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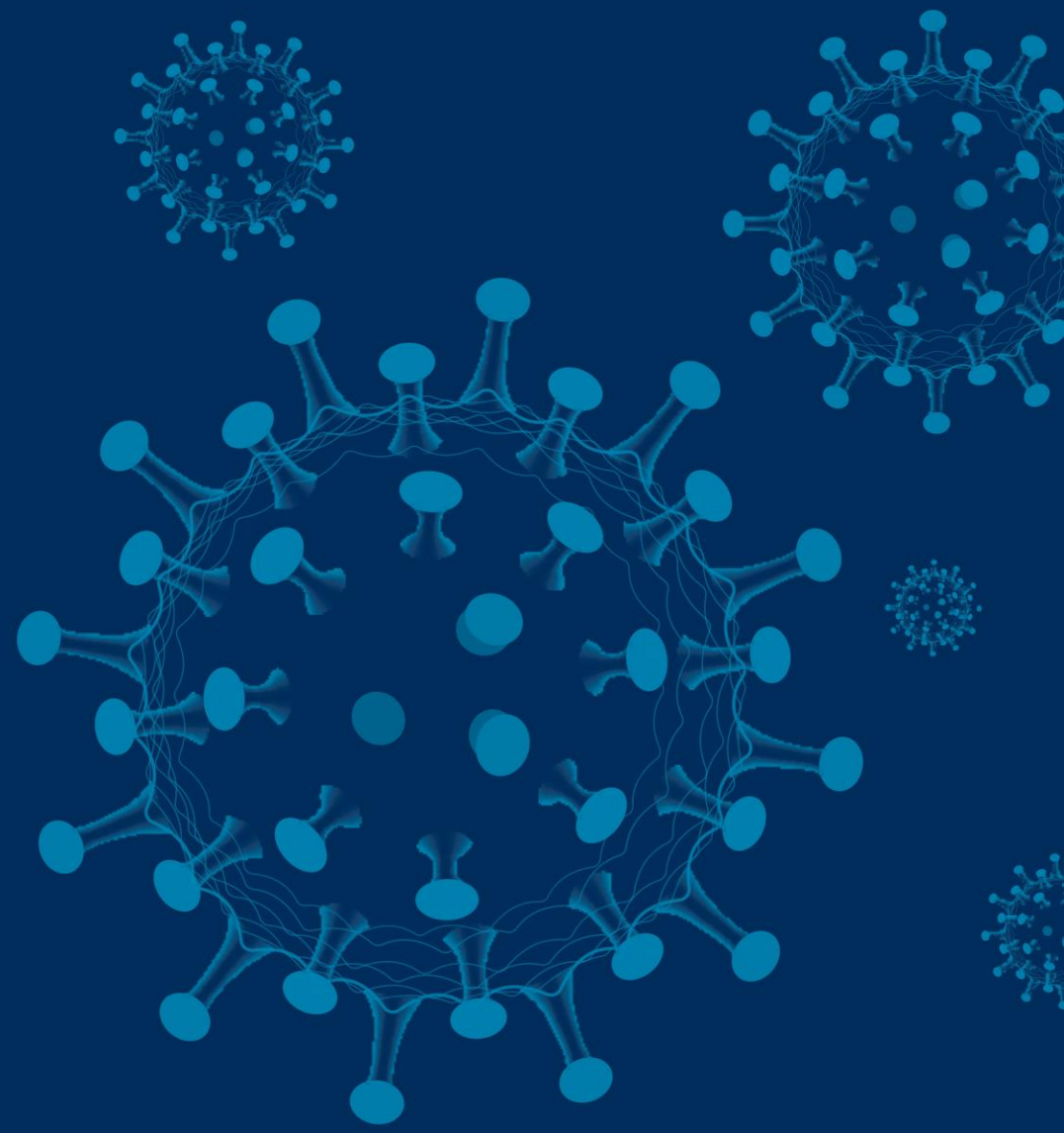
COVID-19

Mid-Summer Covid-19 Update: Achieving, Not Just Dreaming, About How to Improve



July 20, 2020

Speakers

- Kim Eagle, MD, FACC, Moderator
- Bina Ahmed, MD, FACC
- Nicole Bhave, MD, FACC
- Salim Hayek, MD, FACC
- Debabrata Mukherjee, MD, FACC

Presenter Disclosure Information

- Kim Eagle, MD, FACC, Moderator
  - Nothing to disclose
- Bina Ahmed, MD, FACC
  - Nothing to disclose
- Nicole Bhave, MD, FACC
  - Nothing to disclose
- Salim Hayek, MD, FACC
  - Nothing to disclose
- Debabrata Mukherjee, MD, FACC
  - Nothing to disclose

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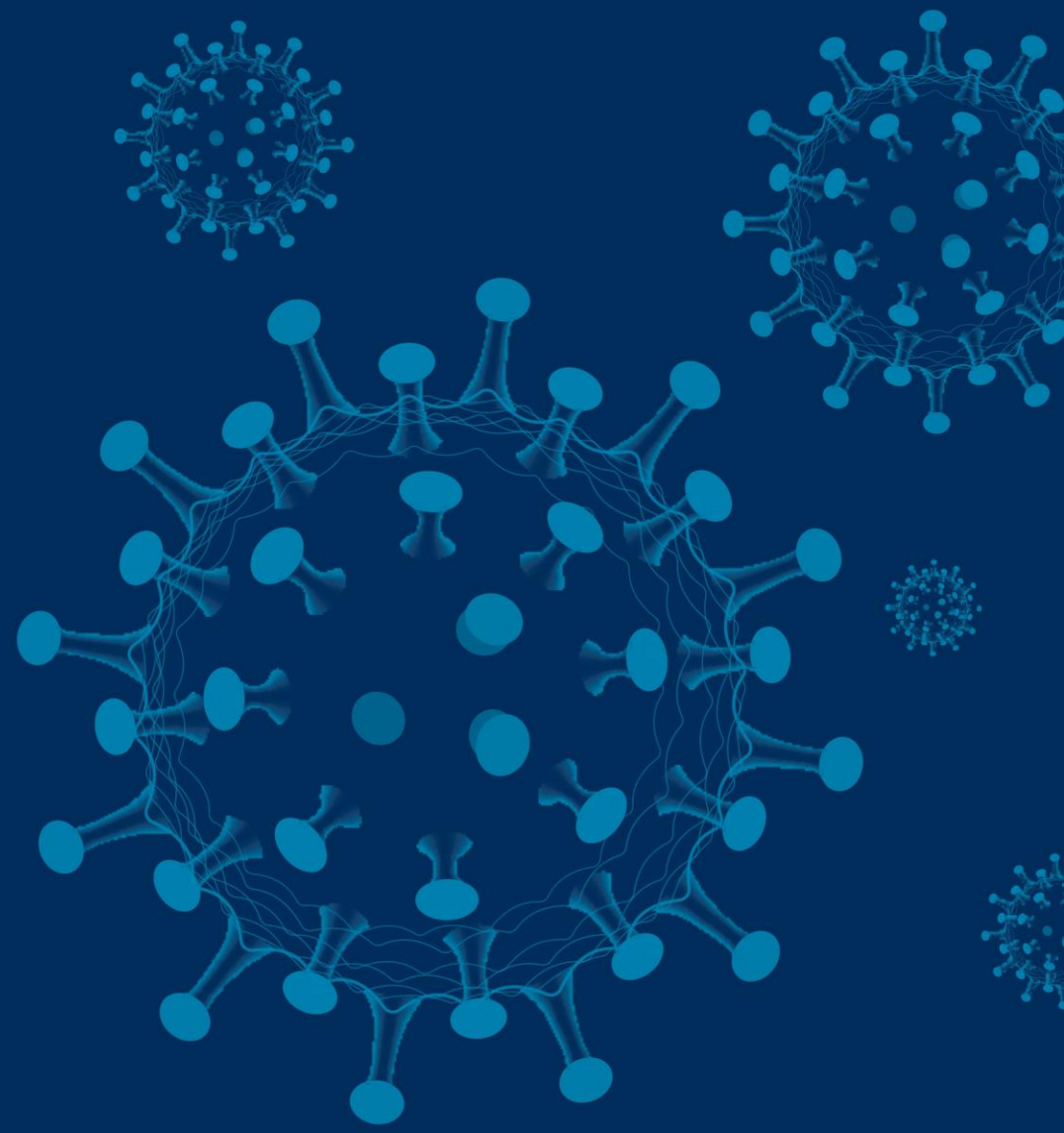
COVID-19

Genome-wide Association Study of Severe Covid-19 with Respiratory Failure

N Engl J Med 2020;Jun 17:[Epub ahead of print.
https://www.nejm.org/doi/full/10.1056/NEJMoa2020283

Salim Hayek, MD, FACC



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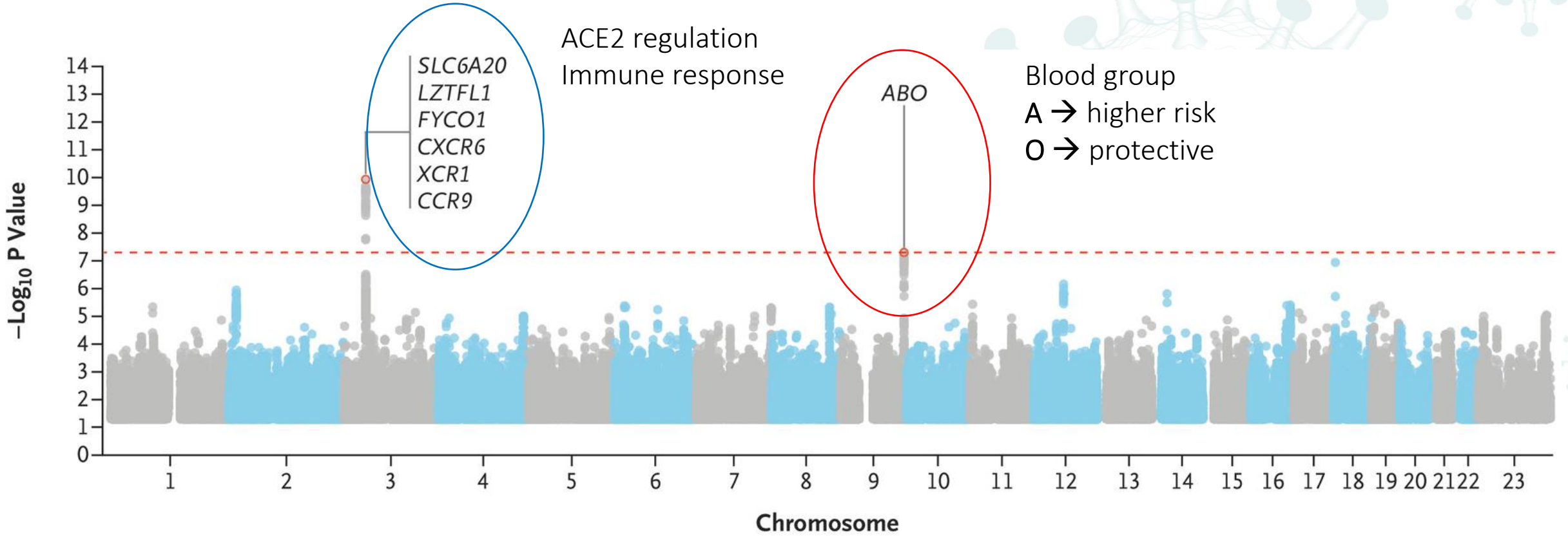
COVID-19

GWAS of COVID-19

- Case-control study of 1980 Italian and Spanish patients with severe COVID-19 and 2381 randomly selected healthy blood donors



