

FINDING BUBBLES:

Using transcranial Doppler to
understand pulmonary physiology

Alexandra S. Reynolds, MD
Hooman Poor, MD



**Mount
Sinai
Hospital**

Disclosures

Neither of us have disclosures to report.

Talk Outline

1. The COVID19 pandemic response in NYC
2. Utility of TCDs in COVID19
3. How TCDs have shed light on a pulmonary disease

The COVID19 pandemic response in NYC

The COVID-19 Timeline

- **December 31, 2019** – Chinese officials confirm dozens of cases of pneumonia of unknown cause.
- **Feb 29, 2020** – First recorded US coronavirus death

Department of Health confirms first coronavirus death in Washington state

Updated: 09:56 AM Saturday, February 29, 2020

By KIRO 7 News Staff

The Washington Department of Health confirmed Saturday the first coronavirus-related death in Washington state, according to a press release.

Health officials said there are new King County cases in addition to the two new cases confirmed Friday evening.

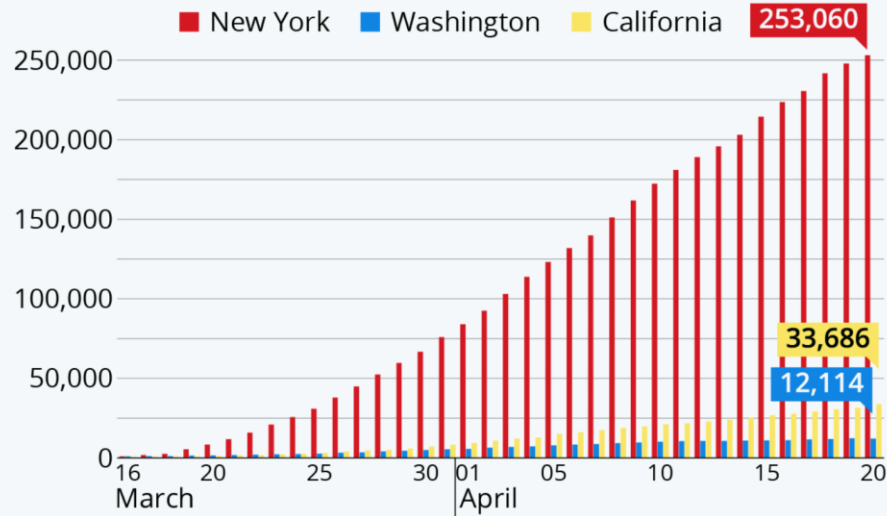
The department is hosting a press conference at 1 p.m. to provide further details.



The New York COVID-19 Timeline

New York Passes 250,000 COVID-19 Cases

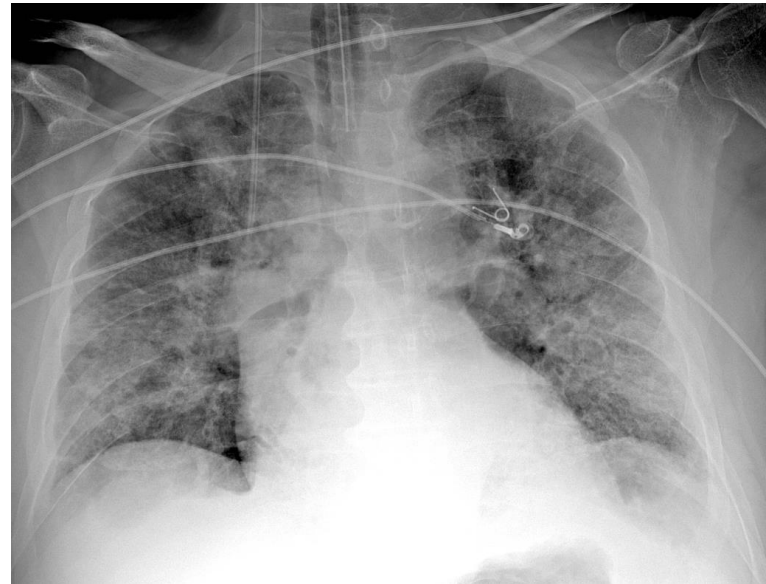
Cumulative number of confirmed COVID-19 cases in selected U.S. states (March 16 - April 20)



