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COVID-19 and Cardiovascular Health: Managing Patients and Incorporating a Telehealth Framework

November 16, 2022

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Welcome

Michael W. Konstan, MD
Principal Investigator, Cardi-OH

Shari Bolen, MD, MPH
Co-Principal Investigator, Cardi-OH

Case Western Reserve University School of Medicine

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About Cardi-OH

Founded in 2017, the mission of Cardi-OH is to improve cardiovascular and diabetes health outcomes and eliminate disparities in Ohio's Medicaid population.

WHO WE ARE: An initiative of health care professionals across Ohio's seven medical schools.

WHAT WE DO: Identify, produce, and disseminate evidence-based cardiovascular and diabetes best practices to primary care teams.

HOW WE DO IT: Best practices resources are available via an online library at Cardi-OH.org, including monthly newsletters, podcasts, webinars, and virtual clinics using the Project ECHO® virtual training model.

Learn more at Cardi-OH.org

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Agenda

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Topics	Presenter(s)	Timing
Welcome and Overview	Michael W. Konstan, MD Shari Bolen, MD, MPH	5 mins.
COVID-19 and Cardiovascular Health: Managing Patients and Incorporating a Telehealth Framework	Tamanna K. Singh, MD	40 mins.
Audience Question and Answer	Amy Zack, MD (Moderator) Tamanna K. Singh, MD	10 mins.
Next Steps and Wrap Up	Shari Bolen, MD, MPH	5 mins.

Tamanna K. Singh, MD
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University

Amy Zack, MD (Moderator)
Case Western Reserve University

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COVID-19 and Cardiovascular Health: Managing Patients and Incorporating a Telehealth Framework

Tamanna K. Singh, MD
Assistant Professor, Cleveland Clinic Lerner College of Medicine
Case Western Reserve University
Co-Director, Sports Cardiology Center
Post-COVID Cardiovascular Recovery Center and reCOVer Clinic
Cleveland Clinic

Objectives

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- Identify cardiovascular complications of COVID-19 infection
- Screen and treat patients for COVID-19 cardiovascular complications
- Use telehealth with post-COVID patients as a means of managing cardiovascular care

Coronavirus Cases:

632,909,744

view by country

Deaths:

6,582,821

Recovered:

611,807,671

https://www.worldometers.info/coronavirus/

COVID-19 Cases: United States

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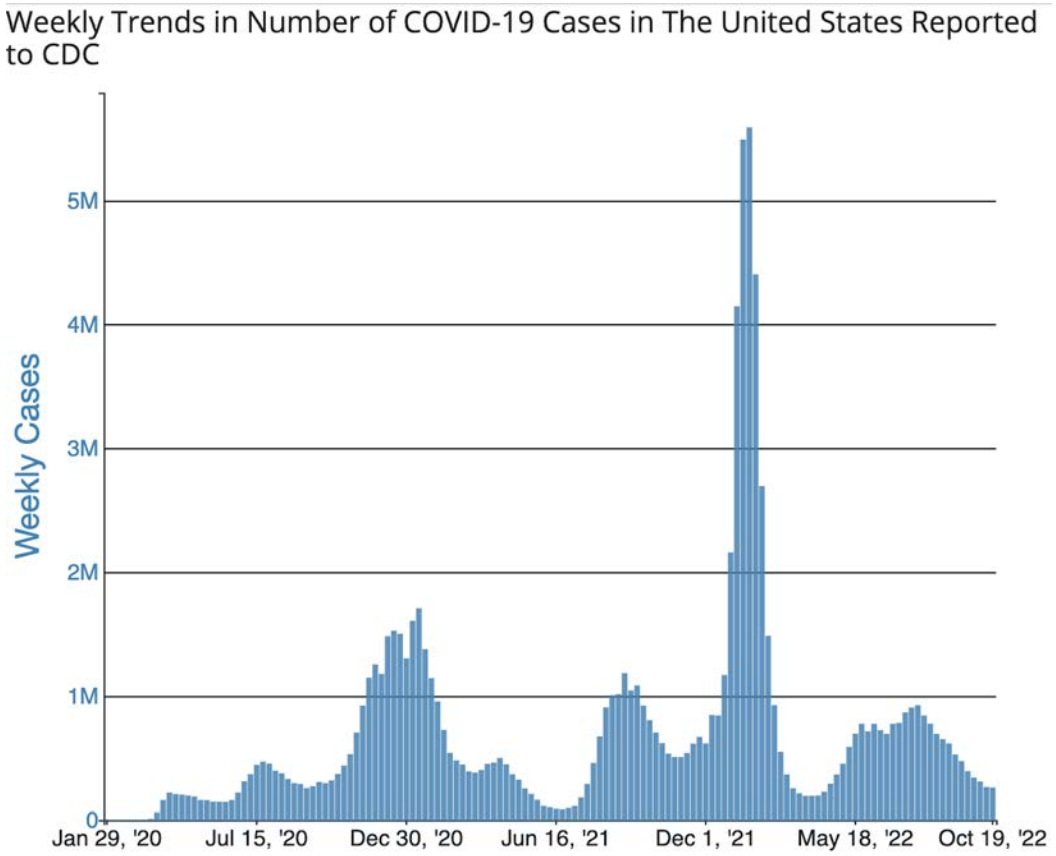

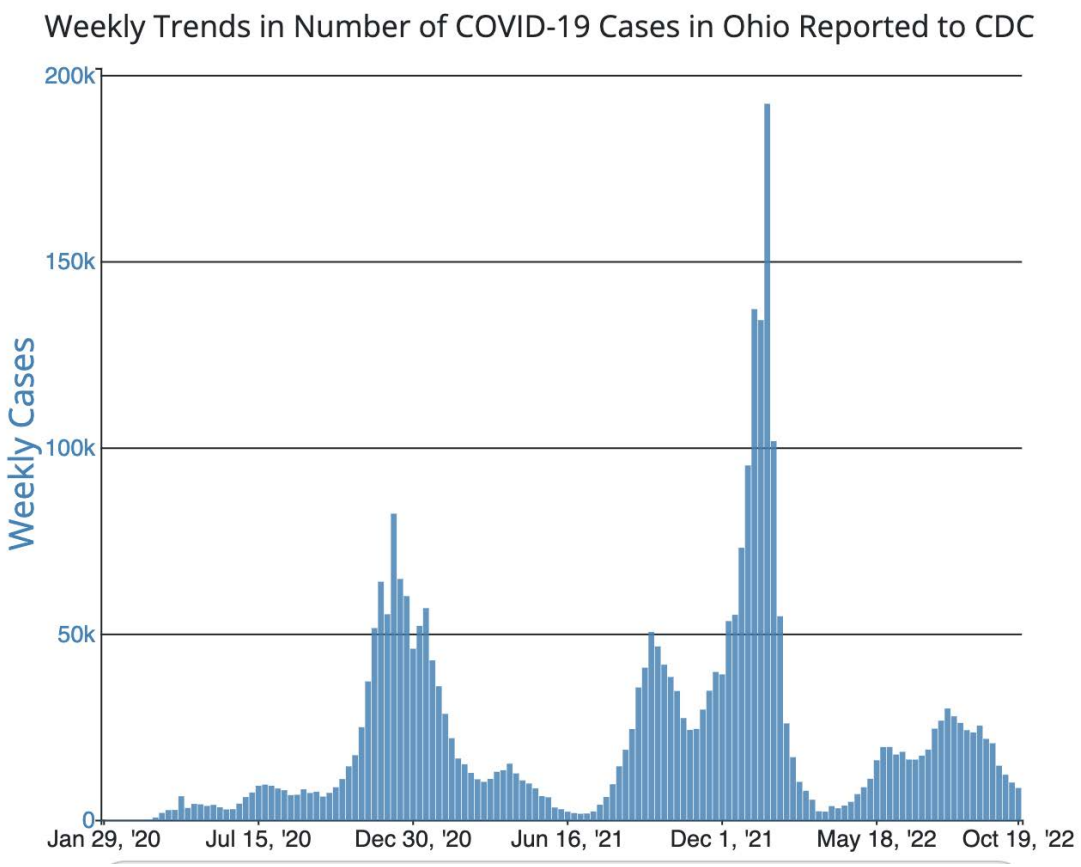

https://covid.cdc.gov/covid-data-tracker/#trends_weeklycases_select_39

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COVID-19 and Cardiovascular Pathophysiology

Pathophysiology of Cardiac Involvement

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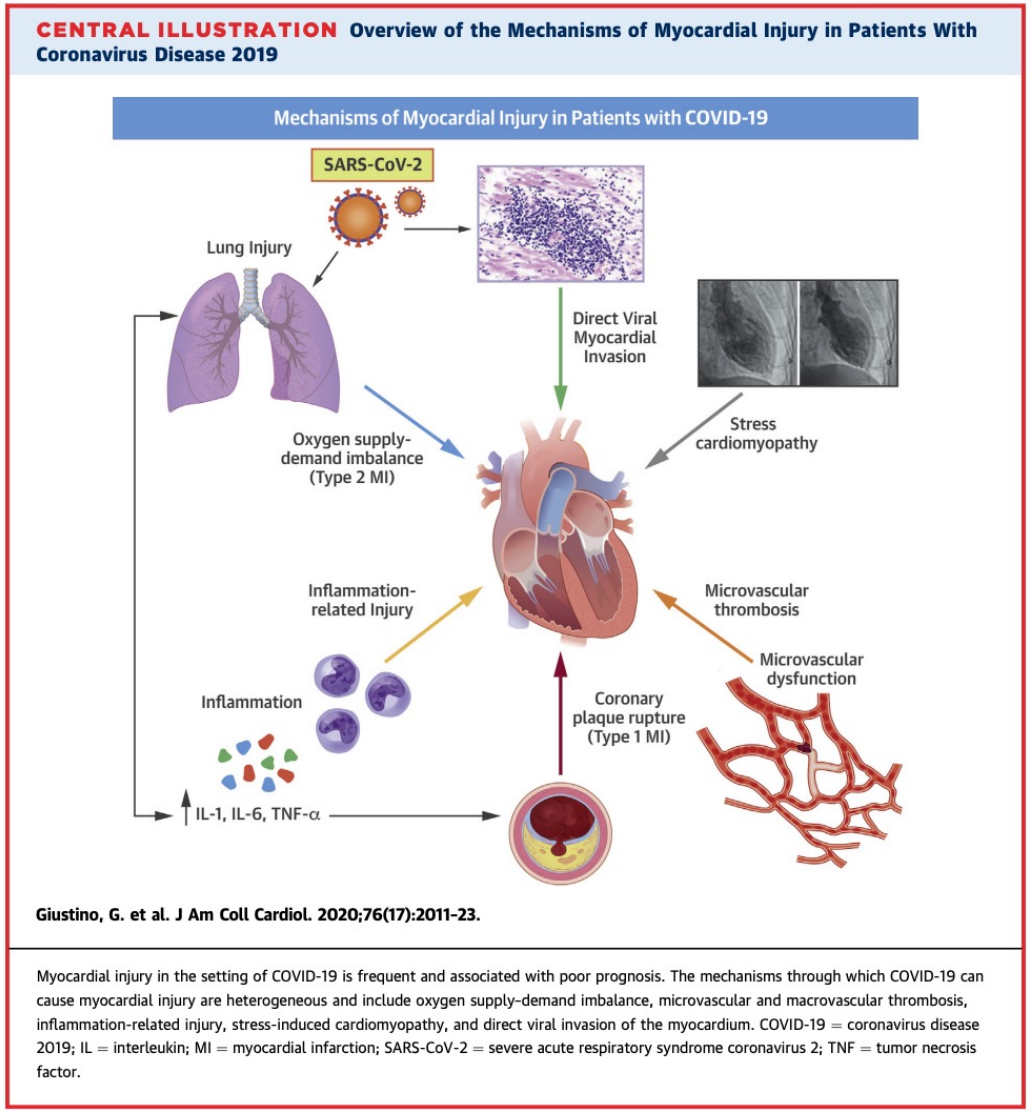
- Cytokine storm
- Endothelial dysfunction / inflammation
- Microvascular thrombosis
- Multiorgan failure



