MASSACHUSETTS GENERAL HOSPITAL
DEPARTMENT OF MEDICINE

HARVARD MEDICAL SCHOOL

Post-COVID Syndromes: Lessons Learned and New Frontiers

MGH/HMS Internal Medicine Course
June 8th, 2022

George A. Alba, MD
Pulmonary and Critical Care, MGH
Associate Director, CORE Clinic
@galbamd

Disclosures

Stock: Verve Therapeutics

Patents: Anti-NEDD9 antibody (US Patent ID# PCT/US2019/059890), Plasma NEDD9 ELISA (US Patent ID# PCT/US2020/066886)

All disclosures are unrelated to the content of this presentation

Learning objectives

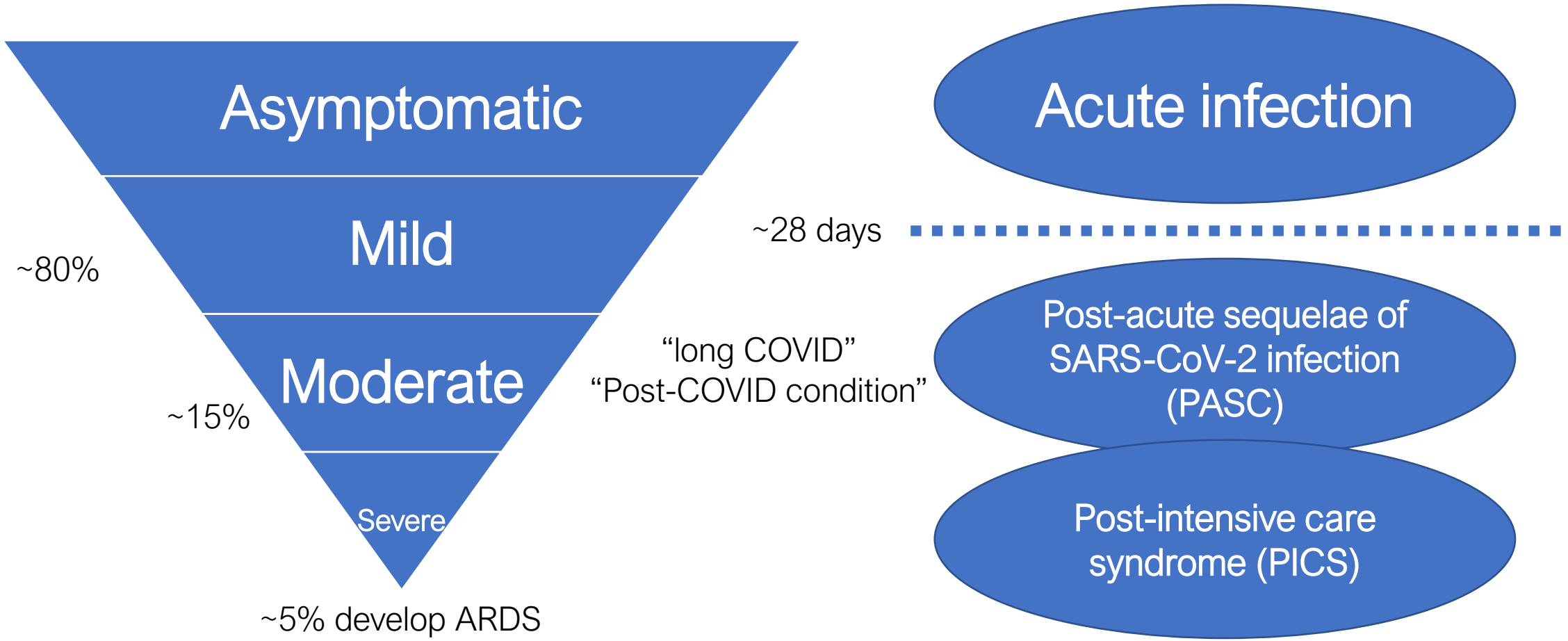
Understand the spectrum of SARS-CoV-2 illness and recovery in adults

Define the post-acute sequelae of SARS-CoV-2 infection (PASC)

Understand the current research into PASC pathophysiology

Outline a clinical approach to the adult patient presenting with PASC

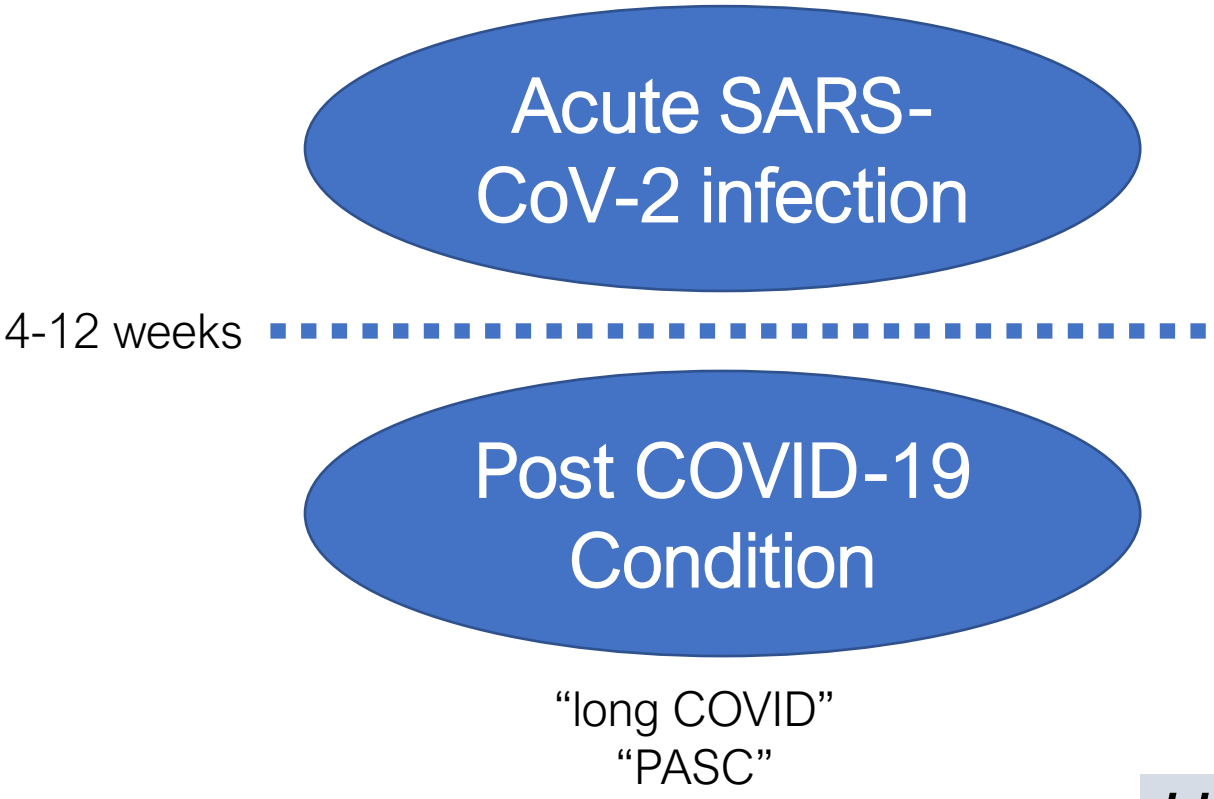
The SARS-CoV-2 spectrum of illness and recovery



Wu et al. JAOran et al. Ann Int Med 2020;173(5):362
MA 2020;323(13):1239
NIH.gov (https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/)

Greenhalgh et al. BMJ 2020.
Xiao et al. Clin Infect Dis 2020.
CDC. https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html.