Ellinghaus D, et al. *N Engl J Med*. 2020

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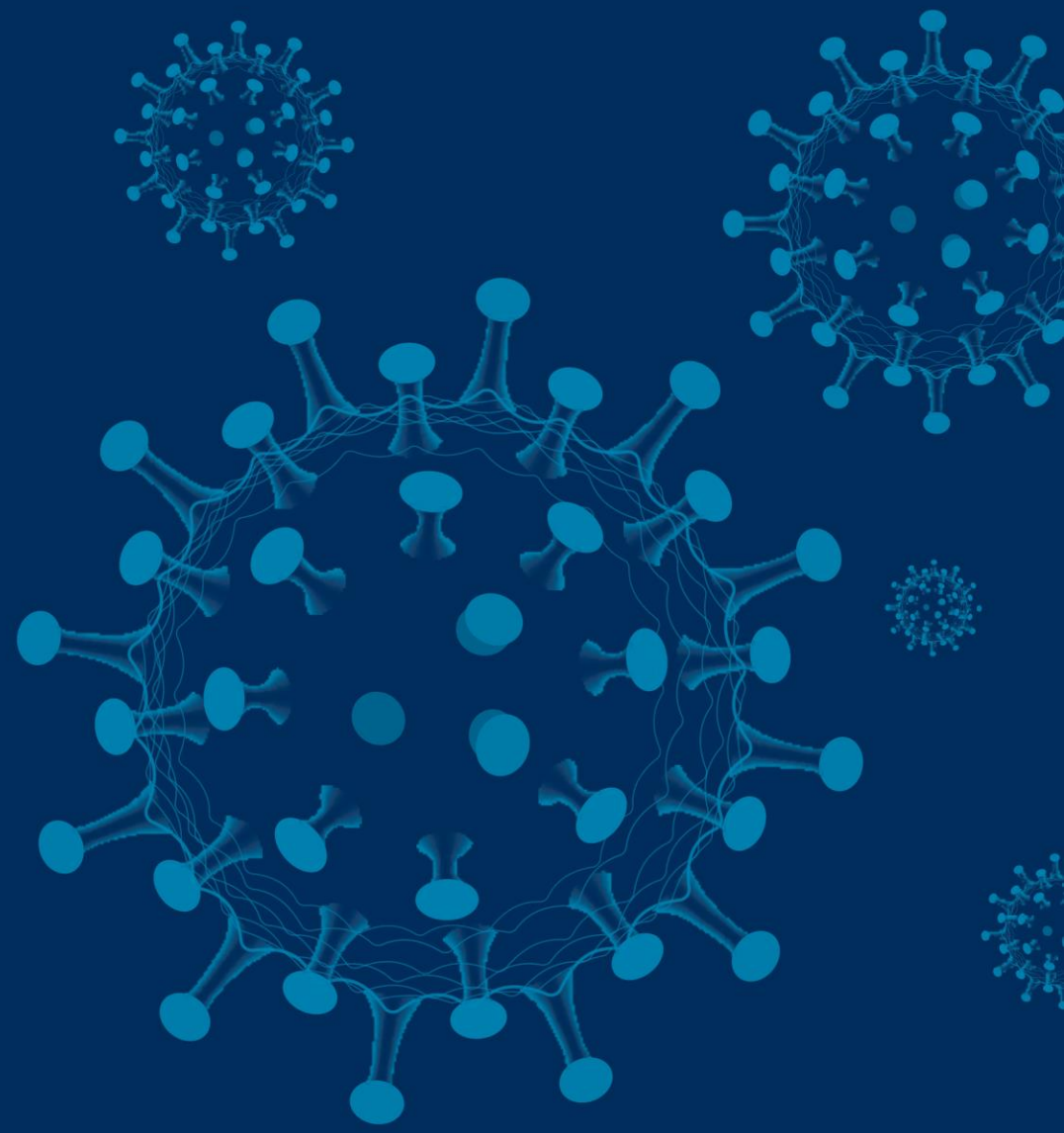
COVID-19

The Spectrum of Cardiac Manifestations in Coronavirus Disease 2019 (COVID-19) - A Systematic Echocardiographic Study.



Circulation 2020;May 29:[Epub ahead of print].
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.047971

Nicole Bhave, MD, FACC

Echocardiographic findings in COVID-19

- **Study question:** Among patients hospitalized with COVID-19, what abnormalities are seen on transthoracic echocardiograms (TTEs)?
- **Methods:** 100 consecutive adults with COVID underwent TTE within 24 hr of admission to Tel Aviv Medical Center
- **Patients:** Mean age 66.1 yr, 63% male, 39% requiring O_2 (10% ventilated), 20% ↑TnI, 30% ↑BNP

Szekely et al., *Circulation* 2020

- **Findings:** Normal TTE (32%), RV dilation ± dysfunction (39%), LV diastolic dysfunction (16%), LV systolic dysfunction (10%)
- **Clinical deterioration→repeat TTE:** 20% - most common finding RV dilation/dysfunction (12/20 patients, including 5 with DVT)
- **Conclusions**
  - In all comers, RV suffers more than LV
  - Findings support selective use of TTE in COVID inpatients

Szekely et al., *Circulation* 2020

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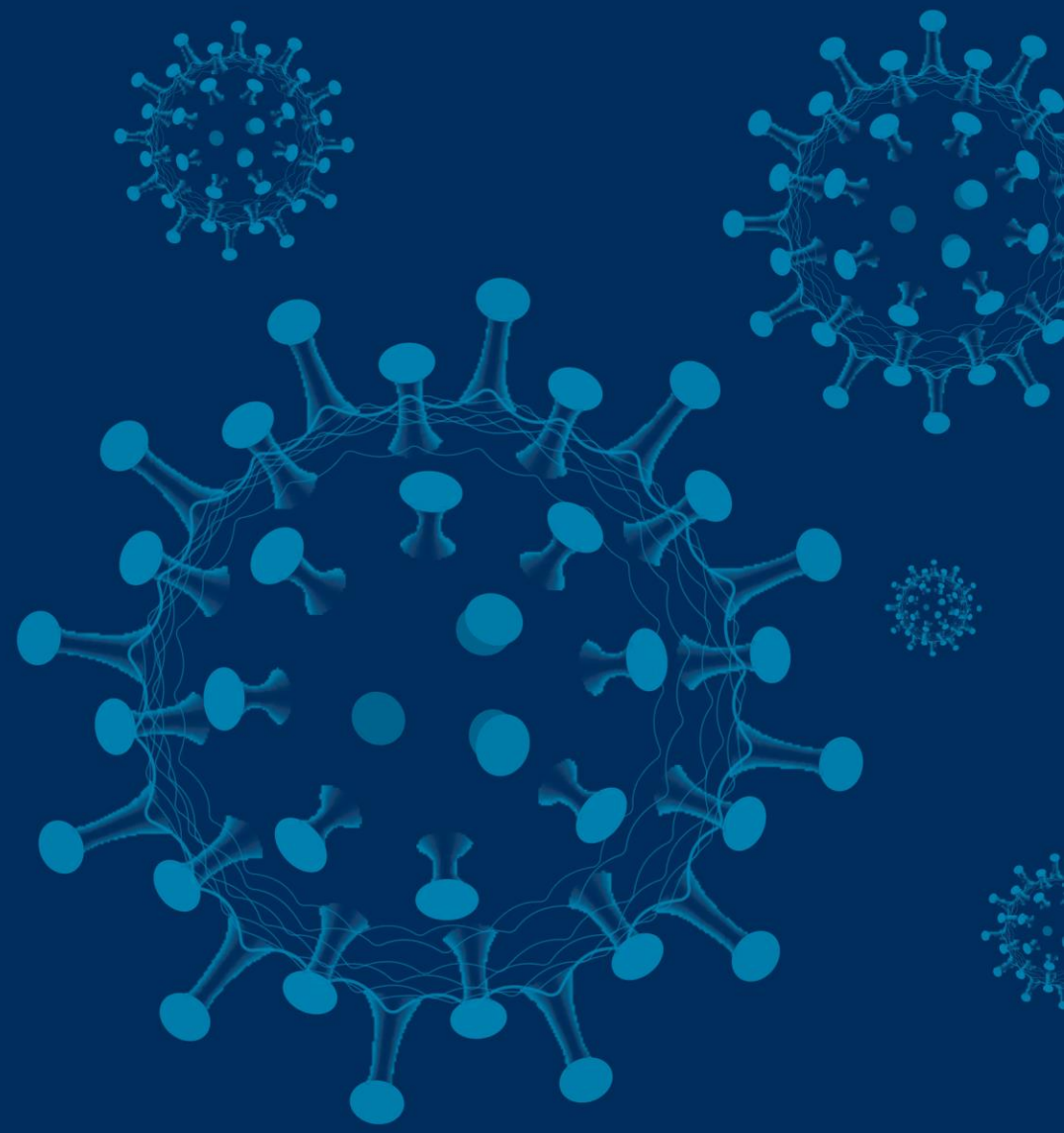
COVID-19

Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure

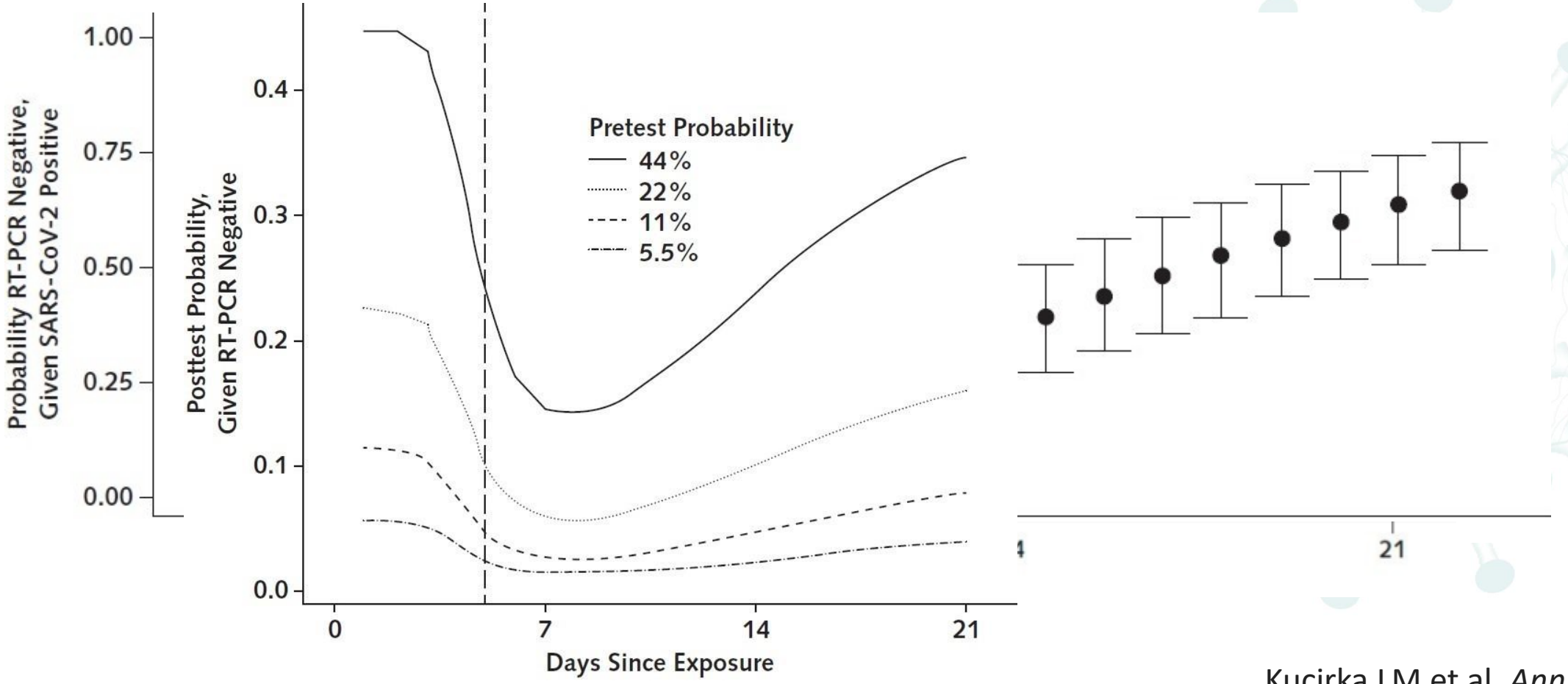
Ann Intern Med 2020;May 13:[Epub ahead of print
https://www.acpjournals.org/doi/10.7326/M20-1495

