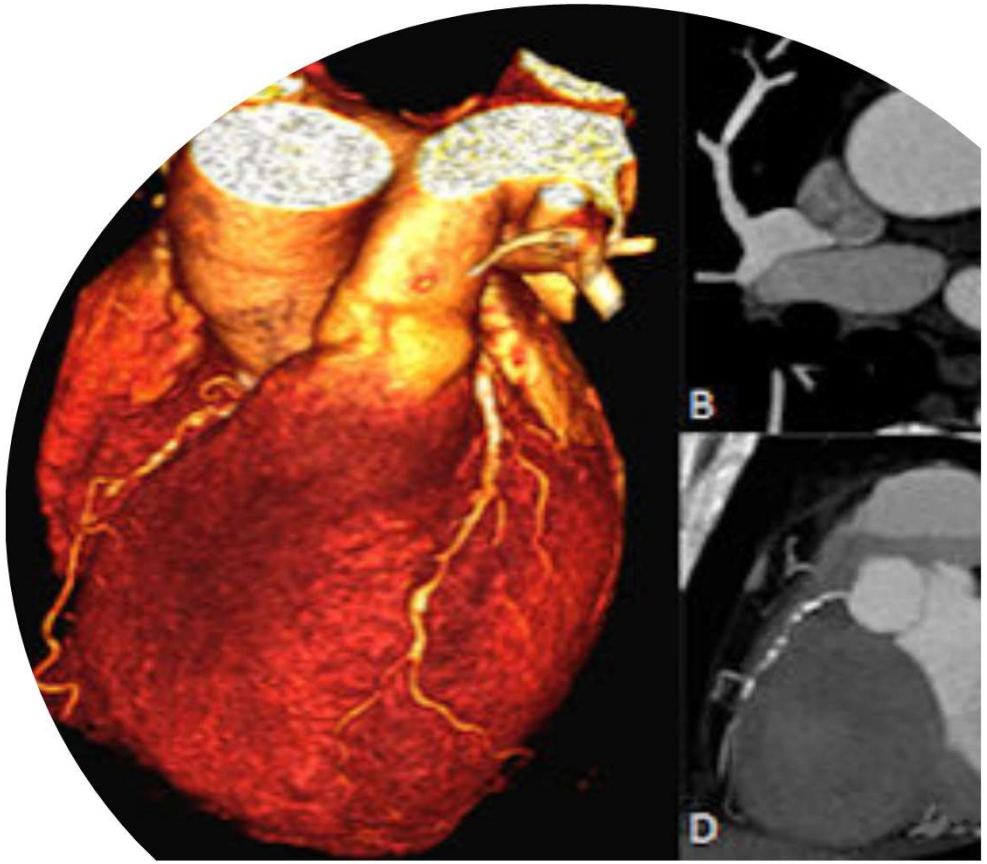
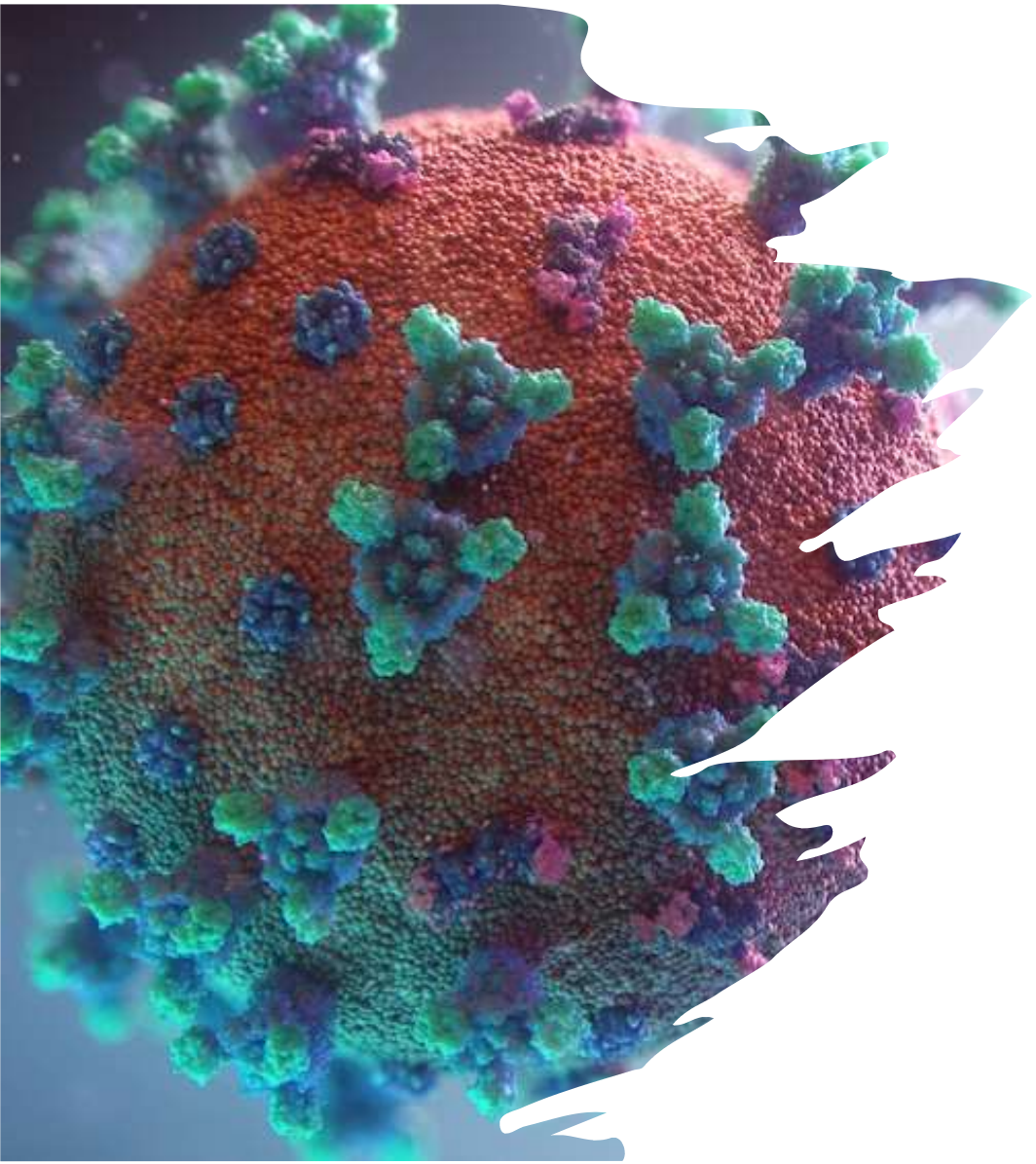
Key Messages

