KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

Cardiac Implications due to COVID-19 Infections

dr. Agnes Lucia Panda, Sp PD, Sp JP (K)

OUTLINE

- Incidence and Mortality
- Pathogenesis/ Mechanism
- Therapeutic Implication
- The New Paradigm of Microangiopathy / Thrombosis

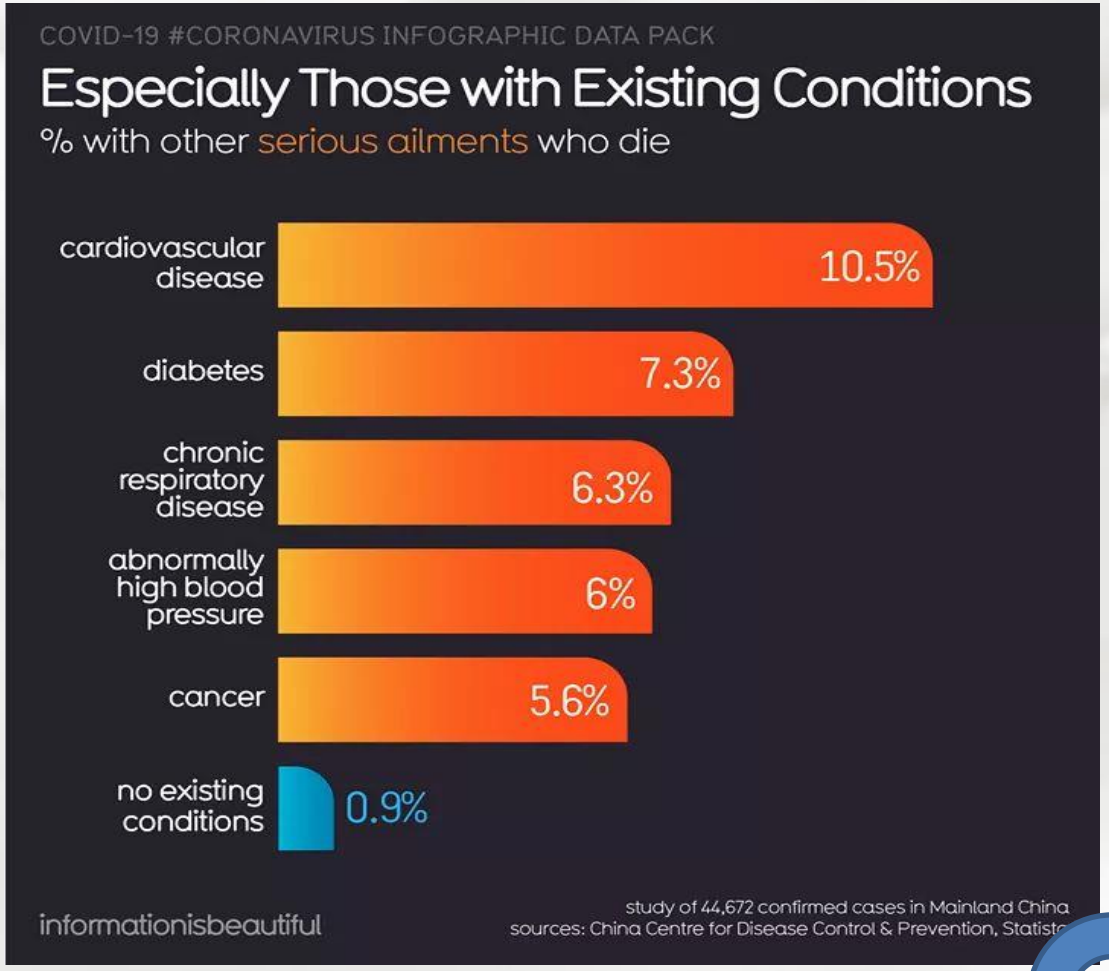
INCIDENCE AND MORTALITY

INTRODUCTION

Cardiovascular Disease (CVD) Manifestation:

Pre- existing (underlying) CVD

De- novo (no underlying) CVD



National Health Commission of China (NHC)

Cardiovascular Disease (CVD) symptoms:

- Palpitations
- Chest tightness

Breathless:

- Respiratory problem
- Cardiovascular disease

} ***BOTH***

Zheng YY, et al. Covid-19 and the cardiovascular disease. Cardiology 2020; 17:259-260

Pre Existing CVD Comorbidity

ELDERLY → Hypertension
Coronary Heart Disease
Chronic Kidney Disease, or
Diabetes → SEVERE SYMPTOMS

Severe symptoms of COVID-19:

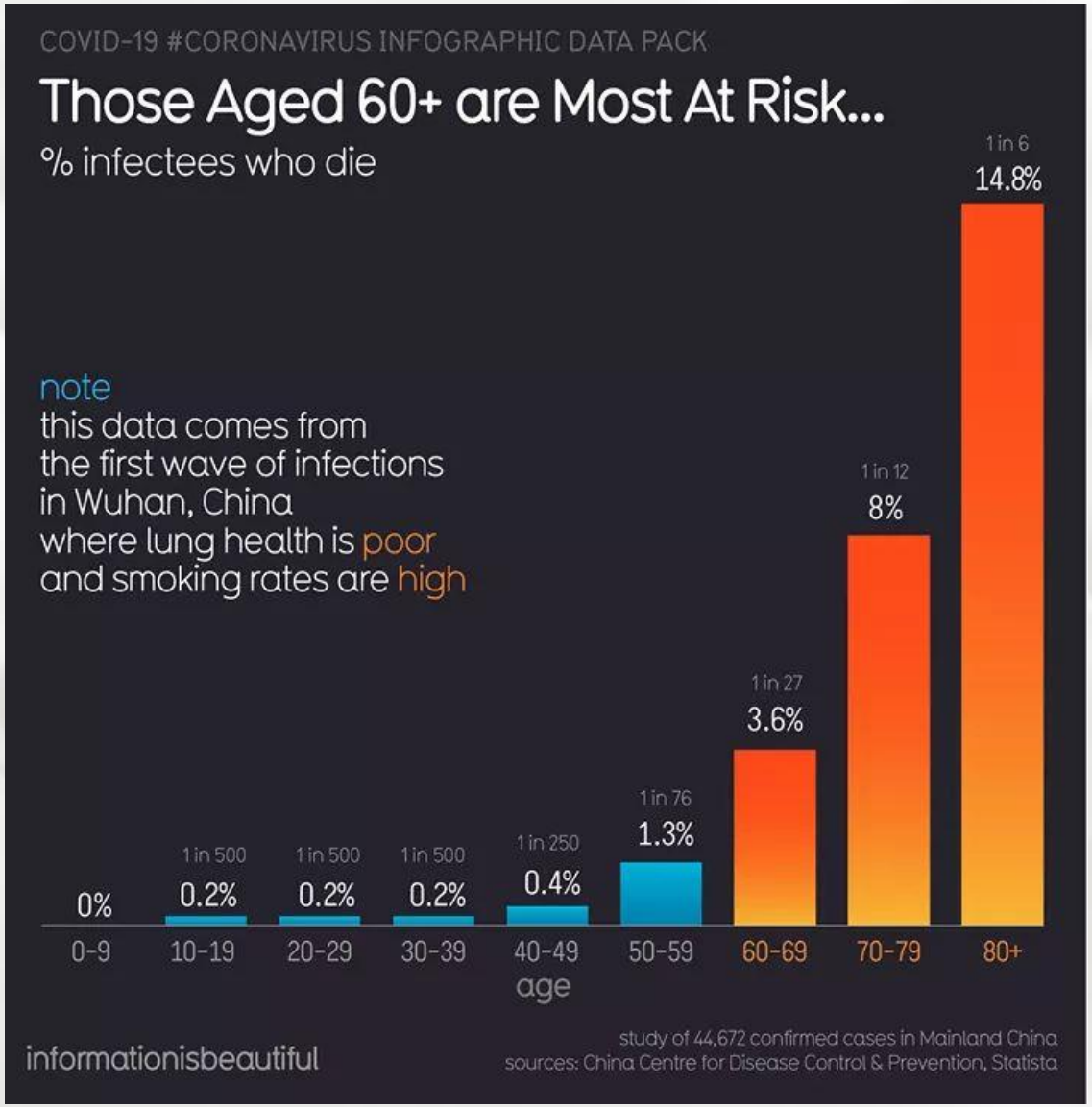
- 58% had Hypertension,
- 25% had Heart Disease
- 44% had Arrhythmia

Mortality data by NHC

35% history of hypertension

17% had a history of coronary heart disease

Underlying CVD → Aggravate Pneumonia
↑ Symptoms Severity



Fei Zhou, et al. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study.2020. The Lancet

De Novo– No Underlying CVD

- Myocardial Injury associated with the Covid-19 occurred in 5 of the first 41 patients COVID-19 in Wuhan

  ⇨ ↑ in high-sensitivity cardiac troponin I (hs-cTnI) levels

- Another report of 138 in Wuhan, 36 patients with severe symptoms were treated in the ICU

  ⇨ ↑ (CK)-MB level and hs-cTnI level

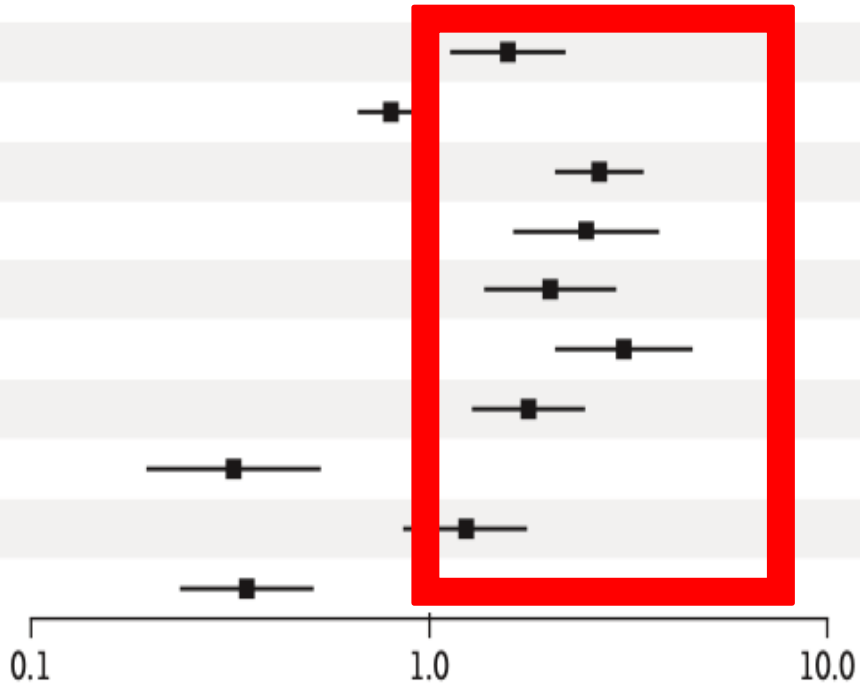
- First autopsy of a 53-year-old woman with chronic renal failure in Jinyintan Hospital showed acute MI (data not published; personal communication with a pathologist from the Chinese Academy of Science)

- **Washington:** 1/3 critically ill COVID-19 develop Cardiomyopathy

Tao Guo, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19).2020. JAMA Cardiol

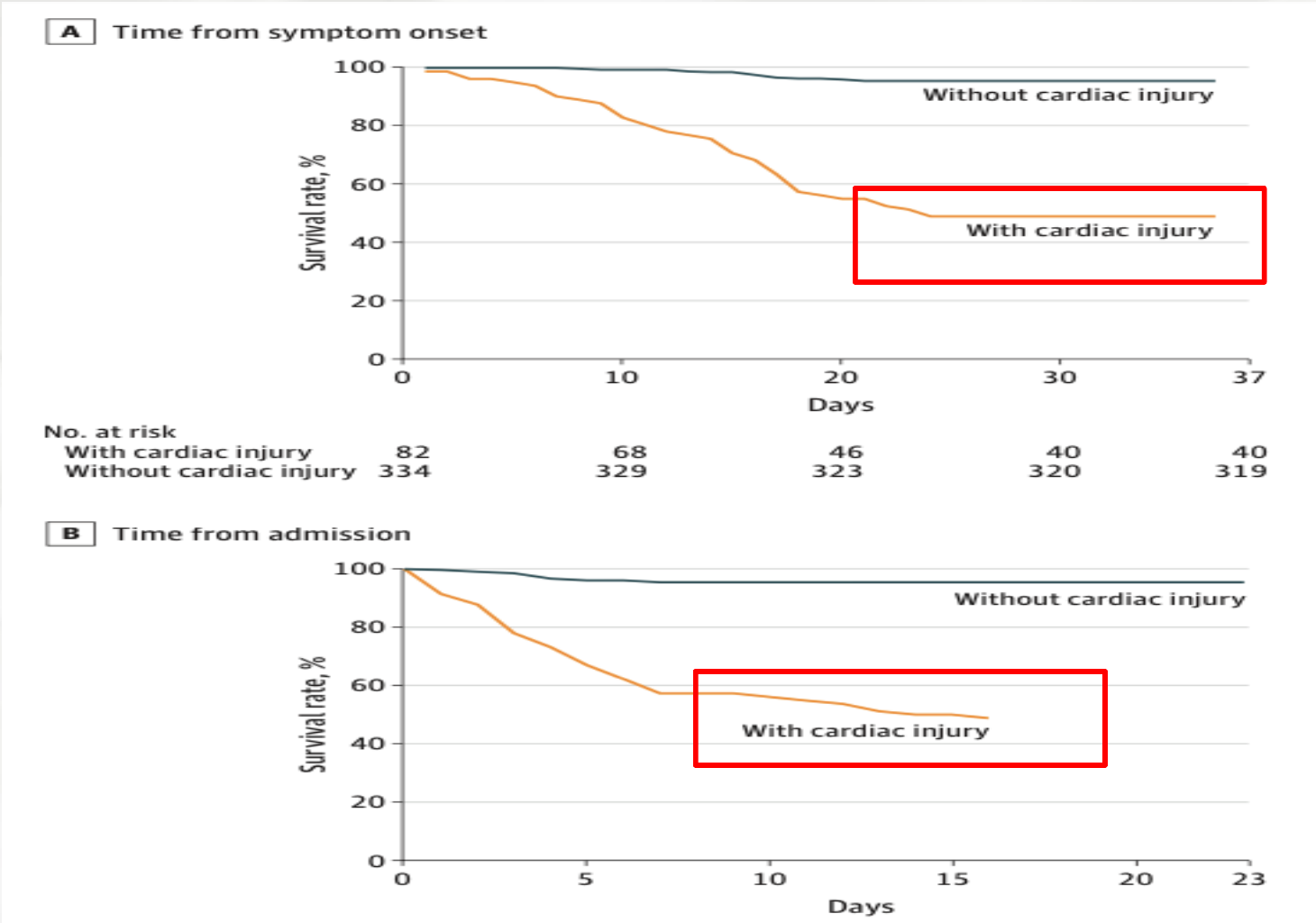
Predictor In Hospital Death

Risk Factor	Risk Factor Present	Risk Factor Absent	Odds Ratio (95% CI)
	no. of patients who died/total no. (%)		
>65 yr of age	147/1474 (10.0)	368/7436 (4.9)	1.93 (1.60–2.41)
Female sex	179/3571 (5.0)	336/5339 (6.3)	0.79 (0.65–0.95)
Coronary artery disease	103/1010 (10.2)	412/7900 (5.2)	2.70 (2.08–3.51)
Congestive heart failure	29/189 (15.3)	486/8721 (5.6)	2.48 (1.62–3.79)
Arrhythmia	35/304 (11.5)	480/8606 (5.6)	1.95 (1.33–2.86)
COPD	32/225 (14.2)	483/8685 (5.6)	2.96 (2.00–4.40)
Current smoker	46/491 (9.4)	469/8419 (5.6)	1.79 (1.29–2.47)
Receiving ACE inhibitor	16/770 (2.1)	499/8140 (6.1)	0.33 (0.20–0.54)
Receiving ARB	38/556 (6.8)	477/8354 (5.7)	1.23 (0.87–1.74)
Receiving statin	36/860 (4.2)	479/8050 (6.0)	0.35 (0.24–0.52)



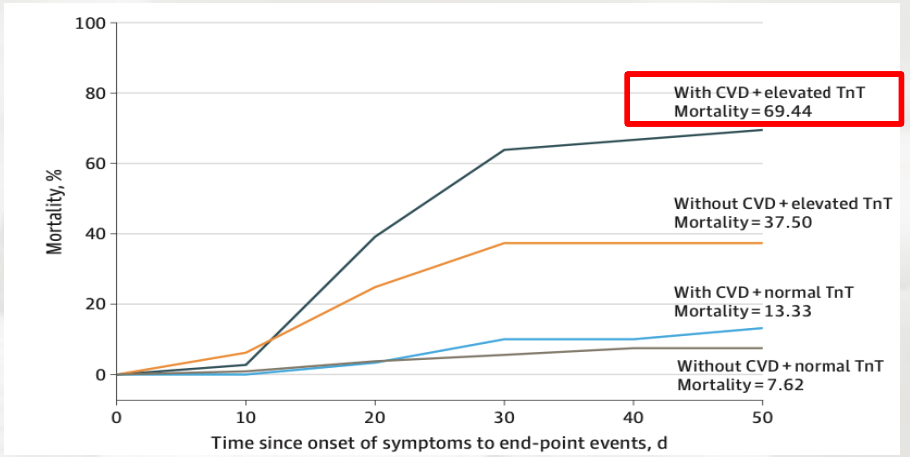
Shi S, Qin et al. Association of Cardiac Injury with Mortality in Hospitalized Patients With Covid-19 in Wuhan, China.2020. JAMA Cardiol.