Source: Johns Hopkins University

Patients presenting with bilateral pneumonia and severe hypoxemia

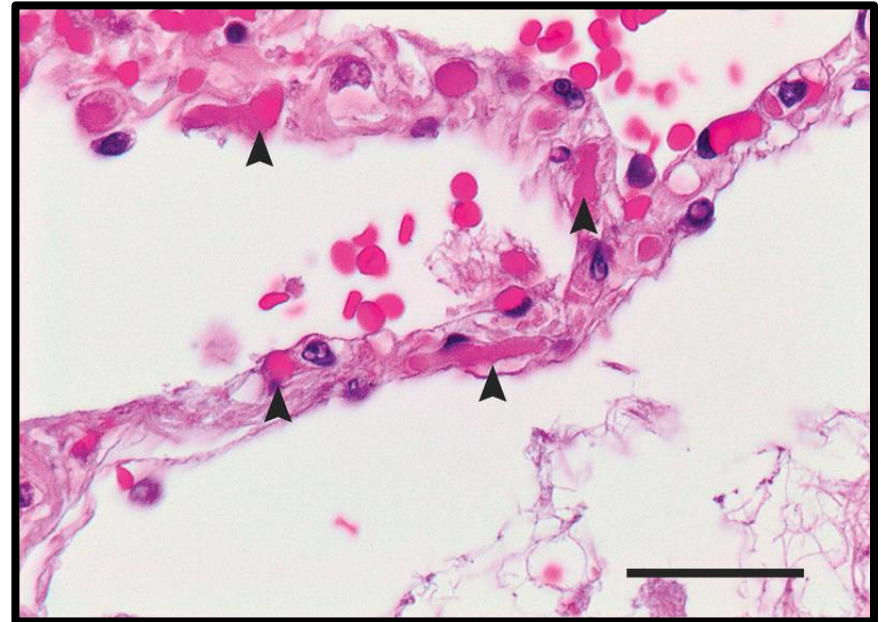
- At least initially, **lung compliance was normal** and not consistent with classic Acute Respiratory Distress Syndrome
- Patients heavily sedated and paralyzed
- Noted that some patients worsened while sitting up



The Role of Coagulopathy

Increasing observation of thrombotic events associated with severe COVID

- STEMI
- Ischemic Stroke
- Pulmonary Embolism



Serum profile of increased inflammation and prothrombotic state

- hypoxemia partly responsive to thrombolysis

Received: 27 April 2020 | Revised: 2 May 2020 | Accepted: 3 May 2020 | Published online: 5 June 2020

DOI: 10.1002/ctm2.44

SHORT COMMUNICATION

CLINICAL AND TRANSLATIONAL MEDICINE WILEY

COVID-19 critical illness pathophysiology driven by diffuse pulmonary thrombi and pulmonary endothelial dysfunction responsive to thrombolysis

Hooman D. Poor¹ | Corey E. Ventetuolo² | Thomas Tolbert¹ | Glen Chun¹ | Gregory Serrao³ | Amanda Zeidman⁴ | Neha S. Dangayach⁵ | Jeffrey Olin³ | Roopa Kohli-Seth⁶ | Charles A. Powell¹

Risk of Stroke

CORRESPONDENCE

COVID-19 CASES

To rapidly communicate information on the global clinical effort against Covid-19, the Journal has initiated a series of case reports that offer important teaching points or novel findings. The case reports should be viewed as observations rather than as recommendations for evaluation or treatment. In the interest of timeliness, these reports are evaluated by in-house editors, with peer review reserved for key points as needed.

Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young

We report five cases of large-vessel stroke in patients younger than 50 years of age who presented to our health system in New York City. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was diagnosed in all five patients.

2020, a total of five patients (including the aforementioned patient) who were younger than 50 years of age presented with new-onset symptoms of large-vessel ischemic stroke. All five patients tested positive for Covid-19. By comparison, every 2 weeks over the previous 12 months, our ser-

Utility of TCDs in COVID-19

The Major Clinical Problems

How do we monitor patients who are sedated and paralyzed?

Why are patients having strokes?

WHY ARE PATIENTS SO HYPOXEMIC BEFORE THEY DEVELOP POOR COMPLIANCE?

 **Cameron Kyle-Sidell, MD**
@cameronks

[@EMNerd_](#) [@emupdates](#) [@CriticalCareNow](#) [@ThinkingCC](#) [@srrezaie](#) [@Turtle1doc](#) [@PulmCrit](#) STOP INTUBATING COVID PATIENTS FOR HYPOXEMIA!!! This is a tracing of a cirrhotic w COVID. Sat does not reflect organ arterial tissue saturation. They do not get tachycardic