COVID-19 & Inflammation

Inflammation & Atherosclerosis

Decreased Use of Critical Cardiovascular Diagnostic Procedures





COVID-19 & Atherosclerosis

Excess systemic inflammation with COVID-19 infection may accelerate development of subclinical & acute cardiovascular (CV) damage

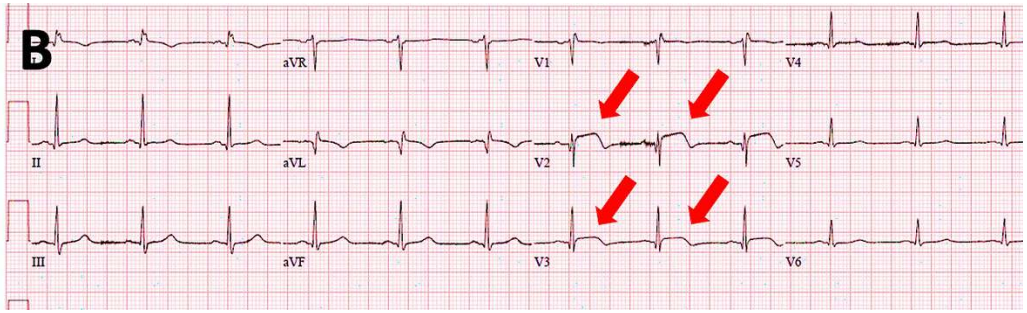
Cytokines released with SARS-CoV-2 infection may activate pre-existing atherosclerotic lesions & accelerate disease progression, particularly in a lesion containing noncalcified plaque coupled with high risk atherosclerotic plaque features (i.e., positive remodeling) leading to plaque growth and worsening stenosis severity

“Echo” Phenomenon

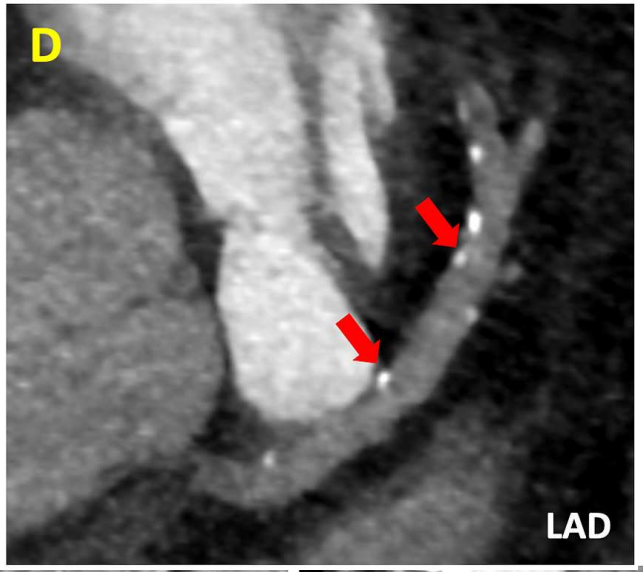
- CAD patients with influenza - ↑ rates of acute coronary syndromes (ACS)
- Also, ↑ ACS risk for CAD patients following an acute infection
- Following an acute infection, there is an upregulation of inflammatory cytokines, enhanced platelet reactivity, & plaque destabilization ↑ ACS risk
- In COVID-19, atherosclerotic plaque may be 2^0 impacted by virally-induced systemic cytokine production - stimulates pre-existing plaques to enhance disruption, progression, & leading to ACS
- H_0 = “echo” phenomenon where an atherosclerotic lesion is 2^0 impacted upon by the SARS-CoV-2 infection

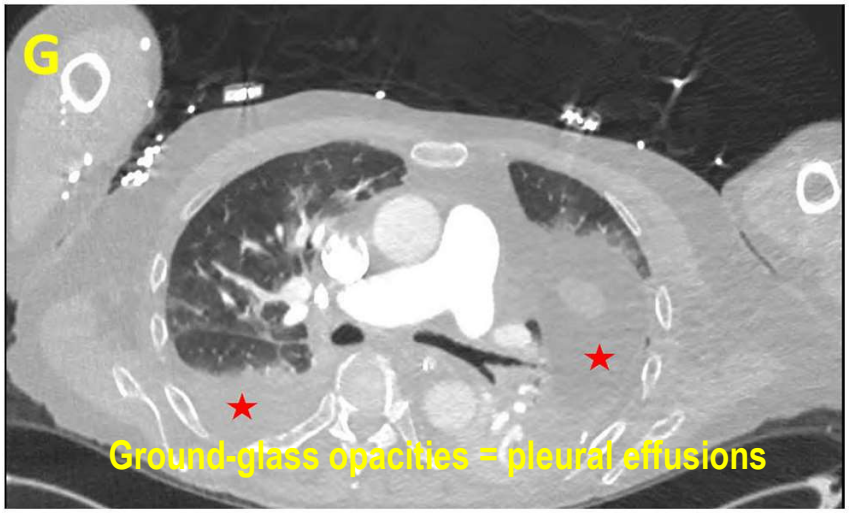
Source: Libby JACC Basic Transl Sci 2020, Nguyen JAMA Cardiol 2016;1:274-81., Kwong N Engl J Med 2018;378:345-353., Madjid Eur Heart J 2007;28:1205-10., Smeeth N Engl J Med 2004;351:2611-8., Corrales-Medina Lancet Infect Dis 2010;10:83-92.