Salim Hayek, MD, FACC



RT-PCR Testing for SARS-CoV-2

- Meta-analysis of 7 studies on RT-PCR testing for SARS-CoV-2



Kucirka LM et al. *Ann Intern Med*. 2020

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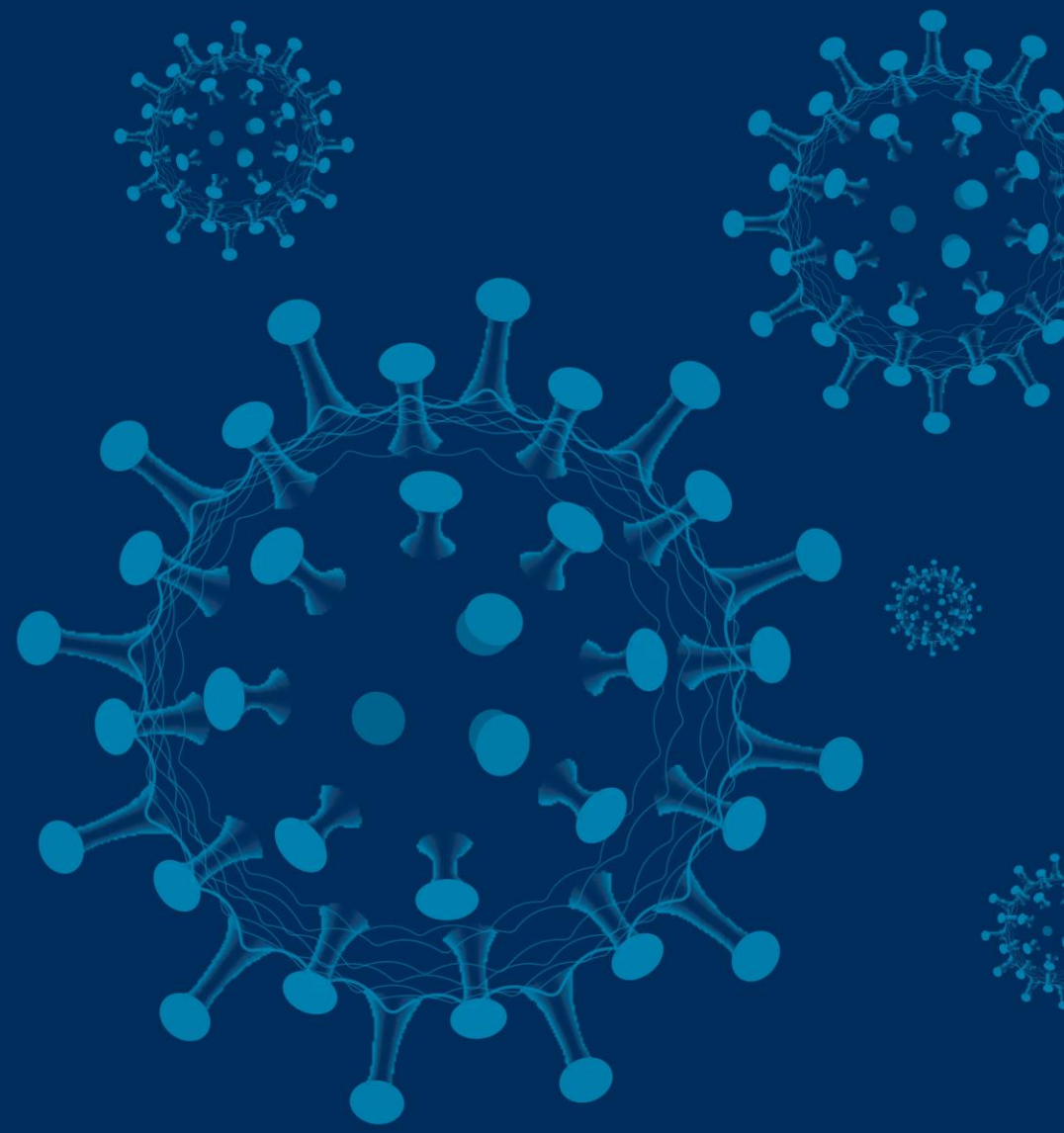
COVID-19

Diagnostic Testing for Severe Acute Respiratory Syndrome-Related Coronavirus-2

Ann Intern Med 2020;May 13:[Epub ahead of print.
https://www.acpjournals.org/doi/10.7326/M20-1301

Salim Hayek, MD, FACC



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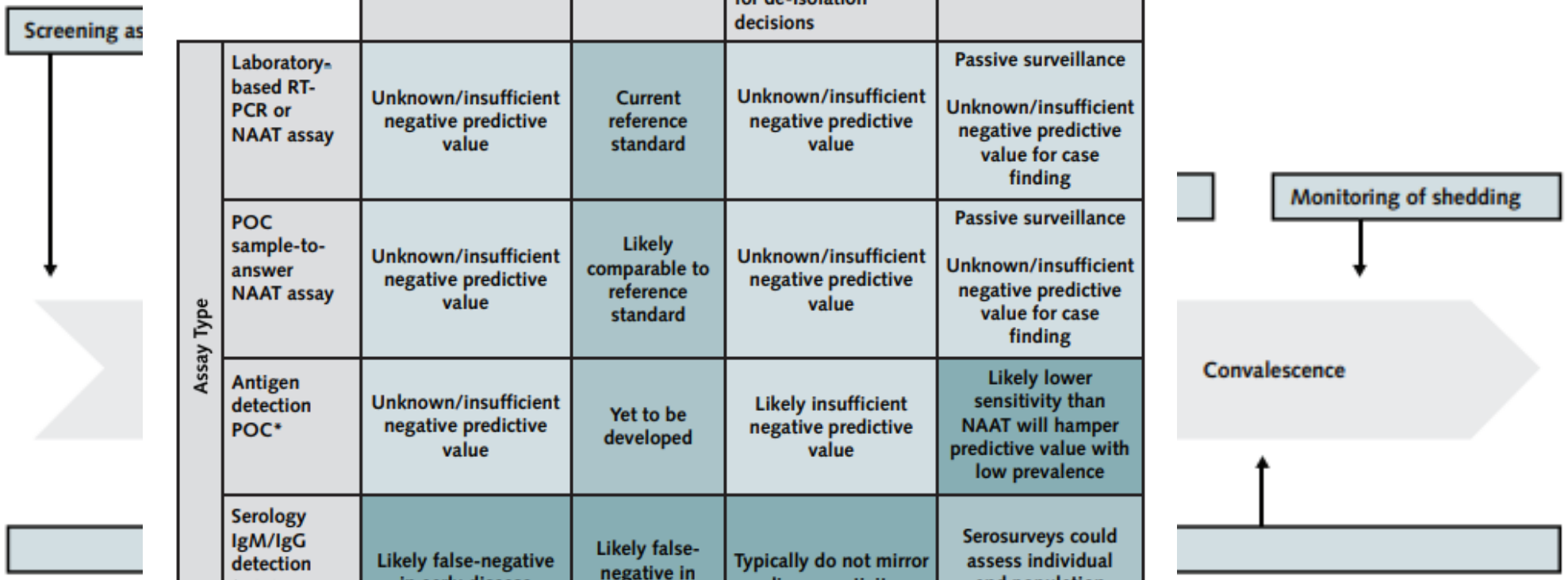
Diagnostic testing for SARS-CoV-2

- Review or SARS-CoV-2

		Selected Use Case			
		Screening during incubation/asymptomatic phase	Diagnosis of symptomatic disease	Screening for viral shedding in convalescence phase for de-isolation decisions	Epidemiologic surveillance
Assay Type	Laboratory-based RT-PCR or NAAT assay	Unknown/insufficient negative predictive value	Current reference standard	Unknown/insufficient negative predictive value	Passive surveillance Unknown/insufficient negative predictive value for case finding
	POC sample-to-answer NAAT assay	Unknown/insufficient negative predictive value	Likely comparable to reference standard	Unknown/insufficient negative predictive value	Passive surveillance Unknown/insufficient negative predictive value for case finding
	Antigen detection POC*	Unknown/insufficient negative predictive value	Yet to be developed	Likely insufficient negative predictive value	Likely lower sensitivity than NAAT will hamper predictive value with low prevalence
	Serology IgM/IgG detection (POC or laboratory based)*	Likely false-negative in early disease	Likely false-negative in early disease†	Typically do not mirror disease activity	Serosurveys could assess individual and population immunity*



Cheng MP et al. *Ann Intern Med*. 2020

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COVID-19

Cardiac Troponin I in Patients With Coronavirus Disease 2019 (COVID-19): Evidence from a Meta-Analysis

Prog Cardiovasc Dis 2020;Mar 10:[Epub ahead of print
https://www.clinicalkey.com/#!/content/journal/1-s2.0-S0033062020300554

Debabrata Mukherjee, MD

Cardiac troponin I in patients with COVID-19: Evidence from a meta-analysis

Lippi G, Lavie CJ, Sanchis-Gomar F. *Prog Cardiovasc Dis.* 2020 Mar 10:S0033-0620(20)30055-4

- An analysis of the current scientific literature to investigate whether the measurement of cardiac troponin I (cTnI) or cardiac troponin T (cTnT) may help predict clinical severity in patients with COVID-19

- 4 studies were finally included in the meta-analysis and included a total number of 341 patients (123 with severe disease; 36%)

- The values of cTnI were increased in COVID-19 patients with severe disease compared to those with milder forms of disease

Cardiac troponin I in patients with COVID-19: Evidence from a meta-analysis

Lippi G, Lavie CJ, Sanchis-Gomar F. *Prog Cardiovasc Dis.* 2020 Mar 10:S0033-0620(20)30055-4

- This study suggests that initial measurement of troponin immediately after hospitalization for SARS-CoV-2 infection, as well as longitudinal monitoring during hospital stay, may help predict the progression of COVID-19 towards a worse clinical picture

- An article from last week by Sandoval et al, Cardiac Troponin for the Diagnosis and Risk-Stratification of Myocardial Injury in COVID-19: JACC Review Topic of the Week published July 8th, 2020 reported that increases in cardiac troponin (cTn) are associated with adverse outcomes such as arrhythmias and death. Troponin increases are more likely to occur in those with chronic cardiovascular conditions and in those with severe COVID-19 presentations