12:56 PM · Mar 27, 2020

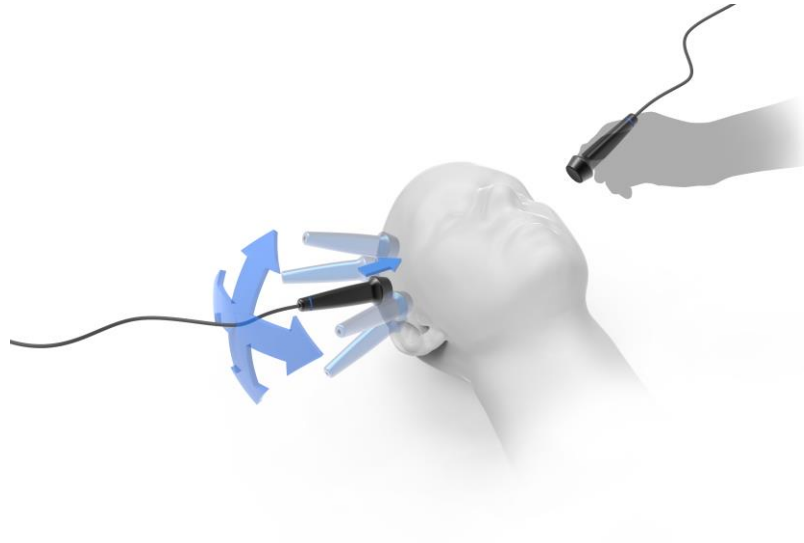
493 See the latest COVID-19 information on Twitter

Utility of TCDs

- ▶ Mechanisms of stroke in COVID-19
- ▶ Feasibility of monitoring patients on anticoagulation
- ▶ Evaluation of cerebral autoregulation in comatose patients

Transcranial Dopplers

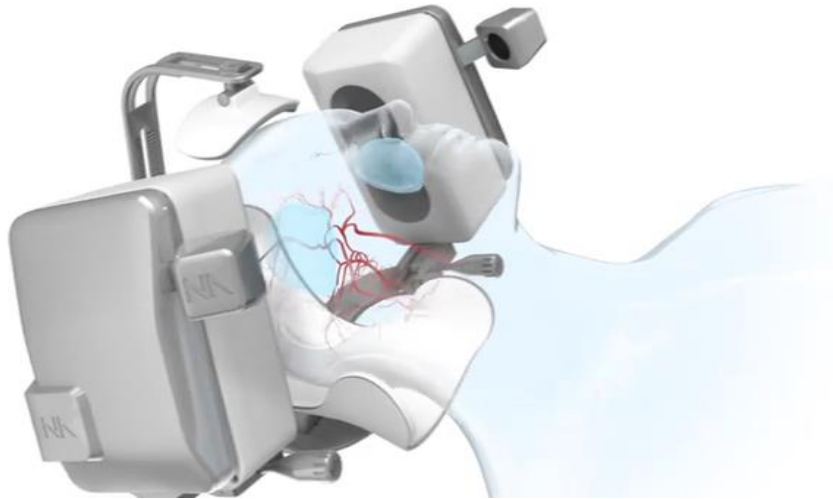
Manual TCD Signal Capture



Protecting the Providers



Automated Transcranial Dopplers



Optimize probe placement

Find transtemporal window

Acquire & maintain signal

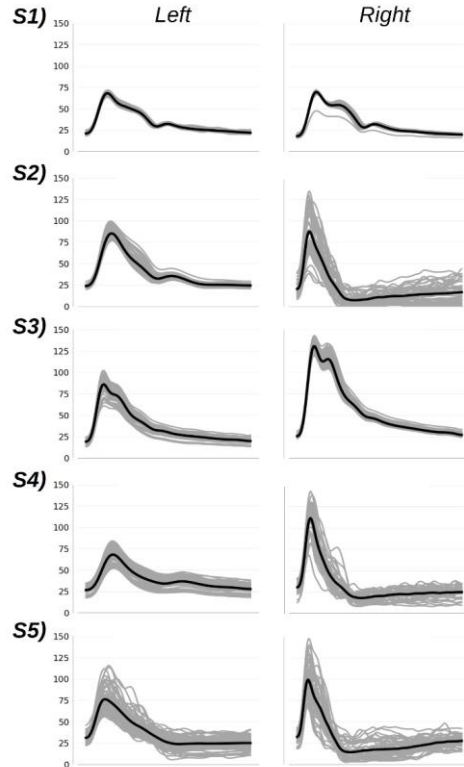
High intensity transient signals

- ▶ HITS studies done to look for spontaneous emboli
- ▶ Done in patients on and off anticoagulation, including those known to be prone to clotting

High intensity transient signals

- ▶ HITS studies done to look for spontaneous emboli
- ▶ Done in patients on and off anticoagulation, including those known to be prone to clotting
- ▶ Of 10 patients scanned for standard 30 minutes, **NO spontaneous emboli seen**