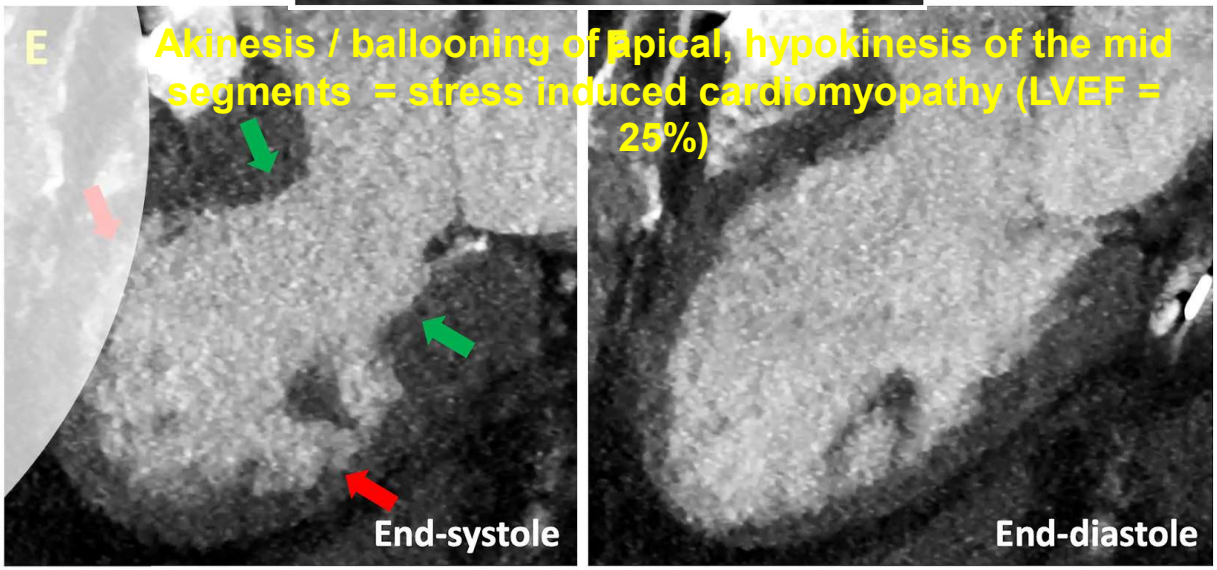
CCTA in Suspected ACS



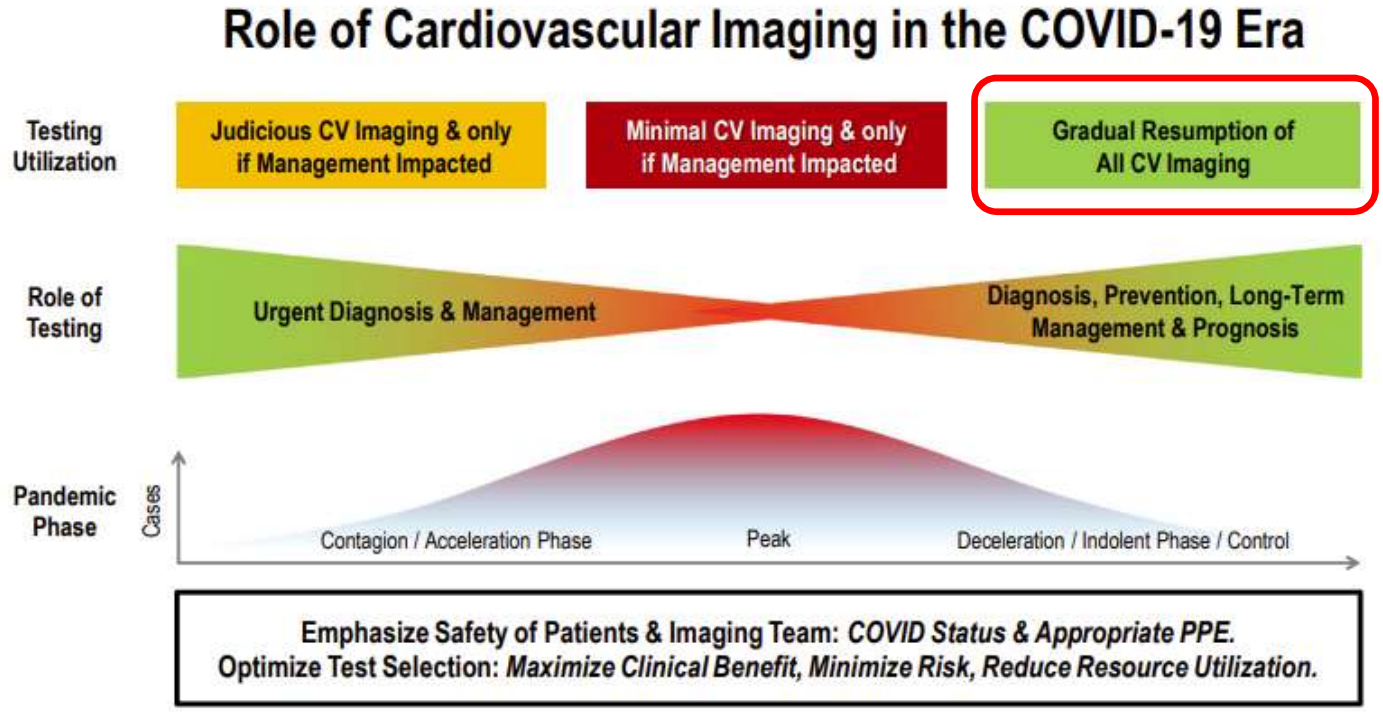
- CCTA useful for COVID-19 with ↑cardiac troponin, & avoid invasive coronary angiography
- Off-hours - Evaluate urgently, 7 days / week
- LV/RV EF + WMA
- Full chest CT