Post-acute sequelae of SARS-CoV-2 infection (PASC)



WHO Clinical Case Definition:

- Probable *or* confirmed SARS-CoV-2 infection
- New or persistent symptoms **12 weeks** from onset of initial symptoms (>2 mo. duration)
- Symptoms may fluctuate or relapse
- Cannot be explained by another diagnosis

U09.9 Post-COVID Condition, Unspecified

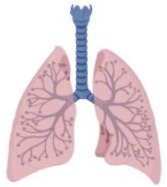
World Health Organization. October 6, 2021. WHO/2019-nCoV/Post_COVID-19_condition/Clinical_case_definition/2021.1

Spectrum and epidemiology of PASC

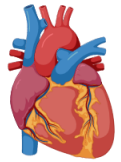
Constellation of Symptoms by Organ System

Fatigue, headaches, dysautonomia, cognitive impairment (“brain fog”)

Anxiety, depression, post-traumatic stress disorder



Dyspnea, decreased exercise capacity, cough



Palpitations, tachycardia, chest pain

Arthralgias

Epidemiology:

~13% ≥ 1 month of symptoms

~4.5% ≥ 2 months

~2.3% ≥ 3 months

Risk factors:

- ↑ age
- ↑ BMI
- Female sex
- ≥ 5 symptoms at onset
- ↑ severity of index illness

Nalbandian A et al. Nat Med. 2021 Apr;27(4):601-615.
Sudre et al. Nat Med. 2021. doi:10.1038/s41591-021-01292-y.

Al-Aly Z et al. Nature. 2021 Jun;594(7862):259-264.
Antonelli M et al. Lancet Infect Dis. 2021 Sep 1;S1473-3099(21)00460-6.

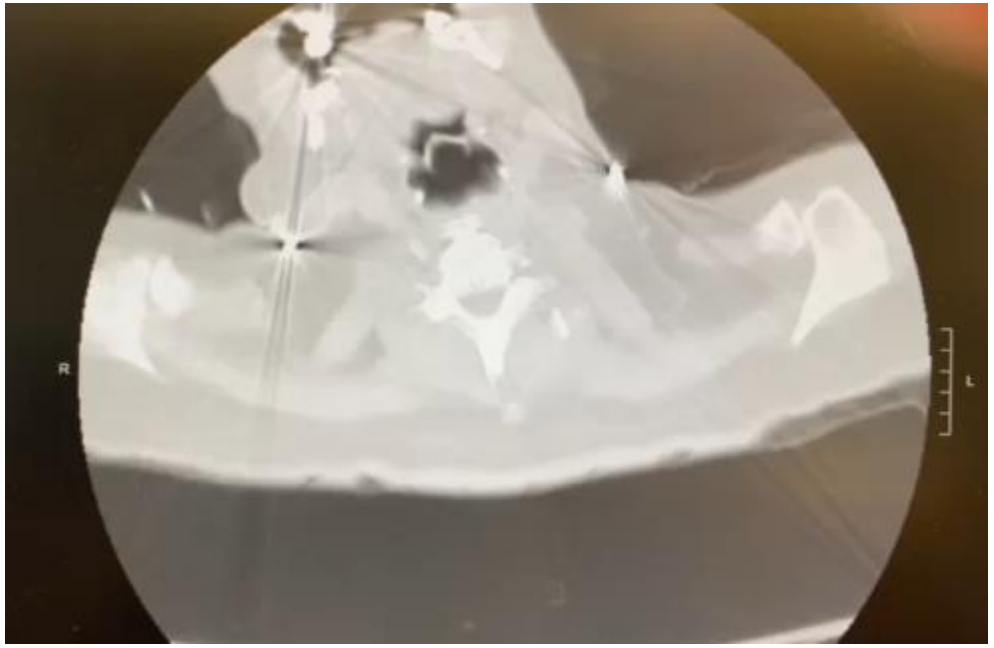
Case 1

46-year-old Latinx man with obesity and type 2 diabetes mellitus who works as a warehouse supervisor hospitalized with critical COVID-19 leading to acute respiratory distress syndrome (ARDS) requiring intubation x 3 weeks.

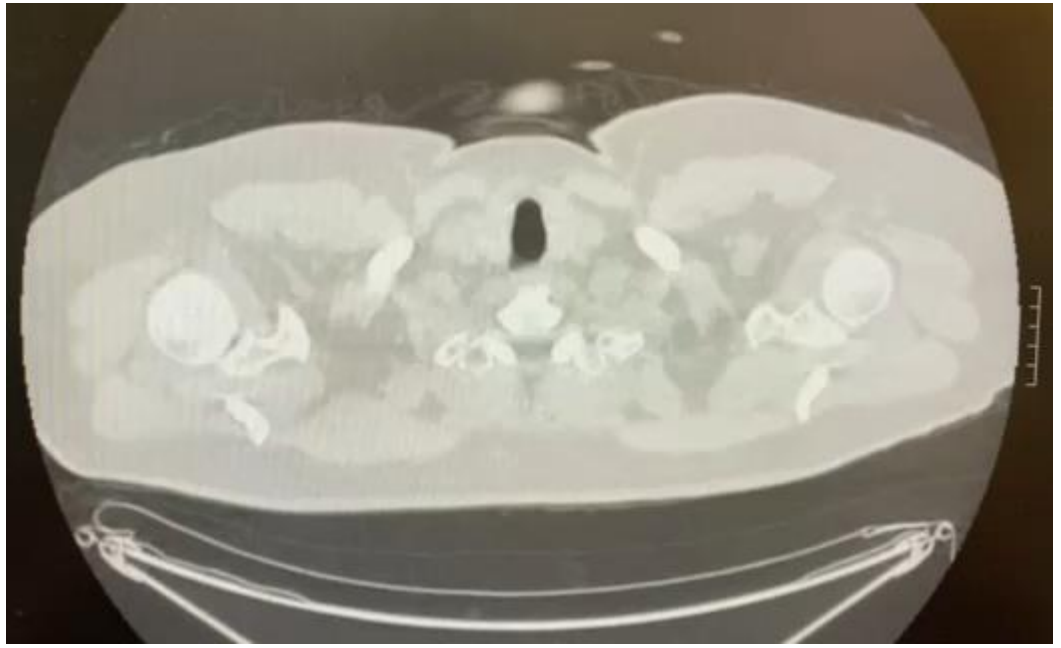
His hospital course was complicated by ventilator associated pneumonia, delirium, withdrawal from sedatives & analgesics, dysphagia, and a sacral decubitus ulcer.

At follow up with you he reports dyspnea on exertion, hypoxemia requiring supplemental oxygen, fatigue, tachycardia, short-term memory deficits, anxiety, and lower back and thigh pain.

