA.120.047011

CSC Expert Consensus on Principles of Clinical Management of Patients with Severe Emergent Cardiovascular Diseases during the COVID-19 Epidemic

Table 1. Patients with severe emergent cardiovascular diseases for whom hospitalization and conservative medical treatment is recommended during COVID-19 epidemic.

Patients with severe emergent cardiovascular diseases
1. Patients with STEMI for whom thrombolytic therapy is indicated*.
2. STEMI patients presenting after exceeding the optimal window of time for revascularization but yet with worsen symptoms, such as severe chest pain, continuous ST-segment elevation, or myocardial infarction-related mechanical complications.
3. High risk NSTE-ACS patients (GRACE score ≥ 140).
4. Patients with uncomplicated Stanford type B aortic dissection#.
5. Patients with acute pulmonary embolism.
6. Patients with acute exacerbation of heart failure.
7. Patients with hypertensive emergency.

STEMI, ST-segment elevation myocardial infarction; NSTE-ACS, non-ST elevation acute coronary syndromes; GRACE, Global Registry of Acute Coronary Events.

*The third- generation thrombolytic agents are preferred.

#For Stanford type A aortic dissection, surgical treatment is recommended.

10.1161/CIRCULATIONAHA.120.047011

CSC Expert Consensus on Principles of Clinical Management of Patients with Severe Emergent Cardiovascular Diseases during the COVID-19 Epidemic

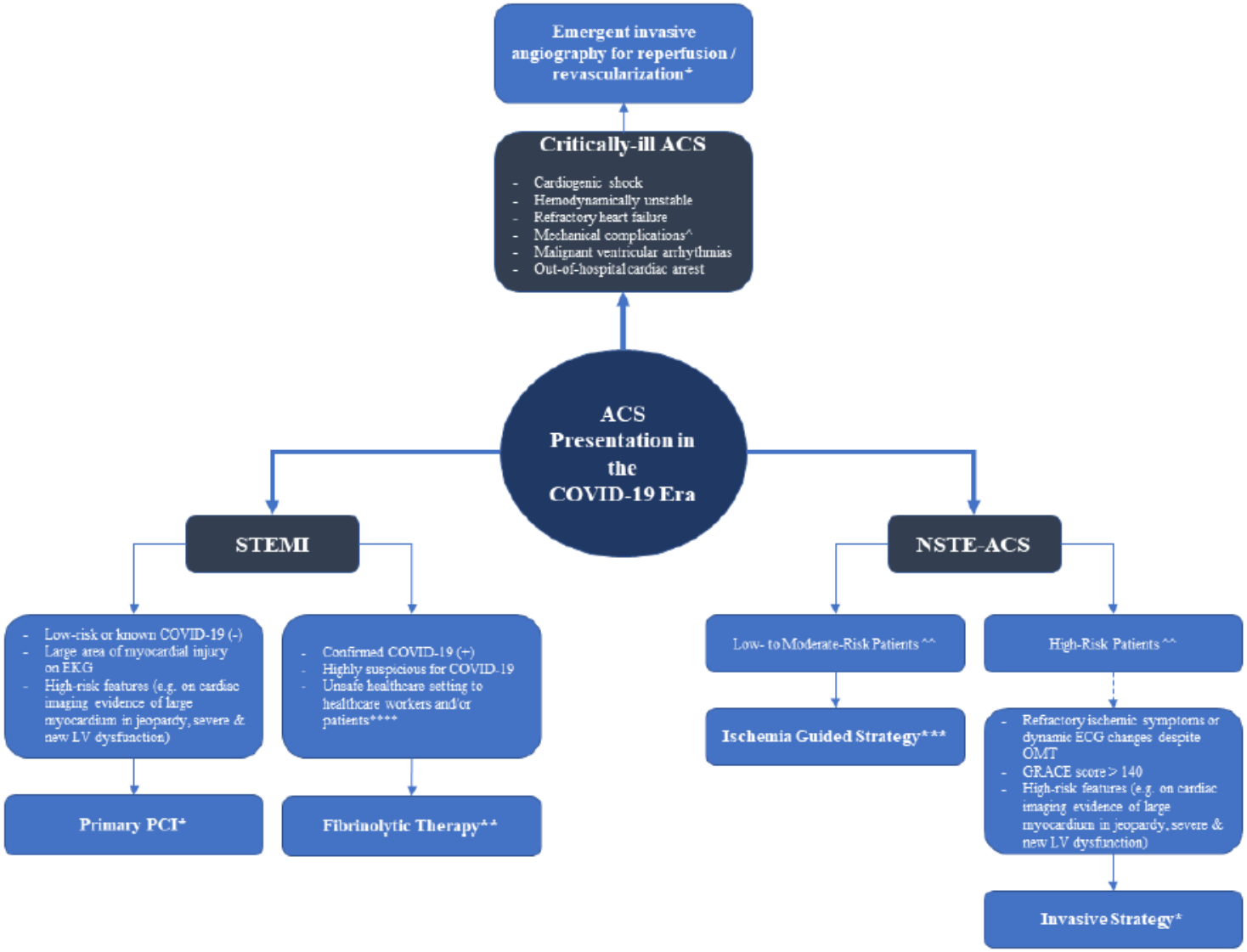
Table 2. Severe cardiovascular diseases requiring urgent or emergent intervention or surgery.

Patients with severe cardiovascular diseases
1. Acute STEMI with hemodynamic instability.
2. Life-threatening NSTEMI indicated for urgent revascularization.
3. Stanford type A or complex Type B acute aortic dissection.
4. Bradyarrhythmia complicated with syncope or unstable hemodynamics mandating implantation of a temporary (bedside implantation as far as possible), or, if indicated, permanent pacemaker.
5. Pulmonary embolism presenting with hemodynamic instability for whom regular intravenous thrombolytic therapy might lead to excessively risk of intracranial bleeding, and trans-catheter low-dose thrombolysis in the pulmonary artery may be required.

STEMI, ST-segment elevation myocardial infarction; NSTEMI, Non-ST segment elevation myocardial infarction.

10.1161/CIRCULATIONAHA.120.047011

Figure 3. Invasive Therapies for ACS Patients in the COVID-19 Era.