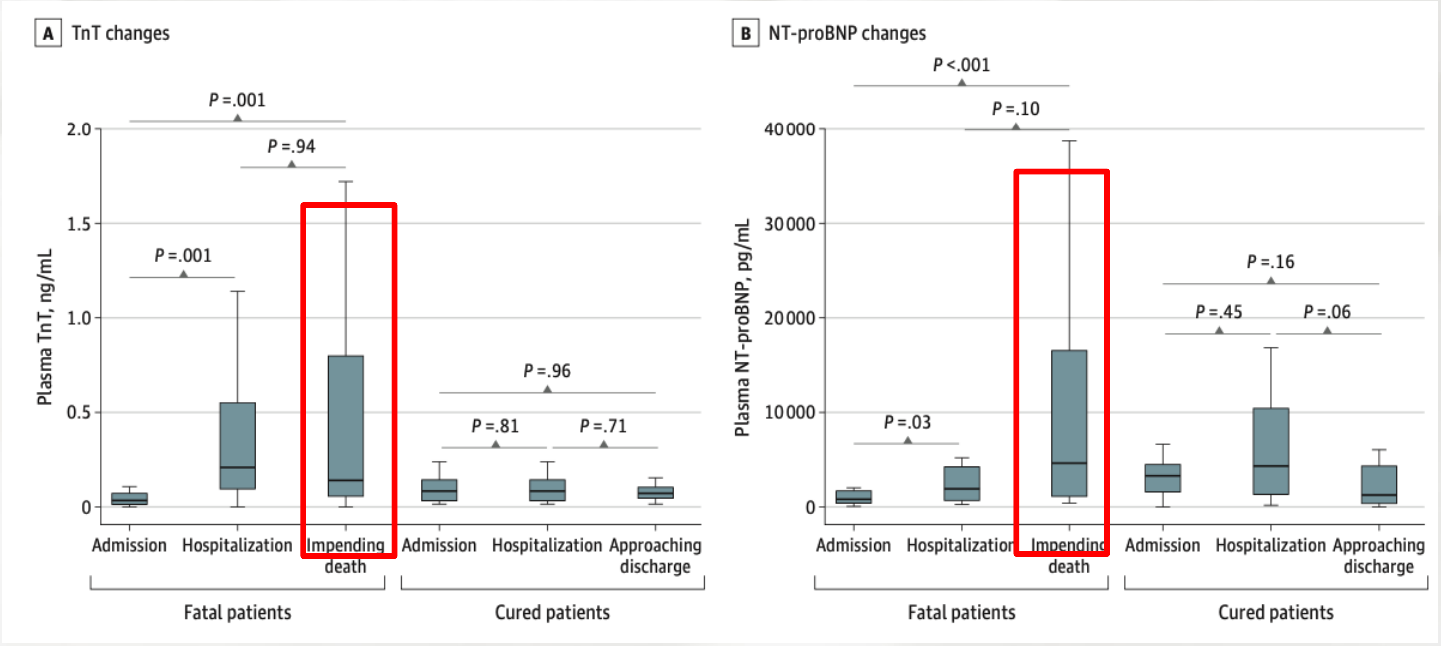
Mortality During Hospitalization Between Patients With vs. Without Cardiac Injury



Shi S, Qin et al. Association of Cardiac Injury with Mortality in Hospitalized Patients With Covid-19 in Wuhan, China.2020. JAMA Cardiol.

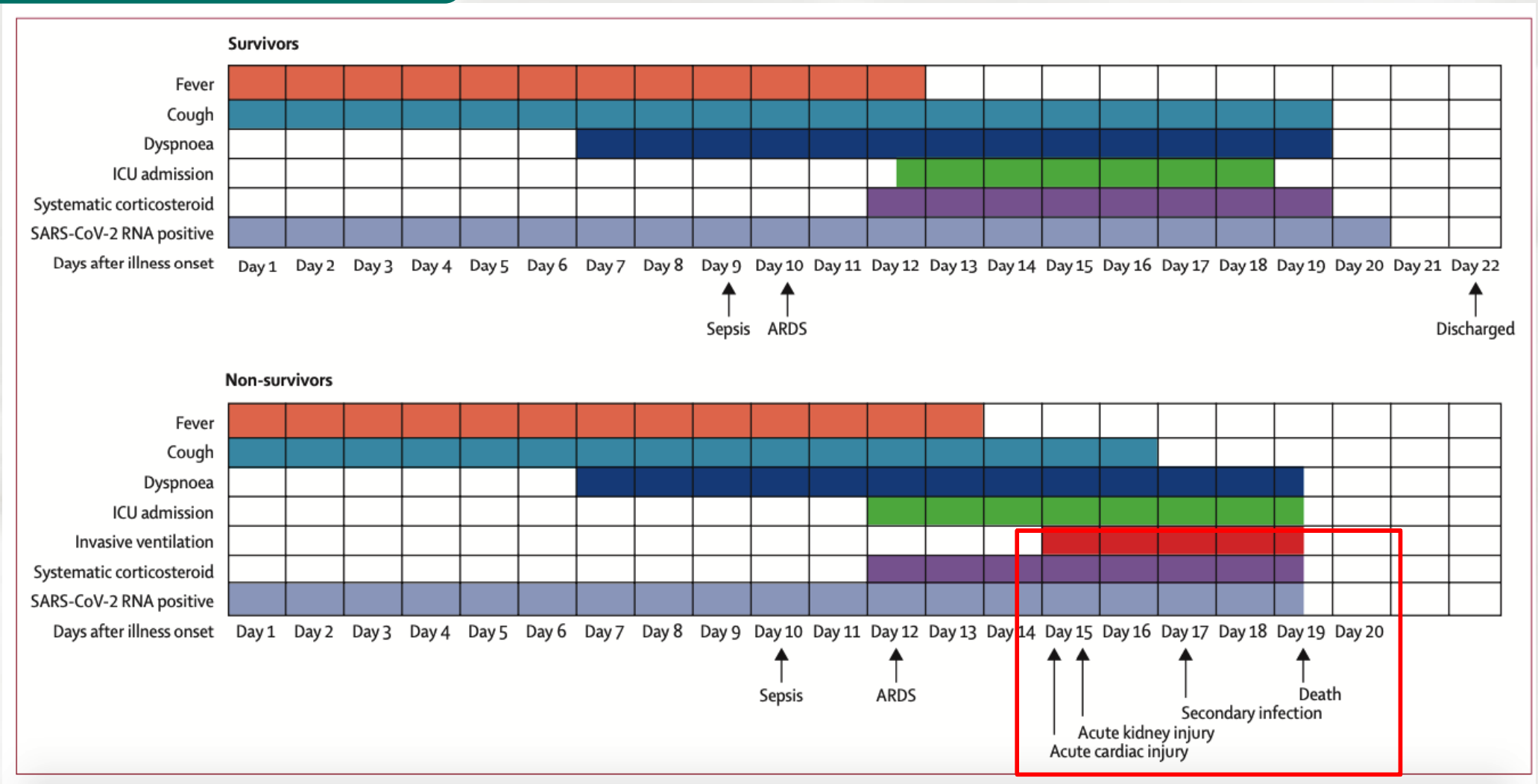
Mortality and Cardiac Marker



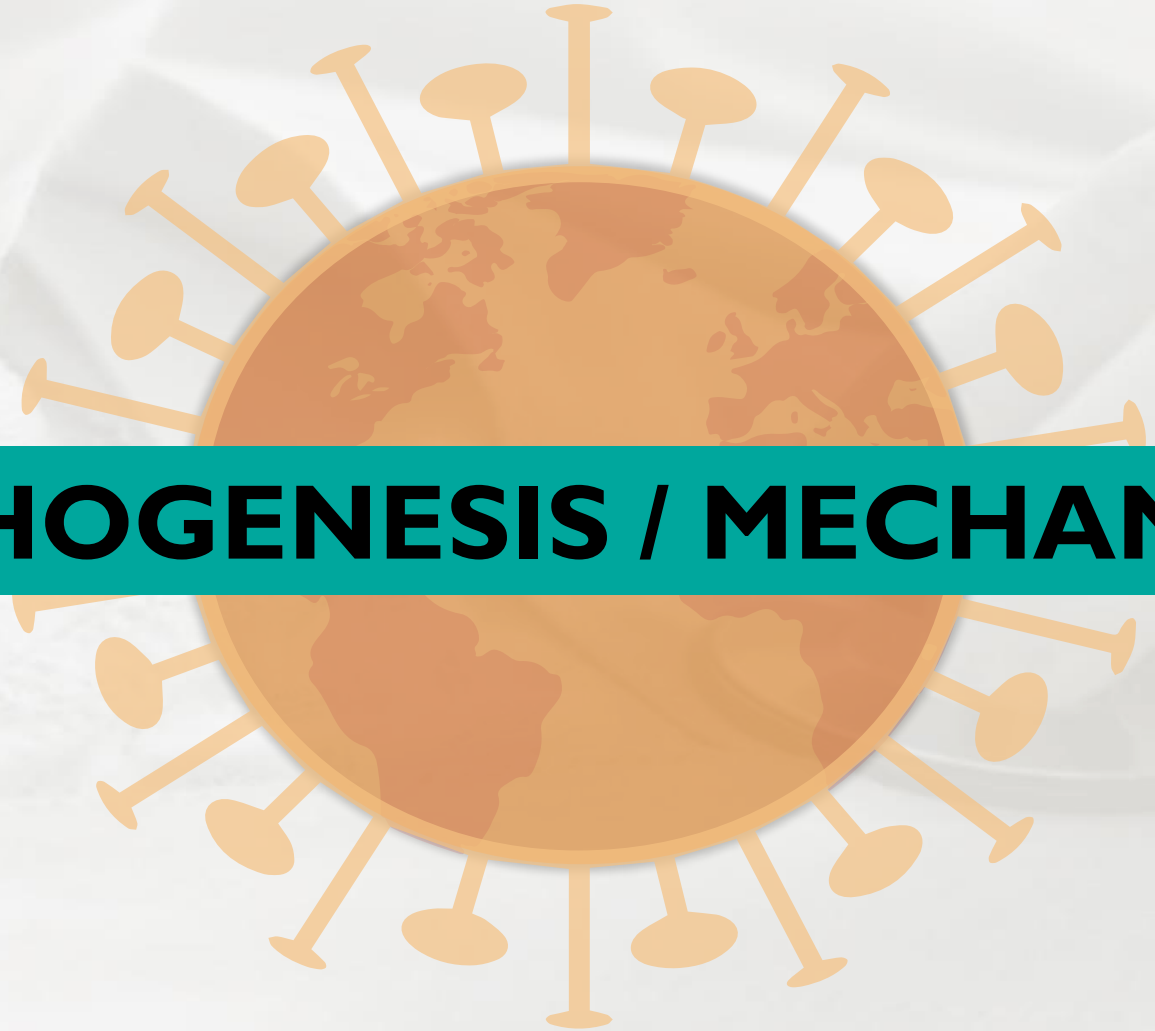


Tao Guo, et al.Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). 2020. JAMA Cardiol.

CLINICAL COURSE

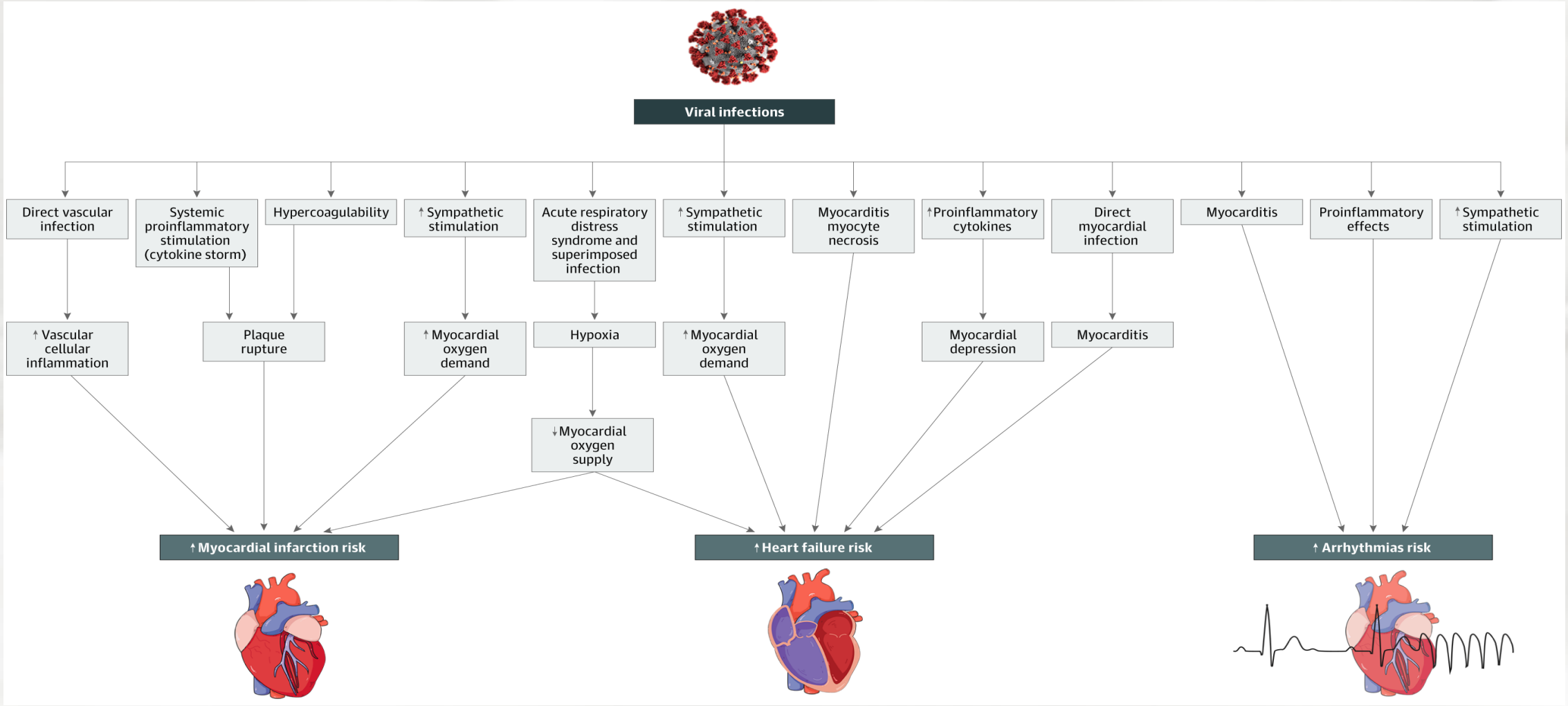


Fei Zhou, et al. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study. 2020. The Lancet.



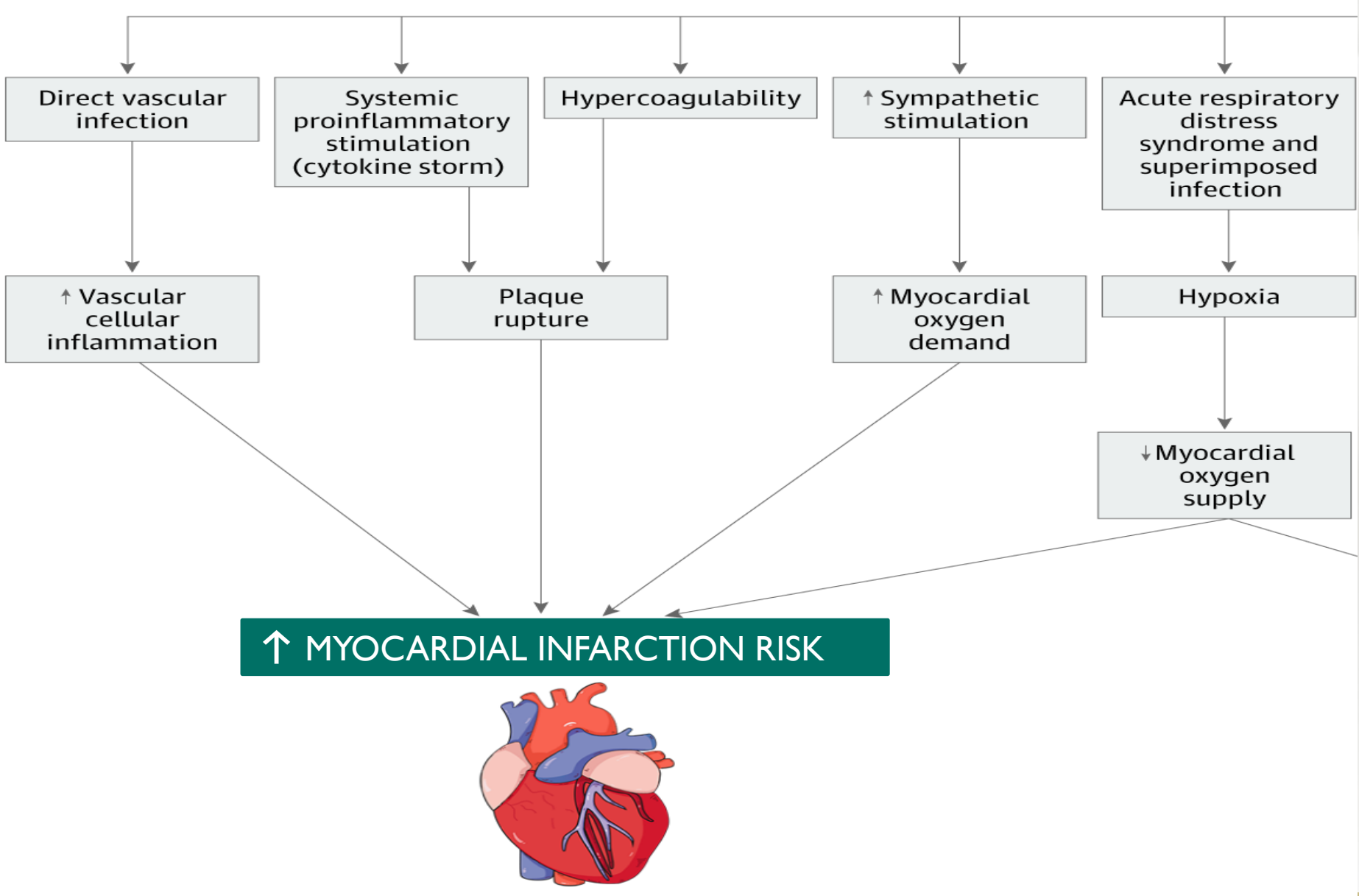
PATHOGENESIS / MECHANISM

Cardiac Implication of COVID-19

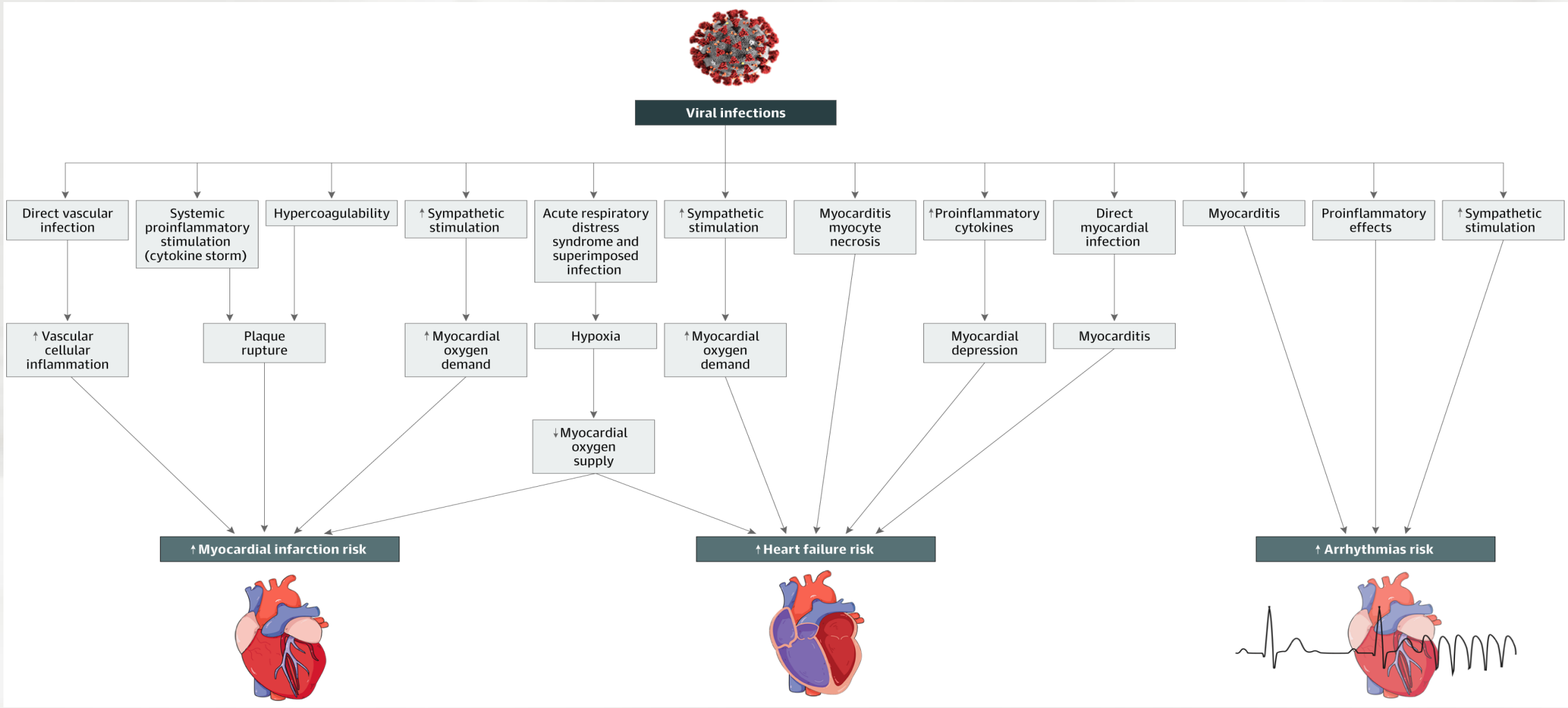


Madjid M, et al. Potential Effects of Corona Viruses on The Cardiovascular System. A Review. 2020. JAMA Cardiol