Case 1

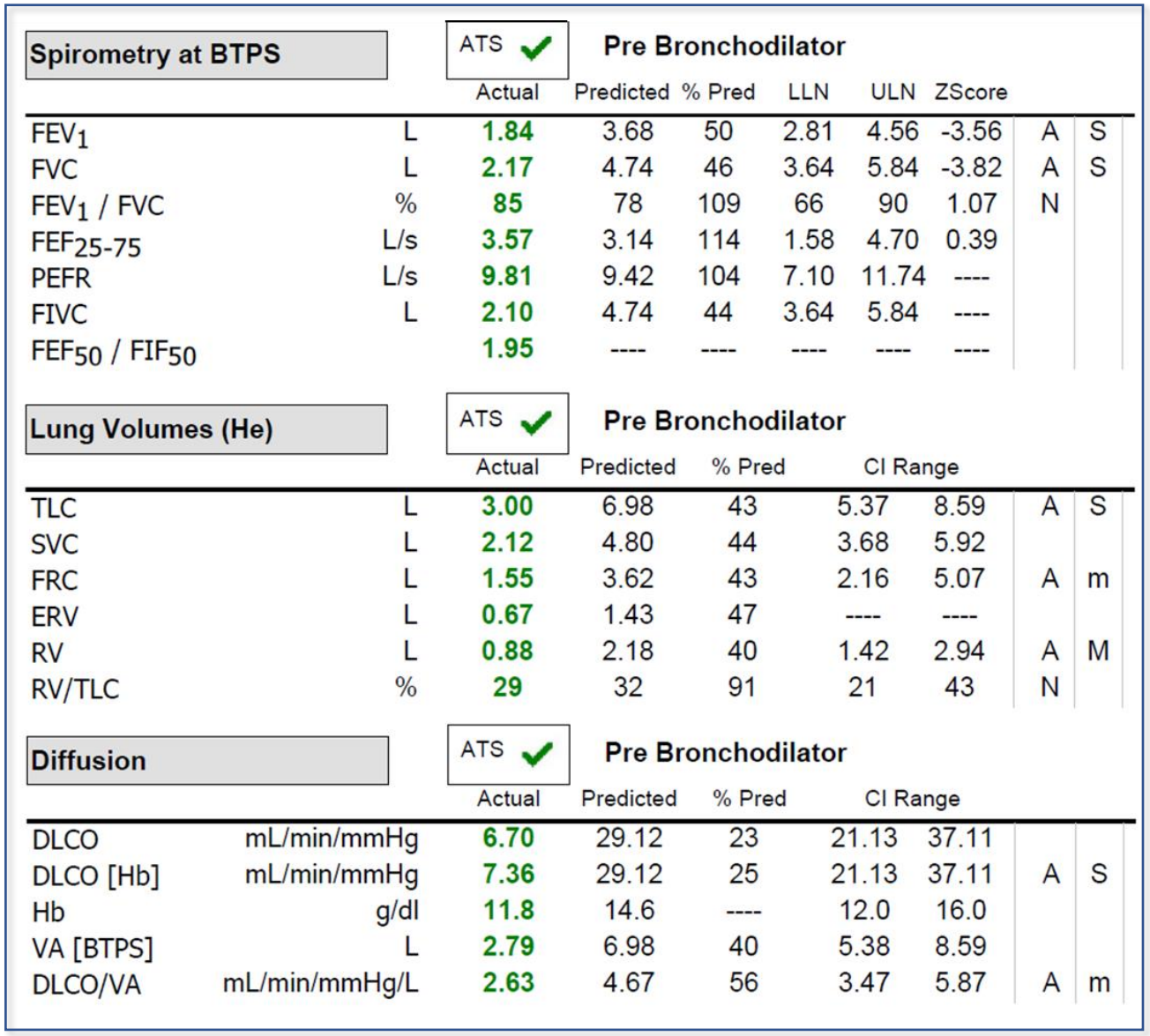


Index ICU admission for ARDS



4 months after discharge

Case 1



Spirometry at BTPS — ATS ✔ — **Pre Bronchodilator**

		Actual	Predicted	% Pred	LLN	ULN	ZScore		
FEV_1	L	1.84	3.68	50	2.81	4.56	-3.56	A	S
FVC	L	2.17	4.74	46	3.64	5.84	-3.82	A	S
FEV_1 / FVC	%	85	78	109	66	90	1.07	N	
FEF_{25-75}	L/s	3.57	3.14	114	1.58	4.70	0.39		
PEFR	L/s	9.81	9.42	104	7.10	11.74	----		
FIVC	L	2.10	4.74	44	3.64	5.84	----		
FEF_{50} / FIF_{50}		1.95	----	----	----	----	----		

Lung Volumes (He) — ATS ✔ — **Pre Bronchodilator**

		Actual	Predicted	% Pred	CI Range			
TLC	L	3.00	6.98	43	5.37	8.59	A	S
SVC	L	2.12	4.80	44	3.68	5.92		
FRC	L	1.55	3.62	43	2.16	5.07	A	m
ERV	L	0.67	1.43	47	----	----		
RV	L	0.88	2.18	40	1.42	2.94	A	M
RV/TLC	%	29	32	91	21	43	N	

Diffusion — ATS ✔ — **Pre Bronchodilator**

		Actual	Predicted	% Pred	CI Range			
DLCO	mL/min/mmHg	6.70	29.12	23	21.13	37.11		
DLCO [Hb]	mL/min/mmHg	7.36	29.12	25	21.13	37.11	A	S
Hb	g/dl	11.8	14.6	----	12.0	16.0		
VA [BTPS]	L	2.79	6.98	40	5.38	8.59		
DLCO/VA	mL/min/mmHg/L	2.63	4.67	56	3.47	5.87	A	m