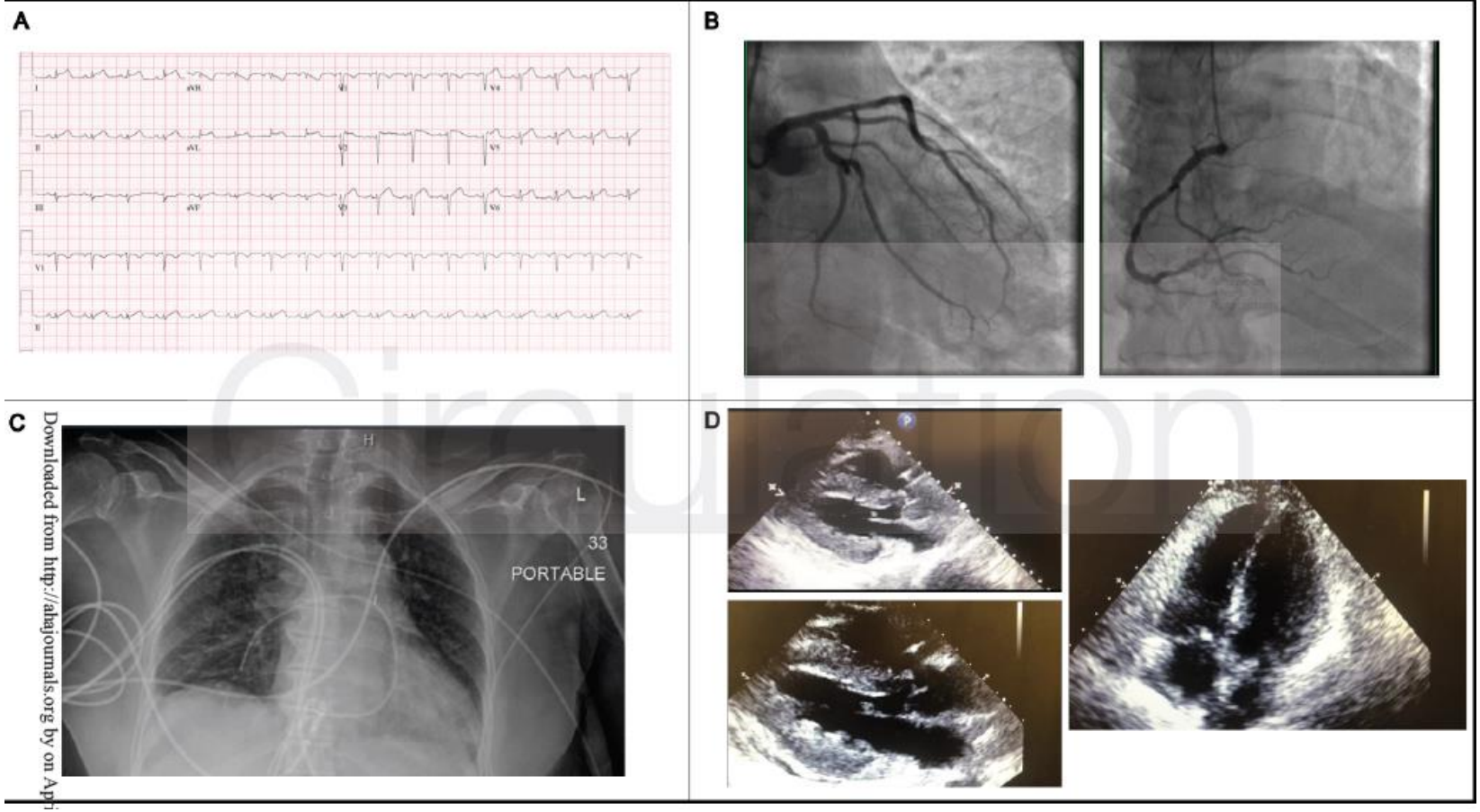


Figure 1. Chest Pain and ST-elevation. Initial electrocardiogram showed sinus tachycardia, low voltage QRS complexes in the limb leads and diffuse ST elevation in leads I, II, aVL and leads V2-V6 (**Panel A**); Coronary angiogram demonstrated mild disease in the left anterior descending artery and left circumflex artery and 40% stenosis in the mid right coronary artery (**Panel B**); Chest radiography demonstrated clear lungs (**Panel C**); Transthoracic echocardiogram with severe increased left ventricular wall thickness and left ventricular ejection fraction approximately 30% with trace circumferential pericardial effusion (**Panel D**).

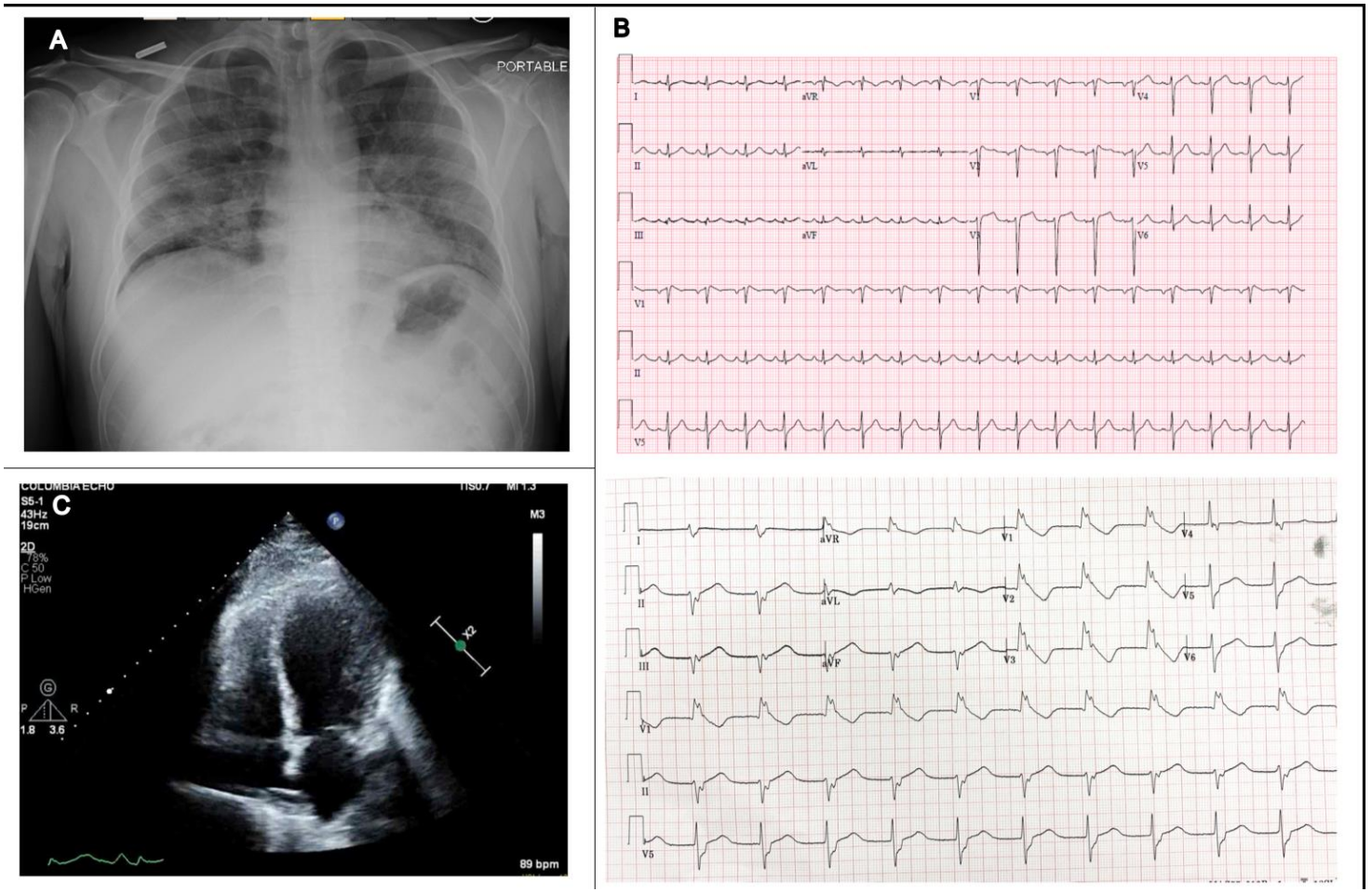


Figure 2. Cardiogenic shock rescued by VAV ECMO. Chest radiograph showed diffuse ill-defined airspace opacities bilaterally (**Panel A**); Initial electrocardiogram (Top) demonstrated sinus tachycardia with incomplete right bundle branch block; Repeat electrocardiogram (Bottom) demonstrated accelerated idioventricular rhythm (**Panel B**); Transthoracic echocardiogram demonstrated left ventricular end-diastolic diameter of 4.5 cm, left ventricular ejection fraction 20-25%, with akinesis of mid left ventricular segments (**Panel C**).