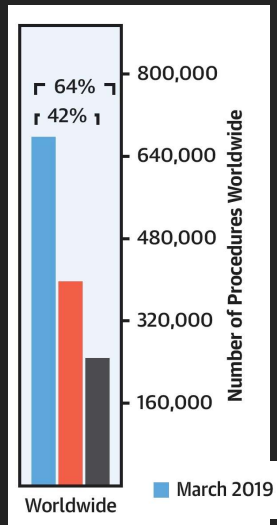


CCTA in the Current Era of COVID-19

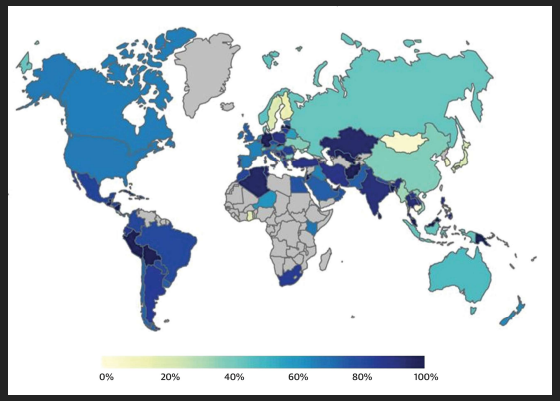


Source: Zoghbi JACC CV Imag 2020;13:1615-1626.

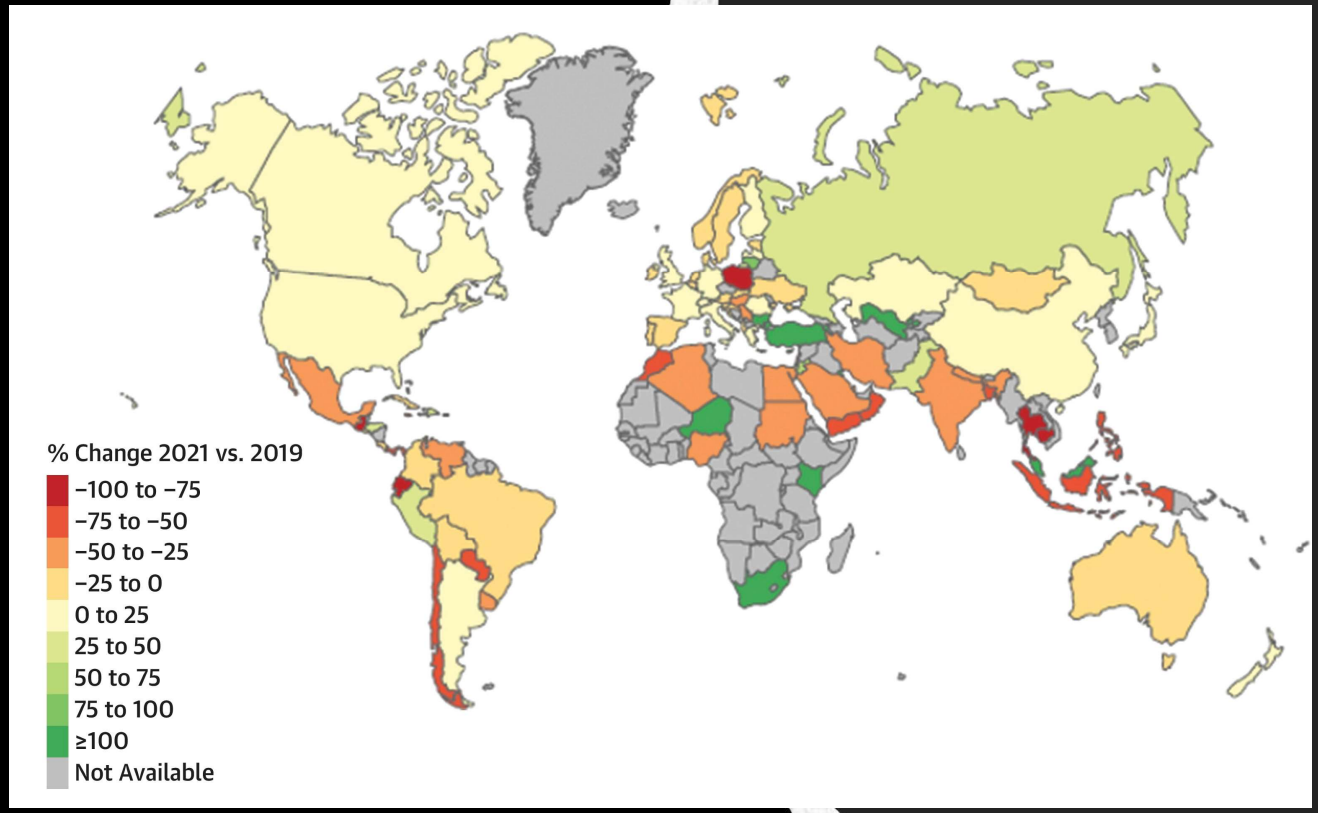
Worldwide Delays in Diagnosis for At-Risk Patients