Normal FEV1/FVC ratio
↓ FEV1
↓ FVC
Suggestive of severe restriction

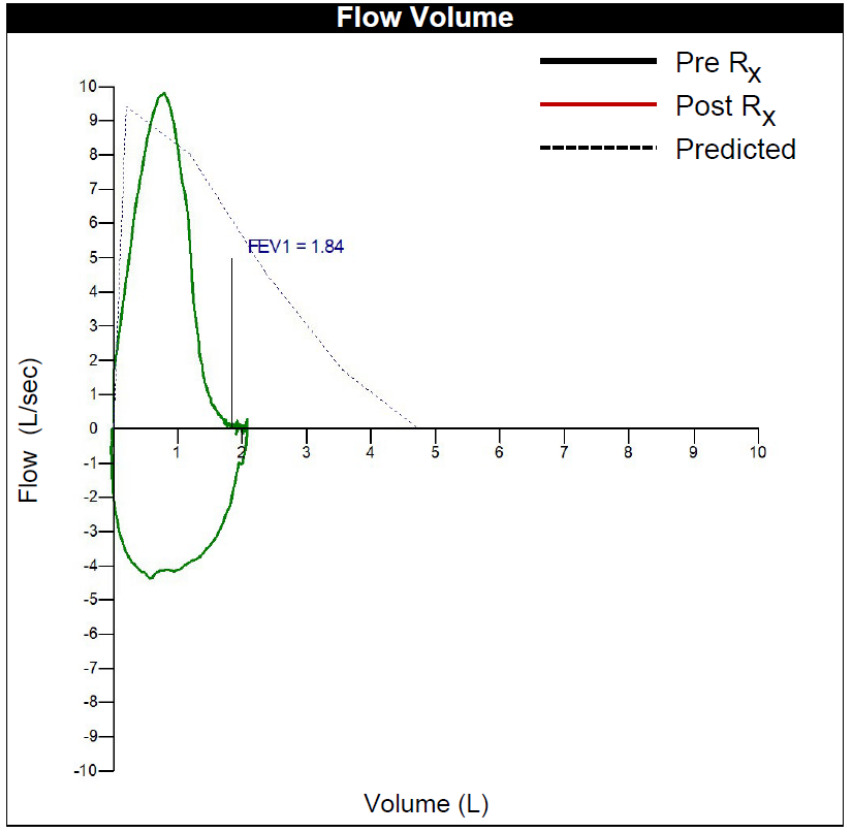
↓ TLC consistent with restriction

D_LCO is severely impaired

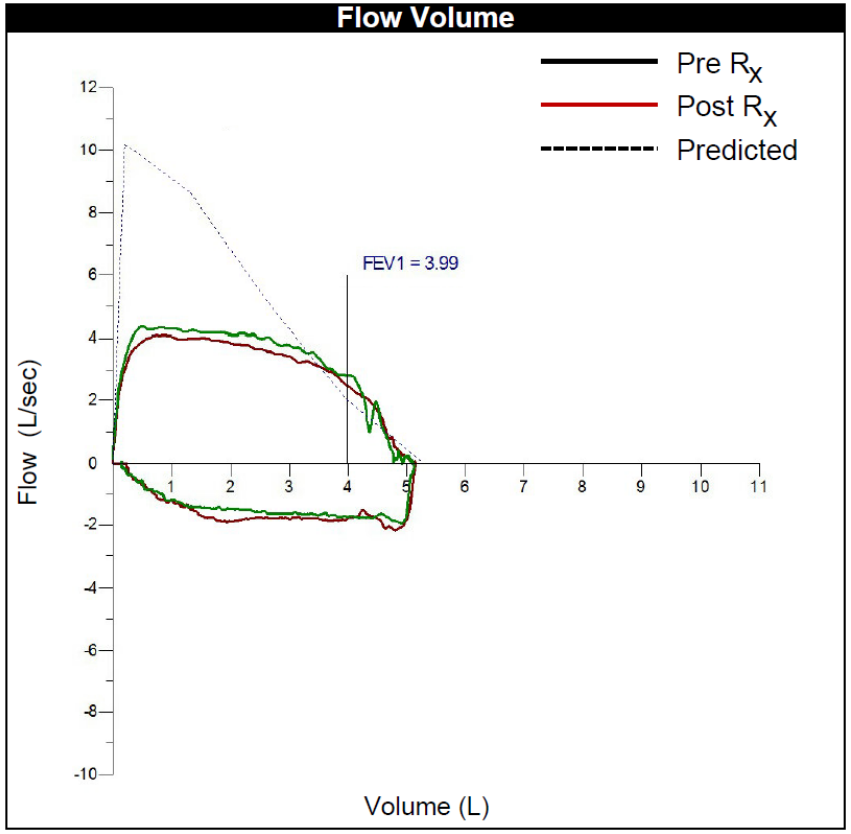
Case 1

Restricted flow-volume loop but otherwise normal contours

Our patient's flow volume loop



Another patient's flow volume loop



Tracheal (fixed) stenosis due following tracheostomy

Case 1

What is the most likely cause of this patient's shortness of breath?

A) Persistent SARS-CoV-2 infection
B) Organizing pneumonia
C) Tracheal stenosis
D) Deconditioning
E) Pulmonary fibrotic sequelae of ARDS
F) Both D and E

Case 1

What is the most likely cause of this patient's shortness of breath?

A) Persistent SARS-CoV-2 infection
B) Organizing pneumonia
C) Tracheal stenosis
D) Deconditioning
E) Pulmonary fibrotic sequelae of ARDS
F) Both D and E

The patient is both deconditioned (due to ICU-acquired weakness) and has pulmonary parenchymal sequelae of ARDS on cross-sectional imaging with resultant restriction and impaired diffusing capacity

Post-Intensive Care Syndrome (PICS)

Post-intensive care syndrome (PICS)

New or worsened impairment in 1 or more of the following domains following an ICU stay and persisting past hospital discharge:

- Physical function
- Cognition
- Mental health

* PICS can also affect family members (PICS-F)

Risk factors for PICS include:

- Multiorgan dysfunction
- Mechanical ventilation
- Sedation
- Delirium
- Immobility
- Systemic steroids
- Hyperglycemia
- Isolation

Particularly relevant to COVID-19

Needham et al. Crit Care Med 2012.
Griffiths et al. Crit Care 2013.
Kamdar et al. AJRCCM 2017.

Pulmonary Sequelae of Acute Respiratory Distress Syndrome (ARDS)

Parenchymal abnormalities after ARDS are common

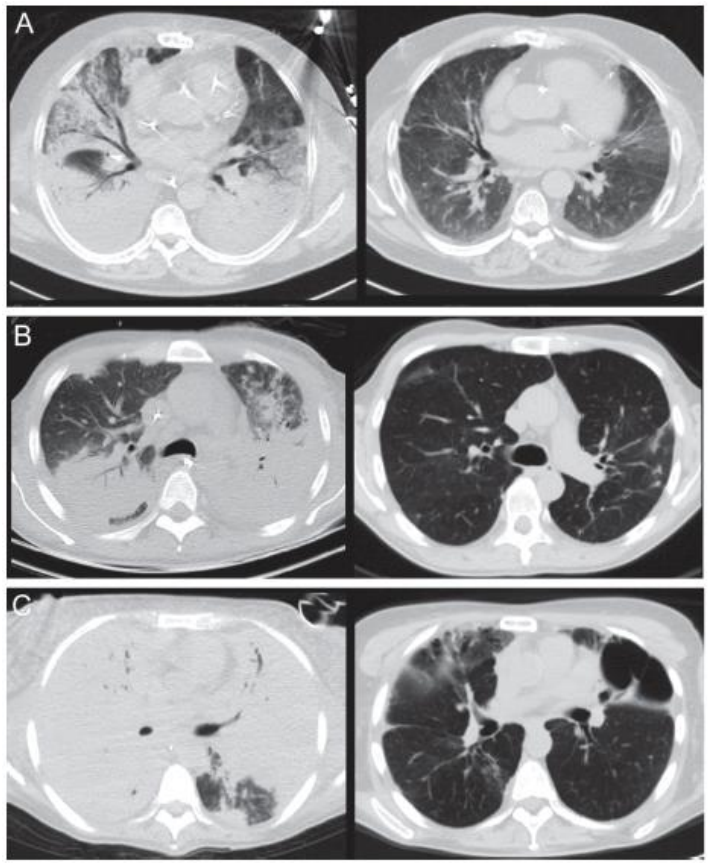
- 50% of patients have ↓ TLC at 1 year
- Impaired D_LCO on PFTs is the most common finding

Following the SARS-CoV-1 outbreak (2003):

- 41% had abnormal peak exercise capacity at 3 months
- 5% of patients had residual parenchymal findings at 15 years

Following the MERS-CoV outbreak (2012):