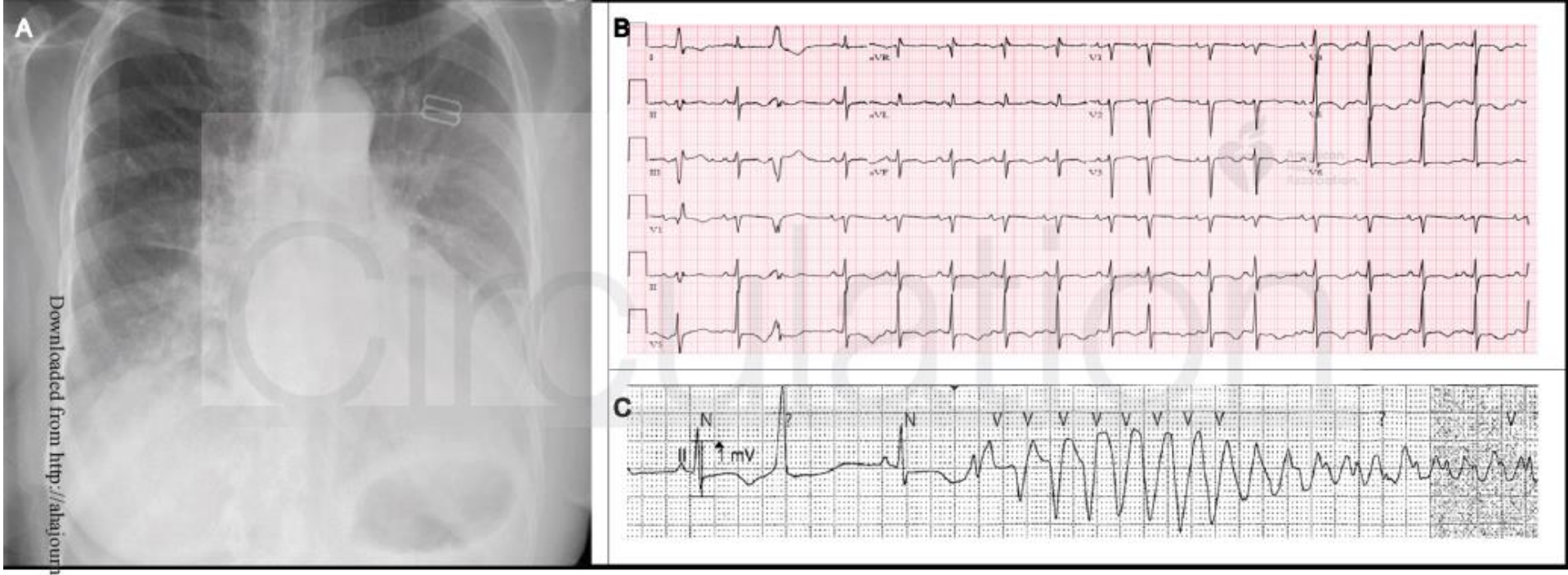


Figure 3. Decompensated Heart Failure. Chest radiography shows pulmonary vascular congestion, patchy airspace opacities at bases and bilateral pleural effusions (**Panel A**); Electrocardiogram shows sinus rhythm with premature atrial and ventricular complexes, lateral T-wave inversions and a prolonged QT interval (**Panel B**). Telemetry strip shows prolonged QT interval and Torsades de Pointes following R-on-T phenomenon (**Panel C**).

The Variety of Cardiovascular Presentations of COVID-19

COVID-19 Associated Cardiovascular Disease

ST Segment Elevation

- Myopericarditis should be strongly considered in patient with chest pain, ECG changes, and biomarker elevation. Maintain a low threshold to assess for cardiogenic shock in this setting
- Use bedside TTE and possibly CCTA to triage cases prior to cardiac catheterization, Consider a conservative strategy in appropriately selected cases
- Consider bedside pulmonary artery catheterization and bedside IABP placement. IABP may be preferred device for cardiogenic shock due to lower management requirements
- Even if clinical presentation is dominated by cardiac manifestations and there is no no fever, COVID-19 should be in differential

Cardiogenic Shock

- Myocardial dysfunction may be caused by direct injury by virus or secondary to cytokine storm
- ECMO provides circulatory (VA) and respiratory support (VV). Low flows on VA ECMO may be sufficient
- Stabilization and recovery of profound cardiac dysfunction related to COVID-19 is possible with temporary mechanical circulatory support
- ECMO requires high resource utilization and should be used judiciously during the COVID-19 pandemic

Decompensated Heart Failure

- Preexisting cardiac conditions (congestive heart failure, atrial fibrillation, hypertension) may be exacerbated by COVID-19
- Invasive hemodynamic monitoring may be beneficial in select cases to manage both cardiac and respiratory failure
- The use of QT-prolonging agents (azithromycin, hydroxychloroquine) should be closely monitored in patients with underlying cardiomyopathies

Heart Transplant Recipient

- Heart transplant recipients exhibit similar symptoms of COVID-19 infection as non-transplant population
- Consider holding anti-metabolite (mycophenolate mofetil or azathioprine) in patients requiring hospitalization for COVID-19 infection
- COVID-19 pandemic imposes challenging decisions for heart transplant programs, including maintaining safety of heart failure patients on waitlist and safety of post-transplant patients