Cardiac Implication of COVID-19

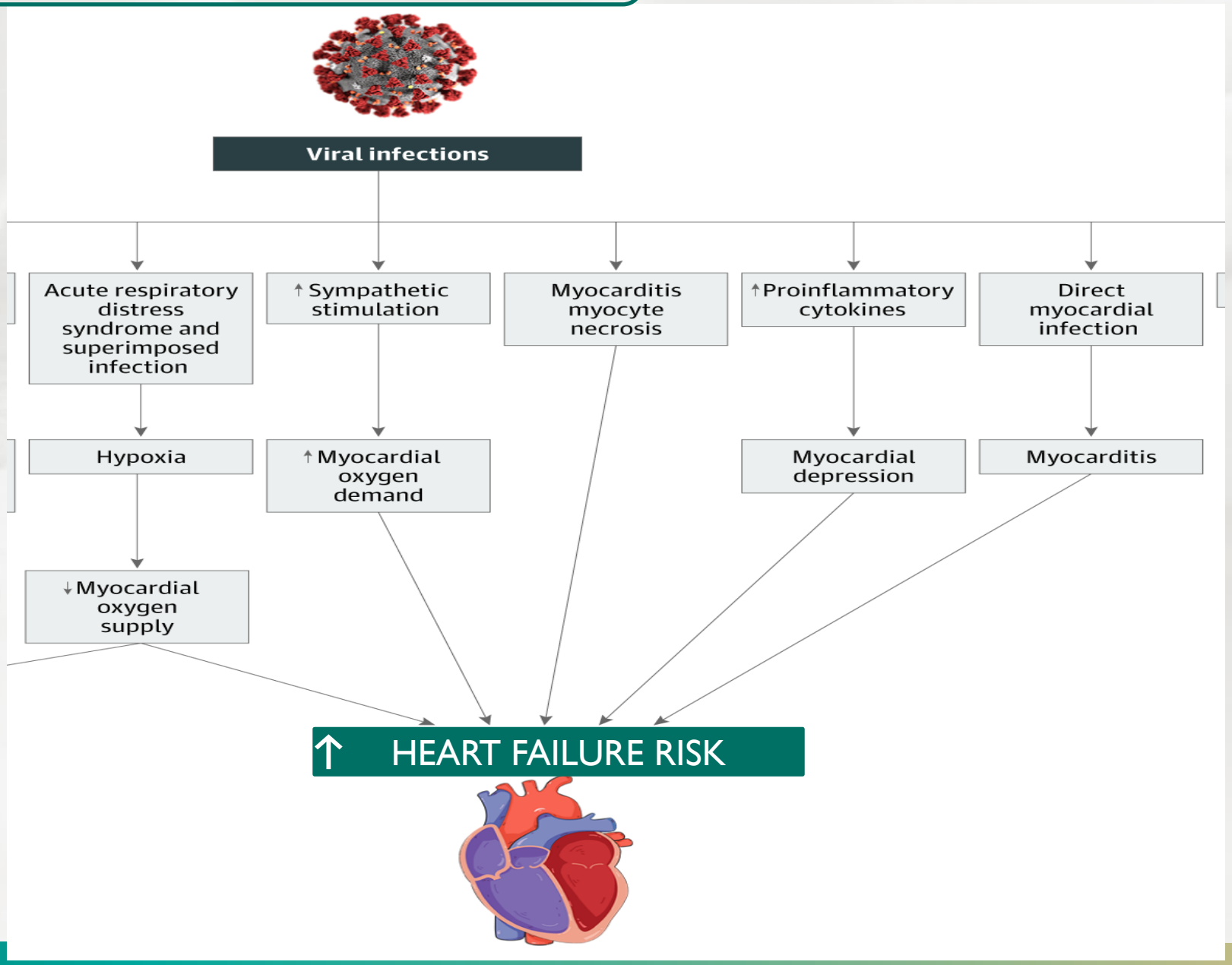


Cardiac Implication of COVID-19

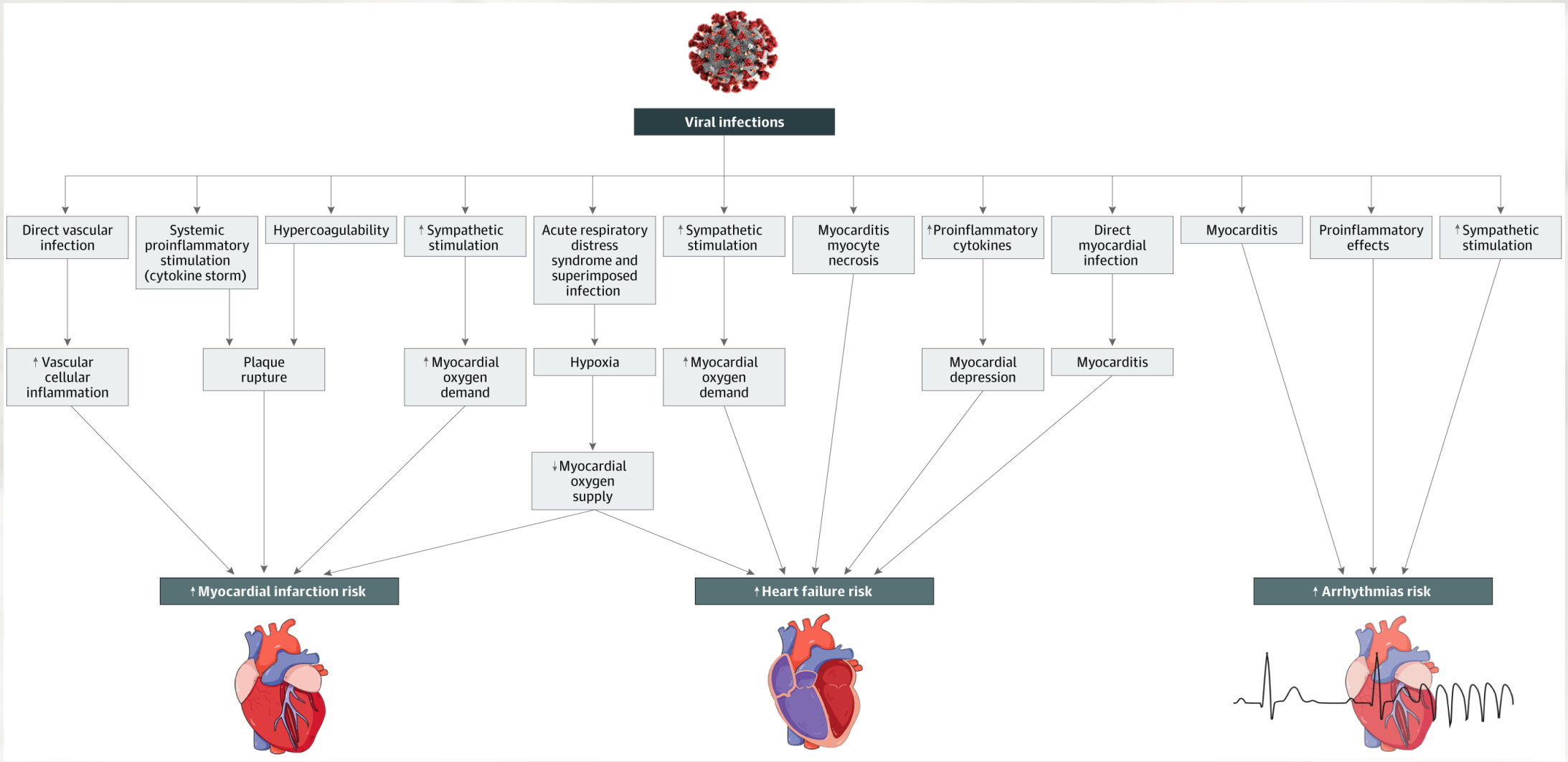


Madjid M, et al. Potential Effects of Corona Viruses on The Cardiovascular System. A Review. 2020. JAMA Cardiol

Cardiac Implication of COVID-19

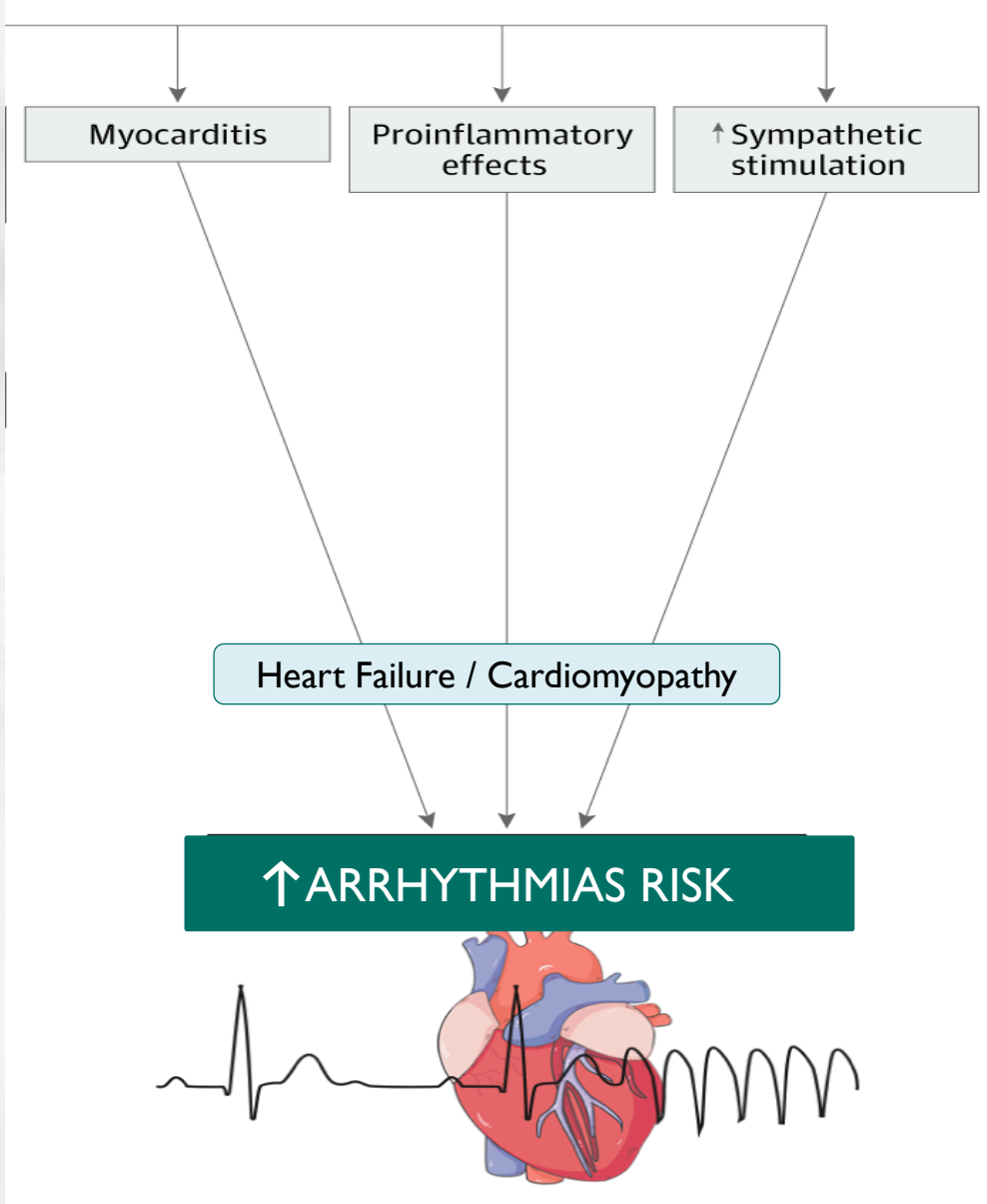


Cardiac Implication of COVID-19

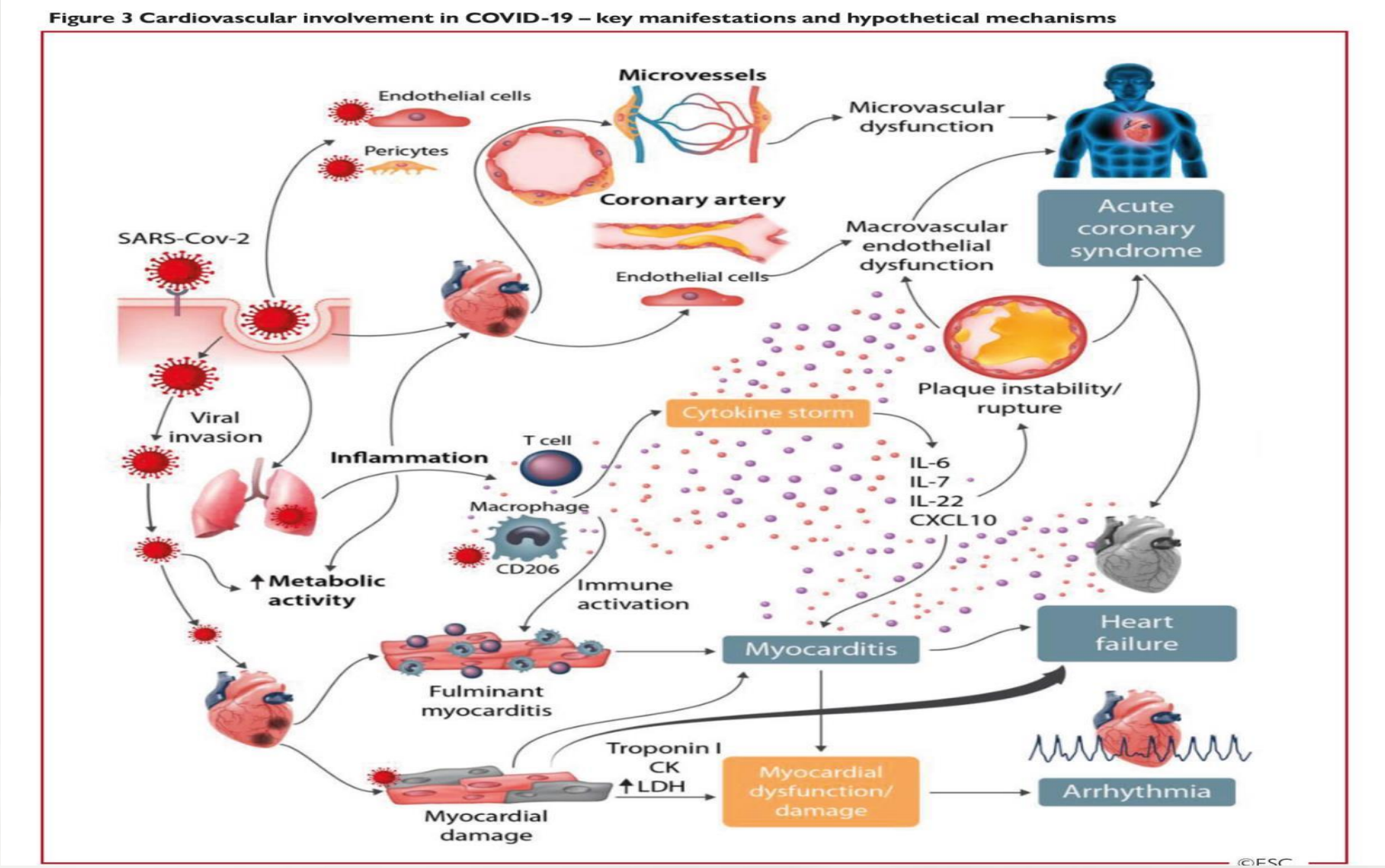


Madjid M, et al. Potential Effects of Corona Viruses on The Cardiovascular System. A Review. 2020. JAMA Cardiol

Cardiac Implication of COVID-19



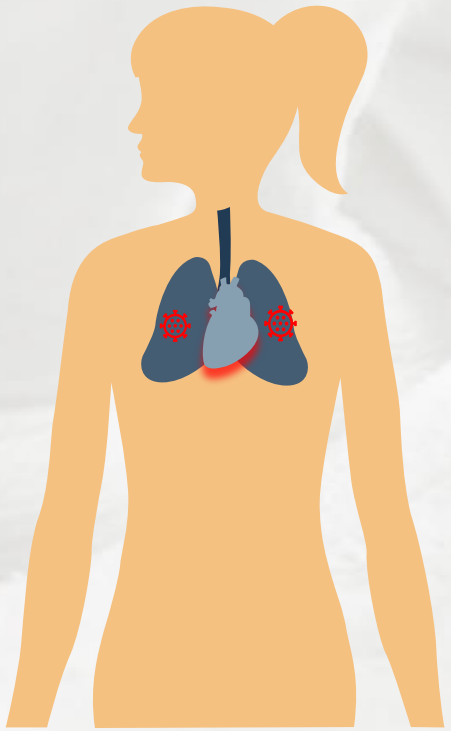
The Link Between Covid-19 and Cardiac Involvement



ESC European Society of Cardiology

ESC Guidance for the Diagnosis and Management of CV Disease during the COVID-19 Pandemic .2020. The European Society of Cardiology.