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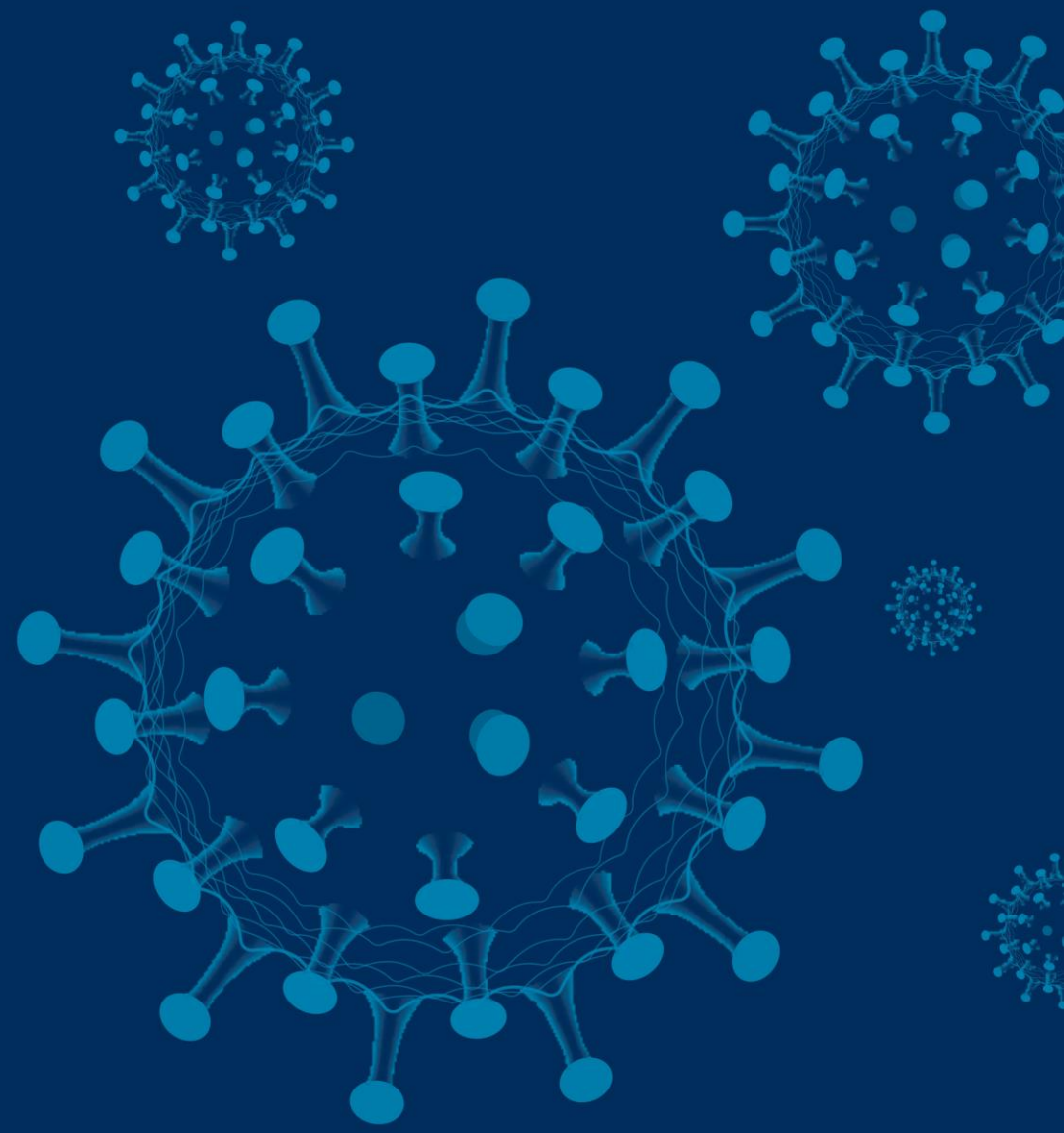
COVID-19

Remdesivir for 5 or 10 Days in Patients With Severe Covid-19



Lancet 2020;Apr 29:[Epub ahead of print]
https://www.thelancet.com/lancet/article/s0140673620310229

Debabrata Mukherjee, MD

Remdesivir for 5 or 10 Days in Patients With Severe Covid-19. N Engl J Med 2020;May 27

Goldman JD, Lye DCB, Hui DS, et al., on behalf of the GS-US-540-5773 Investigators

- The study assessed whether treatment with intravenous remdesivir for 10 days compared to 5 days in patients hospitalized with coronavirus disease 2019 (COVID-19) improves clinical status at day 14 of hospitalization

- Open-label, randomized, multicenter trial, hospitalized 397 patients (≥12 years old) with confirmed severe coronavirus 2 (SARS-CoV-2) infection with radiographic evidence of COVID-19 and oxygen saturation ≤94% or requiring oxygen supplementation were randomized to intravenous remdesivir for 10 days versus 5 days

- There was no difference in clinical improvement at 14 days with a 10-day course of remdesivir compared to a 5-day course in patients with COVID-19 not requiring mechanical ventilation

Remdesivir for 5 or 10 Days in Patients With Severe Covid-19. N Engl J Med 2020;May 27

Goldman JD, Lye DCB, Hui DS, et al., on behalf of the GS-US-540-5773 Investigators

- Some differences in clinical status at baseline, with significantly more patients in the 10-day group requiring mechanical ventilation prior to initiation of treatment, and a higher number needed high-flow oxygen support

- Longer treatment with intravenous (10 days) remdesivir was not associated with clinical improvement compared to a shorter treatment period (5 days)

- Until proven otherwise, a 5-day remdesivir regimen should be given to patients at the early stages of severe disease

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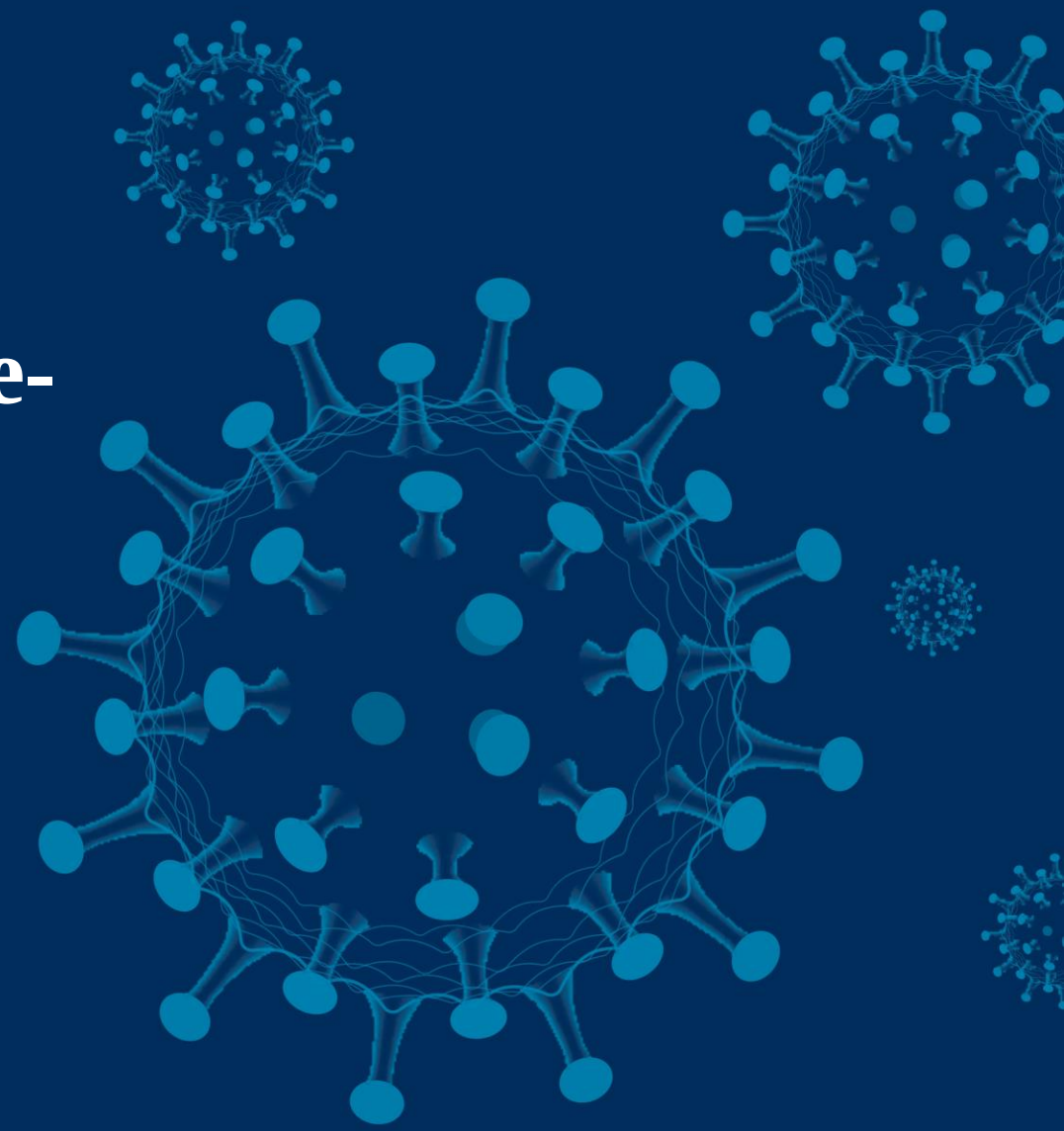
COVID-19

Remdesivir in Adults With Severe COVID-19: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial

N Engl J Med 2020;May 27:[Epub ahead of print].
https://www.nejm.org/doi/full/10.1056/NEJMoa2015301

Debabrata Mukherjee, MD



Remdesivir in Adults With Severe COVID-19: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Lancet 2020;Apr 29:

Wang Y, Zhang D, Du G, et al

- The study assessed whether treatment with remdesivir of adult patients with coronavirus disease 2019 (COVID-19) associated with clinical improvement compared to placebo

- This was a double-blind, placebo-controlled multicenter trial at 10 hospitals in Hubei, China, which enrolled 237 adults (≥18 years) hospitalized with confirmed coronavirus 2 (SARS-CoV-2) infection who met the following criteria: <12 days of symptoms, oxygen saturation of ≤94% on room air, and radiologically confirmed pneumonia

- IV remdesivir was not associated with clinical improvement or mortality in adult patients with COVID-19

Remdesivir in Adults With Severe COVID-19: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Lancet 2020;Apr 29:

Wang Y, Zhang D, Du G, et al

- The study did not reach its target enrollment (n = 453), and its study population was overall less ill, with few patients requiring mechanical ventilation during the disease course

- Preliminary data from the Adaptive COVID-19 Treatment Trial (ACTT) reported that benefit was most apparent in patients requiring oxygen [Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 - Preliminary Report (published May 22, 2020). N Engl J Med. 2020