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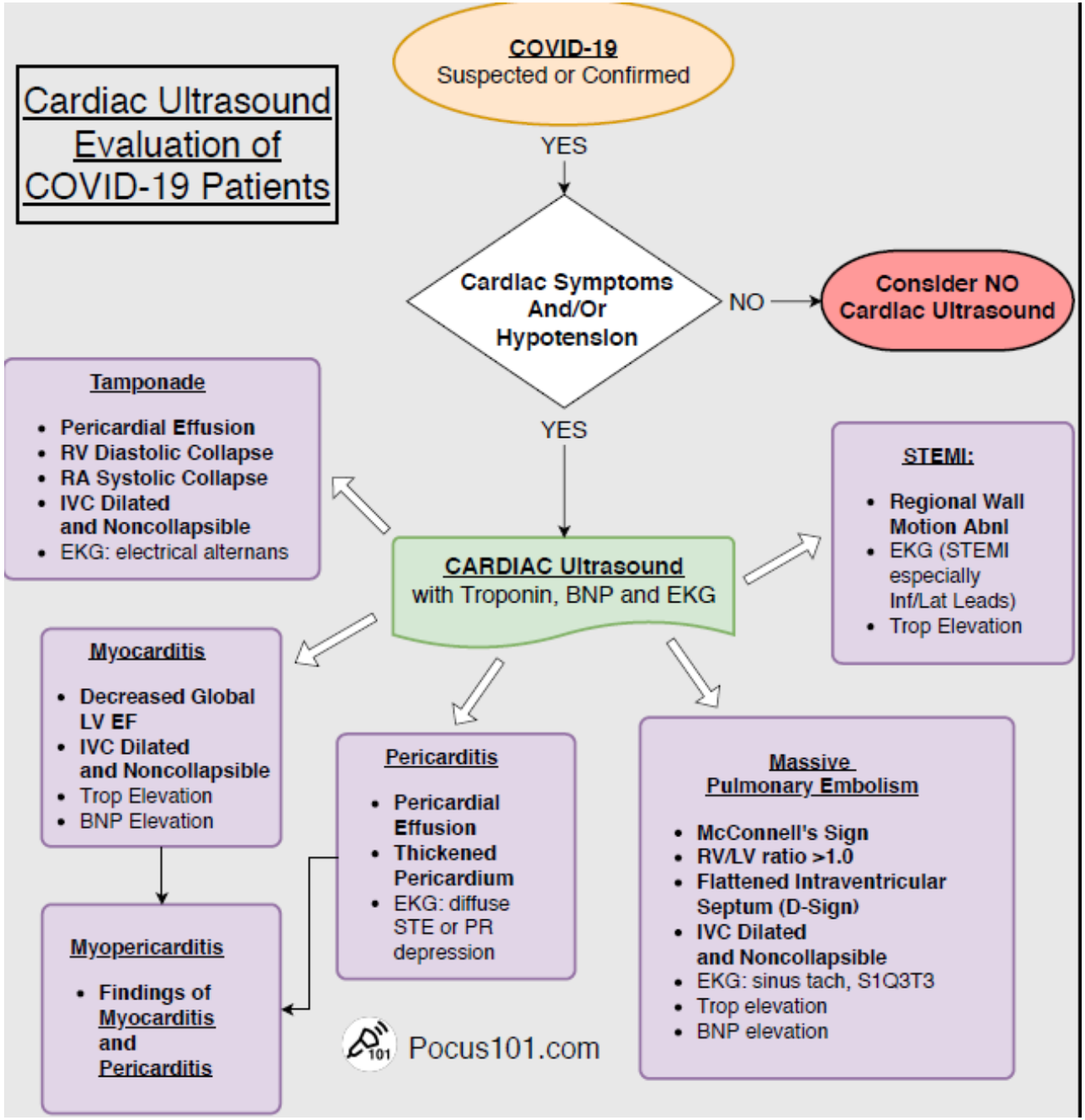
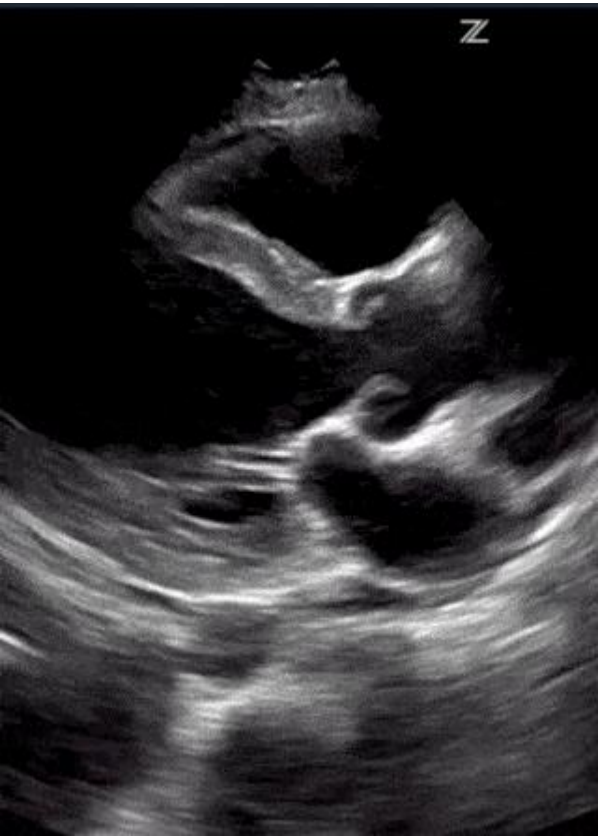
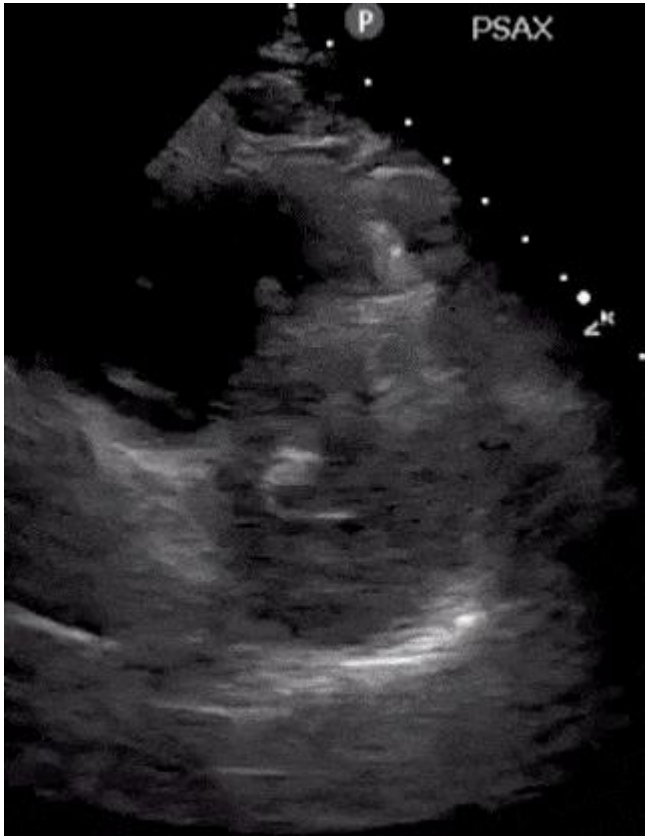
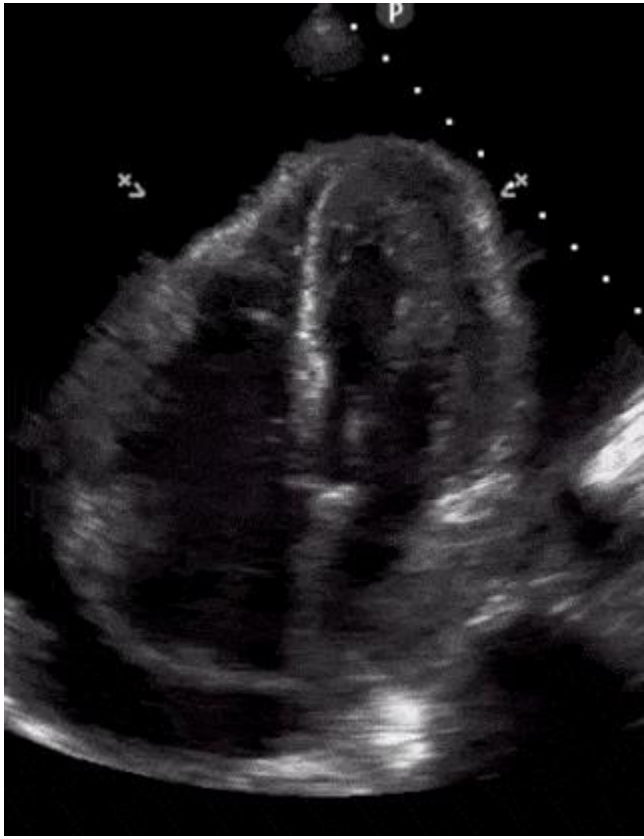