Case of Acute Myopericarditis



Gender	Age	History
Woman	53 y.o	***Positive for Covid-19***

March, 2020

- **Chief complain**: Severe fatique for 2 days
- **Past medical history**: Fever and dry cough for 1 week before

Blood Pressure : 90/50 mmHg

Heart Rate :100 b/m

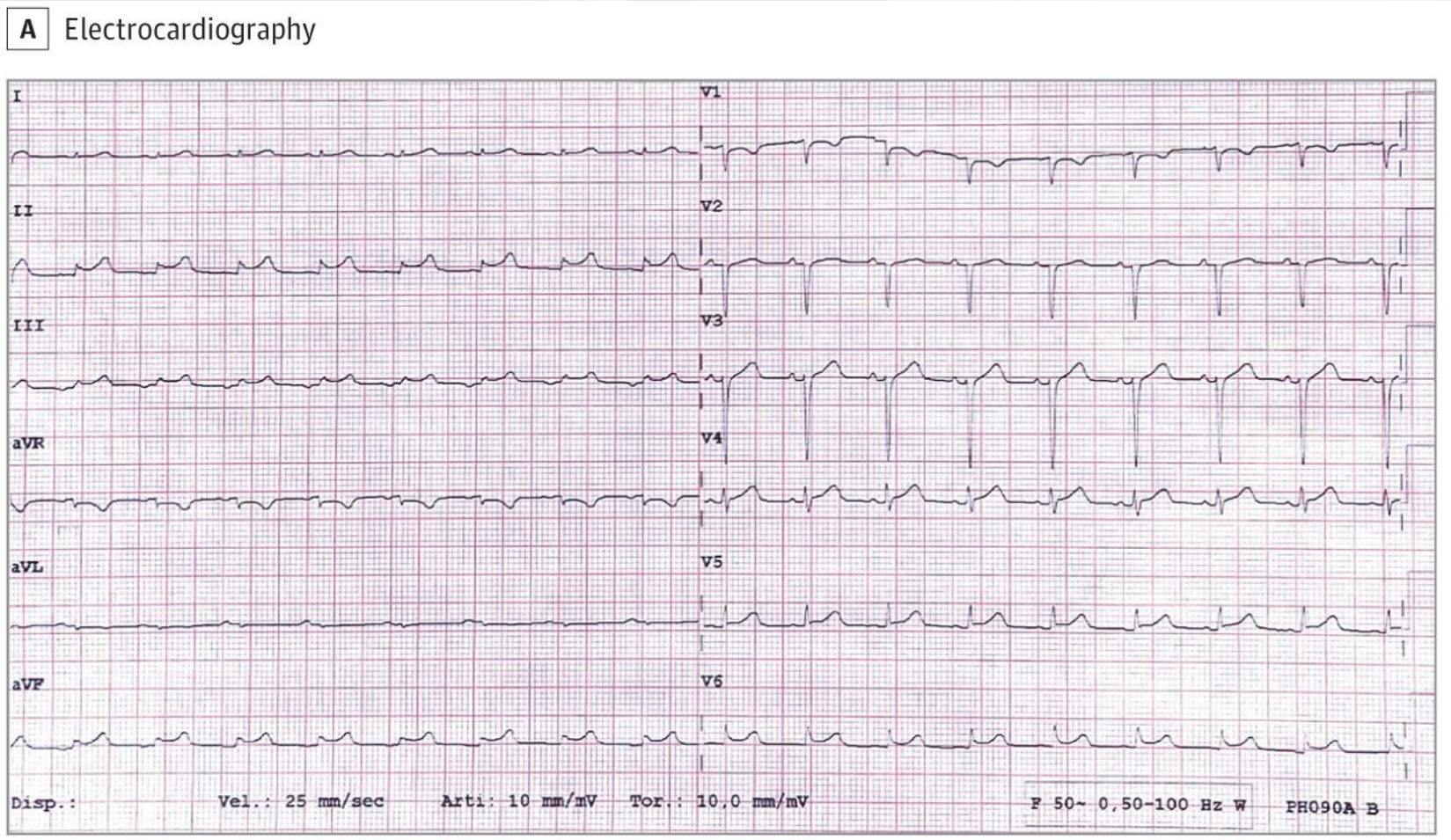
Oxygen saturation: 98%

Temp : 36,6 celcius

Riccardo M., *et al*. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). 2020. JAMA Cardiol.

Case of Acute Myopericarditis

ELECTROCARDIOGRAPHY



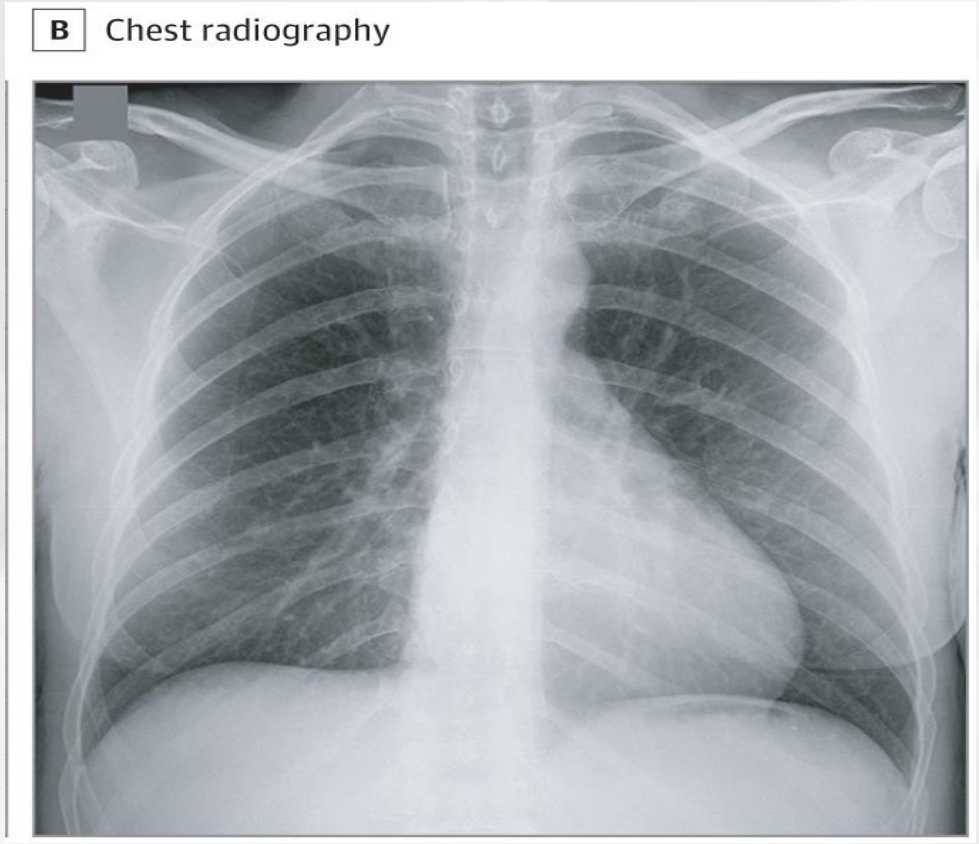
LABORATORY

	RESULT	NORMAL VALUE
CKMB	99 → 195 u/l	<24 u/l
Trop T	1200 → 4500 ng/mL	<50 ng/mL
NT pro BNP	5647 → 8645	<300pg/mL
CRP	13 mg/L	<10 mg/L

Riccardo M., *et al*. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). 2020. JAMA Cardiol.

Case of Acute Myopericarditis

CHEST RADIOGRAPHY FINDING



The patient **did not show any respiratory involvement** during the clinical course.

ECHOCARDIOGRAPHY

- Normal Dimension
- LVH
- Global Hypokinetic with LVEF 40%
- Mild PE

Riccardo M., *et al*. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). 2020. JAMA Cardiol.

Case of Acute Myopericarditis

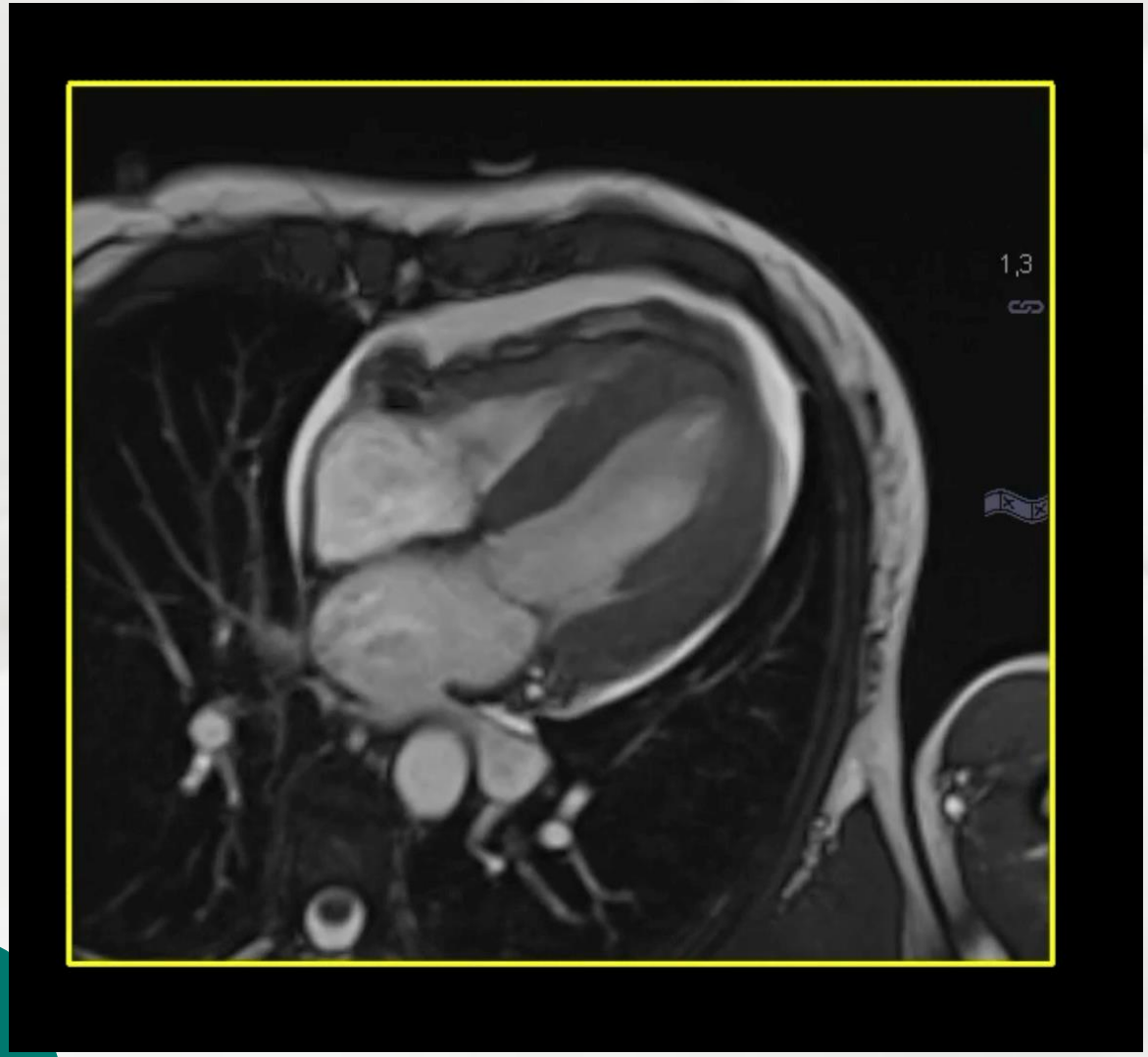
URGENT CORONARY ANGIOGRAPHY

Normal Coronary

Angiographic findings.

Riccardo M., *et al*. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). 2020. JAMA Cardiol.

Case of Acute Myopericarditis

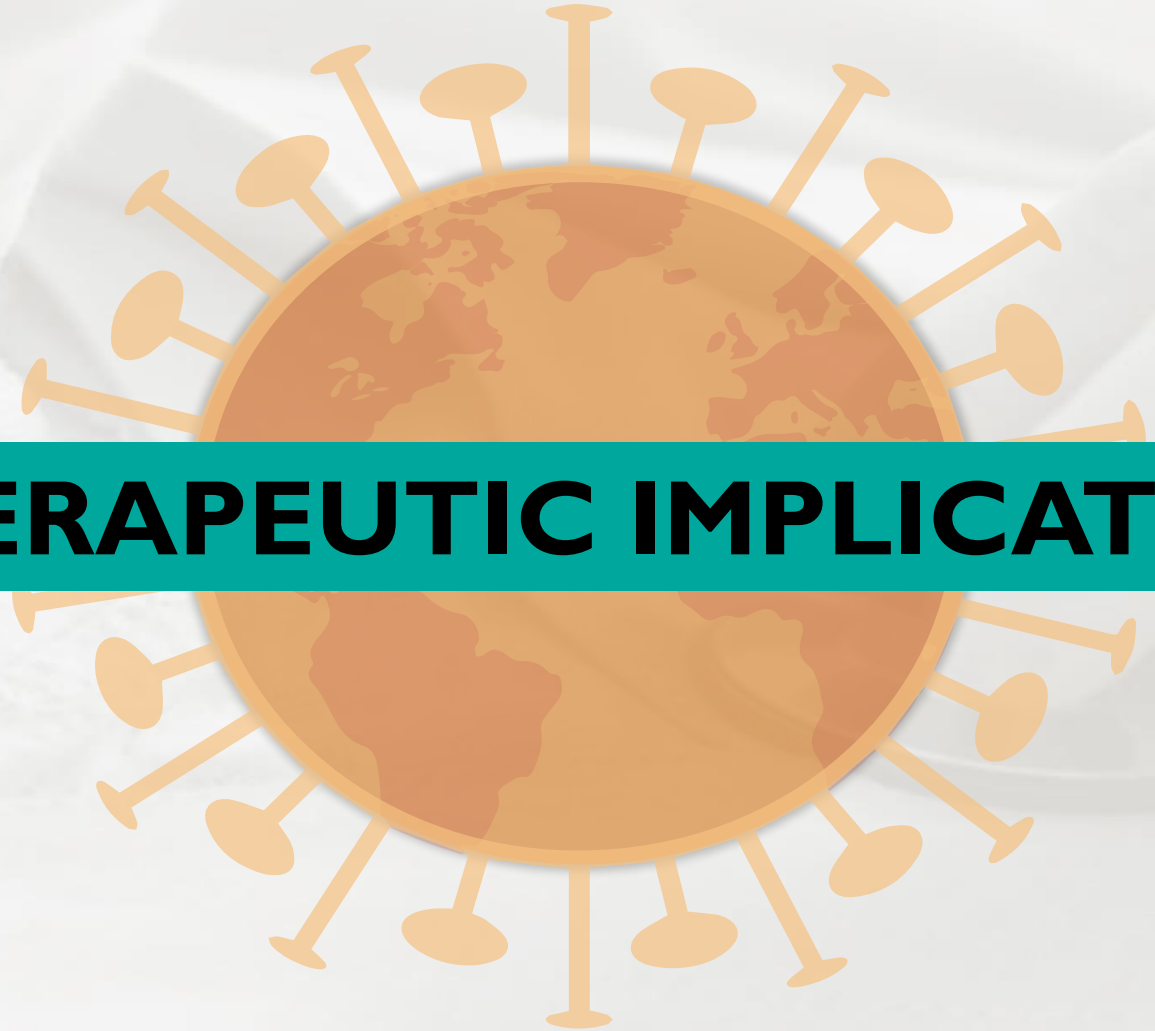


CARDIAC MAGNETIC RESONANCE

- Diffuse Biventricular Hypokinetic with LVEF 35%
- Myocardial Edema
  ⇨ **Acute Myocarditis**

- Mild PE ⇨ Pericarditis

Riccardo M., *et al*. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). 2020. JAMA Cardiol.



THERAPEUTIC IMPLICATION

Management / Therapy Covid-19

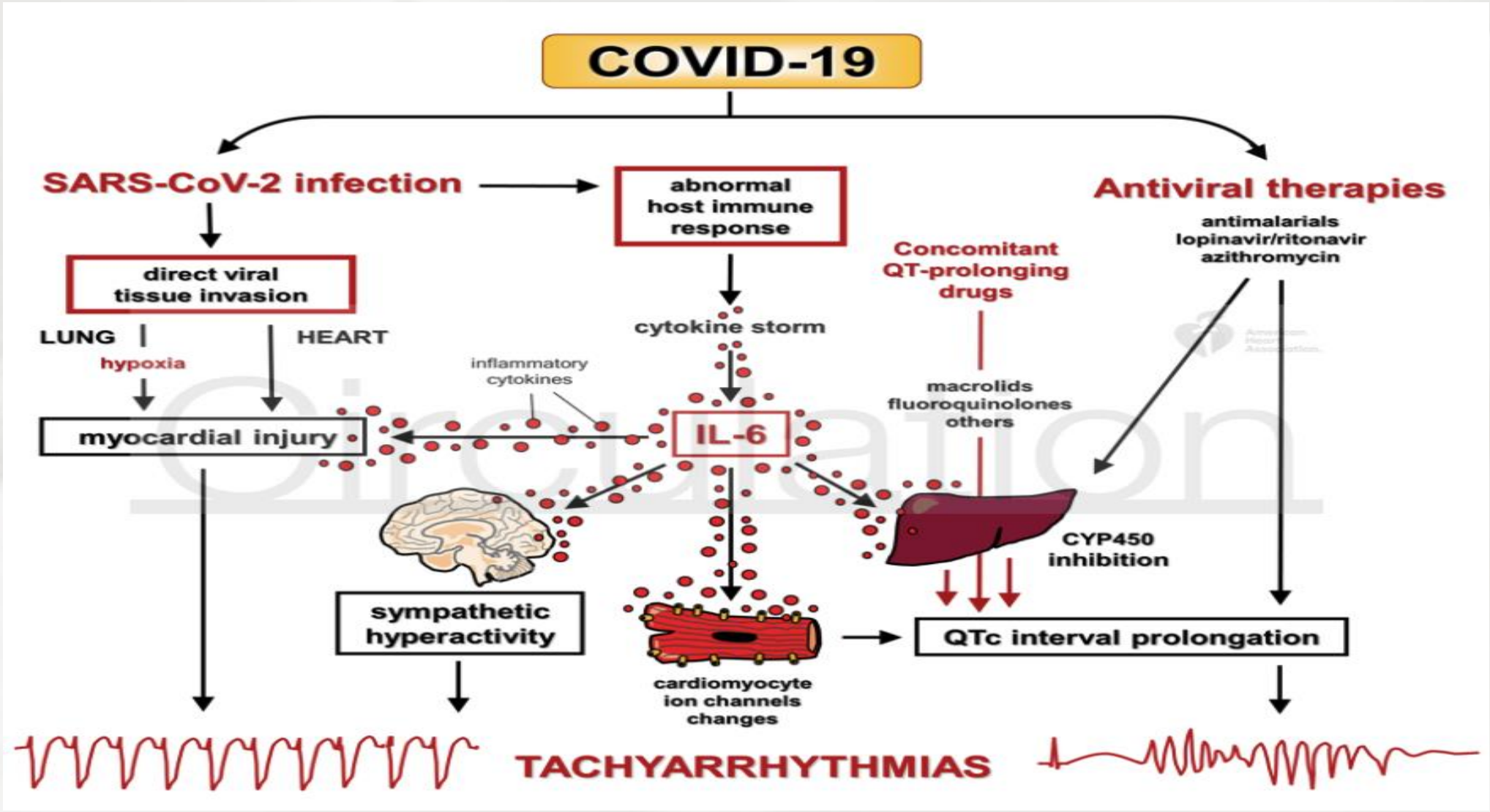
Pharmacological Therapy

Antiviral	Antibiotic	Immunotherapy Agent
• Oseltamivir • Remdesivir (USA approved for emergency use) • Favipiravir (Avigan ®) • Lopinavir/ Darunavir	• Azithromycin • Levofloxacin	• Chloroquine / Hydroxycloroquine • Tocilizumab (Actemra ®)

Drug Related Heart Damage

Many antiviral drugs can cause cardiac insufficiency, arrhythmia, or other cardiovascular disorders.