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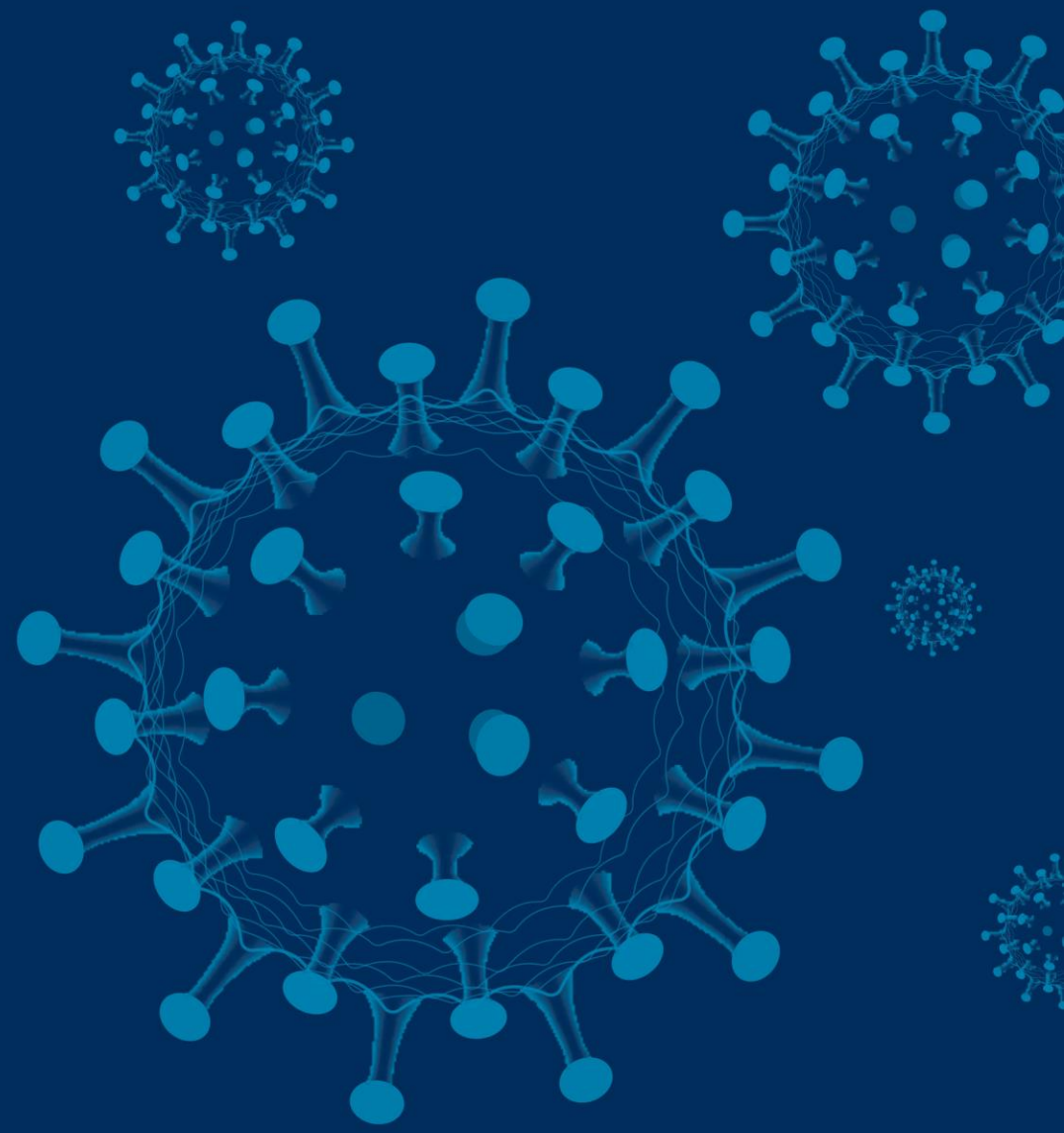
COVID-19

Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial

Lancet 2020;May 22:[Epub ahead of print]
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31208-3/fulltext

Salim Hayek, MD, FACC



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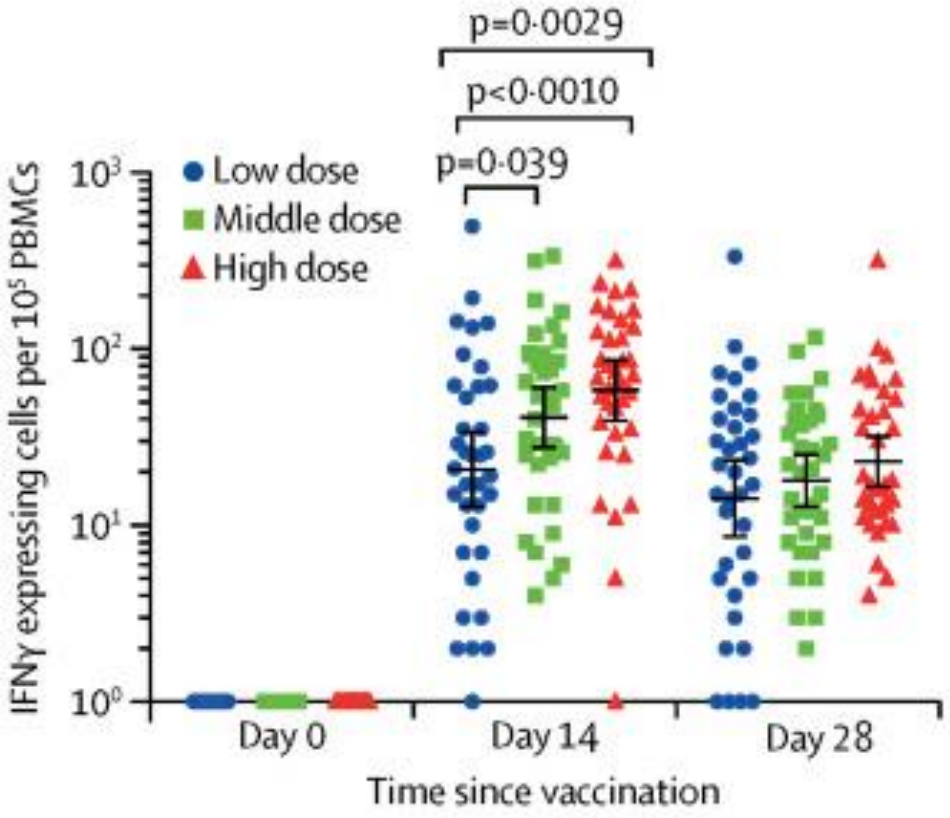
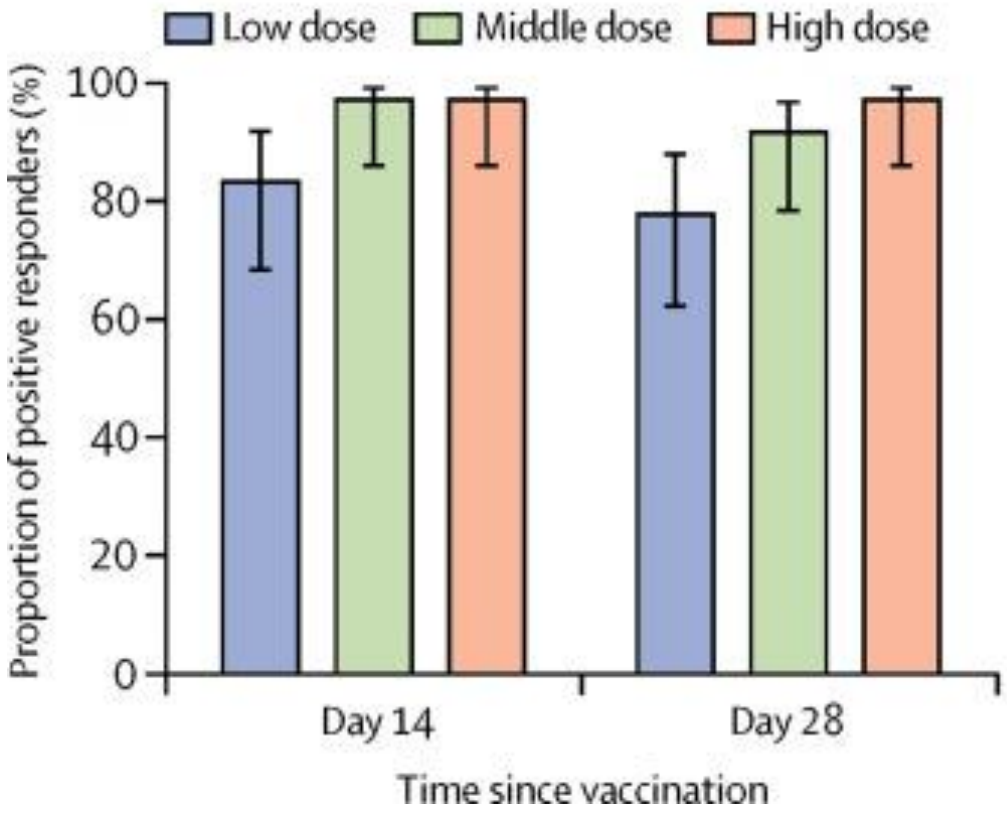
Phase 1 Trial of COVID-19 Vaccine

- Single center, non-randomized phase 1 trial of **Ad5-vectored vaccine**





Zhu FC et al. *Lancet*. 2020

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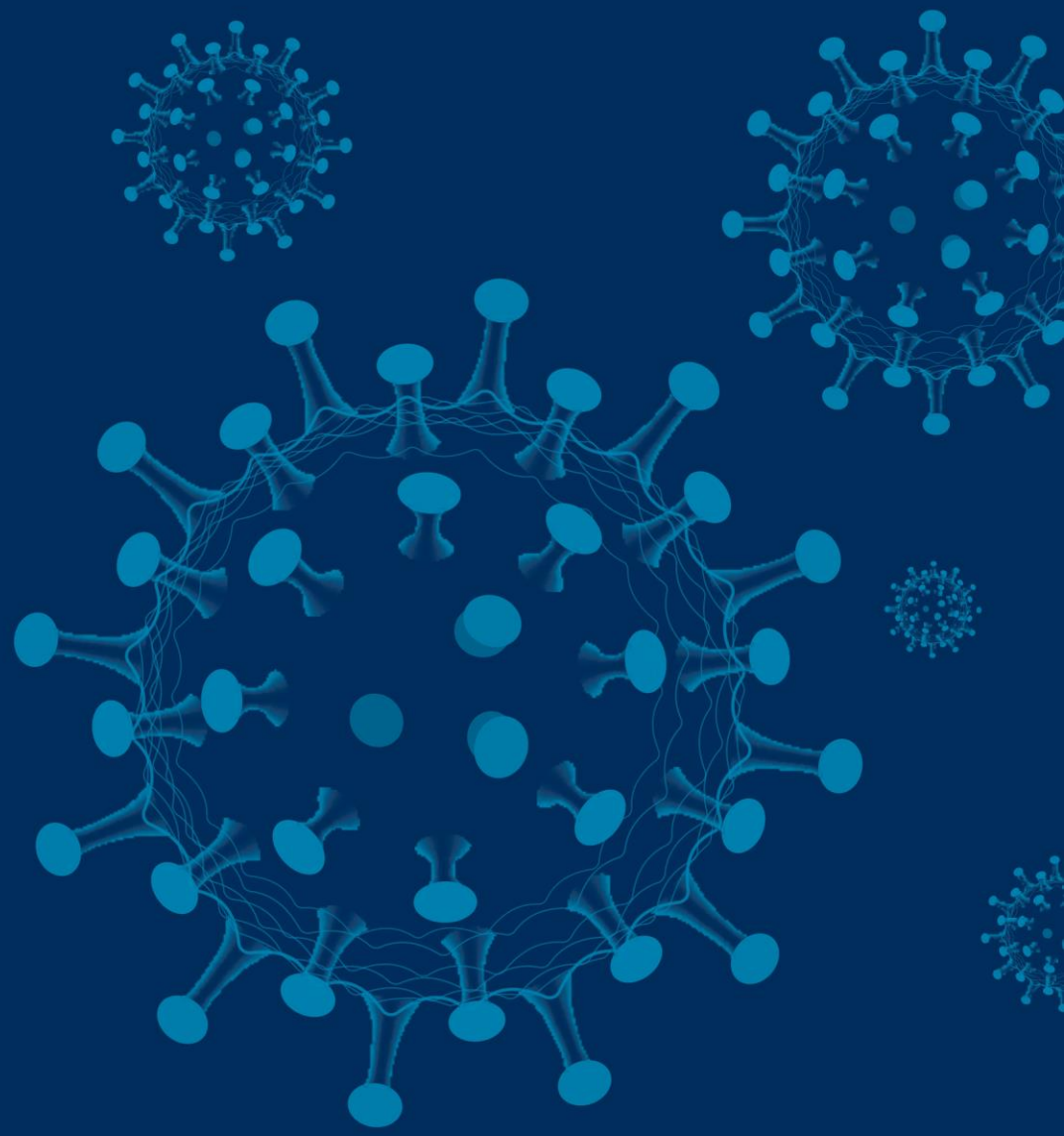
COVID-19

Use of Renin-Angiotensis-Aldosterone System Inhibitors and Risk of COVID-19 Requiring Admission Hospital: A Case-Population Study