Cardiac Ultrasound Evaluation of COVID-19 Patients
COVID-19
Suspected or Confirmed
YES
Cardiac Symptoms And/Or Hypotension
NO
Consider NO Cardiac Ultrasound
YES
Tamponade
Pericardial Effusion
RV Diastolic Collapse
RA Systolic Collapse
IVC Dilated and Noncollapsible
EKG: electrical alternans
CARDIAC Ultrasound with Troponin, BNP and EKG
STEMI:
Regional Wall Motion Abnl
EKG (STEMI especially Inf/Lat Leads)
Trop Elevation
Myocarditis
Decreased Global LV EF
IVC Dilated and Noncollapsible
Trop Elevation
BNP Elevation
Pericarditis
Pericardial Effusion
Thickened Pericardium
EKG: diffuse STE or PR depression
Massive Pulmonary Embolism
McConnell's Sign
RV/LV ratio >1.0
Flattened Intraventricular Septum (D-Sign)
IVC Dilated and Noncollapsible
EKG: sinus tach, S1Q3T3
Trop elevation
BNP elevation
Myopericarditis
Findings of Myocarditis and Pericarditis
Pocus101.com

ECHO Images







Findings of lung ultrasonography of novel corona virus pneumonia during the 2019–2020 epidemic

Qian-Yi Peng[1], Xiao-Ting Wang[2*], Li-Na Zhang[1*] and Chinese Critical Care Ultrasound Study Group (CCUSG)

Table 1 CT and ultrasonographic features of COVID-19 pneumonia

Lung CT	Lung ultrasound
Thickened pleura	Thickened pleural line
Ground glass shadow and effusion	B lines (multifocal, discrete, or confluent)
Pulmonary infiltrating shadow	Confluent B lines
Subpleural consolidation	Small (centomeric) consolidations)
Translobar consolidation	Both non-translobar and translobar consolidation
Pleural effusion is rare.	Pleural effusion is rare
More than two lobes affected	Multilobar distribution of abnormalities
Negative or atypical in lung CT images in the super-early stage, then diffuse scattered or ground glass shadow with the progress of the disease, further lung consolidation	Focal B lines is the main feature in the early stage and in mild infection; alveolar interstitial syndrome is the main feature in the progressive stage and in critically ill patients; A lines can be found in the convalescence; pleural line thickening with uneven B lines can be seen in patients with pulmonary fibrosis

Intensive Care Med
https://doi.org/10.1007/s00134-020-05996-6

Initial Ultrasound Evaluation of COVID-19 Patients

COVID-19
Suspected or Confirmed

YES

Vital Signs Normal?

YES → **STOP!**
NO Ultrasound
(Consider *Discharge*)

NO

LUNG + CARDIAC Ultrasound

*Appropriate PPE and Disinfection of US Machines

DDX:

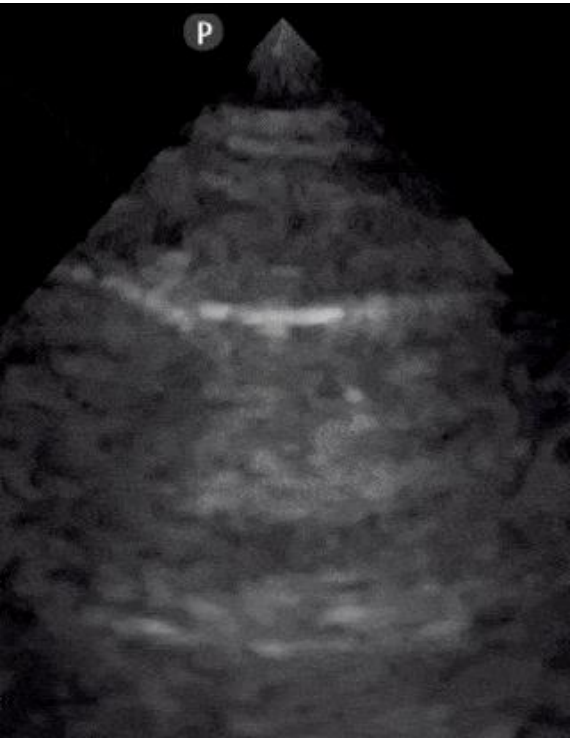
- COVID-19
- Other Viral PNA
- Bac PNA
- Tamponade
- PE
- CHF
- PTX
- COPD
- Hypovolemia

Start Appropriate Treatment

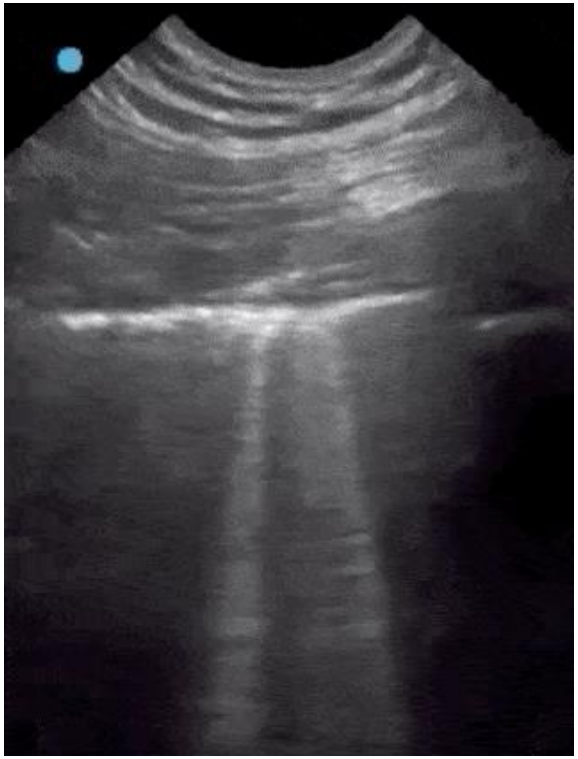
Admit to *ICU* vs *Step Down* vs *Med Surg*
Based on Vital Signs and Pathology