Prone to Devastating Arrhythmia



Lazzerini *et al.* COVID-19, Arrhythmic Risk and Inflammation: Mind the Gap! 2020. Circ AHA Jour

Drug Interaction and Risk of Arrhythmia

Table 15 Arrhythmological considerations of novel experimental pharmacological therapies in COVID-19 infection

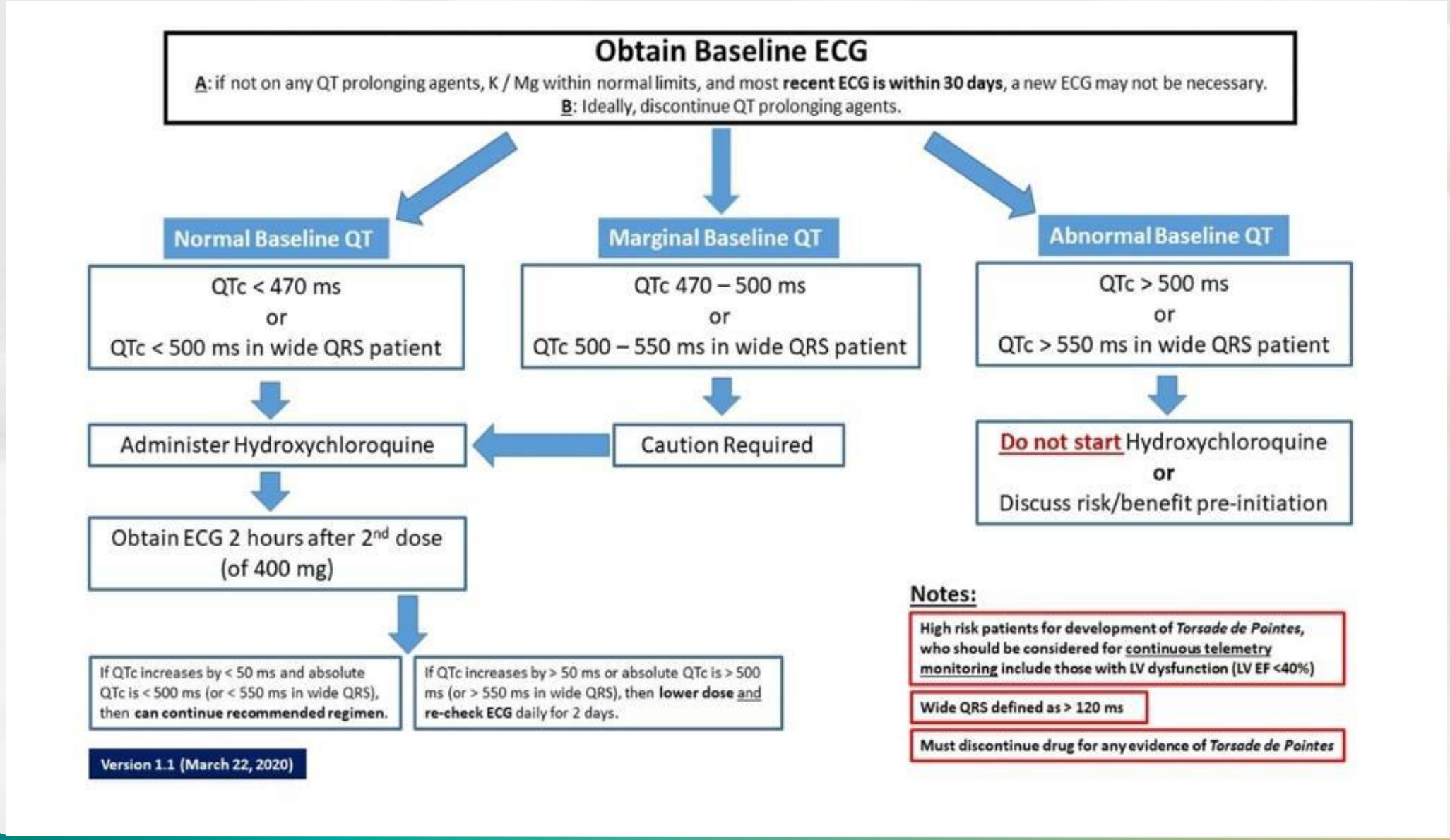
	HR	AV CONDUCTION	QRS INTERVAL	QTC INTERVAL	TDP RISK	AAD DRUGS INTERACTIONS[24]	COMMENTS
CHLOROQUINE	Mild ↓	Mild ↑ Δ_{PR}= 14.8 ms[216]	Mild ↑ Δ_{QRS}= 9.9 ms[216]	Moderate ↑ Δ_{QTc}= 27- 51 ms[216-218] ↑ Δ_{QTc} in 14.2% of pts [219]	Very-low risk of TdP (72 cases of VF/VT/TdP/LQTS in FAERS registry)	**SEVERE[a]** Amiodarone, Flecainide, Mexiletine, Sotalol, Dofetilide **MODERATE[b]** Disopyramide, Propafenone, Quinidine, Digoxin **MILD[c]** Metoprolol, Nebivolol, Propranolol, Timolol, Verapamil	- Very low risk of cardiotoxicity during chronic therapy is reported[220, 221] - In a study in SLE it was negatively associated with AVB (P = 0.01) as was its longer use (6.1 ± 6.9 vs. 1.0 ± 2.5 years, P = 0.018)[219, 222] - Proarrhythmia occurs mostly with overdosage or in chronic therapy (> years)[223] - Proemetic effect is common - Risk of retinopathy, myo/neuropathy during chronic therapy is reported
HYDROXY-CHLOROQUINE	Mild ↓ [220, 221, 224]	Mild ↑	Mild ↑	Moderate ↑ Δ_{QTc}= 25 ms [220, 221]	Very-low risk of TdP (222 cases of VF/VT/TdP/LQTS in FAERS registry)	See Chloroquine	- Very low risk of cardiotoxicity during chronic therapy is reported[220, 221] - Proarrhythmia occurs mostly with overdosage or in chronic therapy (> years)[223] - Less cardiotoxicity reported than with Chloroquine[223] - In a study of pregnant women with Ro/La antibodies, AVBs were more frequent in those not using hydroxychloroquine[225]
AZITHROMYCINE	Mild ↓ [226]	Mild ↑ [226]	Mild ↑ [226]	Moderate-Severe ↑ Δ_{QTc}= 5-32 ms[226-228]	Low risk of TdP Cumulative incidence SCD = 64.6/1 million[229] ROR for Tdp = 4.76 compared to other	**SEVERE[a]** Amiodarone, Dysopiramide, Dofetilide, Flecainide, Propafenone, Sotalol **MODERATE[b]**	In a study during treatment days 1 to 5, patients receiving azithromycin had significantly increased risk of serious arrhythmia (HR = 1.77; 95% CI, 1.20-2.62) compared with patients receiving amoxicillin[233, 234]

ESC European Society of Cardiology

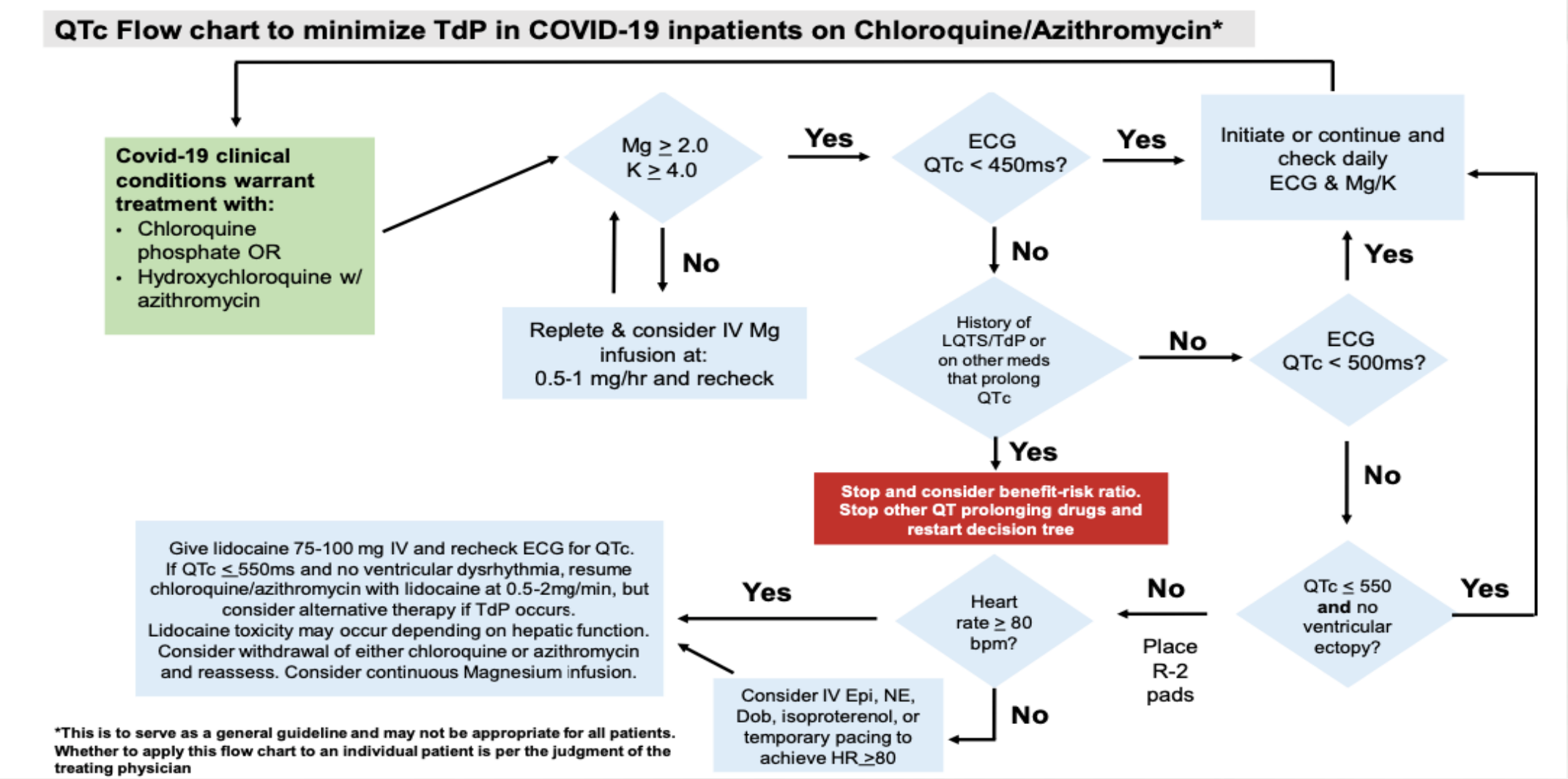
ESC Guidance for the Diagnosis and Management of CV Disease during the COVID-19 Pandemic The European Society of Cardiology 2020.

	HR	AV CONDUCTION	QRS INTERVAL	QTC INTERVAL	TDP RISK	AAD DRUGS INTERACTIONS[24]	COMMENTS
LOPINAVIR/ RITONAVIR	NR	Moderate↑ Δ_{PR}= 33.5 ms[216]	Mild ↑ Δ_{QRS}= 7 ms[235]	Moderate ↑ Δ_{QTc}= 20 ms[216]	Low risk of TdP (27 cases of VF/VT/TdP/LQTS in FAERS registry) HR for Tdp 1.02 (0.26-3.24)[227]	**SEVERE[a]** Amiodarone, Dronedarone, Disopyramide, Dofetilide, Flecainide, Sotalol **MODERATE[b]** Lidocaine, Mexiletine, Propafenone, Quinidine, Digoxin, All Beta-blockers, Ca^{2+} blockers	Cases of AV block are reported
TOCILIZUMAB	No ECG changes described[236]				Unknown	**MILD[c]** Amiodarone, Quinidine	
FINGOLIMOD SIPONIMOD	Moderate-Severe ↓ Δ_{HR}= -23 bpm[237]	Mild-moderate ↑	Unknown	Mild ↑	Unknown	**MODERATE[b]** Beta-blockers, Ca2+ blockers, Ivabradine, Amiodarone, Flecainide, Propafenone	Reported risk of rare, transient and benign bradycardia and AV conduction abnormalities[238]: - In a study of 3591 patients, 31 patients (0.8%) developed bradycardia (<45 bpm), 62 patients (1.6%) had second-degree Mobitz I and/or 2:1 AV blocks[239] - In study of 5573 patients new-onset first-degree AVB was experienced by 132 (2.4%) in-home and 74 (0.5%) in-clinic patients, and Wenckebach (Mobitz type I) second-degree AVB by four (0.07%) and nine (0.1%) patients, with no cases of third-degree AVB.[240] - In study of 66 patients with MS fingolimod lead to an increase of vagal activation which persisted even after 14 months of treatment[237]
REMDESIVIR	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Very limited preclinical data showed safety[241]
INTERFERON ALFACON-1	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Limited data: cases of hypotension, arrhythmia, and cardiomyopathy reported
RIBAVIRIN	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	No cardiac side effect
METILPRED-NISOLONE	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	- May cause electrolyte disturbance - High dose intravenous prednisolone might cause acute sinus bradycardia[242] or in MS patients sirus tachycardia, bradycardia and rarely AF and VT[243]

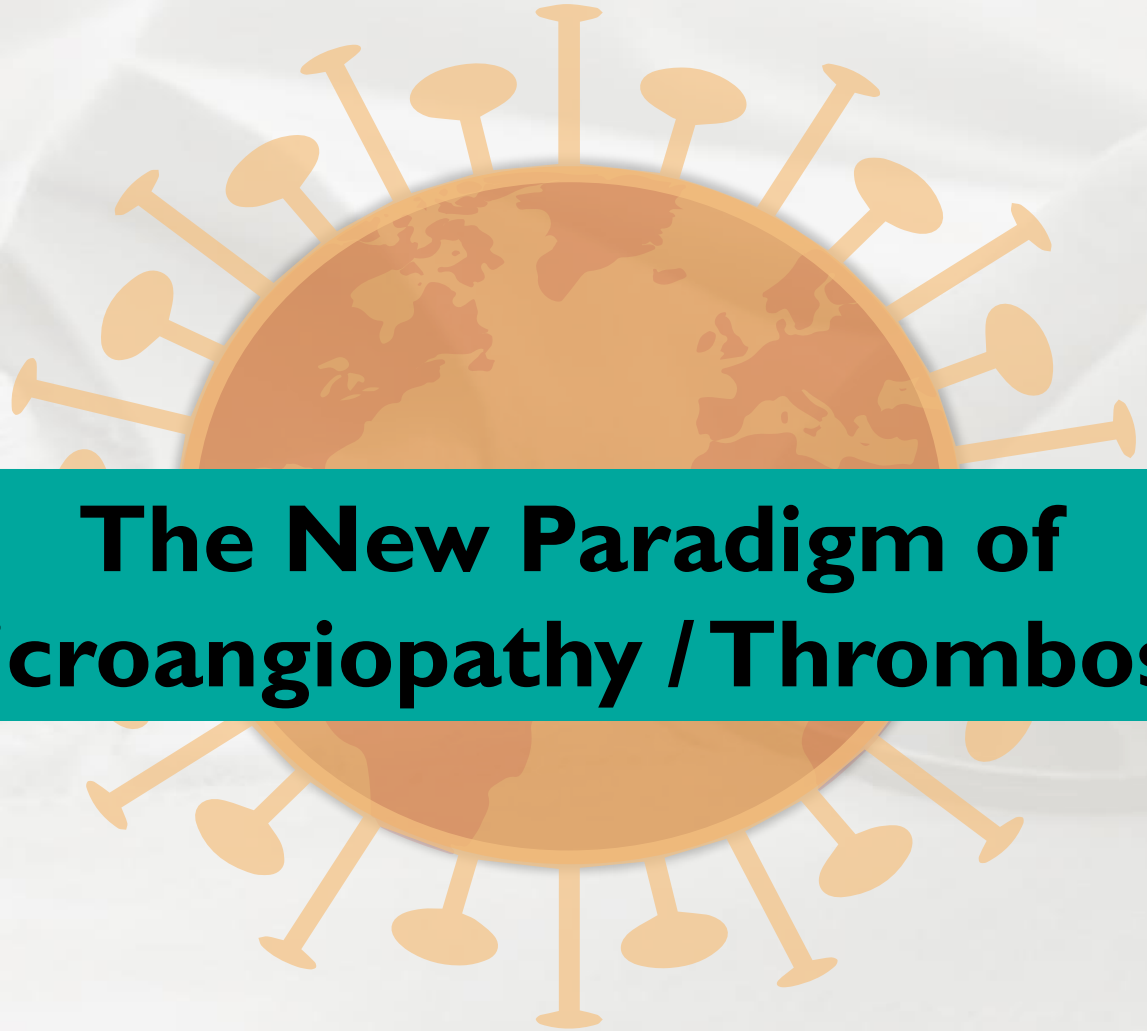
The Importance of QTc



How to Manage The Deadly Combination?



Mitra RL, *et al.* An algorithm for managing QT prolongation in coronavirus disease 2019 (COVID-19) patients treated with either chloroquine or hydroxychloroquine in conjunction with azithromycin: Possible benefits of intravenous lidocaine. 2020. Elsevier



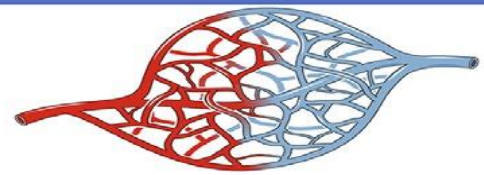
The New Paradigm of Microangiopathy / Thrombosis

The New Paradigm

CYTOKINES

- Rise favored by ACE2 suppression[6,57]
- Cause both direct and indirect myocardial injury[6,59,60]
- High concentrations in critical patients with COVID-19[1]

OXIDATIVE STRESS
ENDOTHELIAL DYSFUNCTION



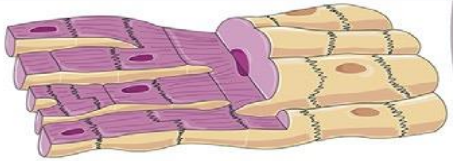
MICROANGIOPATHY

- Favored by prothrombotic state
- High levels of D-dimer in patients with COVID-19[37]
- Vasculitis-like mechanisms involved?