Giustino et al. JACC. Oct 2020. 76(17): 2011-23

Pathophysiology of Cardiac Involvement

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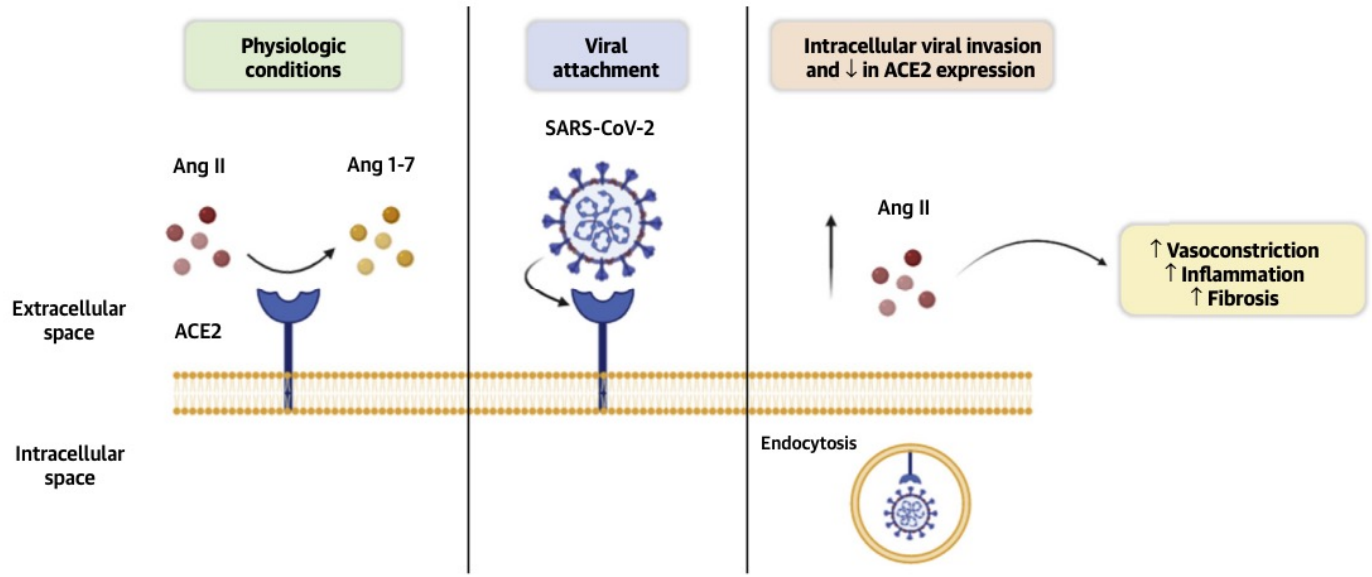
- Outer membrane S protein has high binding affinity to ACE2 receptor
- ACE2 expressed in heart, lung, gut smooth muscle, liver, kidney, immune cells

FIGURE 1 Interaction Between SARS-CoV-2, ACE2 Transmembrane Protein, and Ang II Levels in Patients With COVID-19



In severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the angiotensin-converting enzyme 2 (ACE2) transmembrane protein is internalized, leading to decreased receptor density. The loss of ACE2 receptor density and down-regulation of ACE2 activity leads to an accumulation of angiotensin II (Ang II), which exerts vasoconstrictor, profibrotic, and proinflammatory effects. Image created with BioRender. Ang 1-7 = angiotensin 1-7; COVID-19 = coronavirus disease 2019.

In an observational study with >10,000 patients in the NYU electronic health record system, treatment with ACEI or ARBs was **not** associated with higher incidence of COVID-19 or with severe illness

Giustino et al. JACC. Oct 2020; 76(17): 2011-23

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Cardiovascular Complications Associated with Acute COVID-19

Viral Myocarditis: Autopsy Data

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- Initial presumption of direct myocardial invasion by SARS-CoV-2
- 104 patients with acute heart failure
  - Endomyocardial biopsy: 5-positive for SARS-CoV-2 genome in myocardium
  - Features of myocarditis present (inflammation, microvascular thrombosis, myocardial necrosis)

Wenzel P et al. Cardiovasc Res. 2020;116: 1661-3

Viral Myocarditis: Autopsy Data

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- 39 autopsy cases – acute phase only
  - 24 with SARS-CoV-2 RNA present in myocardial tissue, some with evidence of viral replication
  - 15 without RNA
- Presence of SARS-CoV-2 in cardiac tissue was not associated with mononuclear cell infiltration i.e. what would be seen in myocarditis, thus no clinical myocarditis identified
- Long-term effects of viral activity in myocardium unknown

Lindner D et al. JAMA Card 2020; 5(11):1281-85

COVID-19: CV Manifestations

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- Viral myocarditis
  - Elevated troponin levels in acute infection posed concern for high incidence of myocarditis
  - Reality: quite rare, few case reports on fulminant myocarditis +/- cardiogenic shock
- Arrhythmias are a more common manifestation of SARS-COV2, unclear how frequent they are related to myocarditis

Abbasi J. JAMA. 2021;325(9):808–811

So What Causes Myocardial Injury if Myocarditis is not the Source?

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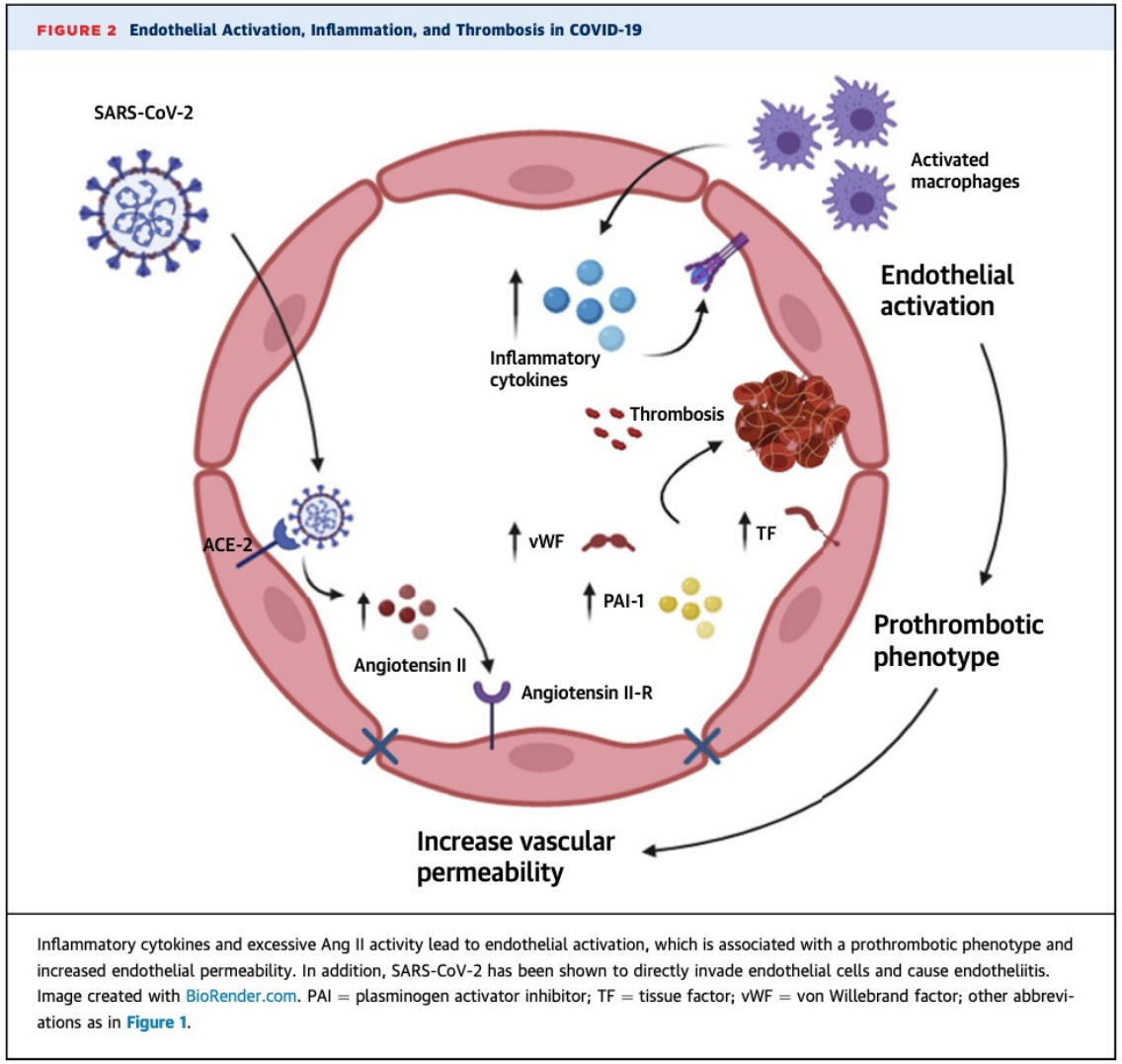
- Systemic inflammation is the culprit
  - Thromboembolic phenomena
  - Arrhythmias
  - Coronary plaque destabilization
  - Oxygen supply/demand mismatch
  - Stress-induced cardiomyopathy