Pocus101.com

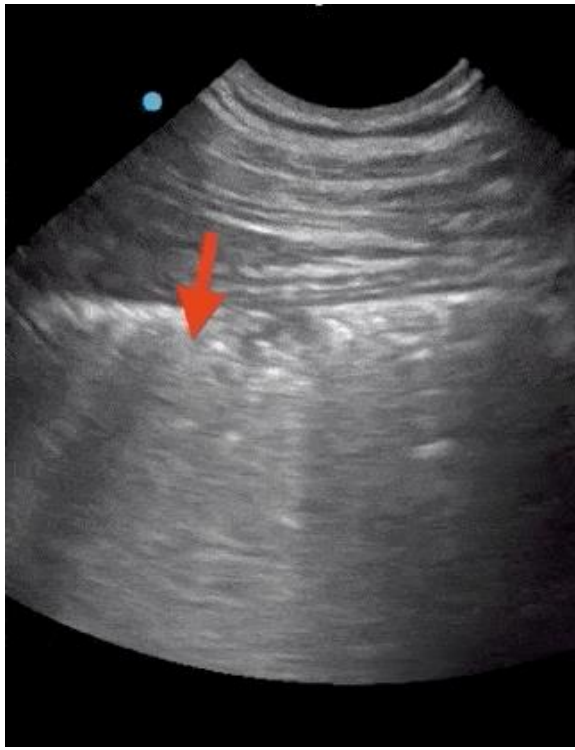
Lung ultrasound images



Normal lung

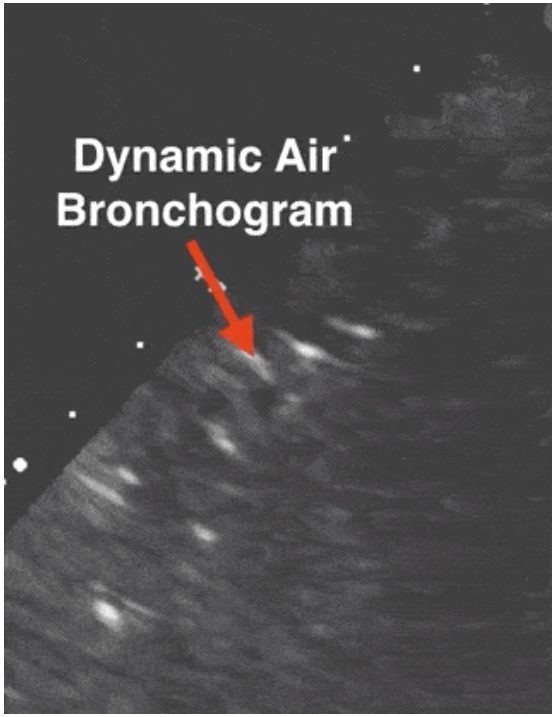


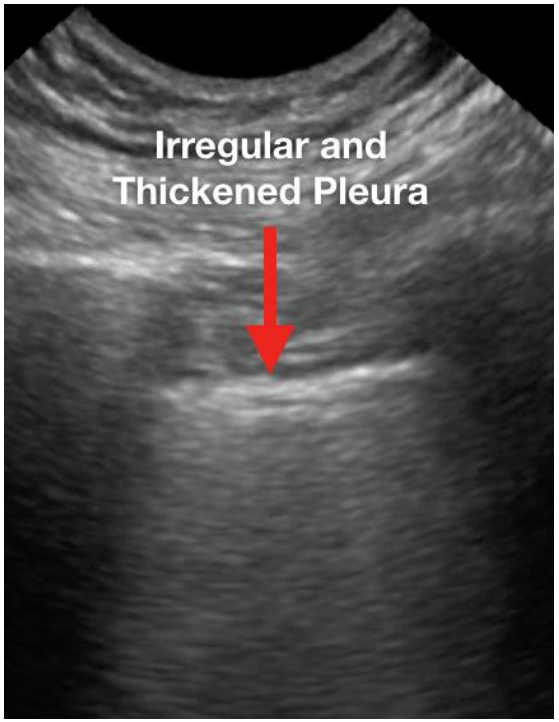
Few B-lines

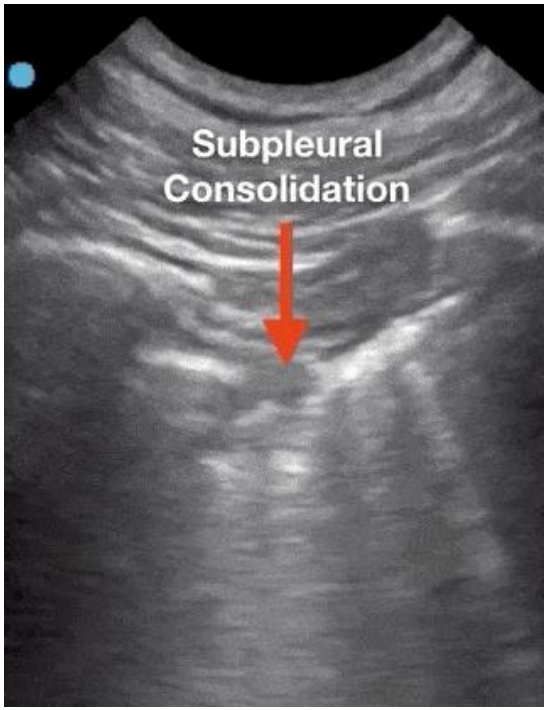


COVID ARDS

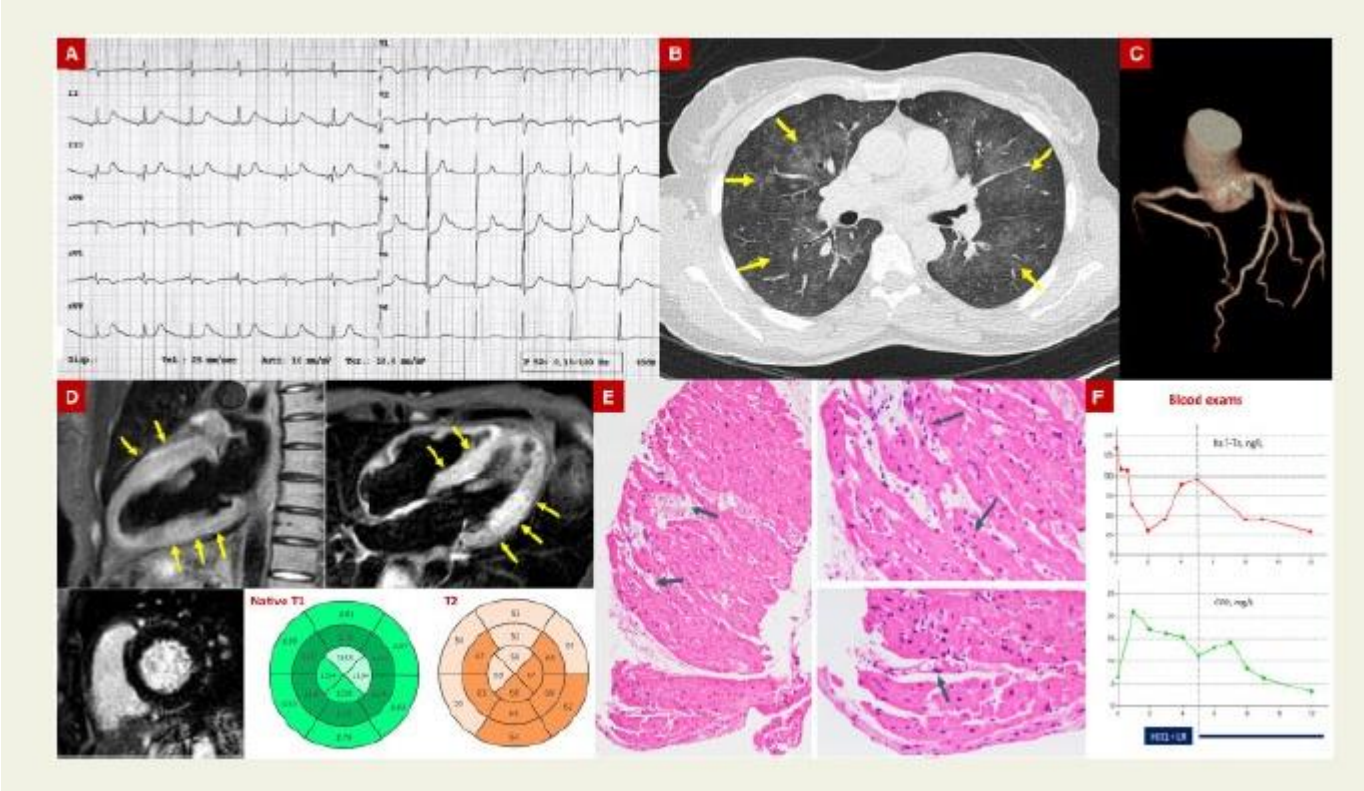
Lung ultrasound images







Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection



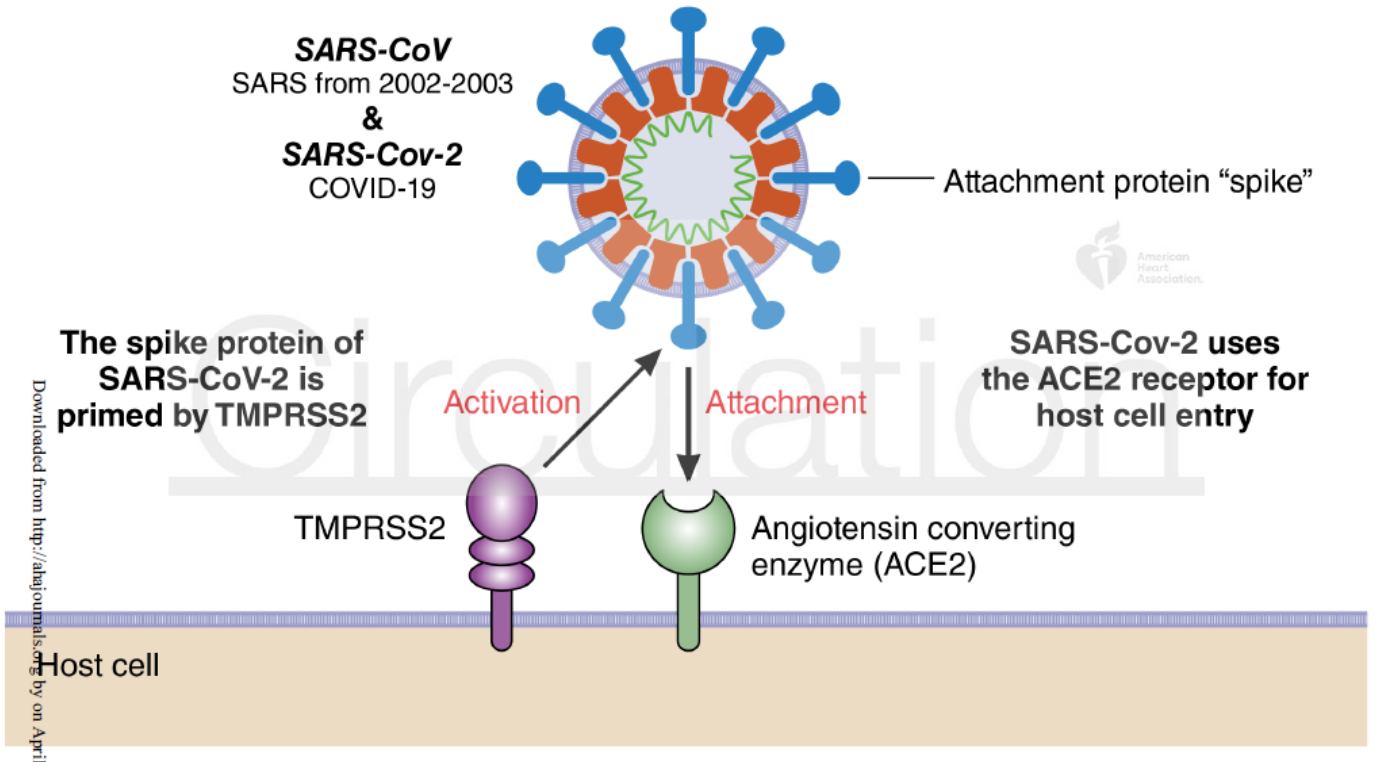
European Heart Journal, ehaa286,
https://doi.org/10.1093/eurheartj/ehaa286

Table 3. Summary of clinical reports describing arrhythmias in COVID-19 patients. Search strategy: ("SARS-CoV-2" OR "COVID-19" OR "novel coronavirus") AND ("arrhythmia" OR "tachycardia" OR "bradycardia" OR "cardiac arrest"), date of search 4 April 2020.

Reference	Location	Type of study	Setting	N	N with arrhythmia	Remarks
Guo et al[6]	Wuhan, China	Single-center retrospective case series	Hospitalized patients	187	11 (6%) VT/VF	Only VT/VF reported. Almost all (9/11 patients with VT/VF) had increased troponin-T levels.
Du et al[22]	Wuhan, China	Multi-center retrospective case series	Fatal cases	85	51 (60%) type of arrhythmia unknown	Report on 85 fatal cases. No information on type of arrhythmia.
Wang et al[5]	Wuhan, China	Single-center retrospective case series	Hospitalized patients	138	23 (17%) type of arrhythmia unknown	No information on type of arrhythmia. Arrhythmic occurrence relates to severity of disease: 44% of 36 ICU patients had arrhythmias.

ICU: intensive care unit, VF: ventricular fibrillation, VT: ventricular tachycardia

Figure 4. SARS-CoV-2 binds to the ACE2 receptor following activation of the spike protein by TMPRSS2



10.1161/CIRCULATIONAHA.120.046941

Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19

Muthiah Vaduganathan, M.D., M.P.H., Orly Vardeny, Pharm.D., Thomas Michel, M.D., Ph.D., John J.V. McMurray, M.D., Marc A. Pfeffer, M.D., Ph.D., and Scott D. Solomon, M.D.