IMMUNOMEDIATED INJURY

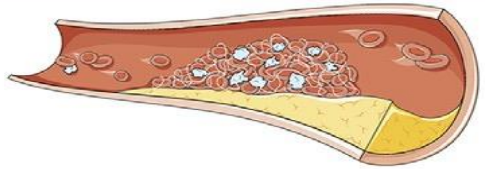
ENDOTHELIAL DYSFUNCTION
PLAQUE INSTABILITY

ALTERED PERFUSION
VASOSPASM



MYOCARDITIS

- SARS-CoV-2 targets myocardial ACE2 receptors[21]
- Only clinically suspected cases[28-30]
- No histological diagnosis in patients with COVID-19 reported so far

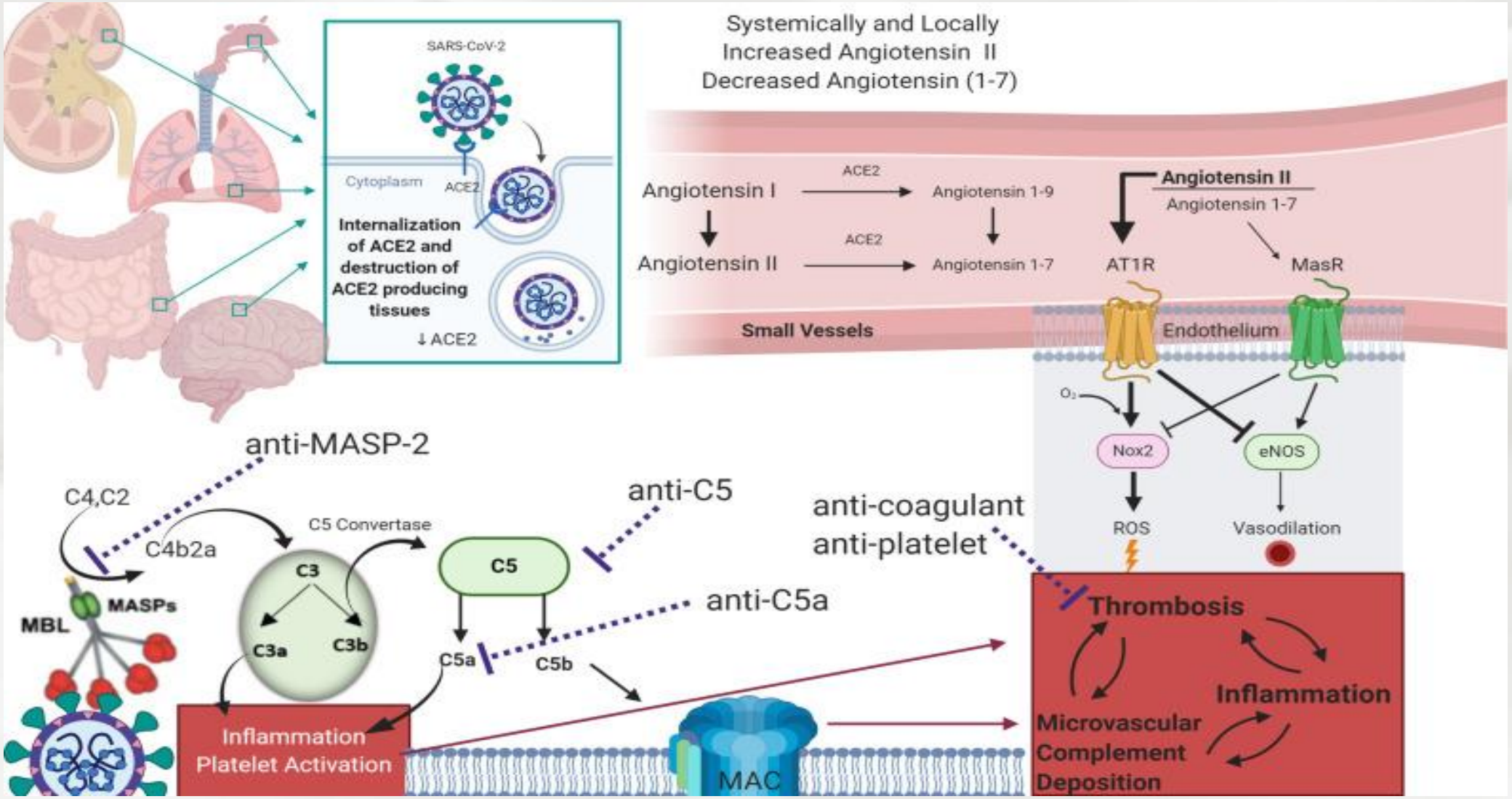


MYOCARDIAL INFARCTION

- Higher troponins in patients with known CAD[6]
- Inflammation and viral invasion cause plaque instability (type I MI)
- Hypoxia and infection cause oxygen supply/demand imbalance (type II MI)

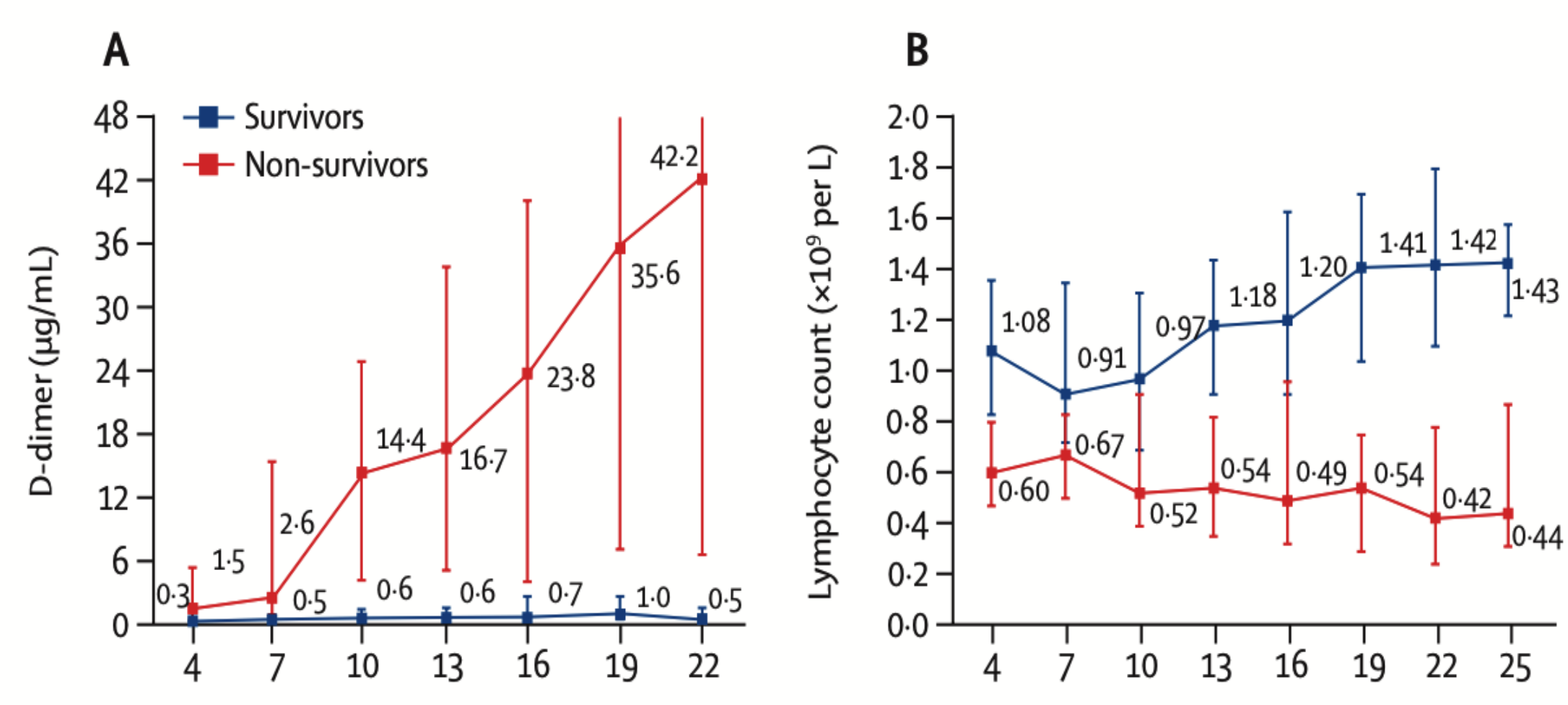
Gregoriot, *et al.* Elevated Troponin in Patients With Coronavirus Disease 2019: Possible Mechanisms. 2020. Elsevier. Jour Card Fail

Microangiopathy Thrombosis



Magro, *et al.* Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. 2020. Elsevier

Mortality and D-Dimer



Fei Zhou, et al. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study. 2020. The Lancet.

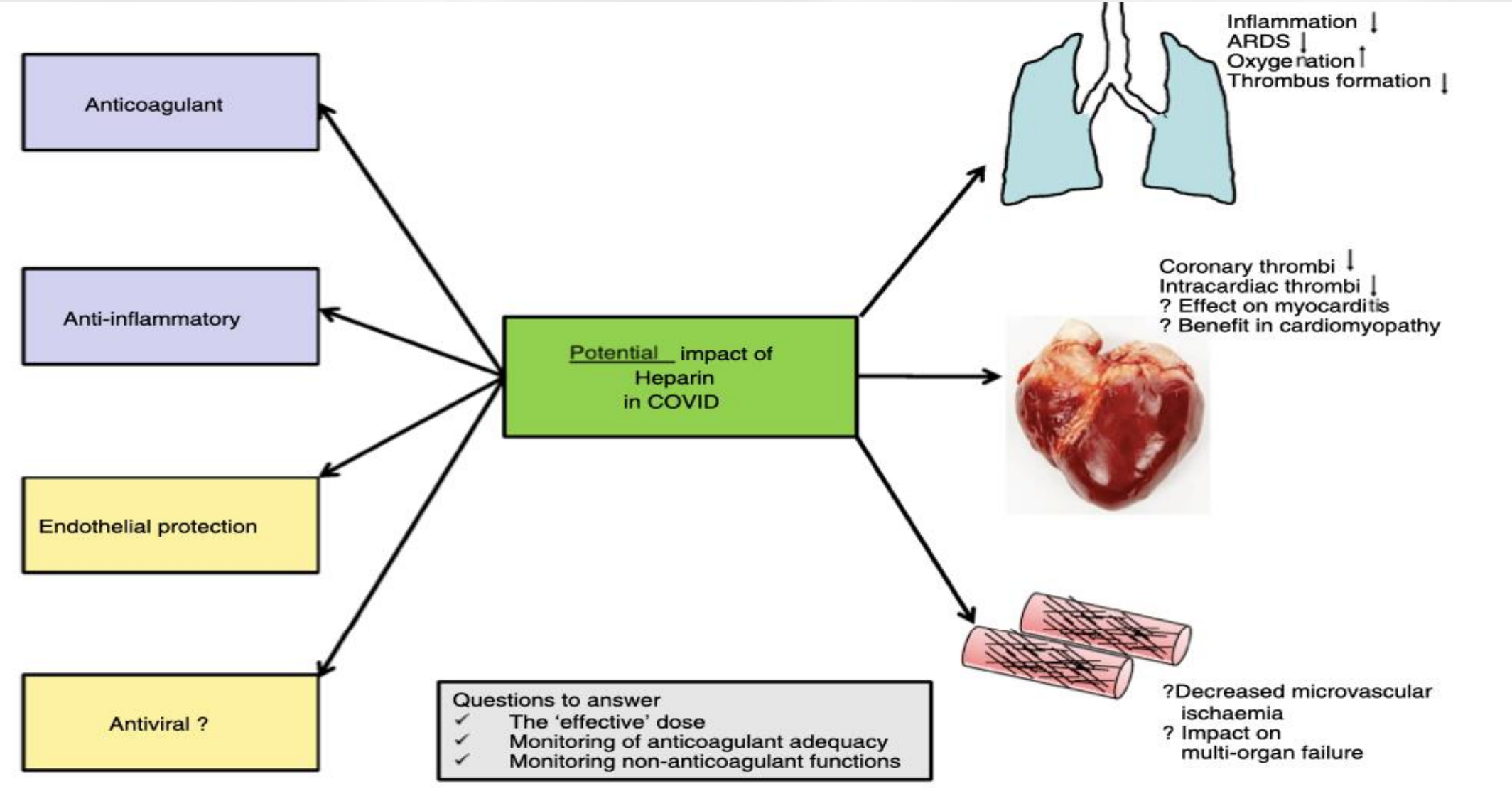
Clinical Manifestation of Microangiopathy Thrombosis

Covid-19 Blue Toes

Lacey Livodoid Rash

Magro, *et al.* Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. 2020. Elsevier

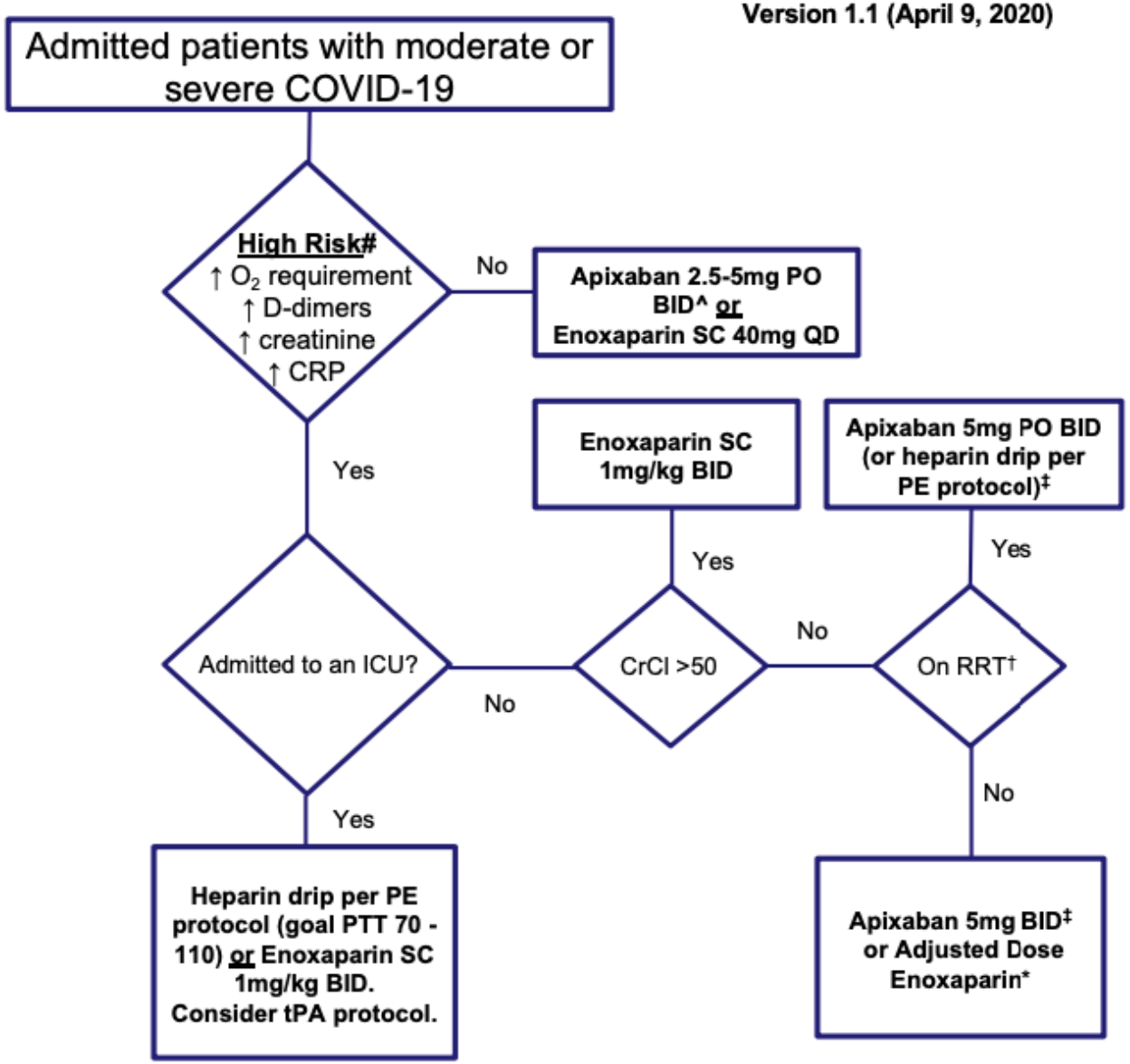
Potential Therapeutic Strategy



Thachil *et al.* The versatile heparin in COVID-19. 2020. Wiley. J Thromb Haemost.