Abbasi J. JAMA. 2021;325(9):808–811

Vascular Complications

- Significant elevations in von Willebrand factor observed in severe infection
- Endothelialitis on histologic examination



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Thromboembolic Disease

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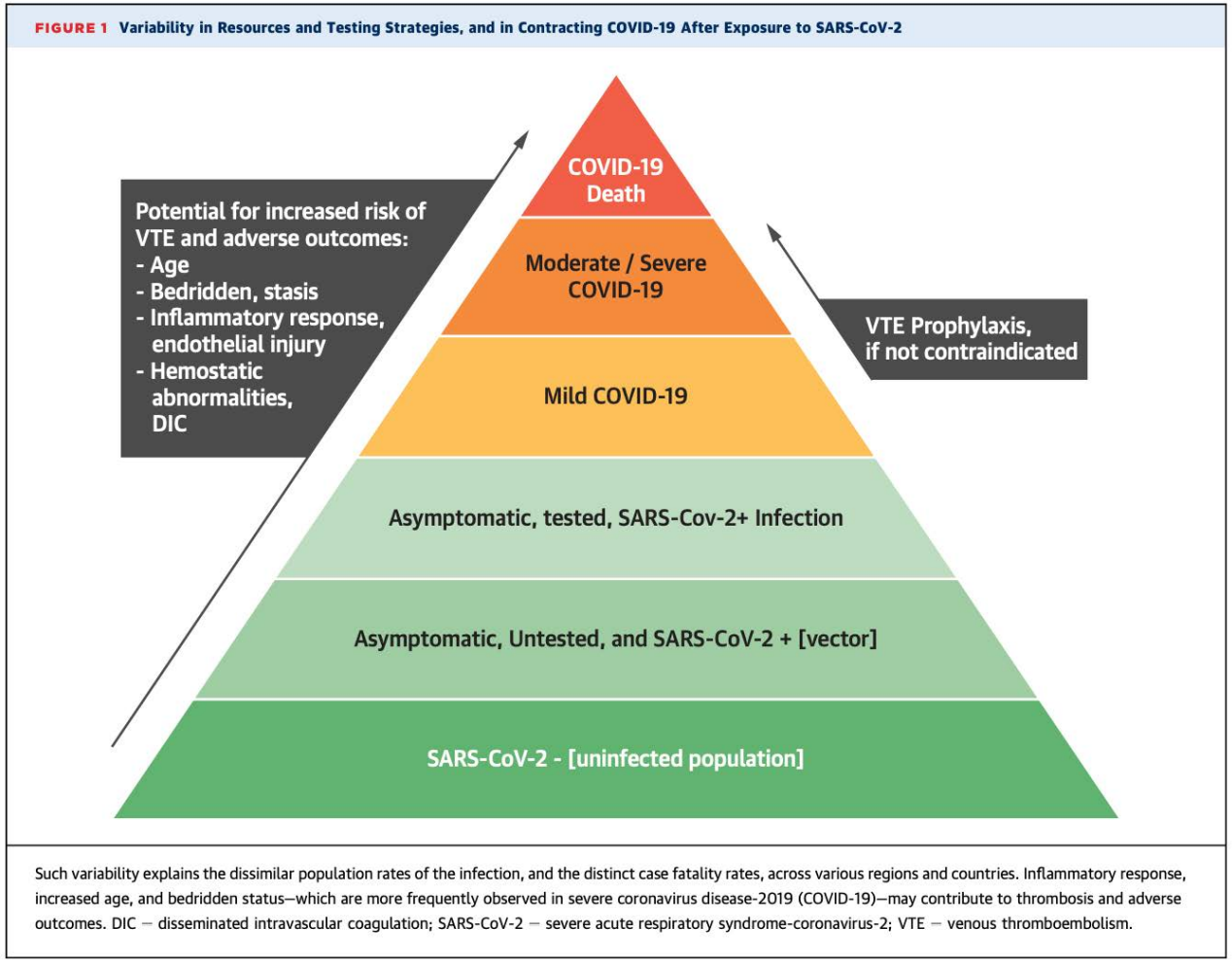

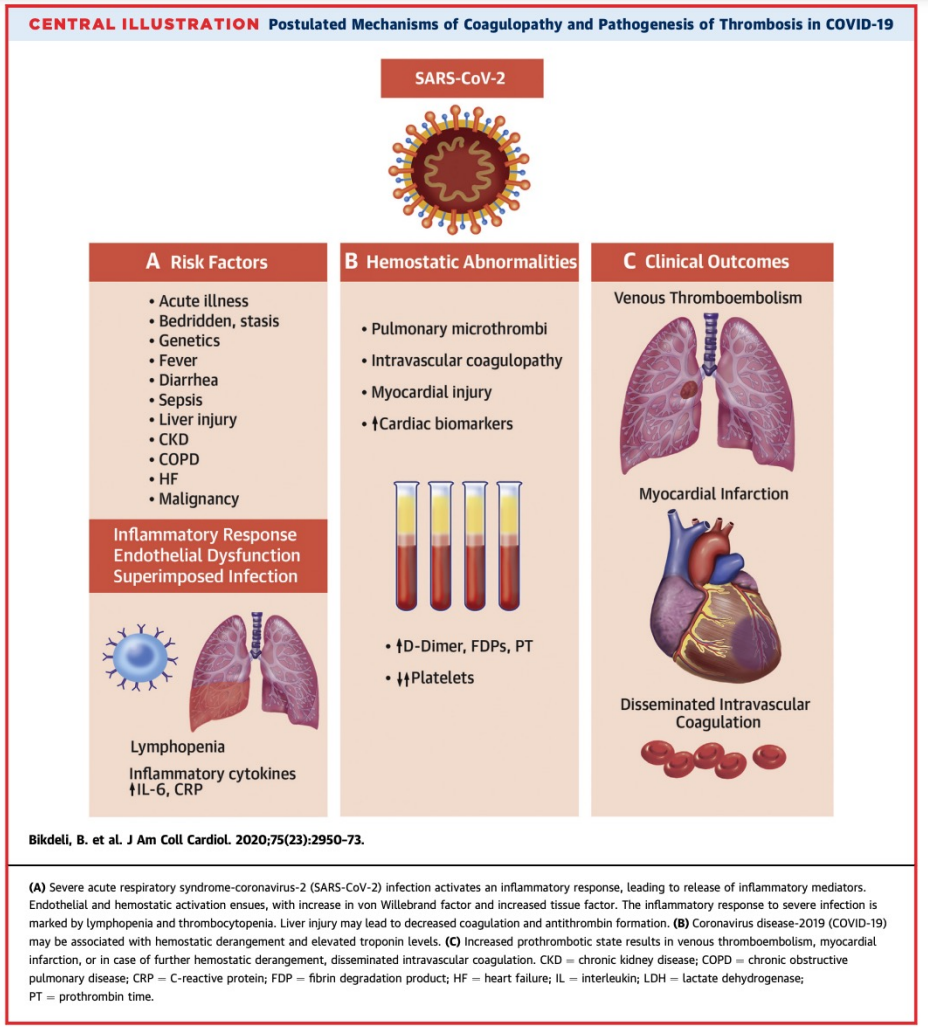

Mild thrombocytopenia + elevated D-dimer → higher risk of ICU admission, mechanical ventilation, death

Bikdeli B et al. JACC. Jun 2020. 75(23): 2950-73

Drug Interactions:
Antiplatelet, Anticoagulant Agents & COVID-19 Therapies

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TABLE 3 Potential Drug Interactions Between Antiplatelet Agents and Investigational Therapies for COVID-19

Investigational COVID-19 Therapy	Mechanism of Action of COVID-19 Therapy	$P2Y_{12}$ Platelet Receptor Inhibitors			Phosphodiesterase III Inhibitor
		Clopidogrel	Prasugrel	Ticagrelor	Cilostazol
Lopinavir/ritonavir	Lopinavir is a protease inhibitor; Ritonavir inhibits CYP3A4 metabolism increasing lopinavir levels.	CYP 3A4 Inhibition (minor pathway): Reduction in clopidogrel active metabolite. Do not coadminister or if available utilize $P2Y_{12}$ platelet function assays for monitoring.† With limited clinical data, prasugrel may be considered as alternative, if no contraindications	CYP3A4 Inhibition: Decreased active metabolite but maintained platelet inhibition. Can administer with caution.	CYP3A4 Inhibition: Increased effects of ticagrelor. Do not coadminister or if available utilize $P2Y_{12}$ monitoring or consider dose-reduced ticagrelor.*	CYP3A4 Inhibition: Recommend decreasing dose to maximum of 50 mg twice a day.
Remdesivir	Nucleotide-analog inhibitor of RNA-dependent RNA polymerases.	Reported inducer of CYP3A4 (minor pathway): no dose adjustment recommended.	Reported inducer of CYP3A4 (major pathway): no dose adjustment recommended.	Reported inducer of CYP3A4 (major pathway): no dose adjustment recommended.	Reported inducer of CYP3A4 (major pathway): no dose adjustment recommended.
Tocilizumab	Inhibits IL-6 receptor: may potentially mitigate cytokine release syndrome symptoms in severely ill patients.	Reported increase in expression of 2C19 (major pathway) and 1A2, 2B6, and 3A4 (minor pathways: no dose adjustment recommended.	Reported increase in expression of 3A4 (major pathway) and 2C9 and 2C19 (minor pathway): no dose adjustment recommended.	Reported increase in expression of 3A4 (major pathway): No dose adjustment recommended.	Reported increase in expression of 3A4 (major pathway): no dose adjustment recommended.
Sarilumab	Binds specifically to both soluble and membrane-bound IL-6Rs (sIL-6Rα and mIL-6Rα) and has been shown to inhibit IL-6-mediated signaling: may potentially mitigate cytokine release syndrome symptoms in severely ill patients.	Reported increase in expression of 3A4 (minor pathways): no dose adjustment recommended.	Reported increase in expression of 3A4 (major pathway): no dose adjustment recommended.	Reported increase in expression of CYP3A4 (major pathway): no dose adjustment recommended.	Reported increase in expression of 3A4 (major pathway): no dose adjustment recommended.

Other drugs being studied to treat COVID-19 include azithromycin, bevacizumab, chloroquine/hydroxychloroquine, eculizumab, fingolimod, interferon, losartan, methylprednisolone, pirfenidone, and ribavirin. Drug-drug interactions between these medications and antiplatelet agents have yet to be identified. *Cangrelor, aspirin, dipyridamole, and glycoprotein IIb/IIIa inhibitors (eptifibatide, tirofiban, abciximab) are not known to interact with investigational therapies for COVID-19. †Monitoring of $P2Y_{12}$ levels can be assessed through the VerifyNow assay, or others. Evaluation of effect of protease inhibitors on $P2Y_{12}$ inhibitors has not been extensively studied. Dose reduction recommendations for $P2Y_{12}$ inhibitors or $P2Y_{12}$ platelet function assay monitoring is not commonly practiced.