Marked ↓ in CV Testing Worldwide



…recovery to pre-pandemic levels is lagging in lower-income countries

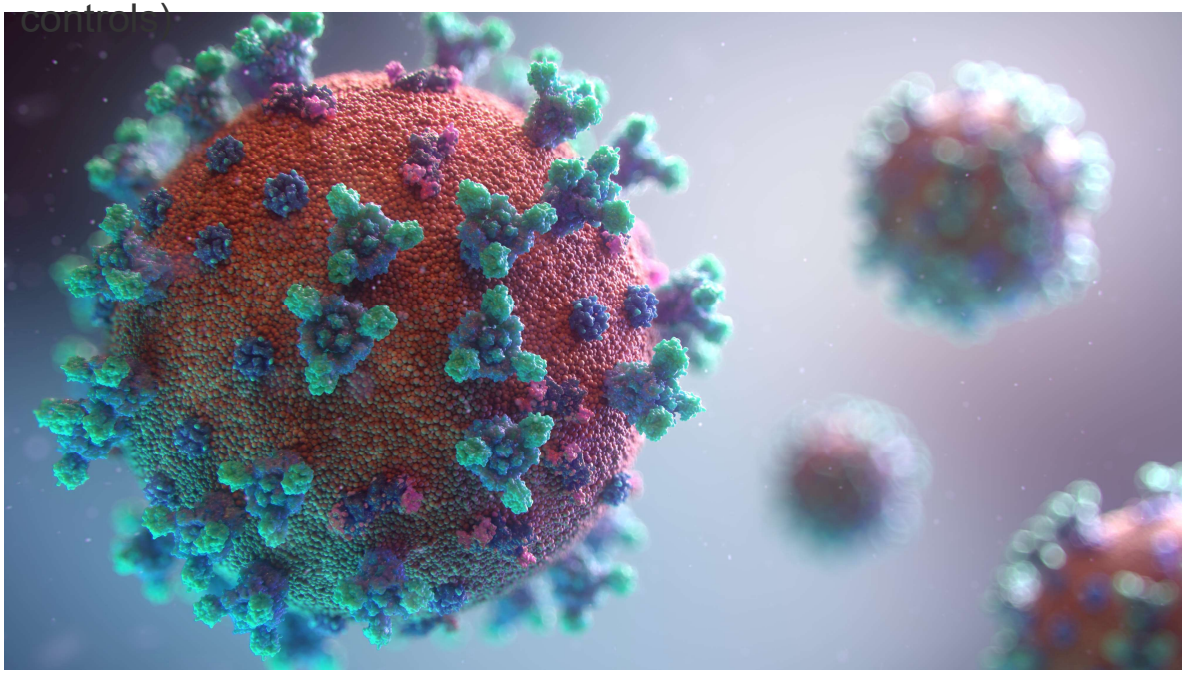


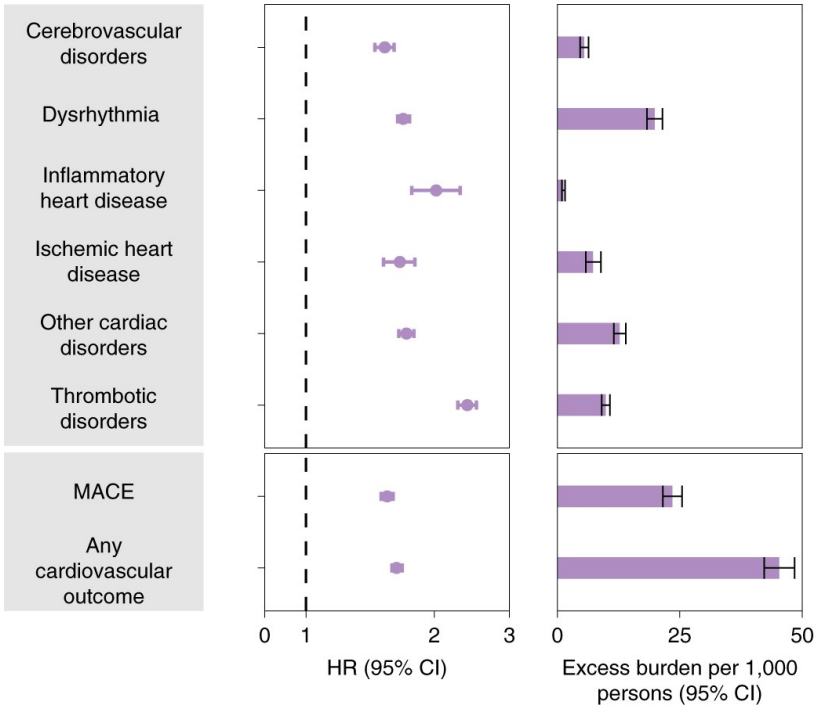
Source: Einstein JACC 2021;77:173–185, JACC 2022;79:2001-2017.

COVID-19 and Cardiovascular Outcomes

At 1-year, COVID-19 was associated with an extra 23.5 incidence of MI, stroke, & mortality