Mount Sinai COVID-19 Anticoagulation Algorithm

Version 1.1 (April 9, 2020)



Inclusion: All admitted patients with moderate or severe COVID-19
Exclusion: High risk of bleeding as judged by treating physician

Obtain at baseline and daily:
- CBC, PT/PTT, D-dimer

Hold anticoagulation if:
- Platelet count <50,000; INR>1.5
- Evidence of current or recent bleeding

If patients take AC at home:
- May switch to therapeutic enoxaparin or heparin (as per algorithm) for the duration of hospitalization, unless contraindicated

Rivaroxaban may be used in place of Apixaban at any indication

Discharged COVID-19 patient on therapeutic anticoagulation while hospitalized

Consider Prophylactic AC for 2 weeks post discharge (Apixaban 5mg PO BID for 2 wks)

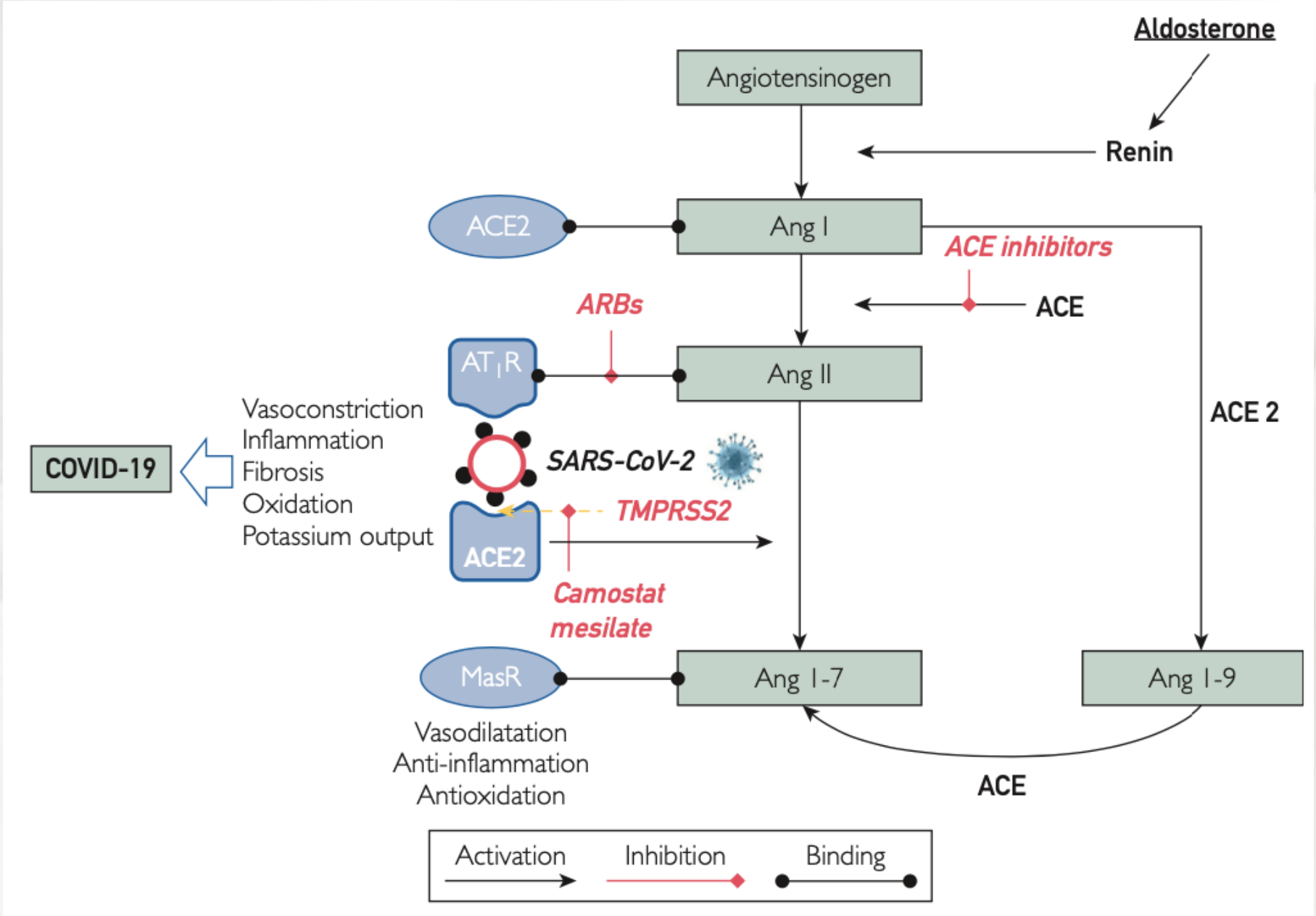
#High Risk: No precise metrics exist. Consider exam (eg O_2 sat<90%, RR >24), ↑O_2 requirement (eg, ≥4L NC), labs (eg, ↑d-dimers, C-reactive protein)
^Efficacy and dose not established; prophylactic or treatment doses acceptable

†RRT – Renal Replacement Therapy
‡ If ≥80 years of age or weight ≤60 kg, reduce apixaban to 2.5 mg BID
* If CrCl <30: enoxaparin 0.5mg/kg BID with anti-Xa level after 3rd dose

TAKE HOME MESSAGES

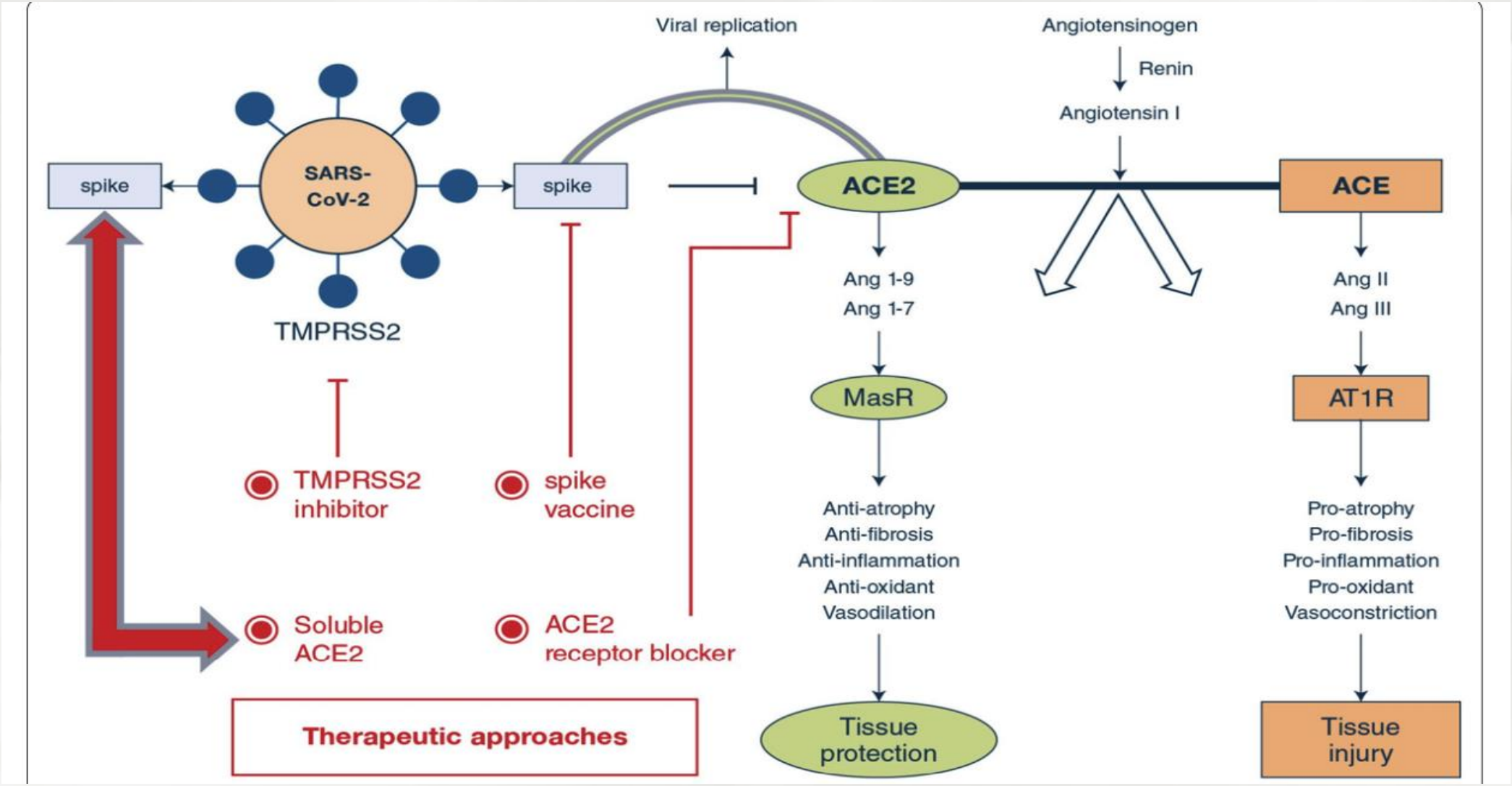
- Covid -19 has a broad cardiac implications that can lead to devastating outcome especially with pre-existing CVD
- Covid-19 has several pathological mechanism that might result in ACS, Myocarditis, HF / Cardiomyopathy and Arrhythmia
- Drug to drug interaction and Covid-19 pathology could cause malignant arrhythmia and should be warrant
- Microangiopathic thrombosis should be recognized as a new therapeutic strategy

THANK YOU



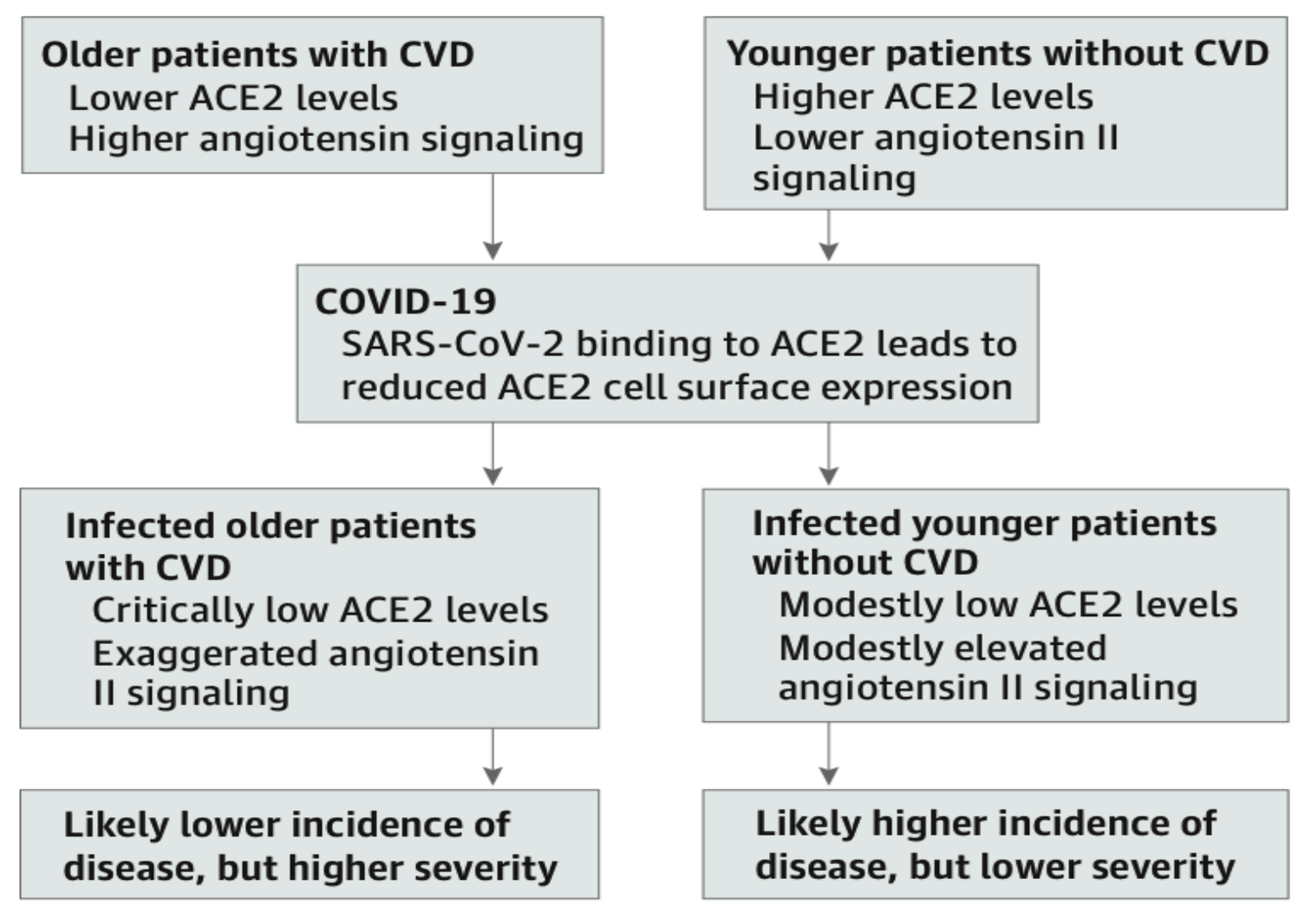
Gomar *et al.* 2020. Angiotensin-Converting Enzyme 2 and Antihypertensives (Angiotensin Receptor Blockers and Angiotensin-Converting Enzyme Inhibitors) in Coronavirus Disease 2019. Mayo Clin Proc

The ACE-2 Pathway



Haibo Zhang, *et al.* Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. 2020. Springer. Intensive Care Med

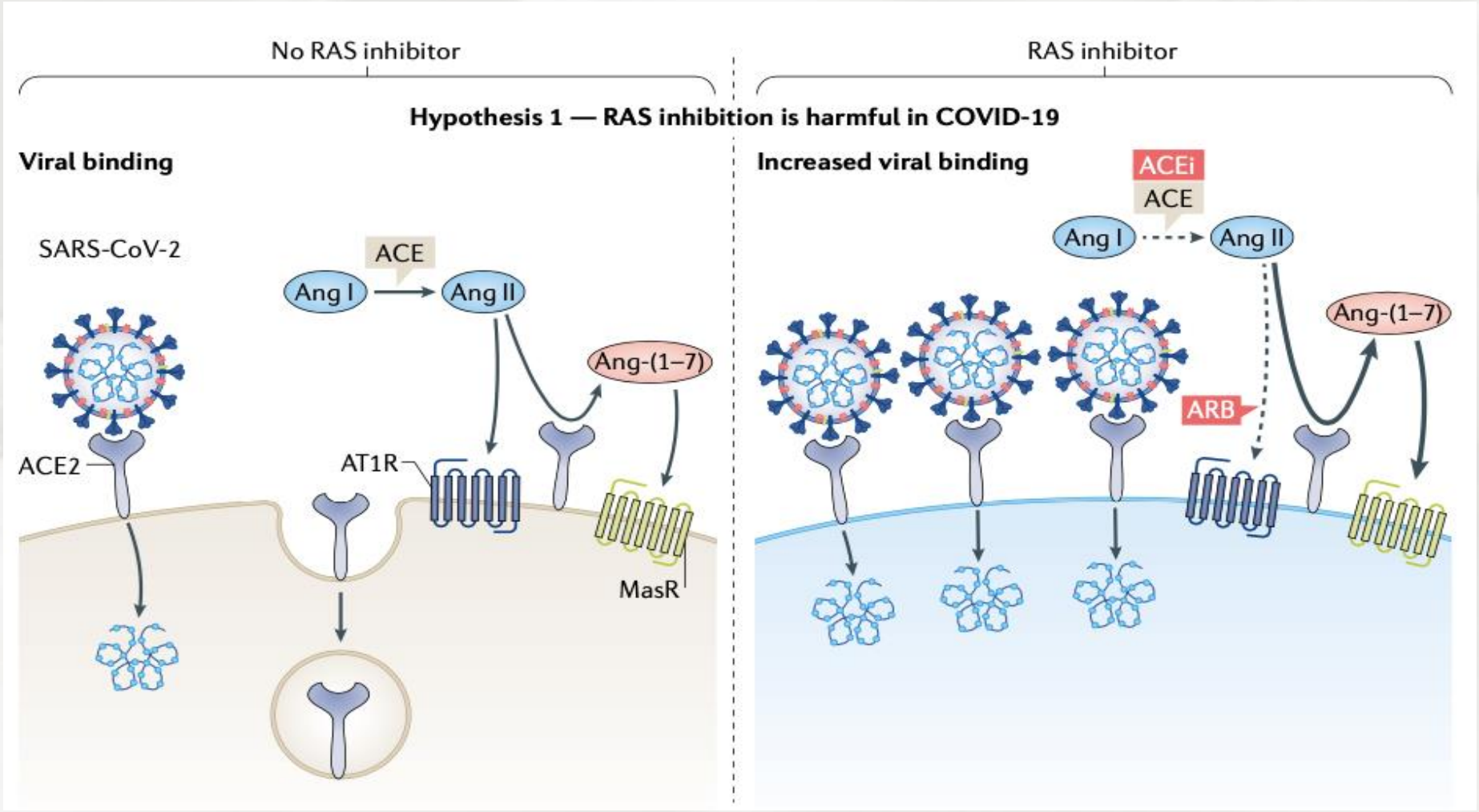
Young VS Old Population



Al Ghatrif, et al. The Dilemma of Coronavirus Disease 2019, Aging, and Cardiovascular Disease Insights From Cardiovascular Aging Science. 2020. JAMA Cardiol

Management Strategy in Cardiology Perspective

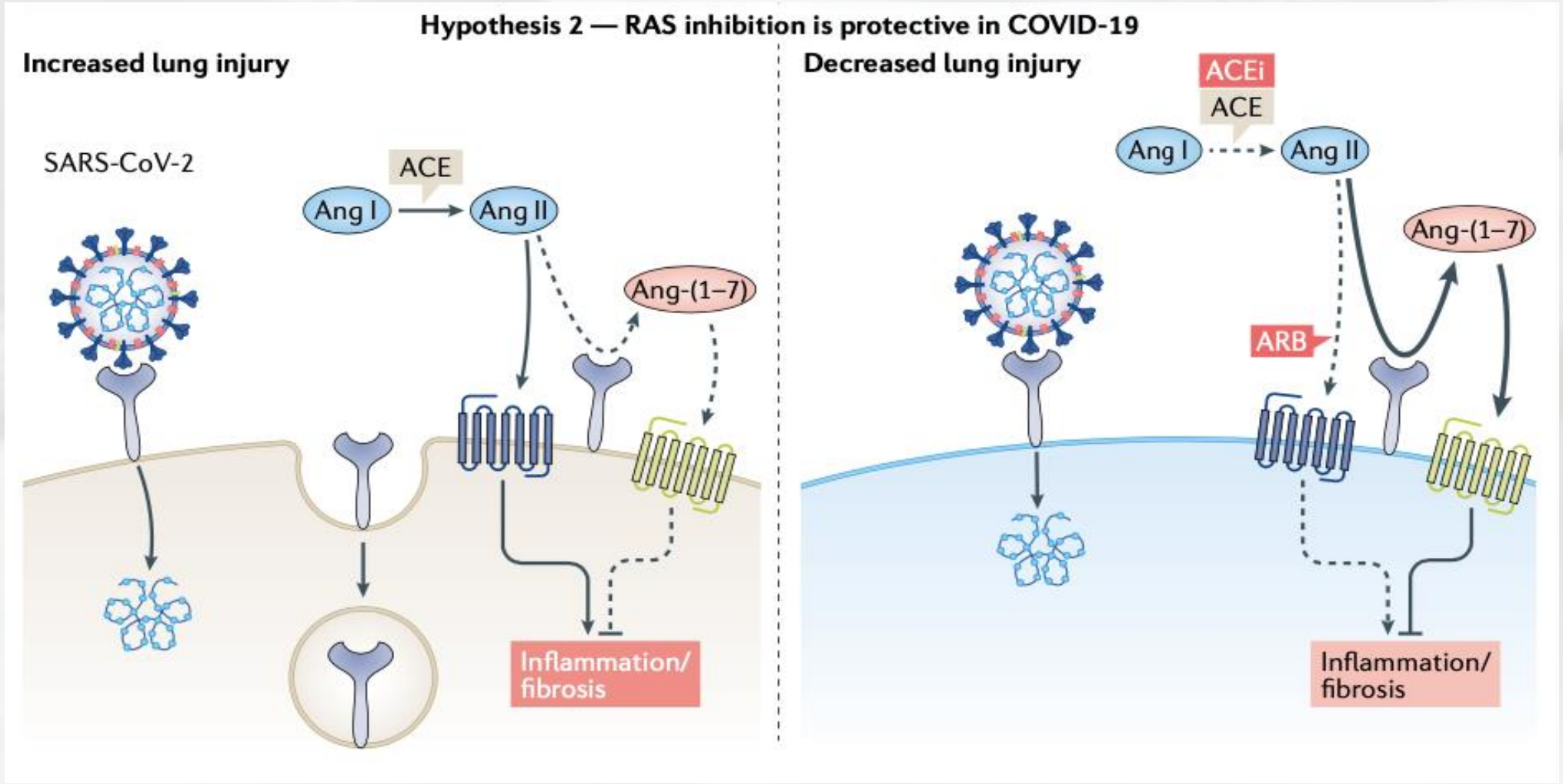
Controversies of ACE-I/ARB in Prexisting CVD Treament