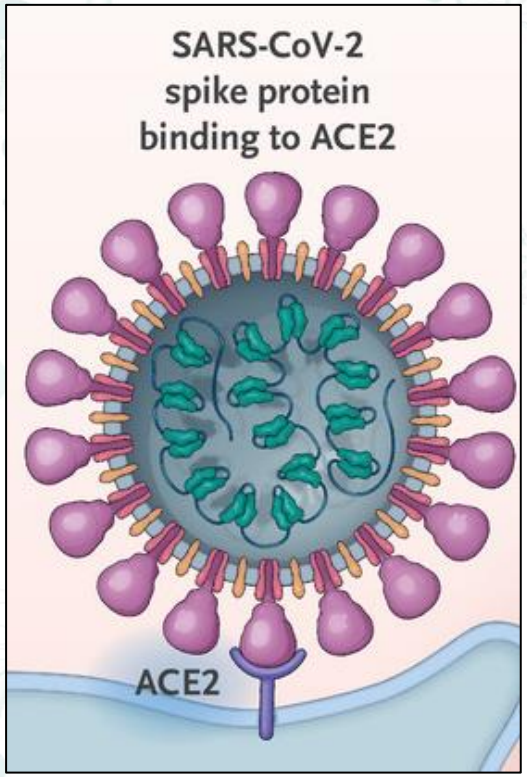
Lancet 2020;May 14:
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31030-8/fulltext

Nicole Bhave, MD, FACC

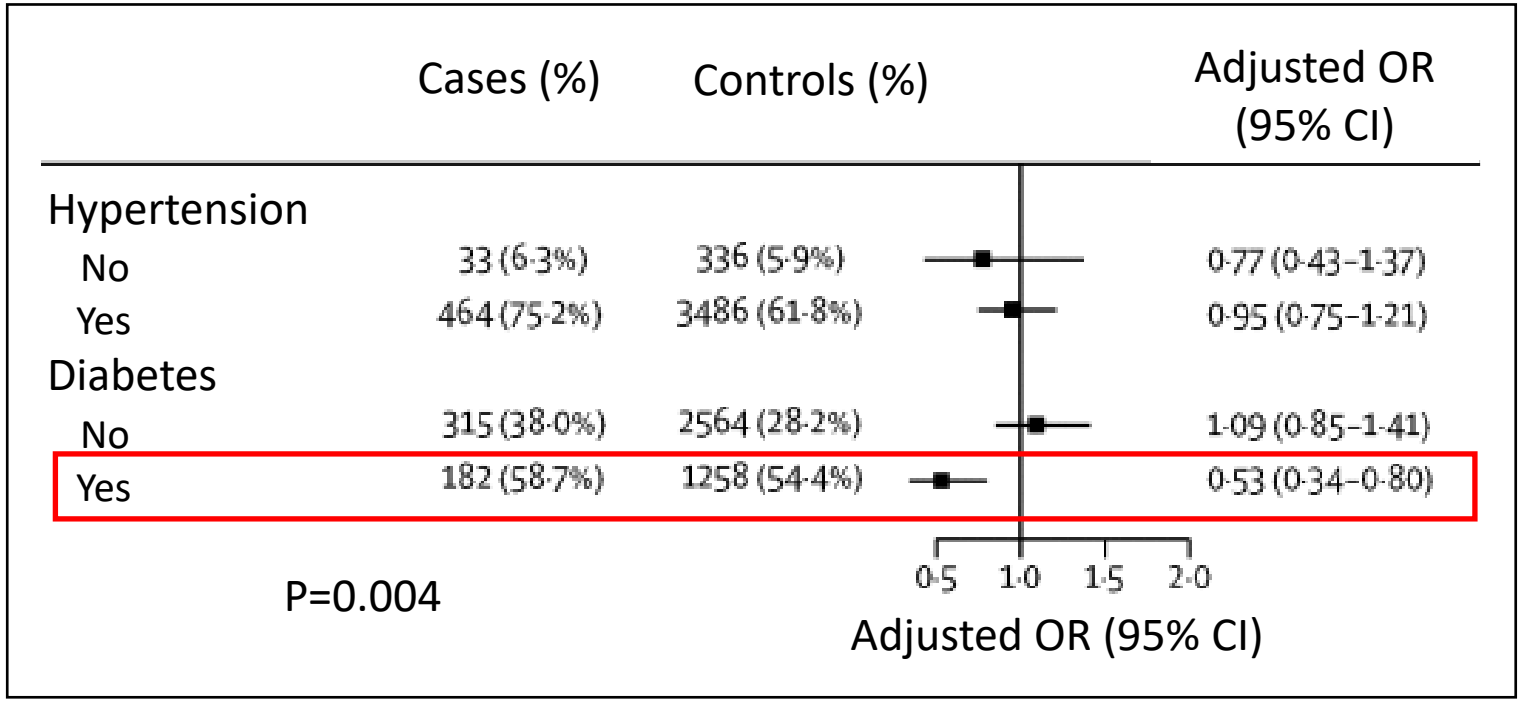
RAAS inhibitors and risk of COVID-19

- **Study question:** What is the risk of COVID-19 requiring hospital admission among patients taking RAAS inhibitors?
- **Methods:** Case-population control study in Madrid; RAAS inhibitors compared with other antihypertensives
- **Key finding:** Adjusted OR for RAAS inhibitors: 0.94 (95% CI 0.77-1.15)

de Abajo et al., *Lancet* 2020



Vaduganathan et al., *N Engl J Med.* 2020



de Abajo et al., *Lancet* 2020

Take-home messages

- RAAS inhibitors do not increase risk of COVID requiring hospitalization
- These drugs may be protective in diabetic patients - further study needed
- Don’t stop drugs in stable patients; reassurance is key

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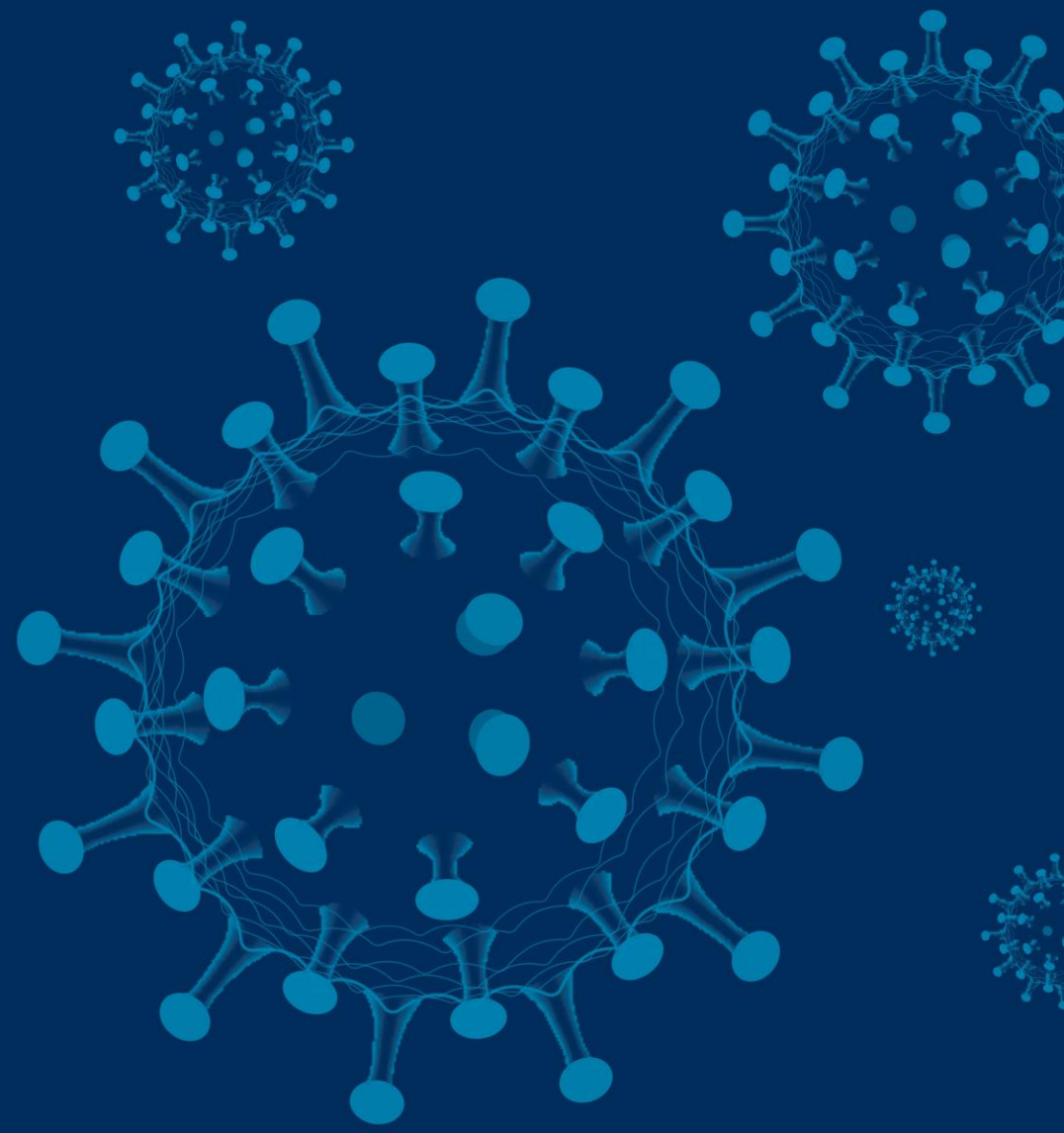
COVID-19 and Renin Angiotensin Blockers: Current Evidence and Recommendations



Circulation 2020;Apr 13:
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.047022

Bina Ahmed, MD, FACC

COVID-19 and Renin Angiotensin Blockers-Current Evidence and Recommendations

Masserli F et al.

- SARS-CoV-2 uses ACE2 receptor as cellular entry point.
- There has been interest in better understanding possible relationship between renin angiotensin system (RAS) modification and SARS-CoV-2 infection
- Clinical implications of use of angiotensin converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB) and SARS-CoV-2 infection
- There is *both* concern about increased risk of infection and adverse outcomes related to ACE-I and ARB use *and* potential benefit of these treatments to limit lung injury among patients with SARS-CoV-2
- Summary of previously published data on the relationship between ACE-I and ARBs and respiratory infections

Circulation. Volume 141, Issue 25, 23 June 2020;Pages 2042-2044

COVID-19 and Renin Angiotensin Blockers-Current Evidence and Recommendations

Masserli F et al.

- Key points:
  - Animal studies suggest less lung injury with use of ARBs. Single human study suggested that patients with pneumonia on ACE-I had decreased mortality
  - CVD and HTN are associated with increased risk of SARS-CoV-2 infection and infection related mortality *and* large number of patients are taking ACE-I or ARB
  - Multiple retrospective analyses have shown no relationship between ACE-I or ARB treatment and SARS-CoV2 outcomes.
  - Current consensus recommendation is to continue with ACE or ARB treatment as clinically indicated during SARS-CoV-2 infection
  - Whether RAS modification with ACE-I or ARBs can be used to reverse lung injury remains to be determined.