- 33% of patients had parenchymal fibrosis at 1 month follow up



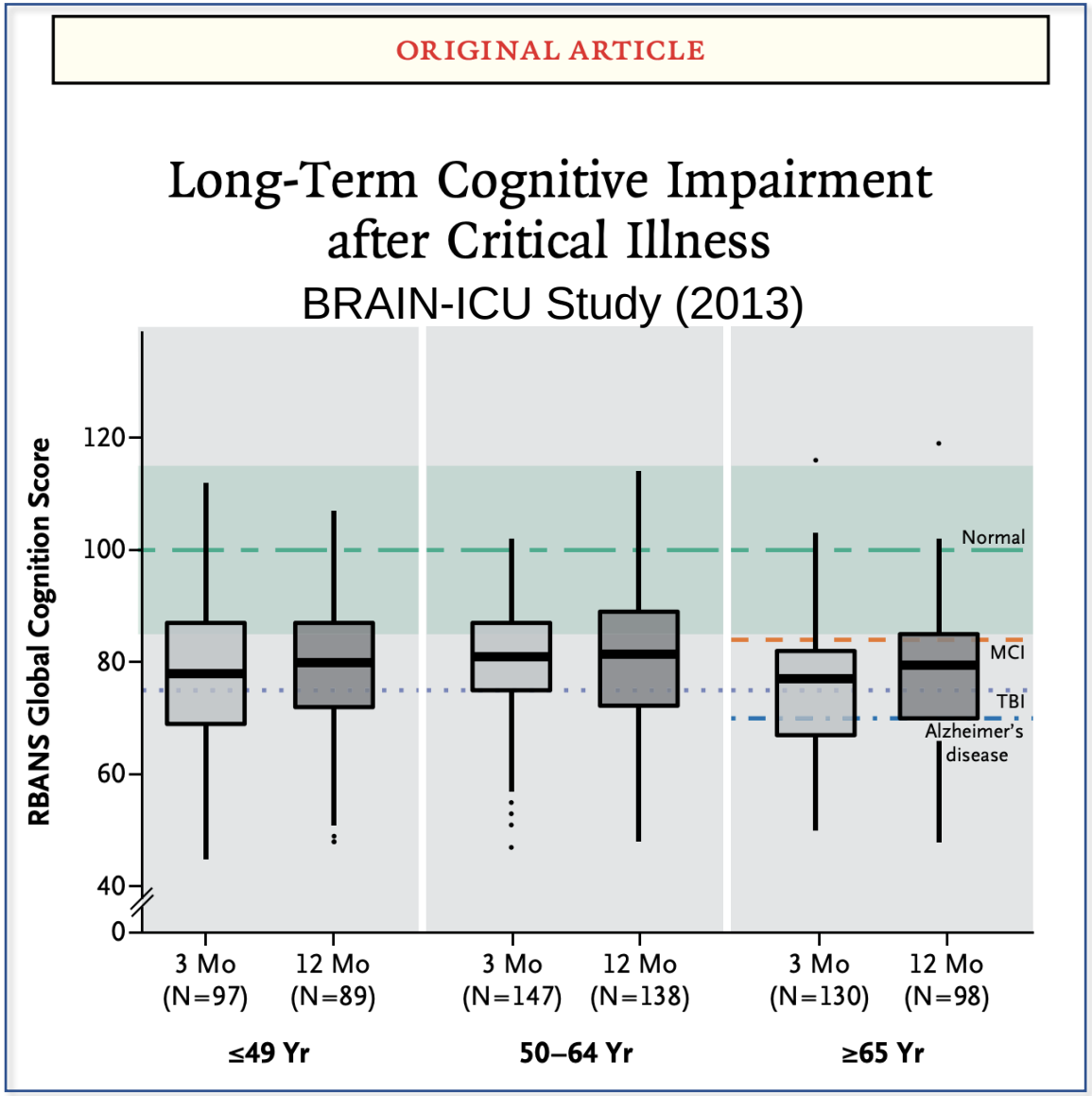
Herridge et al. NEJM 2003.
Chiumello et al. Respir Care 2016.
Thille et al. Lancet Respir Med 2013.
Ong et al. Eur Respir J 2004.
Spagnolo et al. Lancet Respir Med 2020.
Mo et al. Eur Respir J 2020.

PICS: cognitive impairment

RBANS = Repeatable Battery for the Assessment of Neuropsychological Status

Longitudinal study of 821 ICU patients with respiratory failure or shock

- Median global cognitive score (where normal = 100) was:
  - 79 (3 months)
  - 80 (12 months)
- At 3 months, 40% had scores equivalent to individuals with TBI and 26% had scores equivalent to individuals with mild Alzheimer's disease



Pandharipande et al. NEJM 2013.

PICS: cognitive impairment

RBANS = Repeatable Battery for the Assessment of Neuropsychological Status

Longitudinal study of 821 ICU patients with respiratory failure or shock

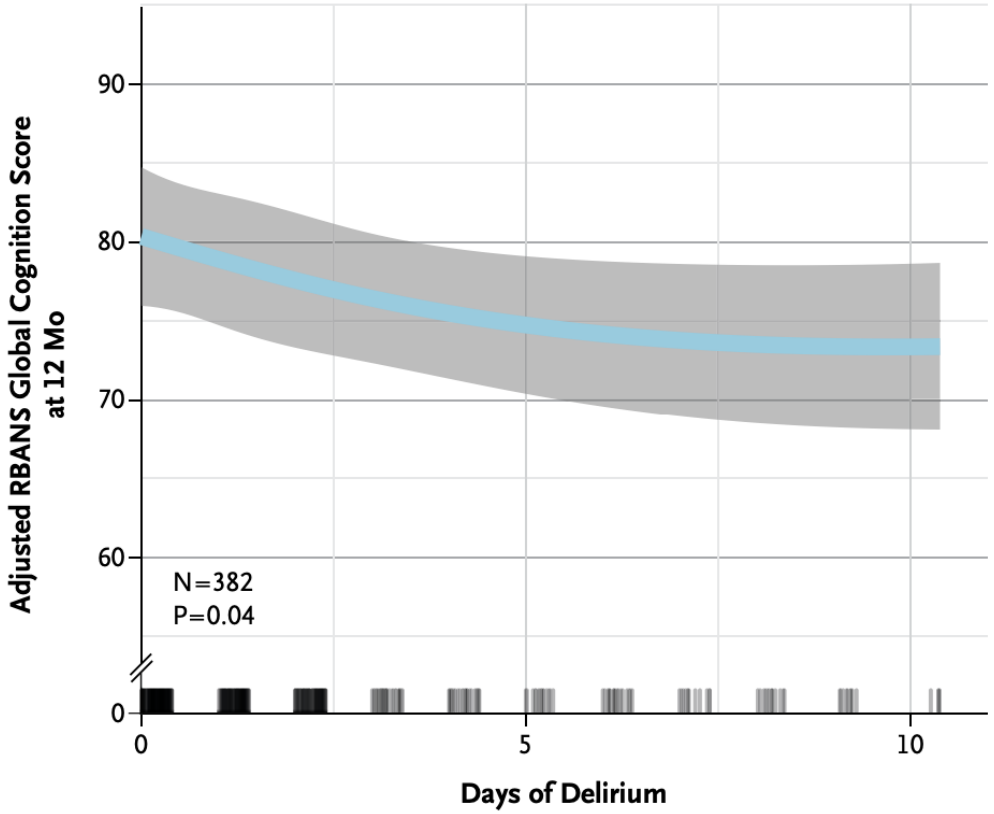
- A longer duration of delirium was independently associated with worse global cognition