IL = interleukin; other abbreviations as in Table 1.

TABLE 4 Potential Drug Interactions Between Anticoagulants* and Investigational Therapies for COVID-19

Investigational COVID-19 Therapies	Vitamin K Antagonists	Dabigatran	Apixaban	Betrixaban	Edoxaban	Rivaroxaban
Lopinavir/ritonavir	CYP2C9 induction: May decrease plasma concentration. Adjust dose based on INR.	P-gp inhibition: May increase plasma concentration. No dose adjustment recommended.	CYP3A4 and P-gp inhibition: Administer at 50% of dose (do not administer if initial dose is 2.5 mg twice daily).†	P-gp and ABCB1 inhibition: Decrease dose to 80 mg once followed by 40 mg once daily.	P-gp inhibition: Do not coadminister.	CYP3A4 and P-gp inhibition: Do not coadminister.
Tocilizumab	–	–	Reported increase in expression of 3A4 (major pathway): No dose adjustment recommended.	–	–	Reported increase in expression of 3A4 (major pathway): No dose adjustment recommended.
Interferon‡,‖	Unknown mechanism: Decreased dose may be needed.	–	–	–	–	–
Ribavirin	Mechanism not well known: Possibly decreased absorption of warfarin in the presence of ribavirin (156); increased dose may be needed.	–	–	–	–	–
Methylprednisolone	Unknown mechanism: Decreased dose may be needed.	–	–	–	–	–
Sarilumab§			Reported increase in expression of CYP3A4 (major pathway): No dose adjustment recommended.			Reported increase in expression of CYP3A4 (major pathway): No dose adjustment recommended.
Azithromycin	Unknown mechanism: Decreased dose may be needed.	P-gp inhibition: May increase plasma concentration. No dose adjustment recommended.		P-gp inhibition: Decrease dose to 80 mg once followed by 40 mg daily.	P-gp inhibition: VTE: Limit dose to 30 mg daily. Nonvalvular AF: No dose recommendation.	
Hydroxychloroquine and chloroquine	–	–	–	–	–	–

Other drugs being studied to treat COVID-19 include bevacizumab, chloroquine/hydroxychloroquine, eculizumab, fingolimod, losartan, and pirfenidone. Drug-drug interactions between these medications and oral anticoagulants have yet to be identified. Bevacizumab has been reported to cause deep vein thrombosis (9%), arterial thrombosis (5%), and pulmonary embolism (1%). It is also reported to cause thrombocytopenia (58%). *Parenteral anticoagulants (including unfractionated or low-molecular-weight heparins, bivalirudin, argatroban, and fondaparinux) are non-CYP-metabolized and do not interact with any of the investigational agents. †These recommendations are based on the U.S. package insert. The Canadian package insert considers the combination of these agents to be contraindicated. ‡Interferon has been reported to cause pulmonary embolism (<5%), thrombosis (<5%), decreased platelet count (1%-15% with Alfa-2b formulation), and ischemic stroke (<5%). §Sarilumab has been reported to cause decreased platelet count, with decreases to <100,000 mm^3 in 1% and 0.7% of patients on 200-mg and 150-mg doses, respectively. ‖Reported with interferon alpha.

CYP = cytochrome P system; INR = international normalized ratio; P-gp = P-glycoprotein; other abbreviations as in Table 1.

Do not co-administer lopinavir/ritonavir and ticagrelor or clopidogrel

1. Adjust Vit K antagonist, apixaban, betrixaban dose with lopinavir/ritonavir
2. **Do not** administer with edoxaban, rivaroxaban
3. Reduce dose of DOACS and Vitamin K antagonists with azithromycin

Bikdeli B et al. JACC. Jun 2020. 75(23): 2950-73

Is There a Role for Empiric Anticoagulation?

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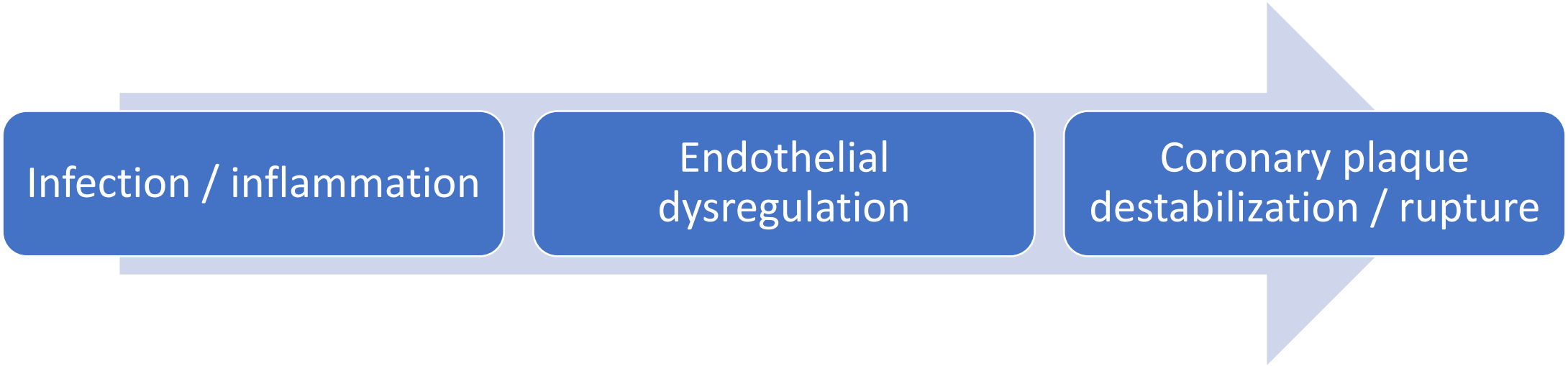
- Clinician-dependent: some use of intermediate or full dose anticoagulation to prevent microvascular thrombosis
- Limited data, no known ”optimal dose” or benefit of prophylactic anticoagulation

Acute Coronary Syndromes



- Incidence of type 1 MI remains unknown
  - Relative infrequency in performing diagnostic angiography in COVID-19 (+) patients to minimize exposure
  - Delayed catheterization while waiting for test results
  - STEMI prioritized over NSTEMI

Giustino et al. JACC. Oct 2020. 76(17): 2011-23

Type 2 Myocardial Infarction

SUSPECTED MECHANISMS
Fixed coronary atherosclerosis limiting myocardial perfusion
Elevated circulating Ang II levels and arteriolar vasoconstriction provoking severe systemic hypertension
Endothelial dysfunction within coronary microvasculature
Acute respiratory distress syndrome or pulmonary vascular thrombosis provoking hypoxemia

- Any severe physiologic stress can provoke elevations in cardiac biomarkers due to provocation of supply : demand mismatch
- Distinguishing patients with Type 1 NSTEMI from those with myocarditis, supply : demand mismatch remains the challenge

Giustino et al. JACC. Oct 2020. 76(17): 2011-23

Myocardial Injury

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- High variability in definition of myocardial injury, contributes to wide incidence range from 7-40%
- Atypical presentation: +/- chest pain, +/- CVD, myocardial and end-organ damage may occur > 2 weeks after onset of initial symptoms
- Consistently associated with increased risk of in-hospital complications, mortality
- Troponin elevation correlates to
  - Higher levels of inflammatory biomarker (e.g. ferritin, IL-6, CRP, D-dimer)
  - Severity of respiratory illness, hypoxemia

Whether myocardial injury is a marker of disease severity or a direct correlate to COVID-19 morbidity and mortality remains unclear.

Giustino et al. JACC. Oct 2020. 76(17): 2011-23

Myocardial Injury

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- Multicenter retrospective analysis in NYC – largest outcomes study
  - 2736 patients: 36% with myocardial injury upon presentation (elevated TnI)
  - After adjusting for baseline confounders: greater TnI elevation was associated with increased risk of in-hospital mortality
- Patients with myocardial injury:
  - Older with more co-morbidities
  - Only ~ 30% had history of coronary artery disease

Lala et al. JACC. Oct 2020. 76: 533-46

Myocardial Injury

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TABLE 1 Selected Studies (With Sample Size ≥100 Patients) Reporting the Incidence and Association of Myocardial Injury With Mortality in Patients With COVID-19

First Author (Ref. #)	Country	No.	Definition of Myocardial Injury	Incidence	Age* (yrs)	Male	Impact of Myocardial Injury on Outcomes
Lala et al. (10)	United States	2,736	Serum levels of TnI >0.03 ng/ml	985/2,736 (36%)	66	59.6%	TnI elevations >0.03-0.09 ng/ml and >0.09 ng/ml were both associated with increased risk of in-hospital mortality after multivariable adjustment (adjusted OR: 1.75; 95% CI: 1.37-2.24, and adjusted OR: 3.03; 95% CI: 2.42-3.80, respectively)
Shi et al. (60)	China	671	Serum levels of TnI >99th percentile URL	Not reported	63	48.0%	TnI elevations >0.026 ng/ml were strongly associated with increased risk of in-hospital mortality (adjusted OR: 4.56; 95% CI: 1.28-16.28)
Shi et al. (4)	China	416	Serum levels of TnI >99th percentile URL	82/416 (19.7%)	64	49.3%	TnI elevations were associated with increased risk of mortality (51.2% vs. 4.5%), ARDS (58.5% vs. 14.7%), AKI (8.5% vs. 0.3%), and coagulopathy (7.3% vs. 1.8%) TnI elevations were associated with increased risk of in-hospital mortality after multivariable adjustment (adjusted HR: 3.41; 95% CI: 1.62-7.16)
Guo et al. (3)	China	187	Serum levels of TnT >99th percentile URL	52/187 (27.8%)	58.5	48.7%	Associated with increased risk of mortality (59.6% vs. 8.9%), ARDS (57.7% vs. 11.9%), VT/VF (17.3% vs. 1.5%), AKI (36.8% vs. 4.7%), and coagulopathy (65.8% vs. 20.0%) Mortality associated with myocardial injury was increased among those with pre-existing cardiovascular disease
Zhou et al. (5)	China	191	High-sensitivity cardiac TnI >28 pg/ml	24/45 (17%)	56	62%	Associated with increased risk of in-hospital mortality (univariate OR: 80.07; 95% CI: 10.34-620.36)

*Mean or median, as reported.