Circulation. Volume 141, Issue 25, 23 June 2020;Pages 2042-2044

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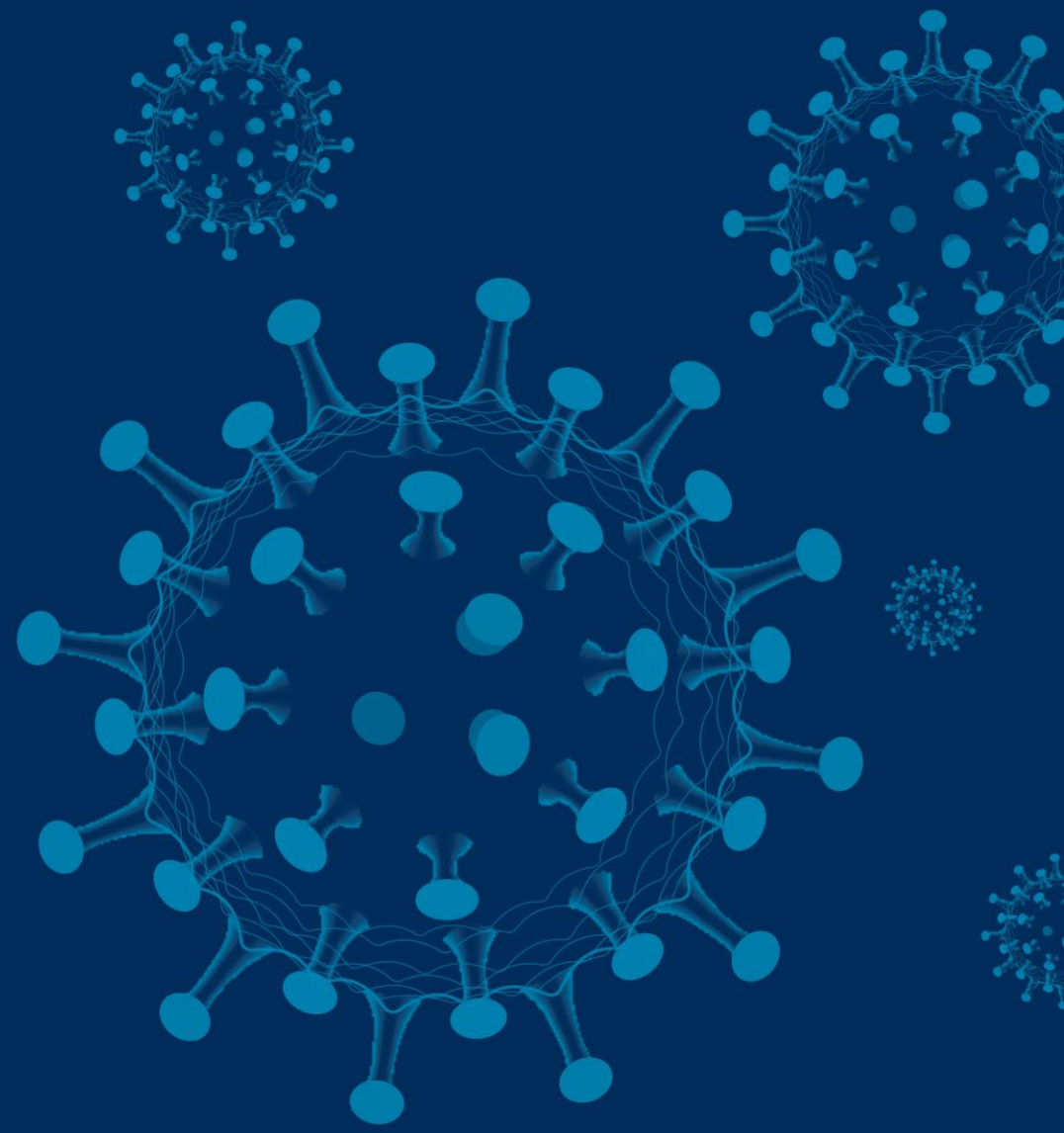
COVID-19

COVID -19 Kills at Home: The Close Relationship Between the Epidemic and the Increase of Out-of-Hospital Cardiac Arrest

Eur Heart J 2020;Jun20
https://academic.oup.com/eurheartj/article/doi/10.1093/eurheartj/ehaa508/5860258

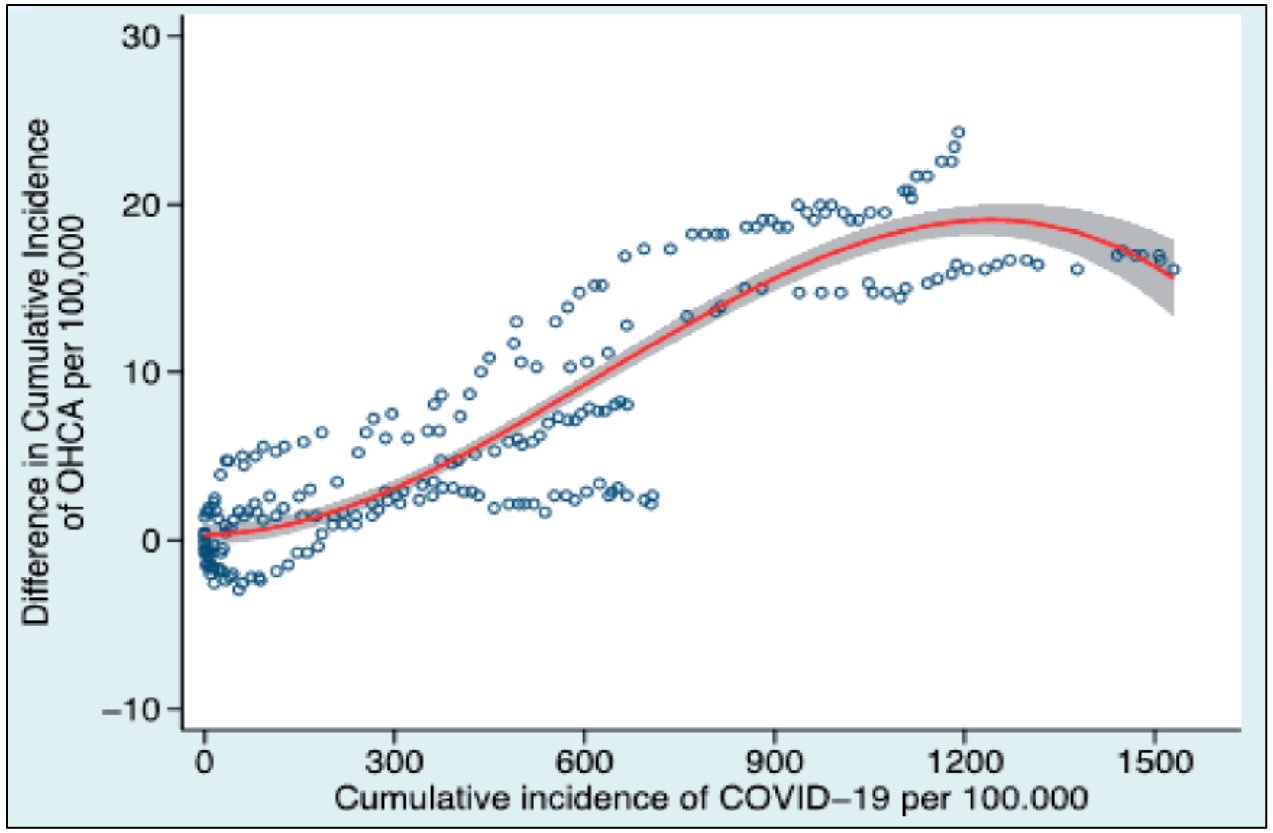
Nicole Bhave, MD, FACC



Out-of-hospital cardiac arrest and COVID-19

- **Study question:** How has the pandemic impacted out-of-hospital cardiac arrest (OHCA) incidence?
- **Methods:** Lombardia Cardiac Arrest Registry, comparing Feb-April 2020 with Feb-April 2019
- **Findings**
  - 52%↑ OHCA in 2020 (490 vs. 321 events)
  - Confirmed/suspected COVID: 125 patients (74% of increase)
  - Pre-hospital ROSC: 8.6% in 2020 vs. 19.8% in 2019 ($p<0.001$)

Baldi et al., *Eur Heart J.* 2020



Baldi et al., *Eur Heart J.* 2020

Conclusions and perspective

- COVID cases closely correlated with OHCA increase
- COVID can kill at home
  - Rapid progression to ARDS
  - Myocardial injury, arrhythmia, PE
- Hypoxia → failed ROSC (unshockable rhythms)
- Profound strain on health care system at height of pandemic

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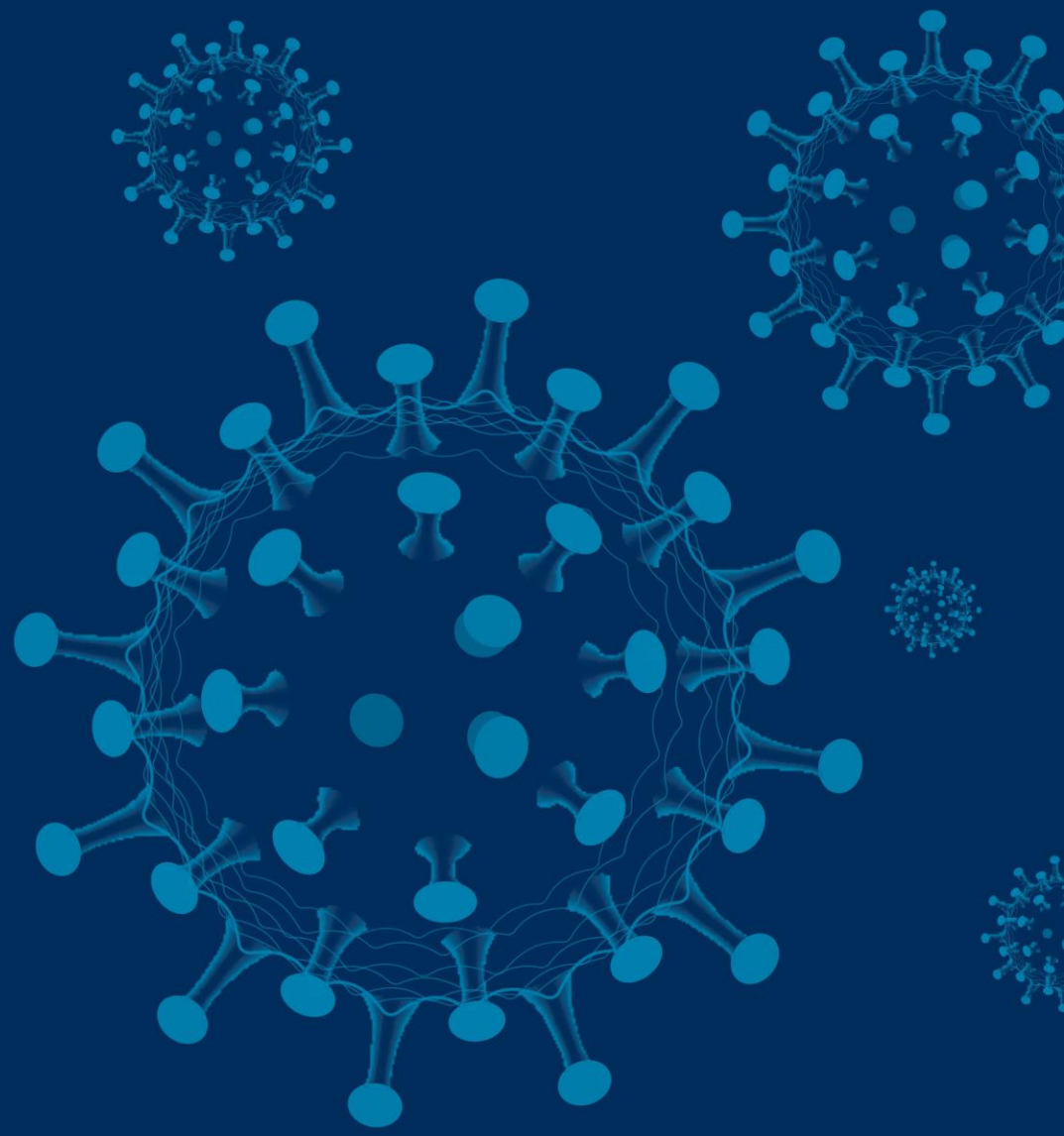
ST-Elevation Myocardial Infarction in Patients With COVID-19: Clinical and Angiographic Outcomes



Circulation 2020;Apr 30
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.047525

Bina Ahmed, MD, FACC

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COVID-19

ST-Elevation Myocardial Infarction in Patients With COVID-19. Clinical and Angiographic Outcomes

Stefanini G et al.