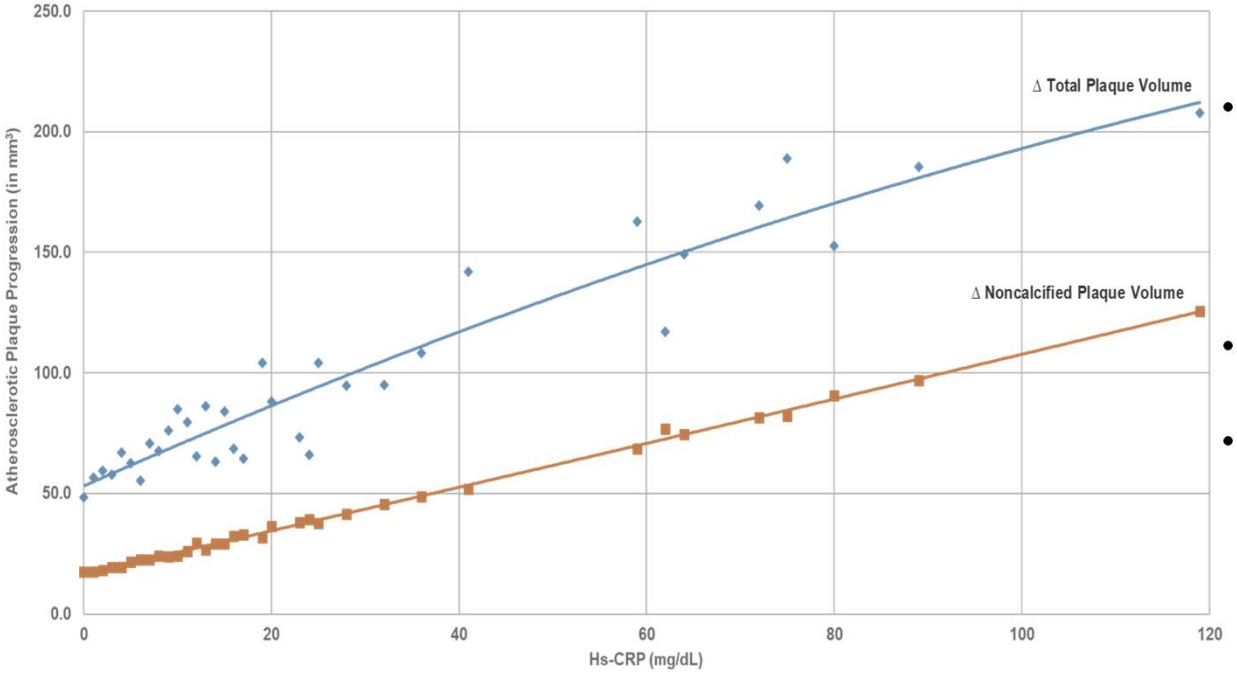
•7.3 extra incidence of Ischemic Heart Disease - 5.4 for acute CAD, 2.9 for MI, and 2.5 for Angina (per 1,000 vs. controls)





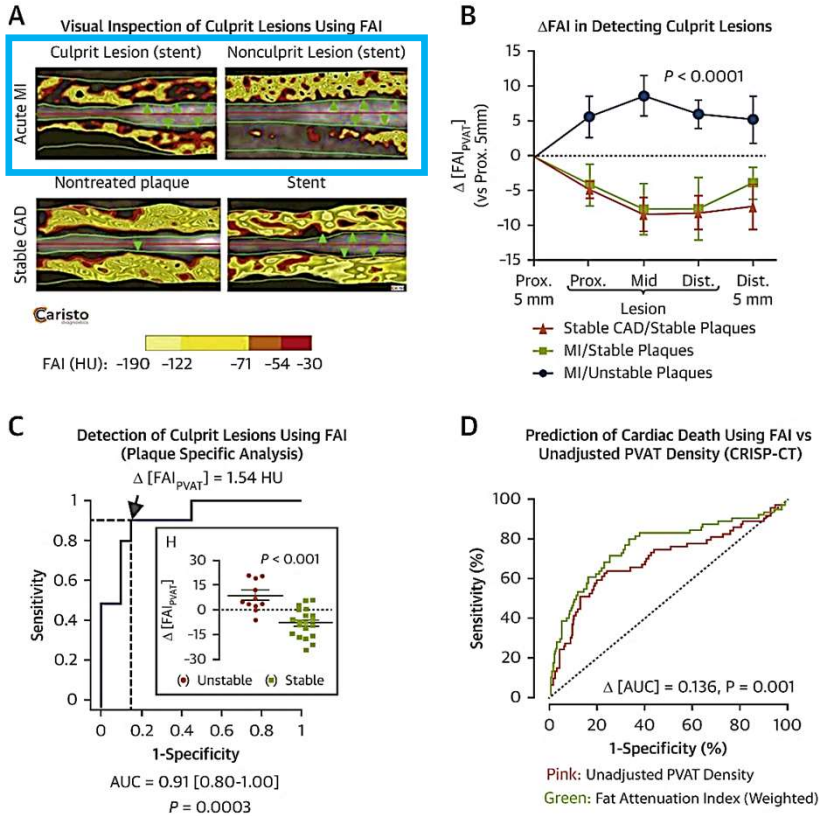
Source: Xie Nature Medicine 2022;28:583-590., Abbasi JAMA 2022;327:1113-1114.

Atherosclerotic Plaque Progression and Inflammation



- Plaque progression >2-fold ↑ with Hs-CRP ≥2 mg/dL for Total and Noncalcified (necrotic core and fibrofatty) plaque ($p<0.01$); even when controlling for risk factors & statin use
- Calcified plaque progression was unrelated to Hs-CRP ($p=0.3$)
- Associations between HIV infection and a greater burden of noncalcified plaque are also reported

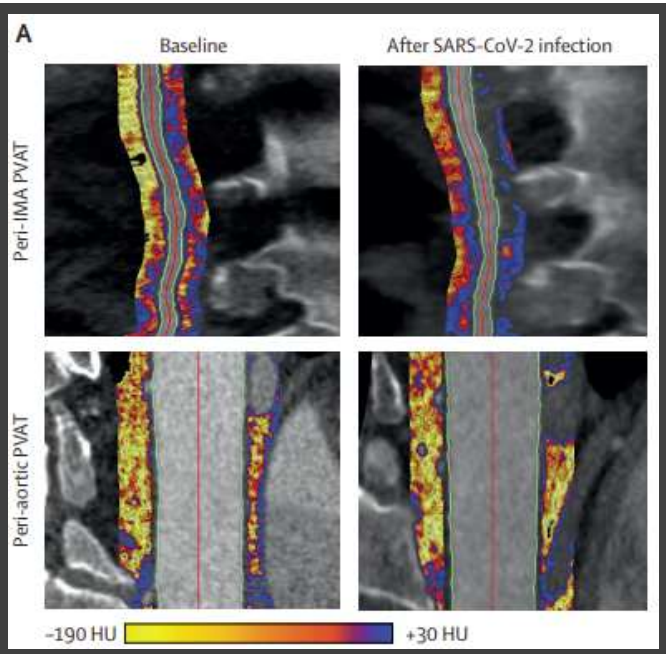
Pericoronary Fat Attenuation Index (pFAI) – Novel Measure of Vascular Inflammation