AKI = acute kidney injury; ARDS = acute respiratory distress syndrome; CI = confidence interval; COVID-19 = coronavirus disease 2019; HR = hazard ratio; OR = odds ratio; TnI = troponin I; URL = upper reference limit; VF = ventricular fibrillation; VT = ventricular tachycardia.

Giustino et al. JACC. Oct 2020. 76(17): 2011-23

How do we Risk Stratify?

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FIGURE 2 Risk Stratification of ACS and Venous Thromboembolism With COVID-19

	LOW-RISK COVID-19	HIGH-RISK COVID-19†
HIGH-RISK ACS OR VTE*	**For ACS:** • GDMT per ACS algorithm • Urgent/emergent angiography and intervention • Consider need and safety of hemodynamic support and monitoring **For VTE:** • Anticoagulant therapy • If recurrent symptoms or deterioration, consider systemic thrombolysis or potentially catheter-directed therapy as an alternative • Consider need and safety of hemodynamic support and monitoring‡	**For ACS:** • GDMT per ACS algorithm • Consider emergent TTE • Urgent/emergent angiography and intervention vs. systemic fibrinolysis • Consider need and safety of hemodynamic support and monitoring in select patients **For VTE:** • Anticoagulant therapy • Consider systemic fibrinolysis • Catheter-directed or surgical therapies in case not suitable for systemic fibrinolysis • Consider need and safety of hemodynamic support and monitoring
LOW/INTERMEDIATE RISK ACS OR VTE	**For ACS:** • GDMT per ACS algorithm • Angiography and intervention only if recurrent/persistent symptoms or decompensation **For VTE:** • Anticoagulant therapy • Catheter-directed or surgical therapies only if recurrent/persistent symptoms or decompensation	**For ACS:** • GDMT per ACS algorithm • Other therapies reserved for select cases such as those with significant recurrent/persistent symptoms or decompensation **For VTE:** • Anticoagulant therapy • Other therapies reserved for select cases such as those with significant recurrent/persistent symptoms or decompensation

Proposed algorithm to risk stratify patients based on severity of acute coronary syndromes (ACS), VTE, and COVID-19 presentations. *High-risk ACS refers to patients with hemodynamic instability, left ventricular dysfunction or focal wall motion abnormality, or worsening or refractory symptoms. High-risk VTE refers to patients with pulmonary embolism who are hemodynamically unstable, evidence of right ventricular dysfunction or dilatation, or worsening of refractory symptoms. †High-risk COVID-19 refers to patients with high suspicion for or confirmed COVID-19, including individuals with high viral load, symptomatic with coughing or sneezing or other respiratory symptoms, and at risk for requiring intubation and aerosolizing viral particles. ‡Hemodynamic support includes intra-aortic balloon pump, percutaneous ventricular assist device, and extracorporeal membrane oxygenation. Hemodynamic monitoring refers to Swan-Ganz catheter for invasive hemodynamic assessment. For potential drug-drug interactions, please refer to Tables 3 and 4. GDMT = guideline-directed medical therapy; TTE = transthoracic echocardiogram; other abbreviations as in Figure 1.

Arrhythmias

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- Substantial increase in incidence in those with myocardial injury (type 1 and 2 MI)
- Additional mechanisms of potentiation
  - Electrical instability from QT prolongation related to metabolic derangements (hypokalemia, hypomagnesemia) and therapeutic strategies (chloroquine, previously hydroxychloroquine, azithromycin)
  - Hyperinflammatory state and cytokine upregulation → prolongation of ventricular action potential duration, cardiac sympathetic hyperactivation

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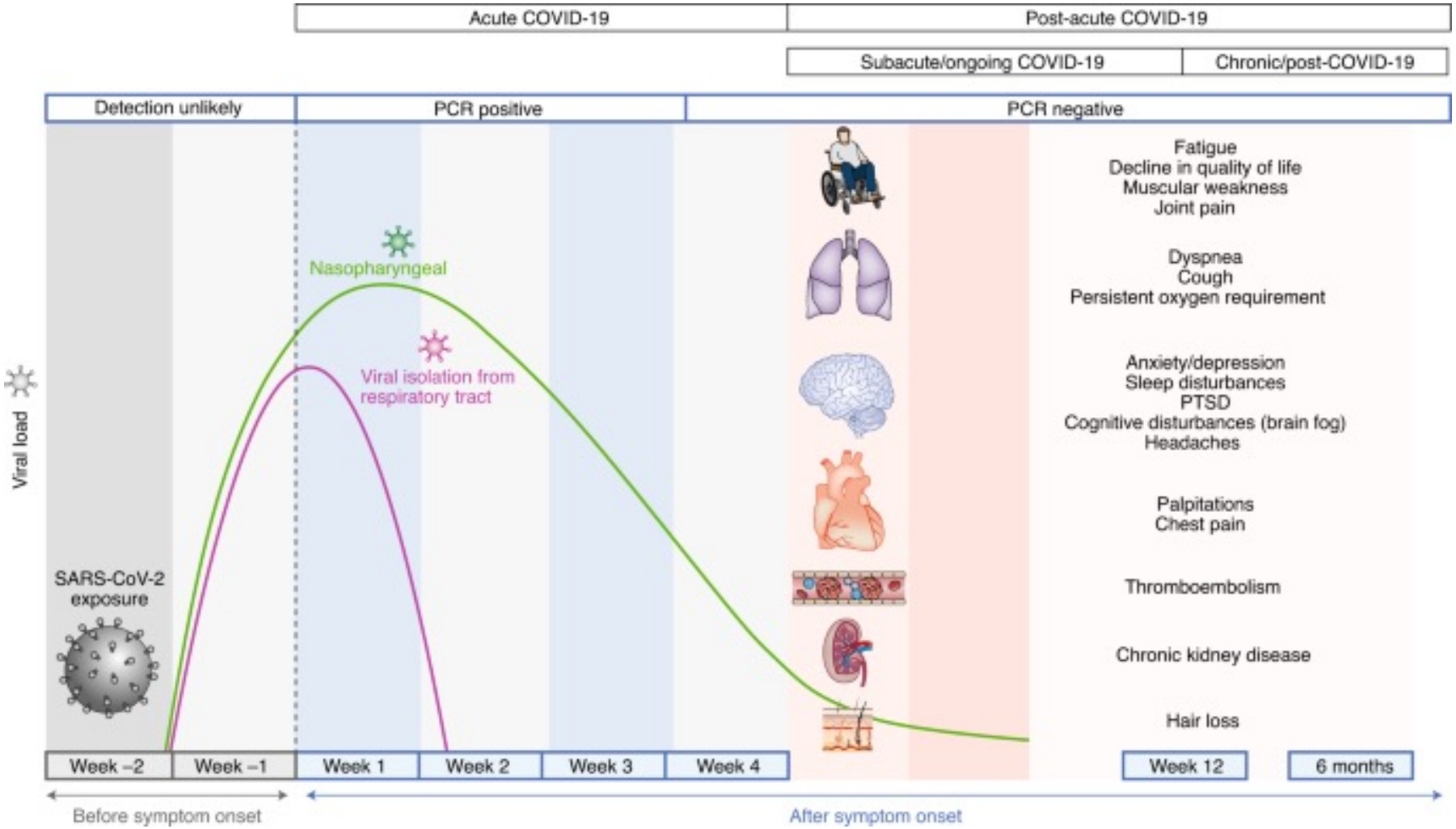
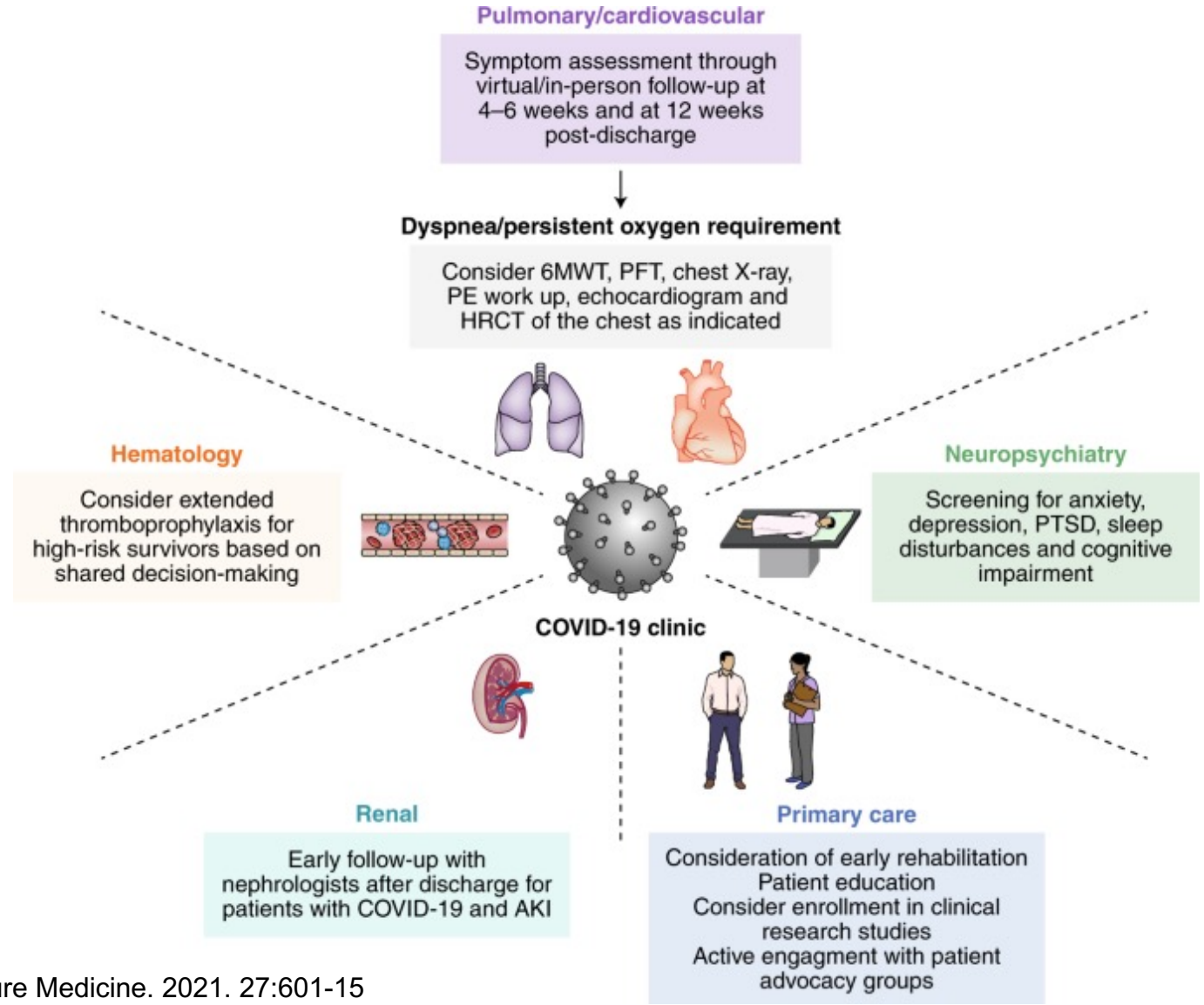
PASC (Post Covid Syndrome) & Cardiovascular Sequelae

Post-Acute Sequelae of SARS-CoV2 Infection (PASC)
(Post-COVID Syndrome)



Nalbandian A et al. Nature Medicine. 2021. 27:601-15

Post-COVID Syndrome Management



Nalbandian A et al. Nature Medicine. 2021. 27:601-15

Potential Mechanisms

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- Chronic fatigue
  - Chronic inflammation – though no association between pro-inflammatory markers and long-term fatigue (only 1 study)
  - Congestion of the glymphatic system – caused by olfactory neuron damage → increased resistance to CSF drainage through cribriform plate → increased toxins in the CNS
  - Cell-mediated immune responses → hypometabolism in frontal lobe and cerebellum
  - Direct SARS-CoV-2 infection of skeletal muscle → damage, weakness, inflammation to muscle fibers and neuromuscular junctions
  - Negative psychosocial and social factors
  - Overlap with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)?