TCD Waveform Analysis in COVID19



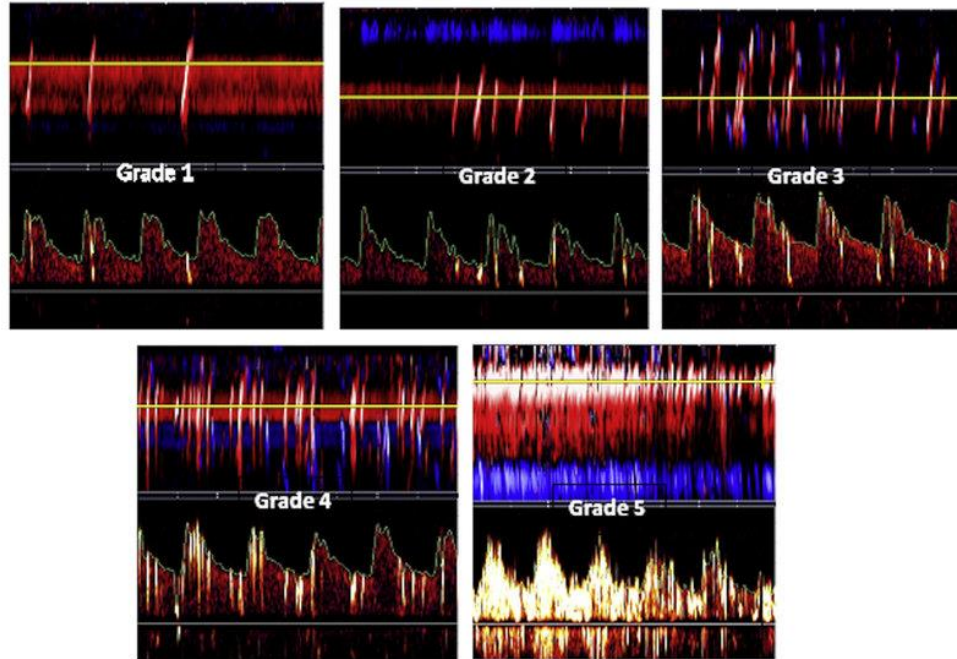
Highly resistive waveforms

- changes in CO₂
- undiagnosed intracranial process
- vasculopathy
- inappropriate autoregulation

Several patients with asymmetries in waveforms

Bubble studies

- ▶ Performed bubble studies to look for right-to-left shunt in patients



Shedding light on a pulmonary disease

**Pulmonary Vascular Dilatation Detected by Automated Transcranial Doppler in
COVID-19 Pneumonia**

Alexandra S. Reynolds, MD¹, Alison G. Lee, MD, MS², Joshua Renz, RVT³, Katherine
DeSantis, MS³, John Liang, MD¹, Charles A. Powell, MD², Corey E. Ventetuolo, MD,
MS⁴ and Hooman D. Poor, MD²

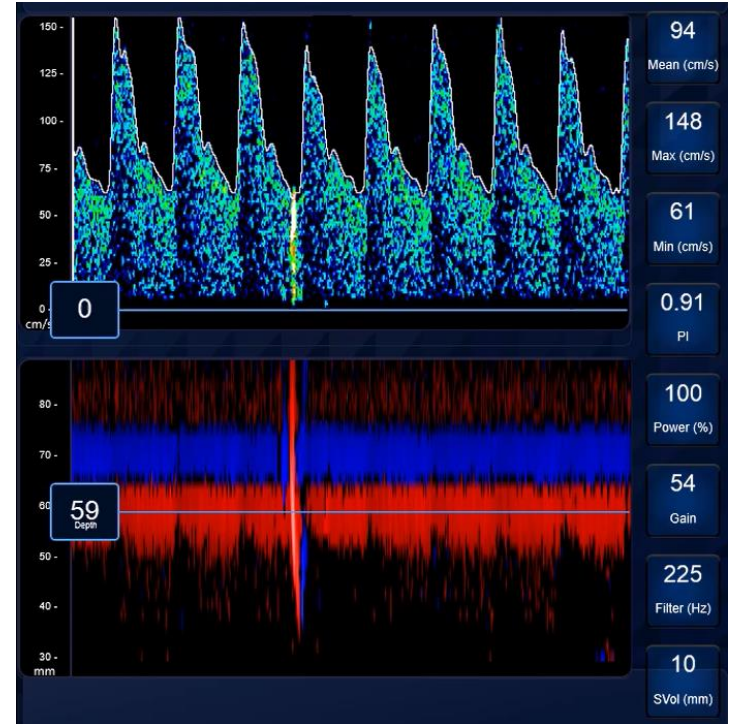
**American Journal of Respiratory
and Critical Care Medicine**