~55% of critically ill COVID patients develop delirium

ORIGINAL ARTICLE

Long-Term Cognitive Impairment after Critical Illness

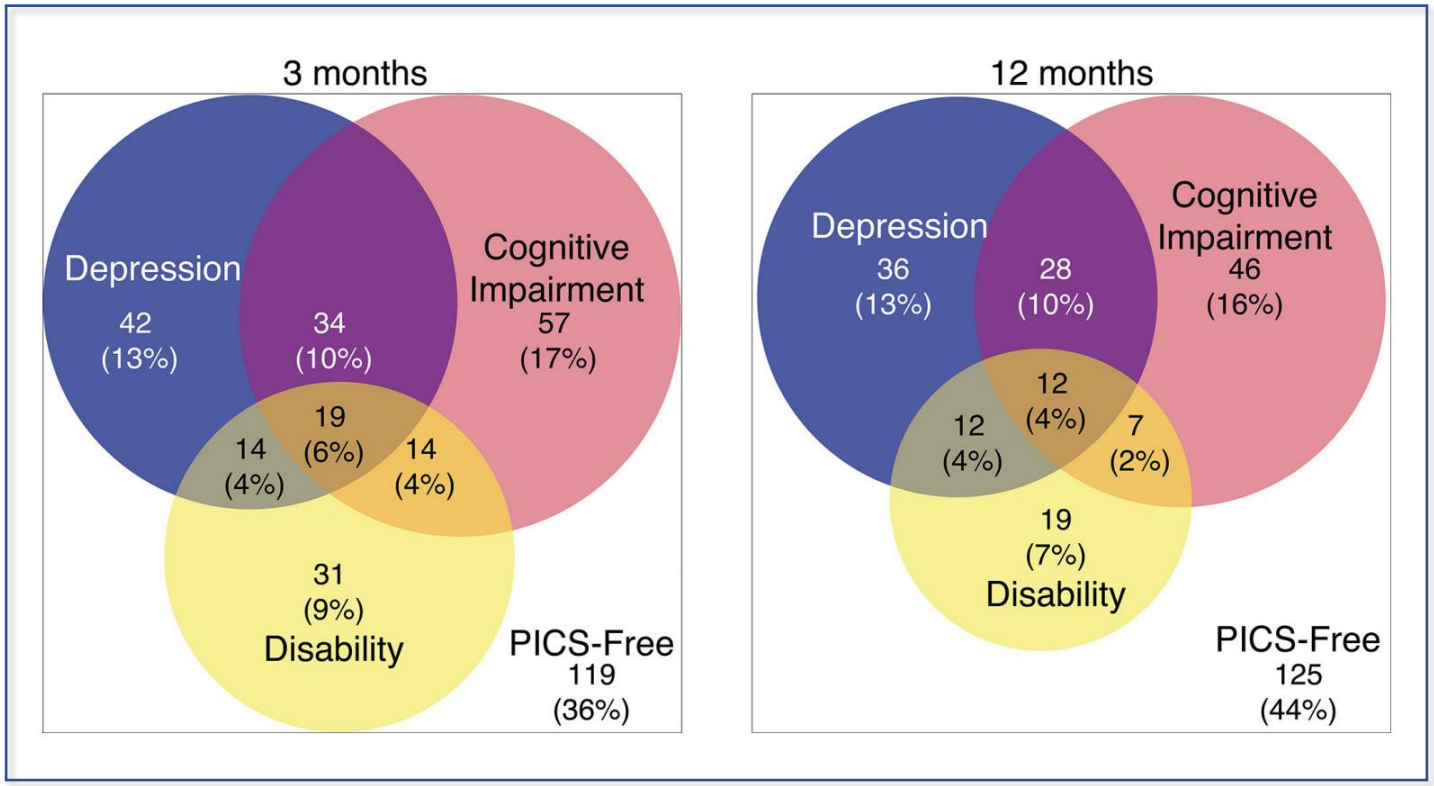
BRAIN-ICU Study (2013)



Pandharipande et al. NEJM 2013.
Pun et al. Lancet Respir Med. 2021.

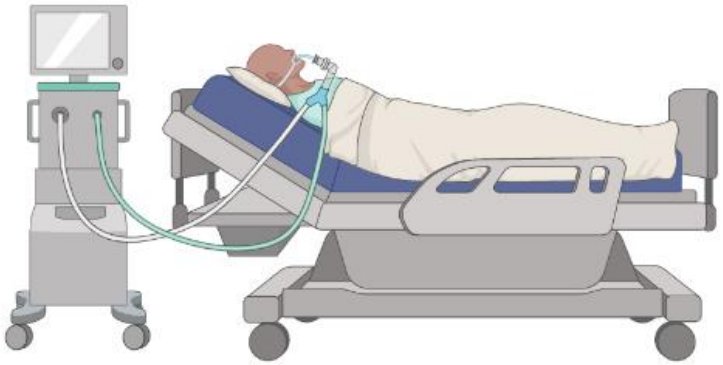
PICS: psychological impairment

- Up to 50% develop anxiety and/or depression
- Up to 25% develop PTSD
- More than one overlapping problem in ~20% at 1 year



Parker et al. Crit Care Med 2015.
Rabiee et al. Crit Care Med 2016.
Needham et al. Crit Care Med 2012.
Marra et al. Crit Care Med 2018.

Post-ICU patients have unique needs



Patients who survived critical illness due to COVID-19

Screen for post-intensive care syndrome (PICS)

- PHQ-4 (anxiety and depression), PTSD-PC-5 (PTSD), and mini-MOCA
- Don't forget family members, financial toxicity, and disparities in these outcomes

Screen for other complications of critical illness

- Supraglottic, glottic, or infraglottic complications of endotracheal intubation or tracheostomy

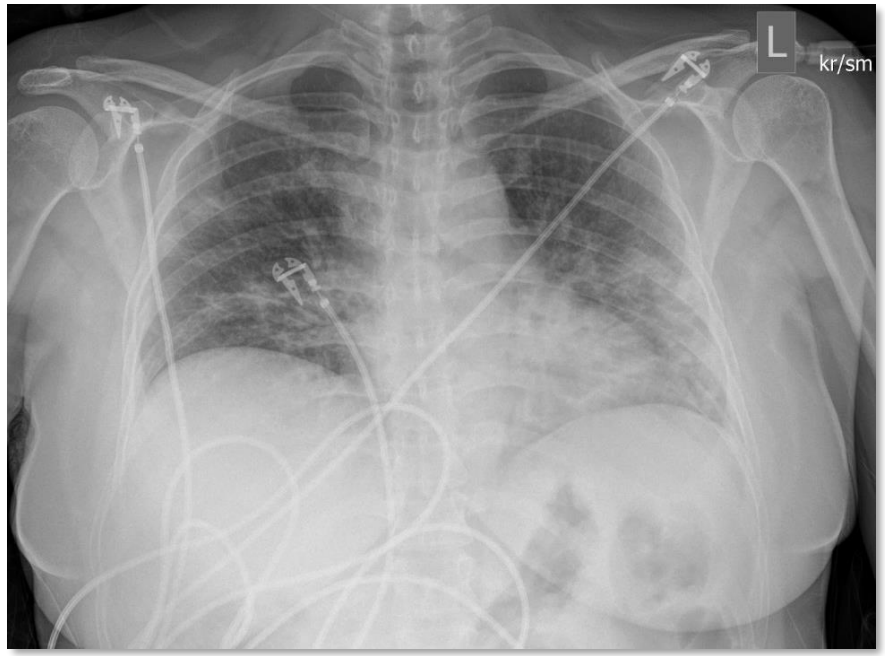
Multidisciplinary evaluation is helpful

- Mental health evaluation and counseling
- Physical and occupational therapy
- Speech language pathology for cognitive therapy
- Pulmonary rehabilitation program
- If available, consider referral to dedicated PICS clinic