Crook et al. BMJ. 2021 Jul 26;347

Long COVID-19 Cardiovascular Complications

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CARDIOVASCULAR SIGNS & SYMPTOMS	CHARACTERISTICS
Exertional intolerance	▪ Inability to do even minimal tasks ▪ Limited by fatigue, palpitations, lightheadedness
Tachycardia	▪ Discordant to exertional intensity ▪ Accentuated postural tachycardia ▪ Inappropriate sinus tachycardia
Chest pain	▪ Exertional ▪ Non-exertional
Lightheadedness, orthostasis, syncope	▪ Positional
Hypertension	▪ Elevated BP in normotensive individuals ▪ Exaggerated BP in previously hypertensive individuals

Cardiac Evaluation

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SYMPTOMS	SUGGESTED CARDIAC TESTING
Chest pain	ECG, echocardiogram Labs: hsTnT, D-dimer, ESR, CRP +/- stress testing, cardiac MRI
Shortness of breath	ECG, echocardiogram Labs: hsTnT, D-dimer, ESR, CRP +/- stress testing
Exertional intolerance	ECG, echocardiogram Labs: hsTnT, D-dimer, ESR, CRP +/- Tilt table, ambulatory rhythm monitor
Orthostasis, lightheadedness	
Palpitations, inappropriate tachycardia	
Syncope	

Long COVID-19 and POTS

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CASE REPORT

BEGINNER

CLINICAL CASE SERIES

Long-Haul Post–COVID-19 Symptoms Presenting as a Variant of Postural Orthostatic Tachycardia Syndrome

The Swedish Experience

Madeleine Johansson, MD, PhD,[a,b,*] Marcus Ståhlberg, MD, PhD,[c,d,*] Michael Runold, MD, PhD,[e] Malin Nygren-Bonnier, PhD, PT,[f,g] Jan Nilsson, MD, PhD,[a] Brian Olshansky, MD,[h] Judith Bruchfeld, MD, PhD,[i,j,†] Artur Fedorowski, MD, PhD[a,b,†]

- Case series of 3 Swedish patients diagnosed with POTS 3 months after acute COVID-19 infection
- Treatment strategies:
  - Supportive (compression stockings, hydration & electrolyte repletion)
  - Medications: propranolol, ivabradine, pyridostigmine

TABLE 1 Diagnostic Criteria of POTS

Diagnostic Criteria
Sustained heart rate increment of not less than 30 beats/min or above 120 beats/min within 10 min of active standing or head-up tilt. For individuals who are younger than 19 years the required increment is at least 40 beats/min.
Absence of orthostatic hypotension (i.e., sustained systolic blood pressure drop of not less than 20 mm Hg).
Reproduction of spontaneous symptoms such as light-headedness, palpitations, tremulousness, generalized weakness, blurred vision, and fatigue. In some patients, tachycardia may evoke vasovagal syncope corresponding to spontaneous attacks from patient's history.
History of chronic orthostatic intolerance and other typical POTS-associated symptoms (for at least 6 months (1)).
Absence of other conditions provoking sinus tachycardia such as anxiety disorders, hyperventilation, anemia, fever, pain, infection, dehydration, hyperthyroidism, pheochromocytoma, use of cardioactive drugs (sympathomimetics, anticholinergics).

This table has been endoresed by the American Academy of Neurology, the American Autonomic Society, the American College of Cardiology, the American Heart Association, the European Federation of Autonomic Societies, the European Heart Rhythm Association, the European Society of Cardiology, and the Heart Rhythm Society. Adopted with permission from Fedorowski (1).

POTS = postural orthostatic tachycardia syndrome.

Long COVID-19 & POTS

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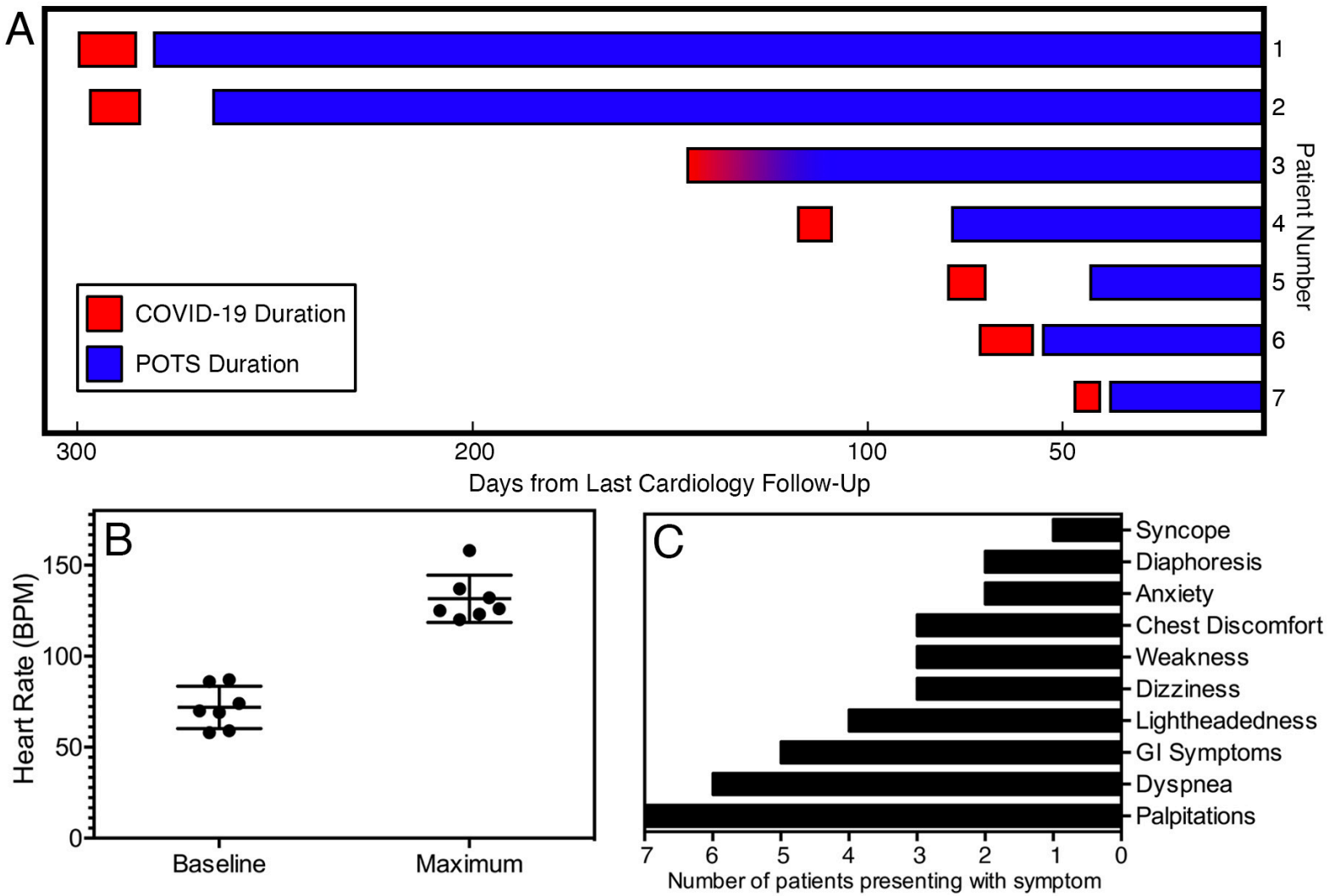
TABLE 3 Typical Clinical Presentation of POTS

Cardiovascular Symptoms (Pathognomonic)	
Cardiovascular system	Main: orthostatic intolerance, orthostatic tachycardia, palpitations, dizziness, lightheadedness, (pre-)syncope, exercise intolerance Other frequent symptoms: dyspnea, chest pain/discomfort, acrocyanosis, Raynaud phenomenon, venous pooling, limb edema
Noncardiovascular Symptoms (Accompanying)	
General symptoms	General deconditioning, chronic fatigue, exhaustion, heat intolerance, fever, debility, bedridden
Nervous system	Headache/migraine, mental clouding ("brain fog"), cognitive impairment, concentration problems, anxiety, tremulousness, light and sound sensitivity, blurred/tunnel vision, neuropathic pain (regional), sleeping disorders, involuntary movements
Musculoskeletal system	Muscle fatigue, weakness, muscle pain
Gastrointestinal system	Nausea, dysmotility, gastroparesis, constipation, diarrhea, abdominal pain, weight loss
Respiratory system	Hyperventilation, bronchial asthma, shortness of breath
Urogenital system	Bladder dysfunction, nocturia, polyuria
Skin	Petechiae, rashes, erythema, telangiectasias, abnormal sudomotor regulation, diaphoresis, pallor, flushing

Adapted with permission from Fedorowski (1).

POTS = postural orthostatic tachycardia syndrome.

Johansson M et al. JACC: Case Reports. Mar 10 2021



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Cleveland Clinic: Case Series

- 7 young, active (5 athletes) patients, predominantly female
- Average time to POTS onset: 73 days
- Treatment strategies: supportive, medications (metoprolol, ivabradine, midodrine, IVIG infusion)

Figure 1. Summary of clinical data for seven patients presenting to outpatient cardiology clinic who subsequently diagnosed with POTS. **A.** Timeline of COVID-19 (red) and POTS (blue) onset and duration. While six patients had clear resolution of COVID-19 symptoms before developing symptoms of POTS, Patient 3 seemed to develop POTS symptoms while still suffering from initial COVID-19 infection. **B.** Tilt table baseline and maximum heart rate represented in categorical scatter plot depicting individual (dot), mean and SD values. **C.** Symptoms patients reported on initial presentation to cardiology outpatient clinic.