ATS Journals

Bubble studies

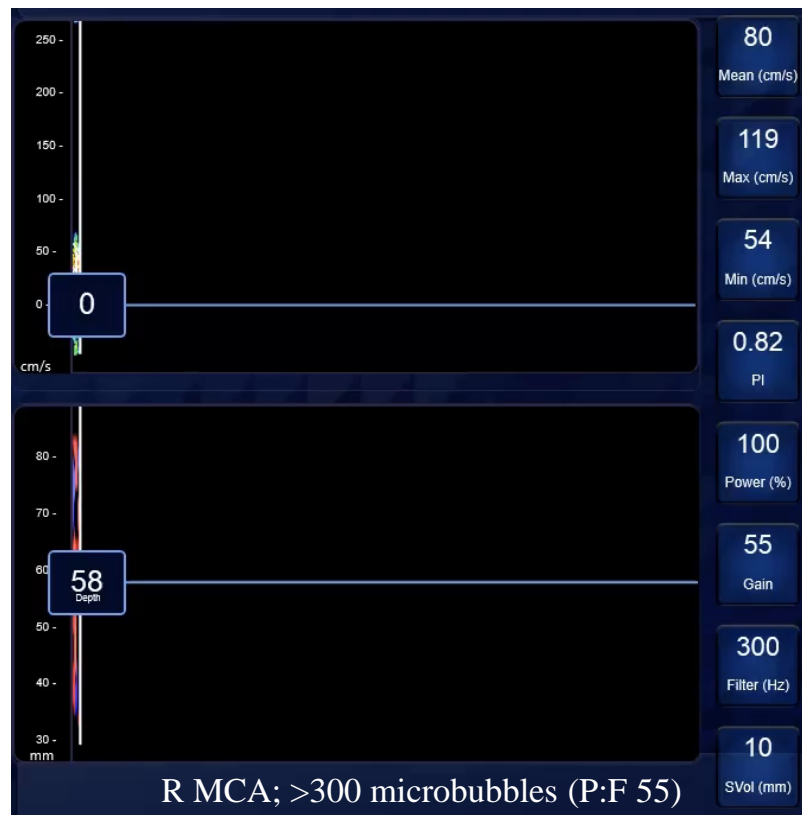
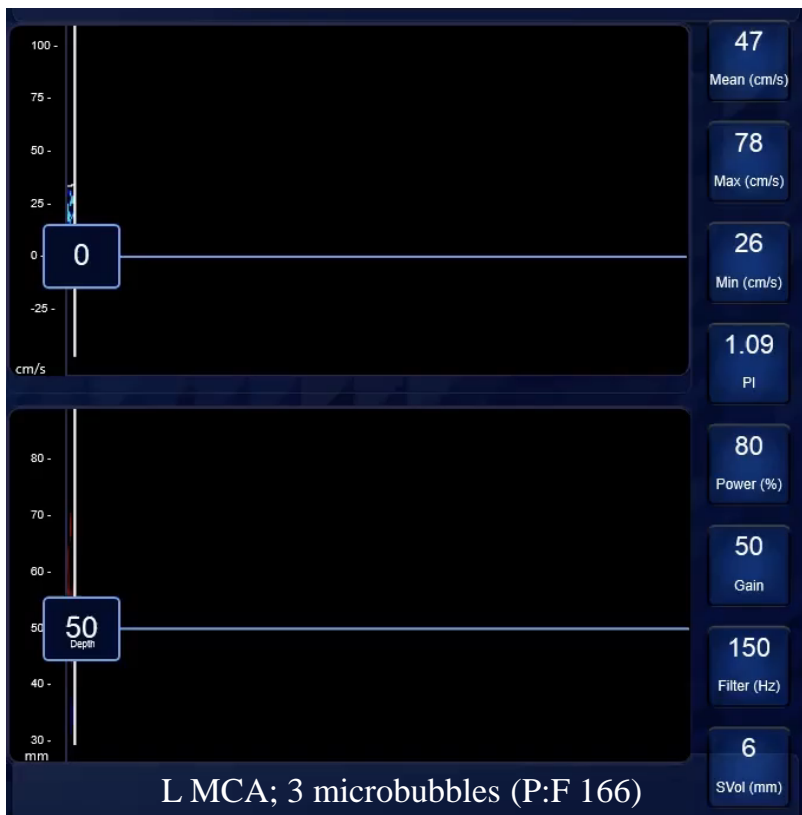
- ▶ Standard study for PFO testing
- ▶ **Of 18 patients, 15 had positive bubble study (83%)**