- Cardiovascular presentation related to SARS-CoV-19 infection can be varied and include acute myocardial infarction (AMI), myocarditis, stress cardiomyopathy, coronary spasm or non-specific myocardial injury
- Due to need for emergent intervention for STEMI patients, there has been concern about ensuring adequate protection from exposure to the ED and cathlab clinical staff while providing timely care to a patient with STEMI.
- Retrospective angiographic analysis from Lombardy, Italy of 28 patients with confirmed COVID-19 who underwent emergent coronary angiography due to STEMI from February to March 2020

Volume 141, Issue 25, 23 June 2020;, Pages 2113-2116

ST-Elevation Myocardial Infarction in Patients With COVID-19. Clinical and Angiographic Outcomes

Stefanini G et al.

- Key Points:
  - Majority (85%) presented with symptoms of STEMI and had localized wall motion on echocardiography.
  - 61% had evidence of a culprit thrombotic lesion requiring revascularization.
  - High mortality (39%) on short term follow up.
  - SARS-CoV-2 can cause myocardial injury by several mechanisms.
  - Challenge is to provide timely reperfusion to the correct patients while minimizing risk to healthcare providers and optimizing utilization of limited resources during the pandemic.

Volume 141, Issue 25, 23 June 2020; Pages 2113-2116

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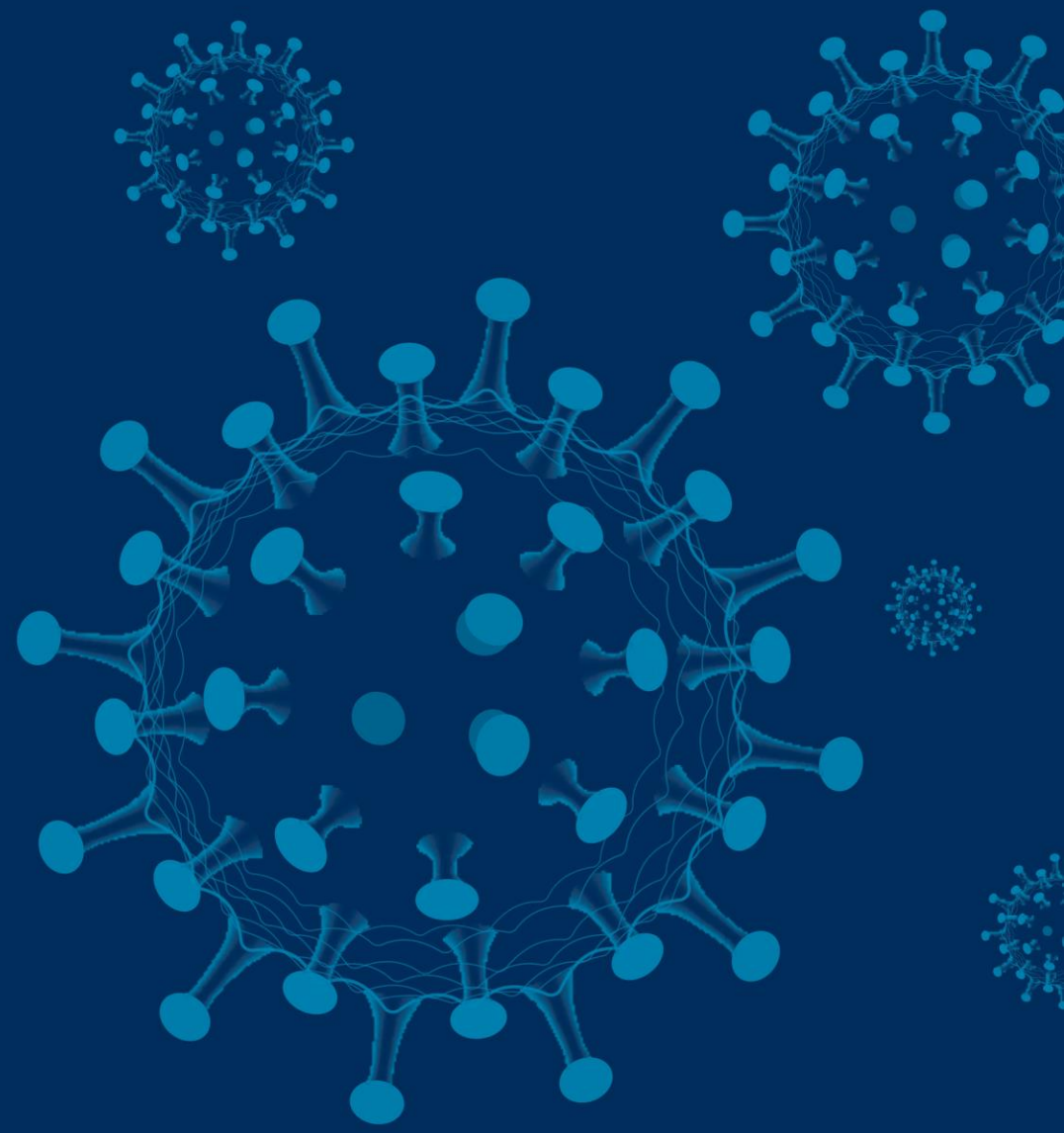
COVID-19

Reperfusion of STEMI in the COVID-19 Era – Business as Usual



Circulation 2020;Apr 13;
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.047122

Bina Ahmed, MD, FACC

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COVID-19

Reperfusion of ST-Segment–Elevation Myocardial Infarction in the COVID-19 Era. Business as Usual?

Daniels M et al.

- Should we re-examine primary PCI as the default approach for patients with STEMI in the COVID 19-Era?
- Fibrinolytic first therapy (FT) is currently the default approach *only* for patients who cannot receive timely PCI.
- Advantages of FT first approach:
  - Known efficacy in subset of patients
  - Mitigate delays in reperfusion (door to needle time quicker than door to balloon time)
  - Resource utilization
  - Limit exposure to healthcare staff

Circulation. Volume 141, Issue 24, 16 June 2020;, Pages 1948-1950

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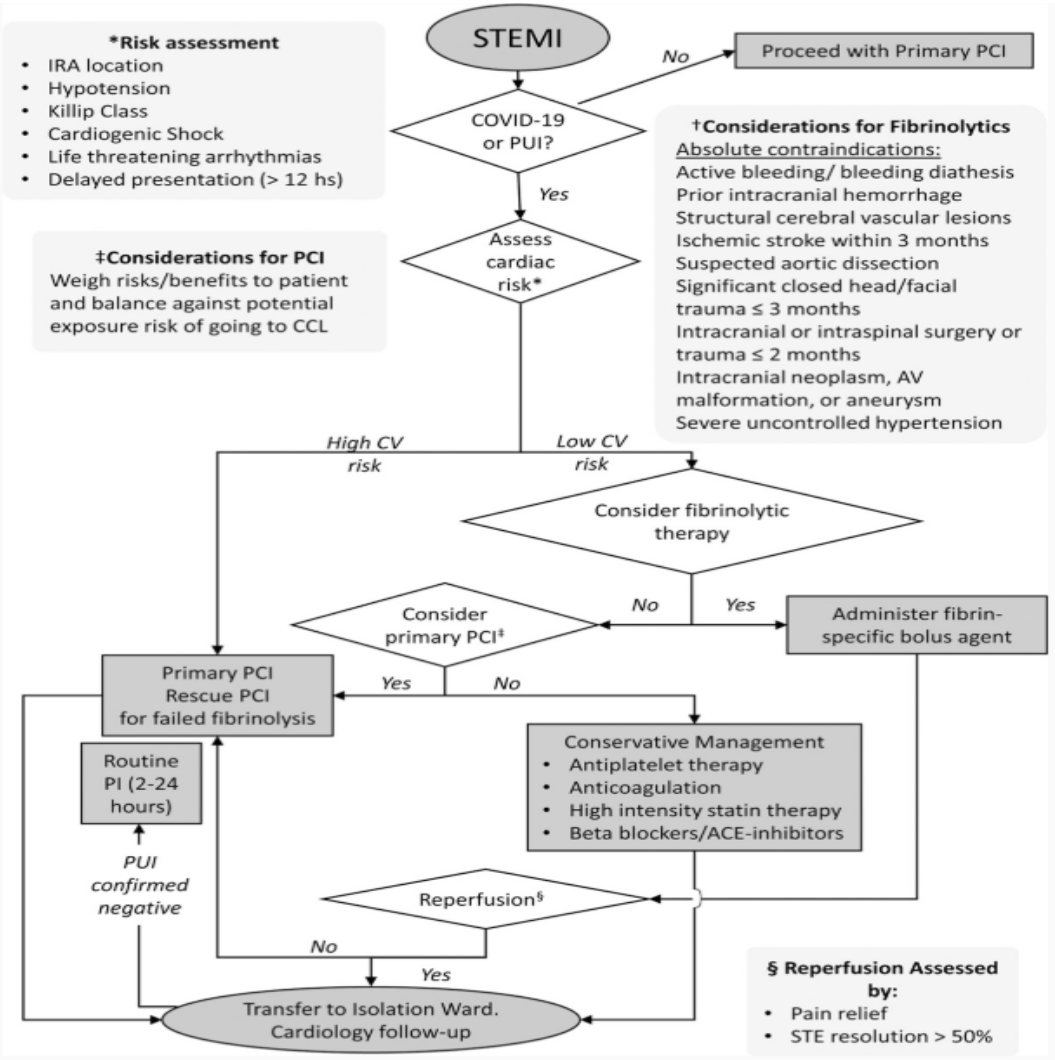
COVID-19



Reperfusion of ST-Segment–Elevation Myocardial Infarction in the COVID-19 Era. Business as Usual?

Daniels M et al.

- Key Points:
  - FT First Pros:
    - Impact of delay in door to balloon times related to COVID-19 with PPCI is unknown
    - Earlier reperfusion, less healthcare personnel exposure and resource utilization
  - FT first Cons:
    - Not standard of care
    - Up to 40% of COVID-19 related STEMI presentations can be secondary to non-thrombotic pathophysiology

Circulation. Volume 141, Issue 24, 16 June 2020;, Pages 1948-1950

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COVID-19

Association between Universal Masking in a Health Care System and SARS-CoV-2 Positivity among Health Care Workers

JAMA. 2020 July 14,
https://jamanetwork.com/journals/jama/fullarticle/2768533

Debabrata Mukherjee, MD

Association between Universal Masking in a Health Care System and SARS-CoV-2 Positivity among Health Care Workers

Wang X, Ferro EG, Zhou G et al

- The investigators used electronic medical records and identified HCWs providing direct and indirect patient care who were tested for SARS-CoV-2
- They identified 3 phases during the study period: a preintervention period before implementation of universal masking of HCWs; a transition period until implementation of universal masking of patients; and an intervention period
- During the intervention period, the positivity rate decreased linearly from 14.65% to 11.46%
- Universal masking at a large health care system in Massachusetts was associated with a significantly lower rate of SARS-CoV-2 positivity among health care workers (HCWs).

Association between Universal Masking in a Health Care System and SARS-CoV-2 Positivity among Health Care Workers

Wang X, Ferro EG, Zhou G et al

- Two reports published last week in Morbidity and Mortality Weekly Report provide additional broader perspective for general population
  - The self-reported prevalence of use of cloth face coverings among those who reported leaving their homes within the previous week increased from 61.9% to 76.4% after announcement by the White House Coronavirus Task Force and the CDC that recommended their adoption in public
  - After public health contact tracing with COVID-19 hair salon stylist clients in Missouri and after 2 weeks of follow-up, no symptoms of COVID-19 were identified among the exposed clients or their secondary contacts. Both stylist and clients wore masks
- Overall, these results support universal masking as part of a multi-faceted strategy along with social distancing measures, and frequent handwashing to minimize infection in health care settings and also in the community

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COVID-19

Panel Discussion

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COVID-19