Clinical Autonomic Research (2021) 31:365–368
https://doi.org/10.1007/s10286-021-00798-2

REVIEW ARTICLE

Check for updates

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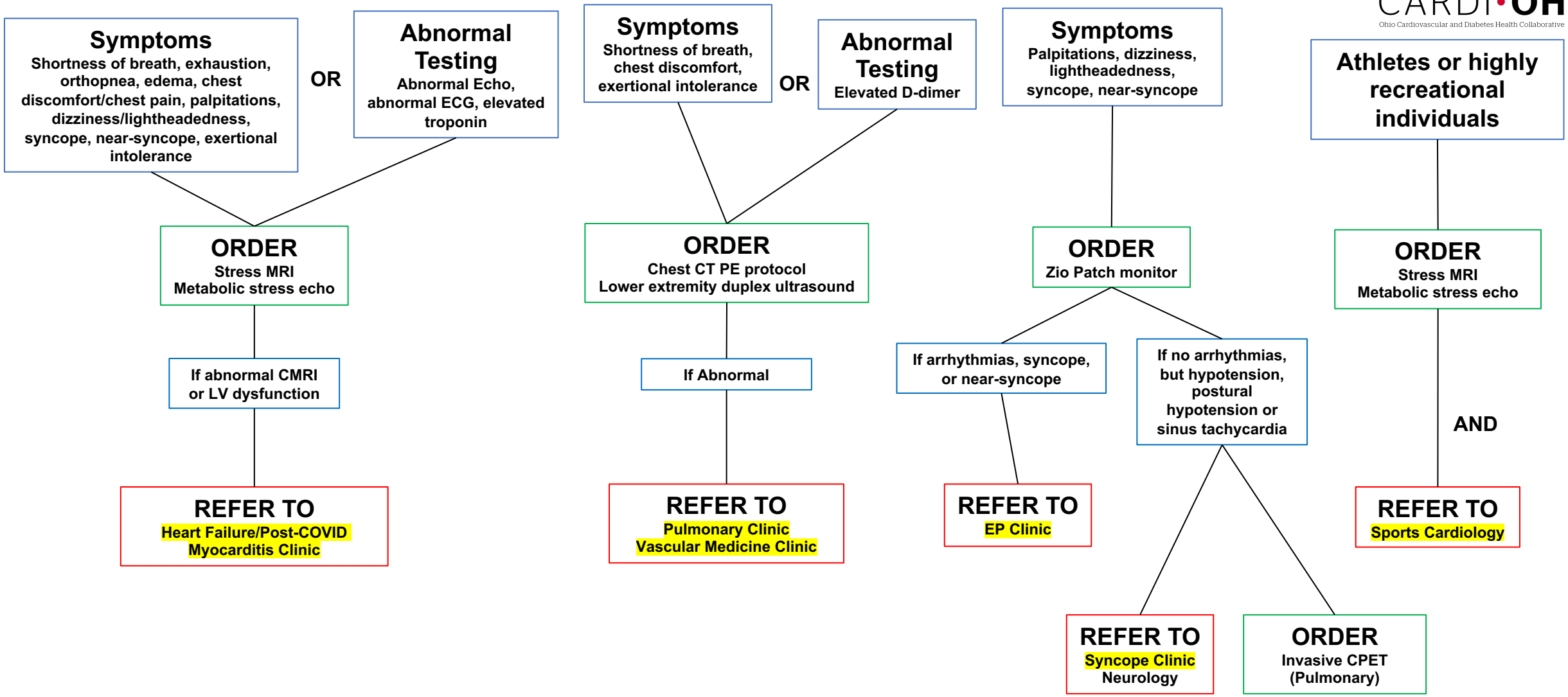
Long-COVID postural tachycardia syndrome: an American Autonomic Society statement

Satish R. Raj[1,2] · Amy C. Arnold[2,3] · Alexandru Barboi[4] · Victoria E. Claydon[5] · Jacqueline K. Limberg[6] · Vera-Ellen M. Lucci[5] · Mohammed Numan[7] · Amanda Peltier[8] · Howard Snapper[9] · Steven Vernino[10] on behalf of the American Autonomic Society

- Long-COVID Symptoms
  - Breathlessness, palpitations, chest discomfort, fatigue, pain, cognitive impairment ("brain fog"), sleep disturbance, orthostatic intolerance, peripheral neuropathy, abdominal discomfort, nausea, diarrhea, joint and muscle pains, symptoms of anxiety/depression, skin rashes, sore throat, headache, earache, tinnitus
- Long-COVID POTS
  - Long-COVID symptoms + excessive orthostatic tachycardia (HR increase > 30 bpm in adults, > 40 bpm in 12-19-year-olds, within 10 min of assuming upright posture in the absence of orthostatic hypotension, with associated symptoms of orthostatic intolerance for at least 3 months

Cardiovascular Evaluation after COVID-19



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Athletes with Long COVID-19 Symptoms

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CARDIOVASCULAR SIGNS & SYMPTOMS	SPORTS RECOMMENDATIONS
Exertional intolerance	▪ Negative cardiac testing → return to sports via graded protocol, without restriction ▪ Pulmonary evaluation
Tachycardia	▪ Negative cardiac testing, including rhythm monitor → return to sports via graded protocol, without restriction ▪ Consider autonomic testing, evaluation for DVT/PE
Chest pain	▪ Negative cardiac testing (+/- cardiac MRI) → return to sports via graded protocol without restriction ▪ If (+) myocarditis/pericarditis: at least 3-6 months restriction to low-intensity exercise +/- treatment if LV systolic dysfunction, pericardial enhancement ▪ If (+) pleuritic → D-dimer or CTPA
Lightheadedness, orthostasis, syncope	▪ If (+) tilt table → cardiac rehab for POTS (modified for athletes) ▪ Supportive & medical therapy (ivabradine, beta blocker, pyridostigmine)
Hypertension	▪ Treat as needed

Post-COVID Treatment Strategies

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- Exercise re-training
  - Graded protocol
  - POTS cardiac rehab
- Medications
  - Arrhythmias – Beta blockers, ivabradine
  - POTS - Acetylcholinesterase inhibitors – pyridostigmine (mestinon)
  - Autonomic dysfunction – Anticonvulsants (gabapentin, pregabalin), beta blockers
  - Chronic myocarditis – dependent upon LVEF
- CBT, group therapy

COVID-19 Clinical Cardiology Care Path

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Cleveland Clinic | reCOVer CLINIC

69% with cardiovascular symptoms

Referral
Direct/Self Referral
ReCOVer Clinic
Outside provider

Intake/Evaluation
History & Exam
ECG, Echo
Labs: hsTnT, TnT, NT pro BNP, ESR, CRP, D-Dimer

Refer to
ReCOVer Clinic for non-cardiac subspecialty referrals
Cardiac Subspecialty Clinic

Follow Up
Directly with cardiac MD or physician extender

Tests to Consider per Standard of Care
Cardiac MRI
Stress testing, (i) CPET
Rhythm monitoring
Tilt Table, Autonomic Testing

reCOVer Clinic

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What can I expect at my first appointment?

- After you schedule a new appointment, you'll receive a questionnaire through MyChart to fill out (preferably) before your appointment.
- Your reCOVer appointment will be in-person or virtual. It will last about 60 minutes.
- Your healthcare provider will take an extensive history and do a physical exam.
- Following your visit, you will be scheduled for several tests and lab work. These will evaluate you for ongoing symptoms.

What type of tests can I expect?

Everyone who is evaluated at the reCOVer Clinic will have:

- A chest X-ray.
- Pulmonary (lung) function tests.
- A 6-minute walk to detect low oxygen.
- An electrocardiogram (EKG or ECG) and echocardiogram (echo) to evaluate how your heart functions.
- A full physical therapy and occupational therapy evaluation.
- Blood work drawn for nutritional, kidney, heart muscle tests.

Appointments & Locations

How can I get an appointment at the reCOVer Clinic?

If you'd like to be seen at the reCOVer Clinic, discuss your ongoing symptoms with your Cleveland Clinic provider. They'll put in an electronic order for you to be seen in the COVID reCOVer Clinic. Our team will then reach out to you to schedule an appointment at one of our locations.

First appointments are usually scheduled virtually or in-person at Independence Family Health Center. We are expanding to offer our services at several locations. When you are contacted by our scheduling team, they'll arrange your first appointment at one of the following locations most convenient for you.

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Telehealth and Cardiovascular Care