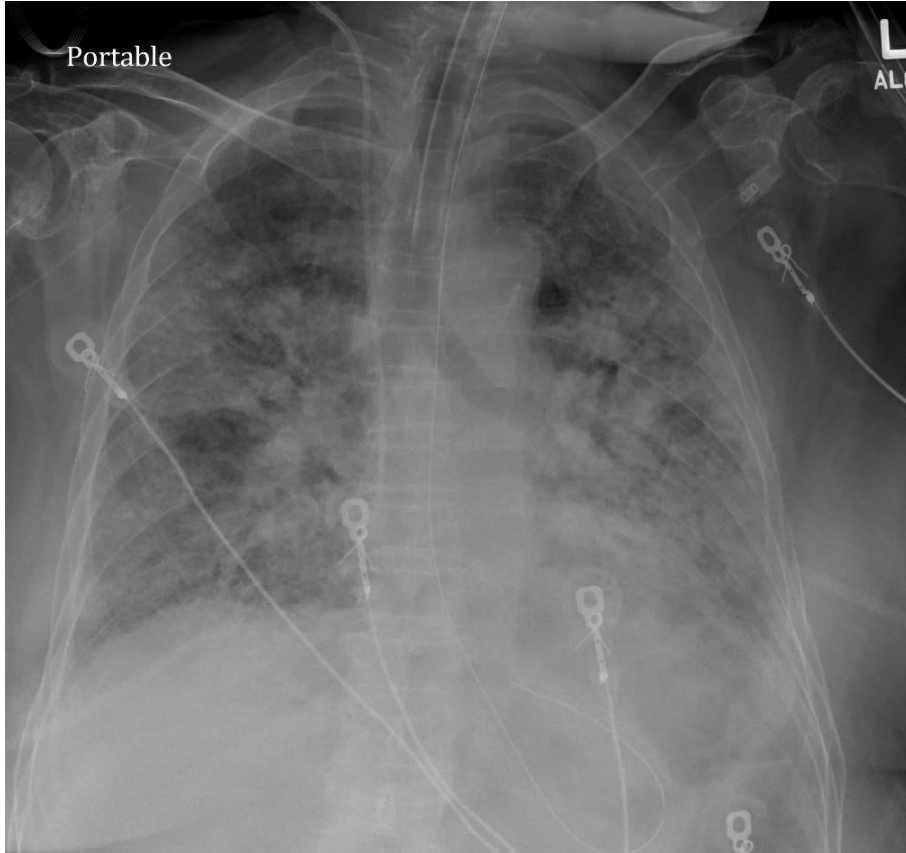
Why use TCD?

- ▶ **More sensitive** than transthoracic echocardiography
- ▶ **Less invasive** than transesophageal echocardiography
- ▶ **Decreased healthcare worker exposure** to aerosolized virus
- ▶ **Quantification** of degree of right-to-left shunt