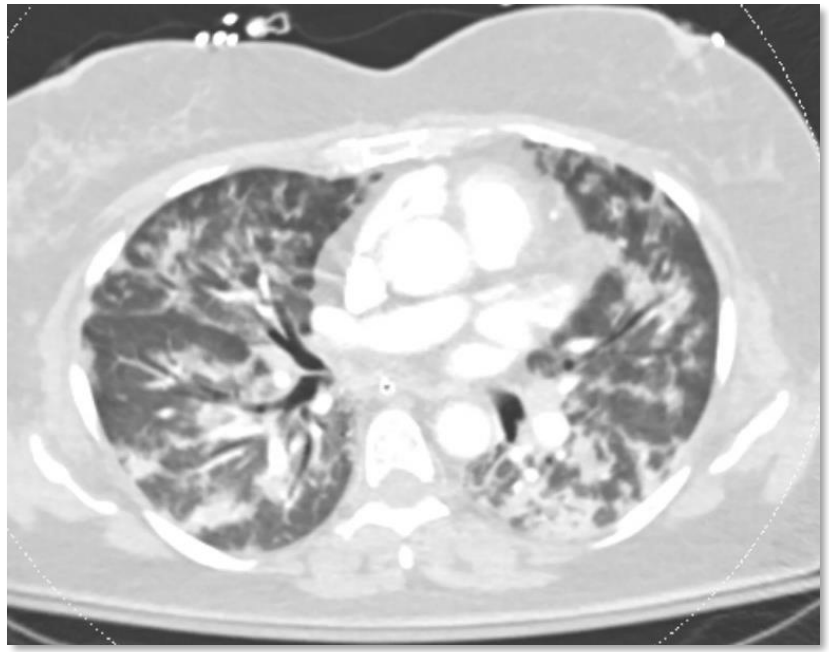
Maley JH, **Alba GA**, Barry JT, et al. PM R. 2022 Jan;14(1):77-95.

Case 2

57-year-old Latinx woman with obesity and OSA hospitalized for 10 days with pneumonia due to SARS-CoV-2 requiring supplemental oxygen and treated with remdesivir and dexamethasone



Admission chest radiograph

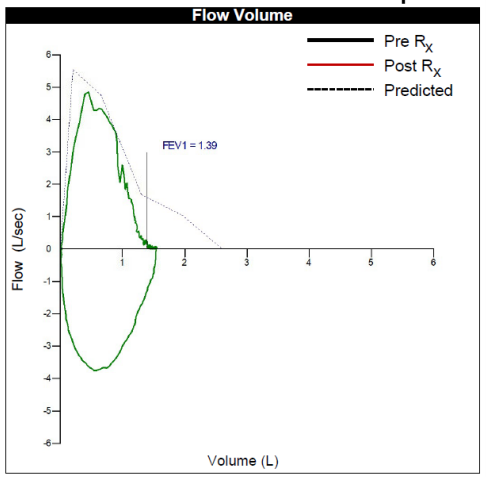


Admission CTPE

Case 2

6 months after discharge she reports chronic non-productive cough, dyspnea with 1 flight of stairs, and exertional tachycardia

Flow-volume loop



No suggestion of tracheal or laryngeal pathology

Spirometry at BTPS — ATS ✔ — **Pre Bronchodilator**

		Actual	Predicted	% Pred	LLN	ULN	ZScore		
FEV_1	L	1.39	2.09	67	1.60	2.59	-2.38	A	M
FVC	L	1.55	2.60	60	1.99	3.22	-2.79	A	MS
FEV_1 / FVC	%	90	81	111	69	92	1.44	N	
FEF_{25-75}	L/s	2.85	2.09	136	1.10	3.08	1.08		
PEFR	L/s	4.86	5.55	88	4.15	6.95	----		
FIVC	L	1.55	2.60	60	1.99	3.22	----		
FEF_{50} / FIF_{50}		1.17	----	----	----	----	----		

Diffusion — ATS ✔ — **Pre Bronchodilator**

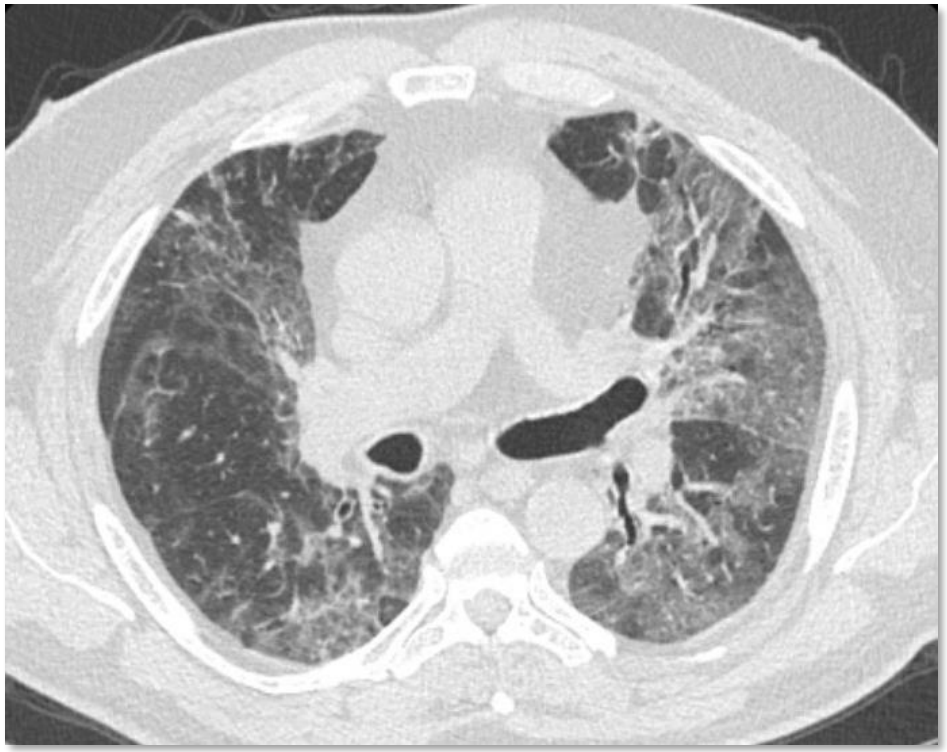
		Actual	Predicted	% Pred	CI Range			
DLCO	mL/min/mmHg	8.68	19.50	45	13.00	26.00		
DLCO [Hb]	mL/min/mmHg	8.97	19.50	46	13.00	26.00	A	m
Hb	g/dl	12.4	13.4	----	12.0	16.0		
VA [BTPS]	L	2.24	4.15	54	4.08	4.23		

Normal FEV1/FVC ratio
↓ FEV1
↓ FVC
Suggestive of restriction

D_LCO is mildly impaired

Case 2

6 months after discharge with persistent respiratory symptoms and evidence of restriction and impaired gas exchange on PFTs



HRCT at first visit

Case 2

What is the most likely cause of this patient's shortness of breath?

A) Persistent SARS-CoV-2 infection
B) Organizing pneumonia
C) Tracheal stenosis
D) Deconditioning
E) Pulmonary fibrotic sequelae of ARDS
F) None of the above

Case 2

What is the most likely cause of this patient's shortness of breath?