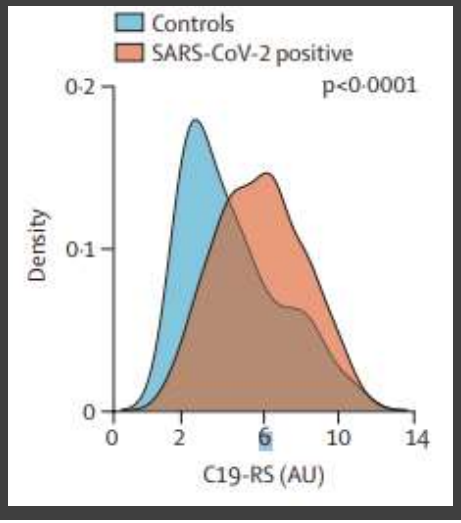
- Circulating inflammatory markers are significantly elevated with ACS & high at the culprit lesion
  - Necrotic core plaque is a stimuli perpetuating inflammation & disease progression
- Coronary inflammation inhibits accumulation of lipid in the perivascular fat & can be imaged with a compositional shift in HU density
  - HU shift across a range from -190 to -30
- pFAI accurate to detect ACS culprit lesion
  - **CV Risk Prediction using CT registry -** pFAI cutoff ≥-70.1 HU*
    - HR: 9 for CAD mortality (p<0.001)
    - HR: 5 for MI (p=0.0012)

*results externally validated.

Radiotranscriptomic Signatures of Vascular Inflammation from Routine CT Pulmonary Angiography



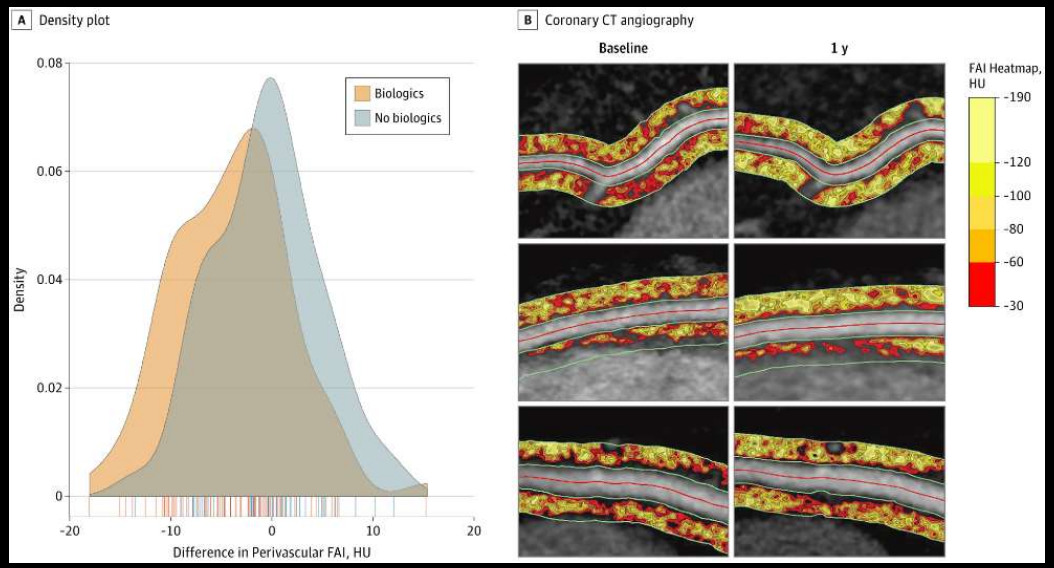
Radiotranscriptomic signature (C19-RS), derived from the perivascular space around the aorta & internal mammary artery describes cytokine-driven vascular inflammation



- Patients with COVID-19 had higher C19-RS (aOR=2·97, p=0·0038)
- C19-RS had prognostic value for in-hospital mortality in COVID-19 in two testing cohorts (high [≥6·99] vs low [<6·99]
  - HR 3·31, p=0·0033

Source: Kotanidis Lancet 2022;4:E705-716.