Varied degree of bubbles seen on TCDs in our cohort



Degree of hypoxemia was inversely correlated with number of bubbles

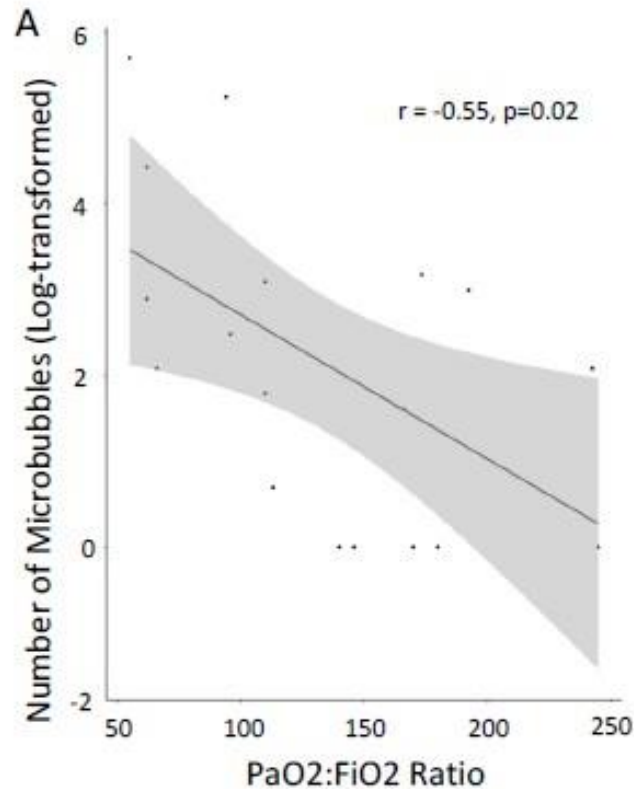


The PaO₂ is the amount of arterial oxygen

The FiO₂ is the amount of oxygen being delivered

The P:F ratio indicates the degree of hypoxemia; **lower is worse**

Degree of hypoxemia was inversely correlated with number of bubbles



The PaO₂ is the amount of arterial oxygen

The FiO₂ is the amount of oxygen being delivered

The P:F ratio indicates the degree of hypoxemia; **lower is worse**

26% positive study in patients with ARDS, no correlation with oxygenation (Boissier 2015)

Intracardiac vs intrapulmonary bubble transit



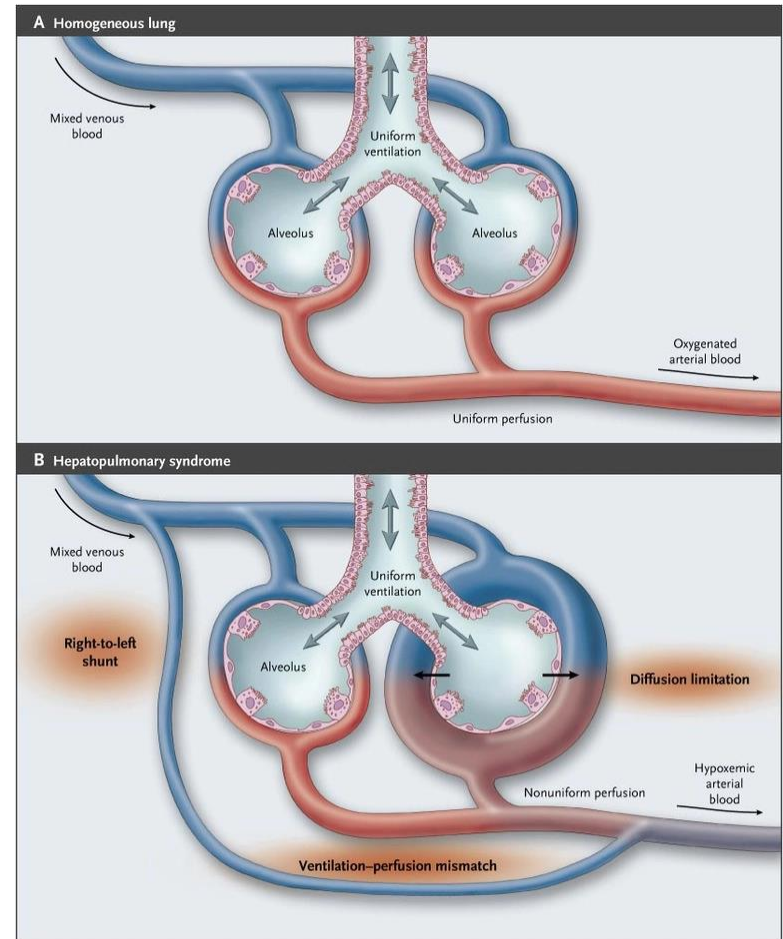
Vincent Lau, Critical Care Western
(<https://youtu.be/i8J1BxGM8wo>)



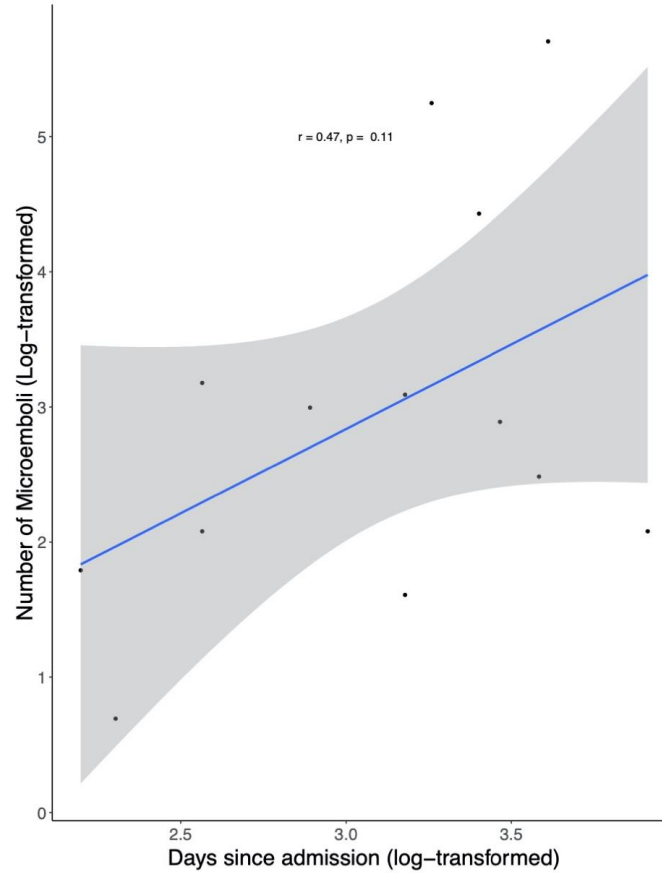
(https://youtu.be/VeI_p-9OowA)