A Virtual Era Brought on by a Pandemic

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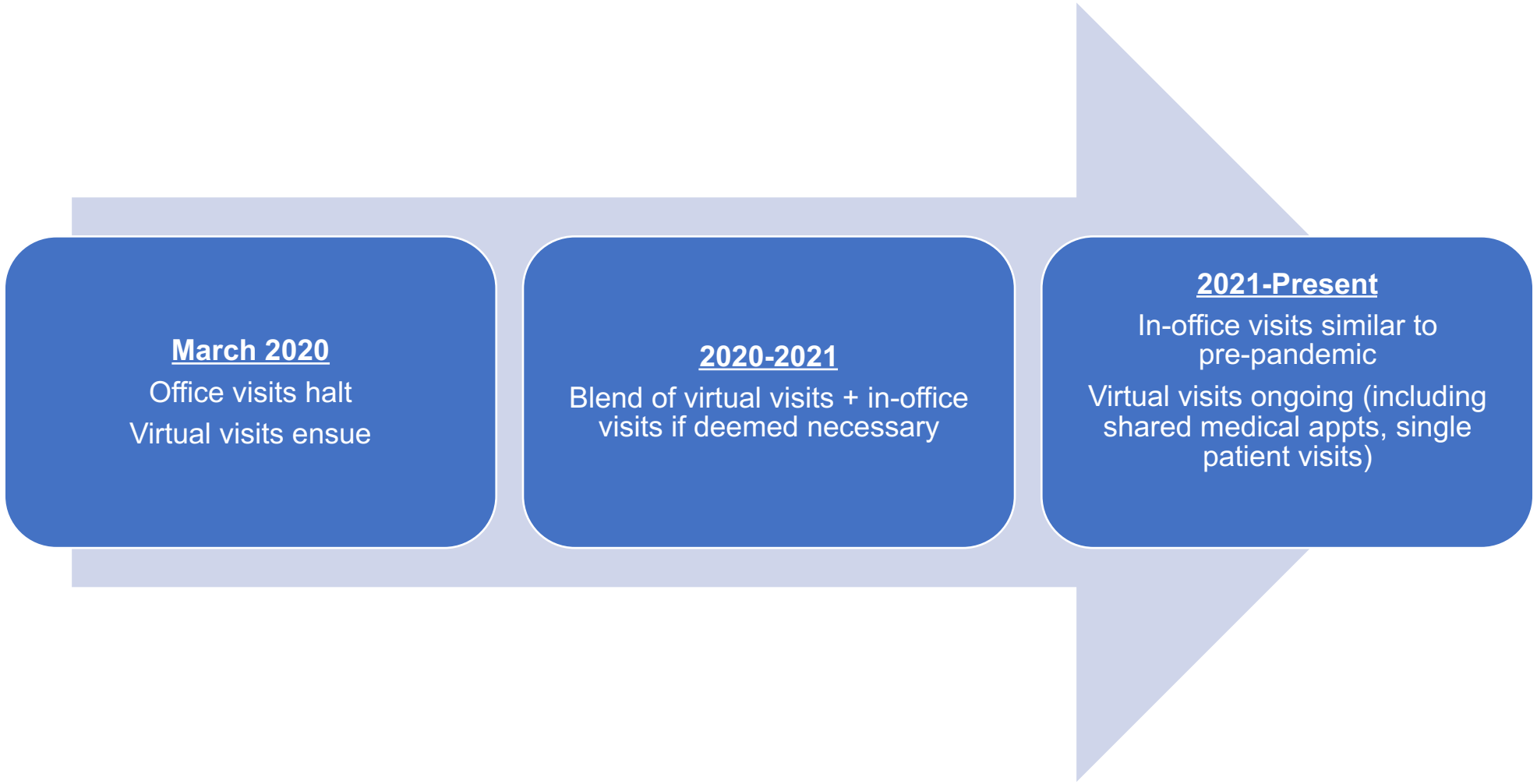

The New York Times

PERSONAL HEALTH

Pandemic Lessons in Improving the Medical System

The pandemic may prompt American medicine to become less expensive, more efficient and more effective at protecting people's health.

Doctors and Patients Turn to Telemedicine in the Coronavirus Outbreak

The use of virtual visits climbs as a way of safely treating patients and containing spread of the infection at hospitals, clinics and medical offices.

Telemedicine Is a Tool. Not a Replacement for Your Doctor's Touch.

The New York Times

Biden Administration Seeks to Expand Telehealth in Rural America

New funding will allow more medical appointments to take place via video in rural communities, where some of the nation's oldest and sickest patients live.

Increased Use of Telehealth for Opioid Use Disorder Services During COVID-19 Pandemic Associated with Reduced Risk of Overdose

Aug 31, 2022

New HHS Study Shows 63-Fold Increase in Medicare Telehealth Utilization During the Pandemic

Dec 03, 2021

Telehealth in the U.S.

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- Types of telehealth
  - Synchronous – direct “real-time” patient-provider interaction
  - Asynchronous – emails, instructions, image/result review
  - Remote patient monitoring – device interrogations, glucose meters, BP monitors, oximeters
- Advantages
  - Increased access
  - Offline communication → efficient care
  - Shared medical appointments
- Disadvantages
  - Lack of health equity if patients lack resources for telehealth
  - No physical exam
  - Reimbursement

Telehealth Purposes

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Table 3. Various purposes of telehealth use during the COVID-19 pandemic (N=543).

Purpose	Number of articles, n (%)
Clinical care	270 (49.7)
Follow-up	83 (15.3)
Medical education	54 (9.9)
Diagnosis	39 (7.2)
Rehabilitation	24 (4.4)
Health communication	20 (3.7)
Triage	19 (3.5)
Surveillance or contact tracing	16 (2.9)
Research	12 (2.2)
Health care worker wellbeing	6 (1.1)

Predominant Specialties:

- Internal medicine – endocrinology, oncology, geriatrics, cardiovascular
- Preventive medicine
- Psychiatry
- Surgery
- Neurology

Doraiswamy et al. J Med Internet Res. 2020 Dec 1; 22(12)

Telehealth & Cardiac Care

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- Symptom follow up
- Medication education and titration
- Blood pressure management
- Counseling
  - Diet and exercise
  - Prevention
- Pharmacist integration with patient visit/care
- Shared visits with family members
- Increased access to rural patients, geriatric patients, athletes and younger individuals who lack transportation/far from campus
- Shared medical appointments

Post-Covid Syndrome & Telehealth

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- Shared medical appointments
  - POTS
  - Wellness
- Increased access
- Exercise recommendations
- Close symptom follow up
- Medication trials and titrations
- Counseling
- Psychosocial support

Next Steps

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- Continue to characterize mechanisms of cardiac involvement with acute and chronic COVID-19 infection
- Understand mechanism(s) of post-COVID syndrome to ultimately develop a treatment that prevents/reduces duration of post-COVID syndrome
- Expand telehealth beyond the pandemic and work towards health equity – address the “digital divide” and develop access points for those who lack resources for virtual visits and are unable to come for in-office visit

In Summary

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- Suspected mechanism for cardiovascular impact of SARS-CoV-2: cytokine storm precipitating endothelial dysfunction, microvascular thrombosis, and multiorgan failure
- Risk stratification by 1) COVID-19 severity and 2) severity of cardiovascular comorbidities may be helpful in risk stratification for acute coronary syndrome and venous thromboembolism
- The exact mechanism(s) for PASC remain unclear though may include: chronic inflammation, glymphatic congestion, cell-mediated immune responses, direct viral infection of skeletal muscle
- Cardiovascular-PASC symptoms may correlate to autonomic dysfunction (e.g. POTS)
- Telehealth utilization for PASC has provided a means for close clinical follow-up, increased access to care, timely medication titrations, and psychosocial support via counseling (individual and group)

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Thank You

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Audience Question and Answer

Amy Zack, MD

Case Western Reserve University School of Medicine

Speakers

REMINDER:
Submit questions using the 'Q&A' feature

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Tamanna K. Singh, MD
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University

Amy Zack, MD (Moderator)
Case Western Reserve University

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Next Steps and Wrap Up

Shari Bolen, MD, MPH
Case Western Reserve University School of Medicine

CME Reminder

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- Registration is required for CME credit:

URL in chat window **OR** Use QR Code

We Want to Hear from You!

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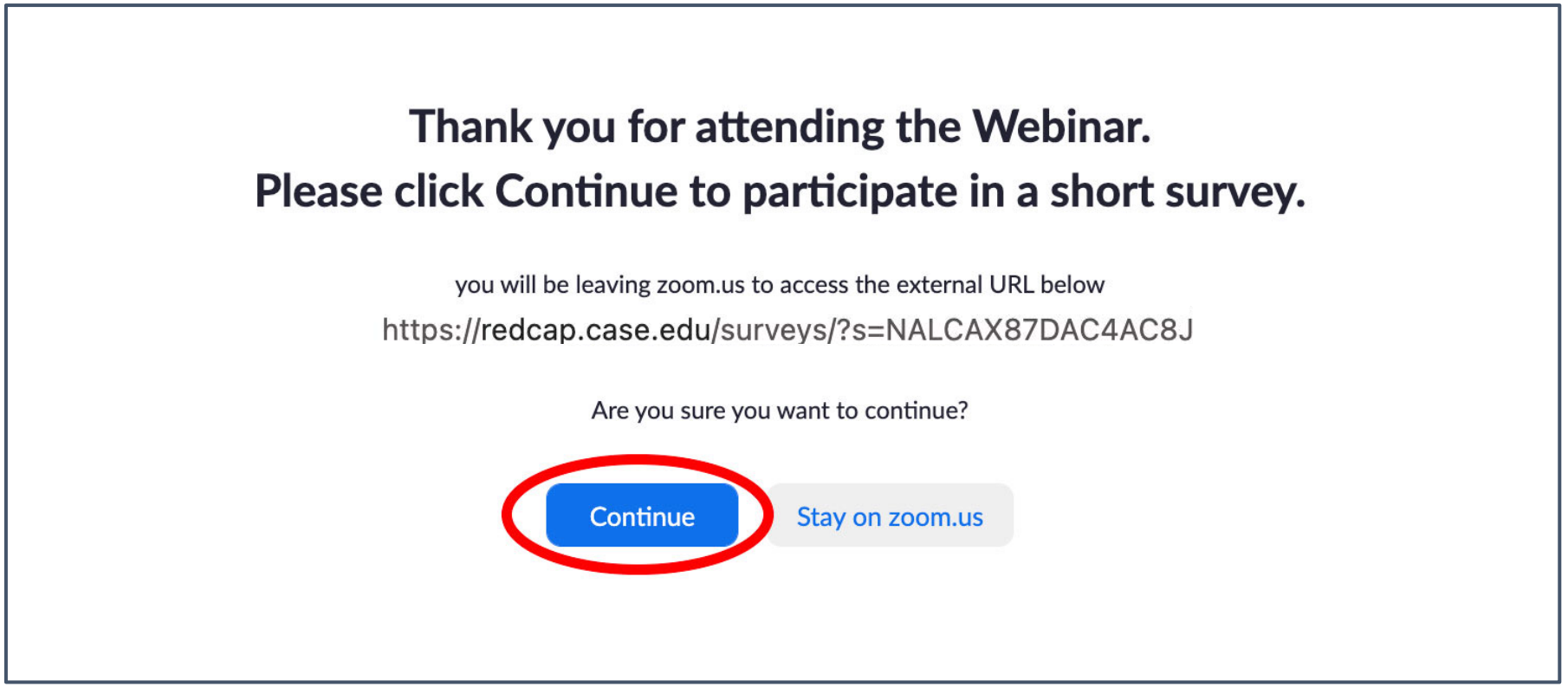
Please complete a brief evaluation of the webinar.



Hit the **Continue** button in your new browser tab to access the evaluation survey.
The survey link will also be emailed to you.

Spring 2023 ECHO Clinic

Innovations in Diabetes and Cardiovascular Health

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Project ECHO®

Date: Thursdays, 8 - 9 a.m. ET
January 12 to March 30, 2023

How Does it Work?

- Uses a hub-and-spoke model to share best practices with Ohio primary care teams
- Features expert-led didactic and interactive case-based learning discussions

Why Join?

- Professional development and continued learning
- Knowledge sharing with practices across the state
- Increased efficiency and joy in work
- Improved patient retention and health outcomes

Register at Cardi-OH.org
Free CME credits

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THANK YOU!

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