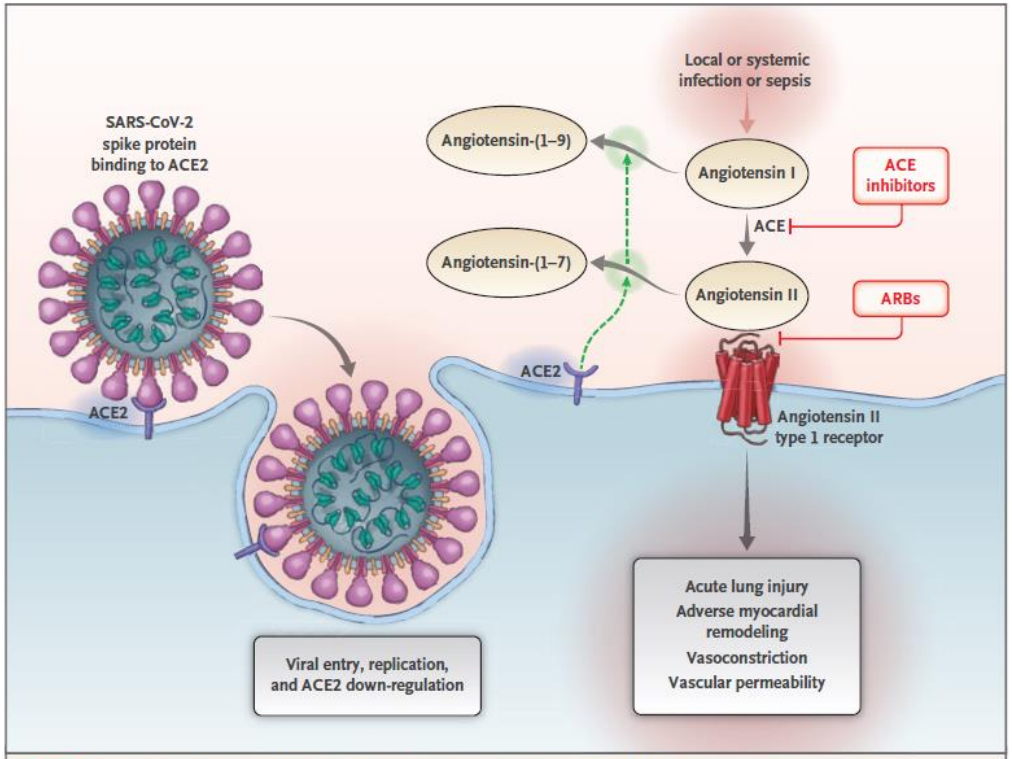


Figure 1. Interaction between SARS-CoV-2 and the Renin–Angiotensin–Aldosterone System.
Shown is the initial entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into cells, primarily type II pneumocytes, after binding to its functional receptor, angiotensin-converting enzyme 2 (ACE2). After endocytosis of the viral complex, surface ACE2 is further down-regulated, resulting in unopposed angiotensin II accumulation. Local activation of the renin–angiotensin–aldosterone system may mediate lung injury responses to viral insults. ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.

Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19

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Key Points Related to the Interplay between Covid-19 and the Renin–Angiotensin–Aldosterone System

- ACE2, an enzyme that physiologically counters RAAS activation, is the functional receptor to SARS-CoV-2, the virus responsible for the Covid-19 pandemic
- Select preclinical studies have suggested that RAAS inhibitors may increase ACE2 expression, raising concerns regarding their safety in patients with Covid-19
- Insufficient data are available to determine whether these observations readily translate to humans, and no studies have evaluated the effects of RAAS inhibitors in Covid-19
- Clinical trials are under way to test the safety and efficacy of RAAS modulators, including recombinant human ACE2 and the ARB losartan in Covid-19
- Abrupt withdrawal of RAAS inhibitors in high-risk patients, including those who have heart failure or have had myocardial infarction, may result in clinical instability and adverse health outcomes
- Until further data are available, we think that RAAS inhibitors should be continued in patients in otherwise stable condition who are at risk for, being evaluated for, or with Covid-19

The NEW ENGLAND JOURNAL of MEDICINE

COVID-19 Illness and Heart Failure: A Missing Link?

Mandeep R. Mehra, MD, MSc, Frank Ruschitzka, MD

Table: Clinical Cardiovascular Concerns in COVID-19 Illness

COVID-19 Infection	Concern	Interpretation
Asymptomatic or early mild disease with constitutional symptoms (fever, dry cough, diarrhea and headache)	Should background cardiovascular medications be modified?	• There is no clear evidence that ACEi or ARB should be discontinued • NSAIDs should be avoided
Moderate disease with pulmonary complications and shortness of breath (including hypoxia)	Is there a cardiovascular contribution to the lung complications?	• Check troponin (evidence of myocardial injury and prognosis) • Check natriuretic peptides • Consider cardiac echocardiography to evaluate for evidence of underlying structural heart disease, high filling pressures • Avoid overuse of intravenous fluids which may worsen underlying pulmonary edema
Advanced stage disease with hypoxia, vasoplegia and shock	Is there evidence of cardiogenic contribution to shock and what therapy may be potentially curative?	• Check for evidence of hyperinflammation or a cytokine release storm (elevated troponin, natriuretic peptides, CRP and serum ferritin>1000 ng/ml (measure IL-6 levels if available) • If cardiac function is reduced (LVEF <0.50%), consider supportive care with inotropic therapy but move to consider anti-cytokine therapy with drugs such as tocilizumab and corticosteroids

ACEi = Angiotensin Converting Enzyme Inhibitors; ARB= Angiotensin Receptor Blockers; CRP= C Reactive Protein; IL = Interleukin [Note that therapy in COVID-19 remains experimental]

Secondary Impact of the COVID-19 Pandemic on Patients With Heart Failure

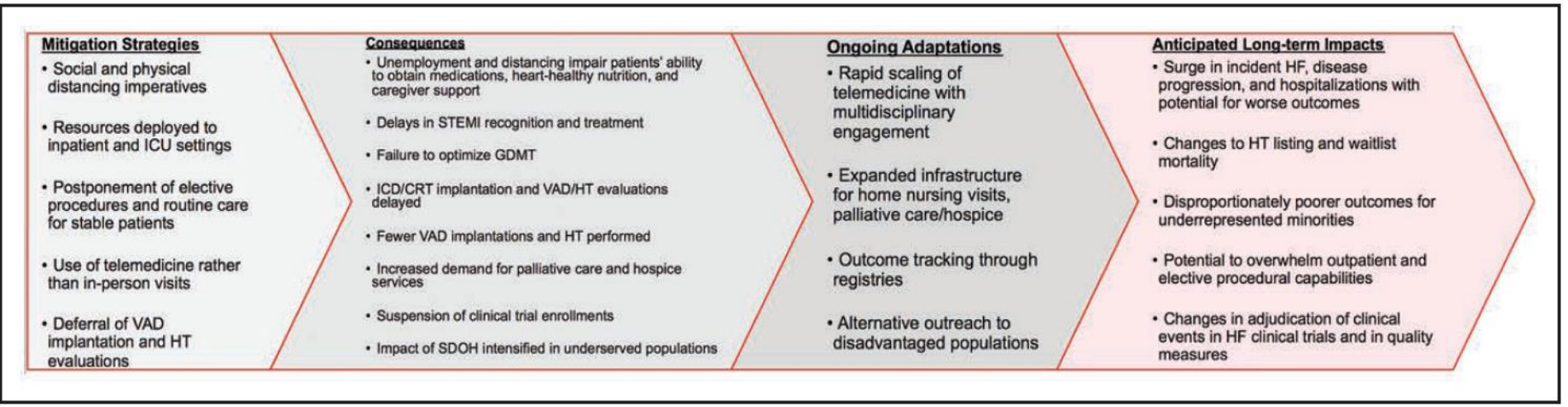

Figure. Mitigation strategies, consequences, ongoing adaptations to, and anticipated impacts of disruptions in heart failure care delivery imposed by the coronavirus disease 2019 (COVID-19) pandemic.

Figure 1. Acute cardiovascular manifestations of COVID-19