Pulmonary Vasodilation

- ▶ analogous to hepatopulmonary syndrome
- ▶ dilated capillaries allow microbubbles to traverse pulmonary circulation
- ▶ results in lung units with low ventilation/perfusion ratios

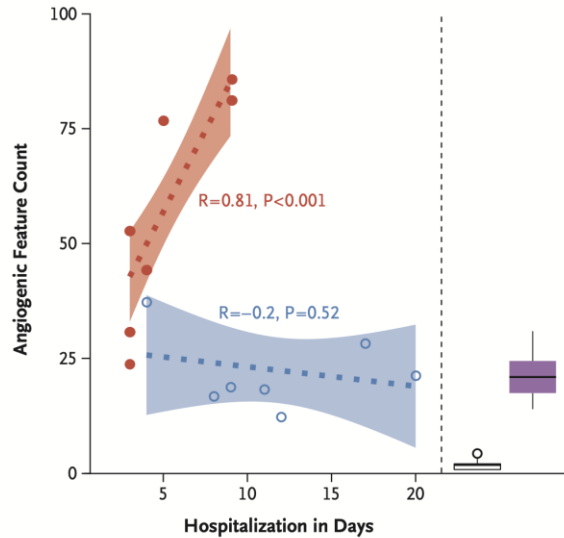


The Time Component

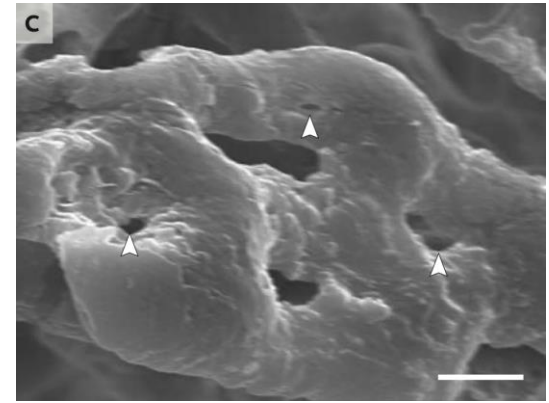
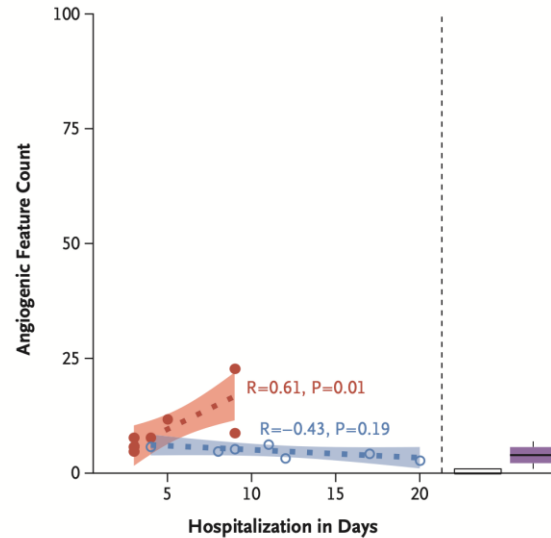


An alternative explanation

C Intussusceptive Angiogenic Features over Time



D Sprouting Angiogenic Features over Time



- ▶ Sprouting and intussusceptive angiogenesis has been seen in post-mortem analysis of COVID19 infected lungs
- ▶ There is a clear time component to this development

Conclusions

- ▶ There is abnormal right-to-left transit of bubbles in severe COVID-19 pneumonia
- ▶ The percent of patients with this abnormal transit is much higher than rates of PFO in the general population or in ARDS
- ▶ The amount of bubbles seen correlates with the degree of hypoxemia

Future directions

Follow up study ongoing

- ▶ Including patients on varying types of noninvasive and invasive oxygenation
- ▶ Multiple studies on same patient as they worsen/improve
- ▶ Studies at 45 degrees, supine

Pathology confirmation of suspected mechanism

Therapeutic targets