Pericoronary Fat (pFAI) in Immune Disorders – Impact of Psoriasis Treatment



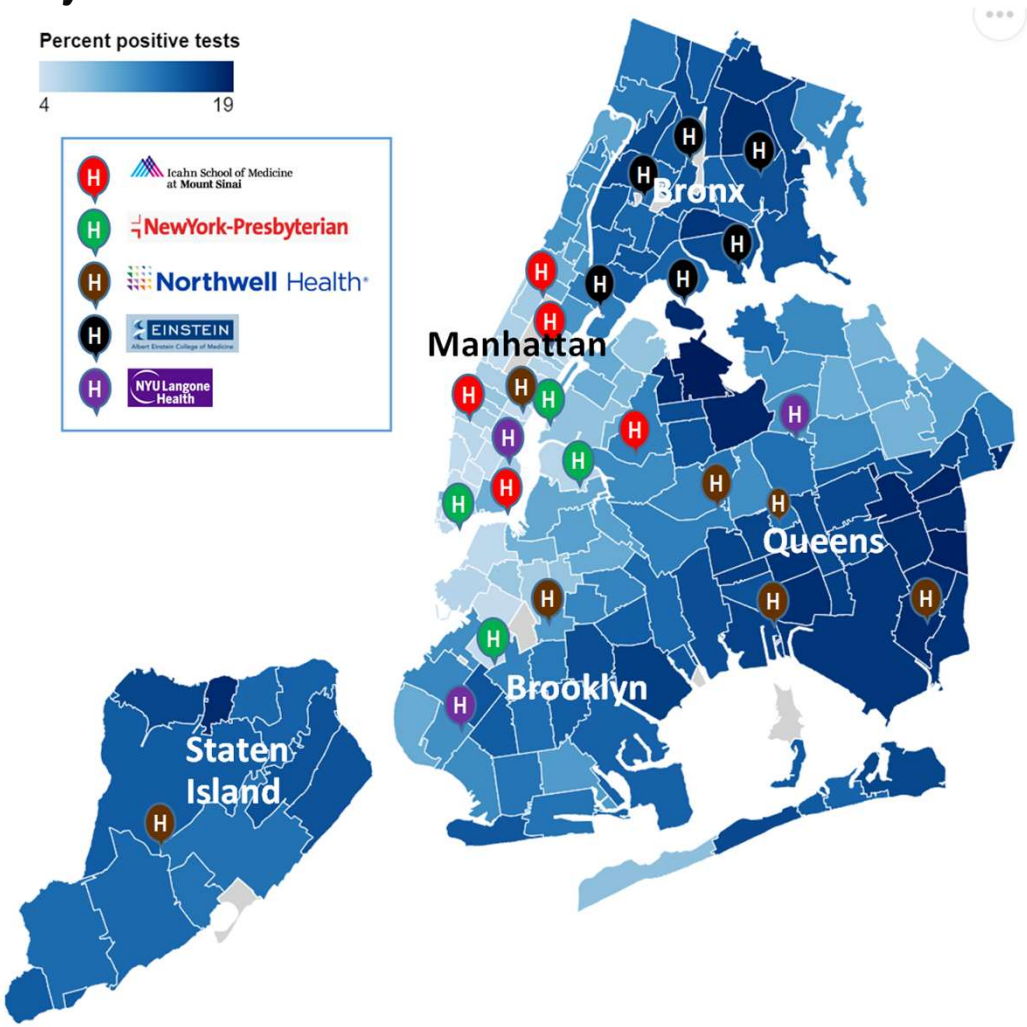
- Serial pFAI fat following intercurrent biologic (anti–tumor necrosis factor α, anti-interleukin-12/23, or -17) therapy in moderate-severe psoriasis
- 1-year of rx =
  - ↓ in the FAI ($p<0.001$)
  - ↓ in Hs-CRP +
  - Skin disease improvement

Source: Elnabawi JAMA Cardiol 2019;4(9):885-891.

NIH-NHLBI Sponsored

COVID-19 Registry

New York City & COVID-19 Wave #1



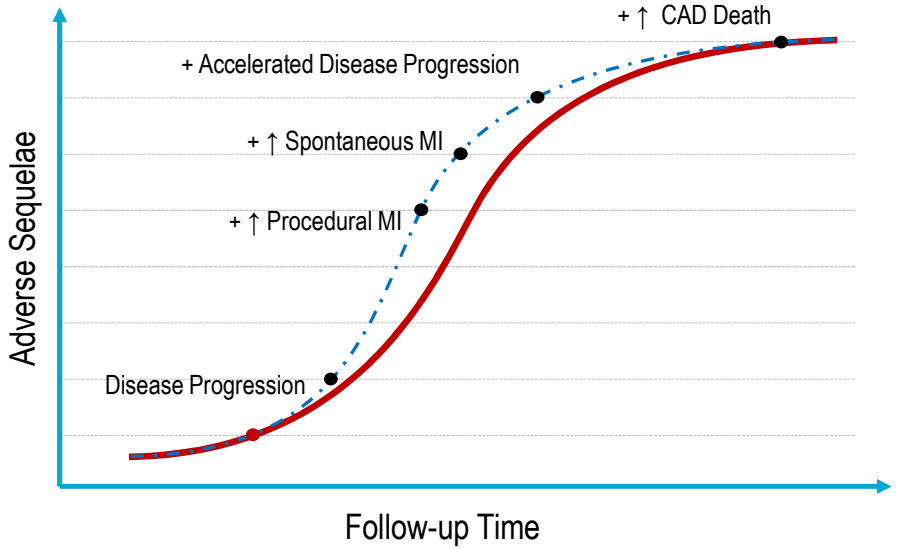
NIH-NHLBI COVID-CT Registry - Does COVID-19 Accelerates Atherosclerotic Plaque Progression?

***Hypotheses**:*

- *Systemic inflammation is a key promoter in the formation & progression of atherosclerotic plaque.*
- *Inflammatory milieu following COVID-19 will result in overall plaque growth, and notably that of higher risk, noncalcified plaque.*
- *Worsening perivascular fat attenuation index in patients infected with SARS-CoV-2 substantiates COVID-19 as the culprit pathway adversely impacting coronary artery inflammation.*

NIH-NHLBI 1R01HL159433-01
Co-PIs: Shaw / Narula

Proposed Mechanistic Pathways Following COVID-19 Infection



- Mechanistic Pathway of Progressive Atherosclerosis is Well Known!
- Do No Underestimate Psychologic Stress / Anxiety → Accentuates Atherosclerosis Progression, Especially Among "Essential Workers"

Intensify Preventive Strategies + Symptom-Guided Medical Therapy

Impact of COVID-19 on Cardiovascular (CV) Disease

- Unimaginable Consequences of this Worldwide Pandemic

  COVID-19 pandemic has produced devastating effects worldwide with loss of health, life, and livelihoods

- Delays in Testing / Treatment – Worsening Disease / Symptoms with Consequential Impact on Morbid / Fatal Outcomes in CV Disease

- Re-Capture Those At-Risk, Especially Patients with Prior Diagnostic Testing


Thank You
Mount
Sinai