South AM, *et al*. Controversies of renin–angiotensin system inhibition during the COVID-19 pandemic. 2020. Nature Review

Management Strategy in Cardiology Perspective

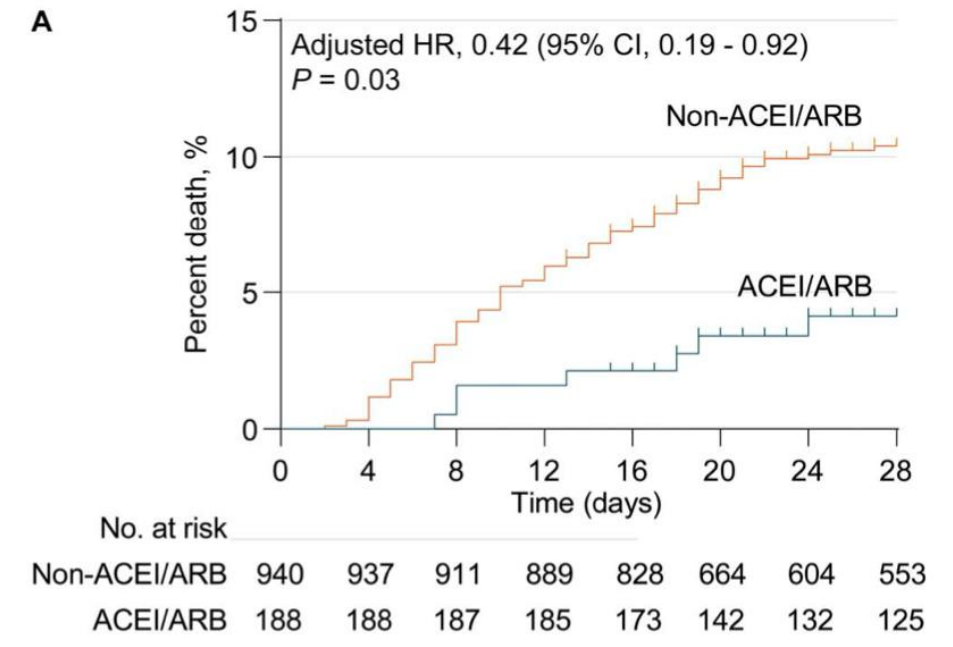
Controversies of ACE-I/ARB in Prexisting CVD Treament

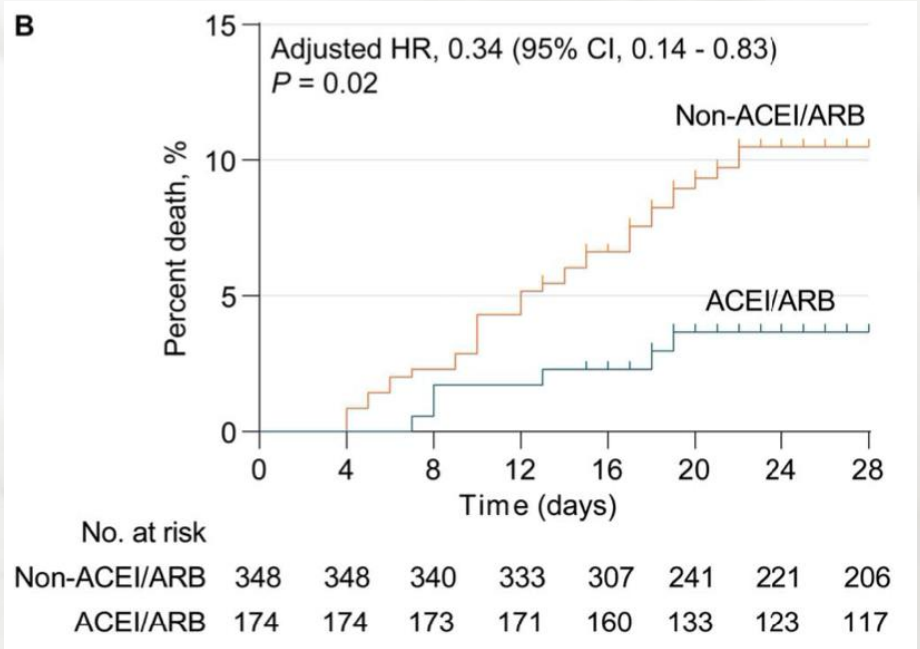


South AM, *et al*. Controversies of renin–angiotensin system inhibition during the COVID-19 pandemic. 2020. Nature Review

ACEI/ARB Strategy

Hypertension Hospitalized With COVID-19





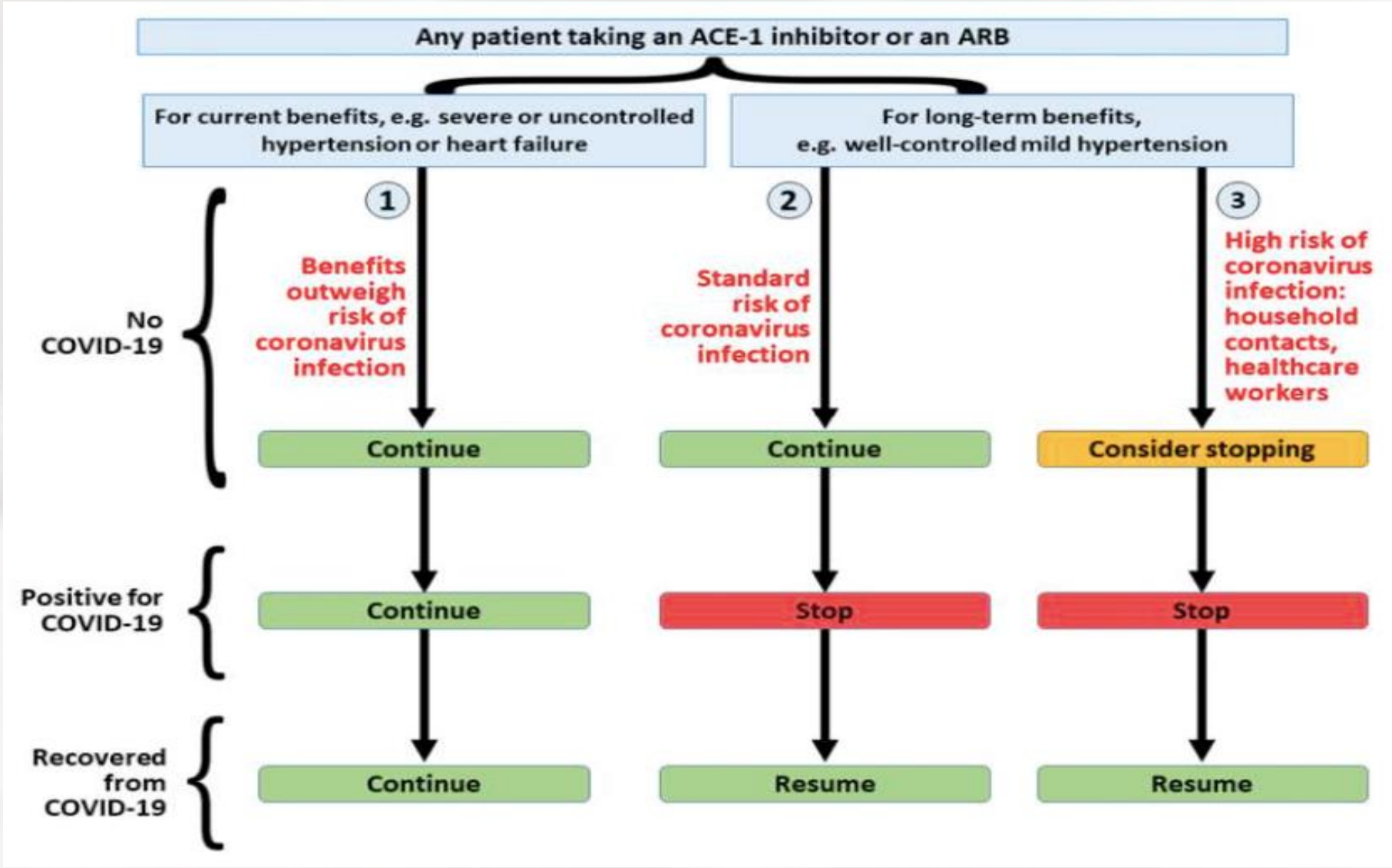
User of ACEI/ARB before COVID-19

Naive

You May Continue or Give ACEI/ARB in COVID-19 patient

Peng Zhang, *et al* .Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19. 2020. AHA Jour

ACEI/ARB Strategy



CEBM – University of Oxford, EK, 2020

ASEAN FEDERATION OF CARDIOLOGY

c/o National Heart Association of Malaysia
Heart House, D-13A-06, Menara Suezcap 1, KL Gateway, No.2 Jalan Kerinchi, Gerbang Kerinchi Lestari
59200 Kuala Lumpur, MALAYSIA
Tel: 603-7931 7900 Fax: 603-7932 1400
E-mail: AFCsecretariat@malaysianheart.org

AFC Position Statement on ACE-I and ARBs use related to COVID-19 outbreak

Scientists have shown that COVID-19 glycoprotein binds to the cell membrane protein angiotensin-converting enzyme 2 (ACE-2) to enter human cells. The structure of the ACE-2 receptor protein is on the surfaces of the respiratory cells. To COVID-19, ACE-2 is a receptor, an entranceway, in the airways and alveoli, as well as in blood vessel linings. Hypothetically, treatment with ACE-I or ARBs could possibly amplify the effects of COVID-19 and that patients on these antihypertensives may fare worse. Some medical professionals have become concerned and patients have possibly stopped taking ACE-I or ARBs medication.

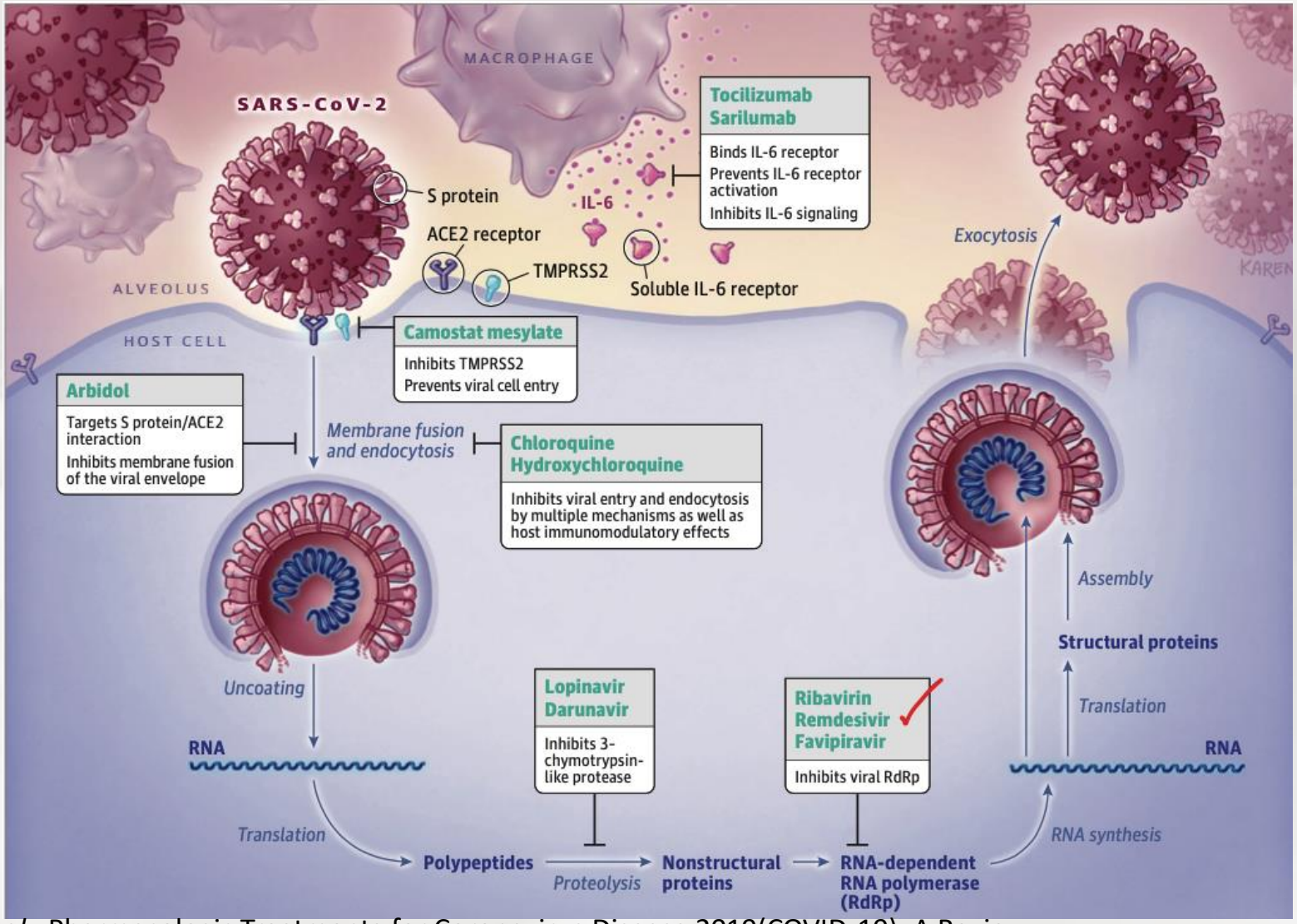
However, there is no clinical evidence or trial in human to show that we should discontinue ACE inhibitors or ARBs as stopping these drugs could precipitate acute events and worsened cardiac failure. There is currently no guideline that stated otherwise. The AFC (ASEAN Federation of Cardiology) would like to emphasize that this speculation of the unsafely of ACE-I or ARBs pertinent to COVID-19 is not evidence-based.

The American Heart Association, American College of Cardiology, European Society of Cardiology, European Society of Hypertension, and International Society of Hypertension have all issued similar recent statements urging continuation of the renin-angiotensin-aldosterone system antagonists in patients, despite theoretical concerns that their use might worsen outcomes in the event of infection with COVID-19.

Anwar Santoso, *MD, Ph.D, FAsCC*
President of AFC

Ng Wai Kiat, *MD, FAsCC*
Secretary General of AFC

Therapeutic Antiviral Target



Sanders JM, *et al.* Pharmacologic Treatments for Coronavirus Disease 2019(COVID-19). A Review. 2020. JAMA Clin Rev and Edu

Supplemental Table – Comparison of COVID-19 with Systemic Vasculopathies

Features	Common findings in vasculitidies	Severe CoViD-19
Infectious Triggers	Many known viral triggers: Hepatitis B/C, Varicella, HIV, Epstein-Barr Virus, Cytomegalovirus, SARS-CoV-1	SARS-CoV-2
Lung	vascular inflammation.	Organizing pneumonia, modest peri-vascular inflammation.
Reported organ involvement	CV, neuro, GI, renal, skeletal muscle	Cardiomyopathy, renal, gastrointertinal Anosmia, Delirium
Thrombotic events	Arterial / venous involvement. (Varies by specific disease).	Massive d-dimer elevations that correlates with death. DVT, pulmonary embolism, catheter thrombosis
Systemic inflammation	Mildly elevated inflammatory cytokines. (IL-6 generally < 100) Acute Phase Reactants: High CRP, ESR, Ferritin. Low albumin.	Mildly elevated inflammatory cytokines (IL-6 generally < 100) Acute Phase Reactants: High CRP, ESR, Ferritin. Low albumin, PCT

Abbreviations: HIV – Human immunodeficiency virus; CRP – C-reactive protein; ESR – erythrocyte sedimentation rate; PCT – procalcitonin; ECMO – extra-corporeal membrane oxygenation; DVT – deep venous thrombosis

Mount Sinai COVID-19 Anticoagulation Algorithm

Definition of high risk for progression to ICU

- There is insufficient evidence to precisely define "high-risk" or provide specific cut-off values for individual factors
- Clinicians should consider a combination of exam findings (e.g, labored breathing, RR >24, decreased O_2 sat<90%), increased O_2 requirement (eg, ≥4L NC), and lab biomarkers (eg, elevated CRP, elevated creatinine, rising d-dimer >1.0).

Rationale for early anticoagulation

- Pathophysiology of COVID-19 associated respiratory disease is consistent with pulmonary vascular thromboemboli with increased dead space ventilation
- Autopsy studies have demonstrated venous thromboembolism in deceased coronavirus patients[1]
- Early anticoagulation is necessary to prevent propagation of microthrombi at disease presentation
- Anticoagulation may be associated with decreased mortality[2]

Rationale for choice of anticoagulant

- Heparins bind tightly to COVID-19 spike proteins[3,4]
- Heparins also downregulate IL-6 and directly dampen immune activation[5]
- DOACs do not appear to have these anti-inflammatory properties
- Rivaroxaban can be used in place of Apixaban in this algorithm

References

1. Xiang-Hua et al. Am J Respir Crit Care Med, 182 (3), 436-7. PMID: 20675682
2. Tang et al. J Thromb Haemost 2020 Mar 27. PMID: 32220112
3. Belouzard et al. Proc Natl Acad Sci, 2009 106 (14), 5871-6. PMID: 19321428
4. de Haan et al. J Virol. 2005 Nov; 79(22): 14451–14456. PMID: 16254381
5. Mummery et al. J Immunol, 2000. 165 (10), 5671-9. PMID: 1106792

Incidence of Thrombosis in COVID-19

Venous and arterial thromboembolic events in hospitalized COVID-19 patients.

	Intensive care unit			General ward			Total		
Thromboembolic events	n	% of closed cases (n = 48)	% of imaging tests performed*	n	% of closed cases (n = 314)	% of imaging tests performed*	n	% of closed cases (n = 362)	% of imaging tests performed
At least one thromboembolic event	8	16.7% (95%CI 8.7%–29.6%)	–	20	6.4% (95%CI 4.2%–9.6%)	–	28	7.7% (95%CI 5.4%–11.0%)	–
VTE	4	8.3%	22%	12	3.8%	46%	16	4.4%	36%
PE (± DVT)	2	4.2%	25%	8	2.5%	36%	10	2.8%	33%
Isolated pDVT	1	2.1%	7%	3	1.0%	44%	4	1.1%	21%
Isolated dDVT	0	–	–	1	0.3%	13%	1	0.3%	13%
Catheter-related DVT	1	2.1%	50%	0	–	–	1	0.3%	50%
Ischemic stroke	3	6.3%	–	6	1.9%	–	9	2.5%	–
ACS/MI	1	2.1%	–	3	1.0%	–	4	1.1%	–

ACS, acute coronary syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; pDVT, proximal deep vein thrombosis; dDVT, distal DVT; PE, pulmonary embolism; VTE, venous thromboembolism.

Corado, et al . Venous and arterial thromboembolic complications in COVID-19 patients T admitted to an academic hospital in Milan, Italy.2020. Thrombosis Research: Elsevier