A) Persistent SARS-CoV-2 infection

B) Organizing pneumonia

C) Tracheal stenosis

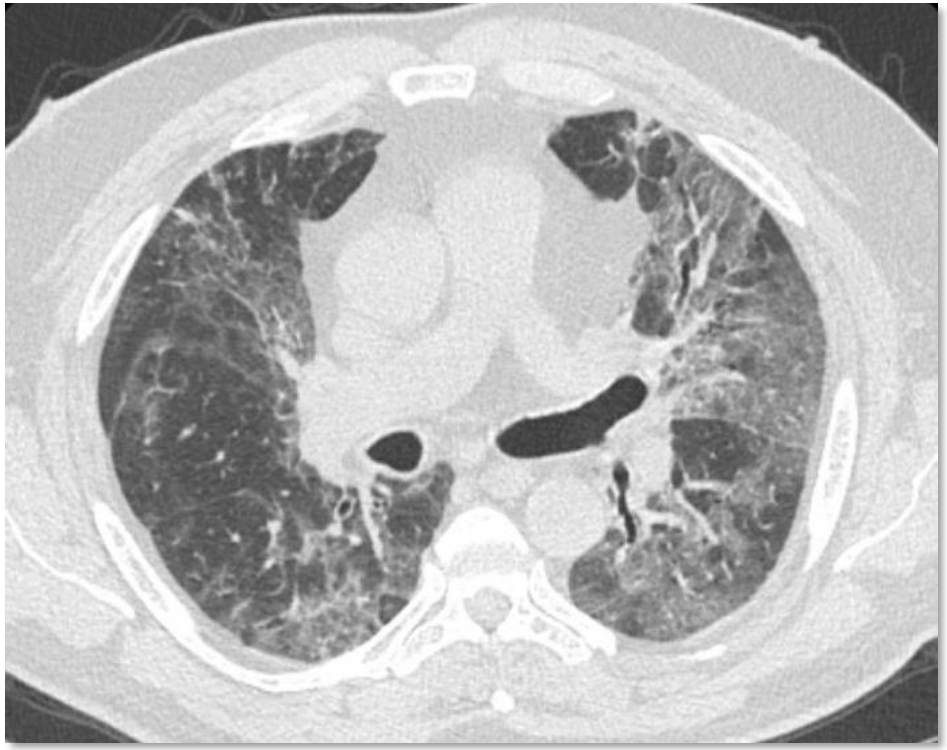
D) Deconditioning

E) Pulmonary fibrotic sequelae of ARDS

F) None of the above

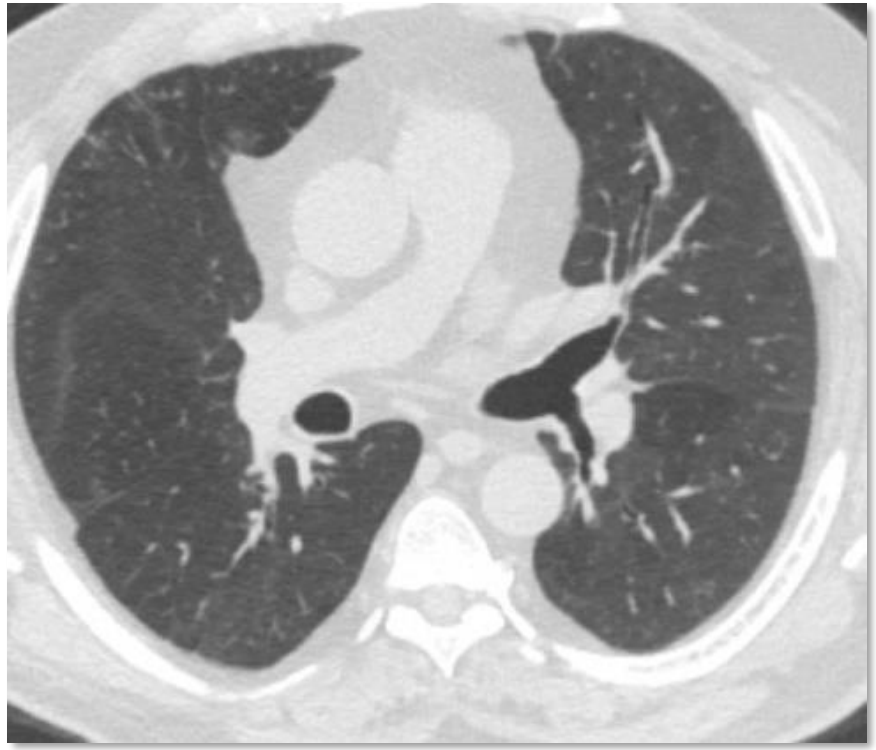
Case 2

Treated with prednisone 0.5 mg/kg x 1 month and then tapered over the next 8 weeks with resolution of her cough and improvement in dyspnea



HRCT at first visit

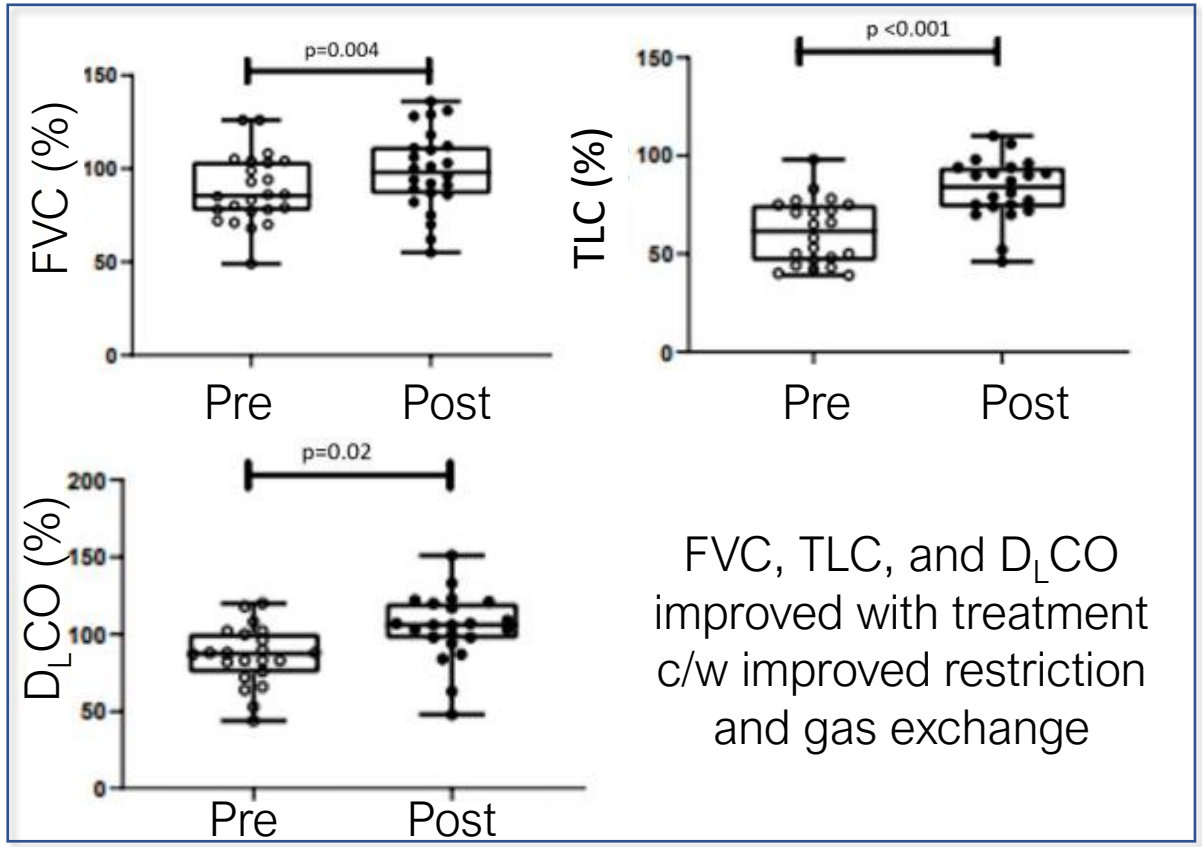
Prednisone
40 mg QD



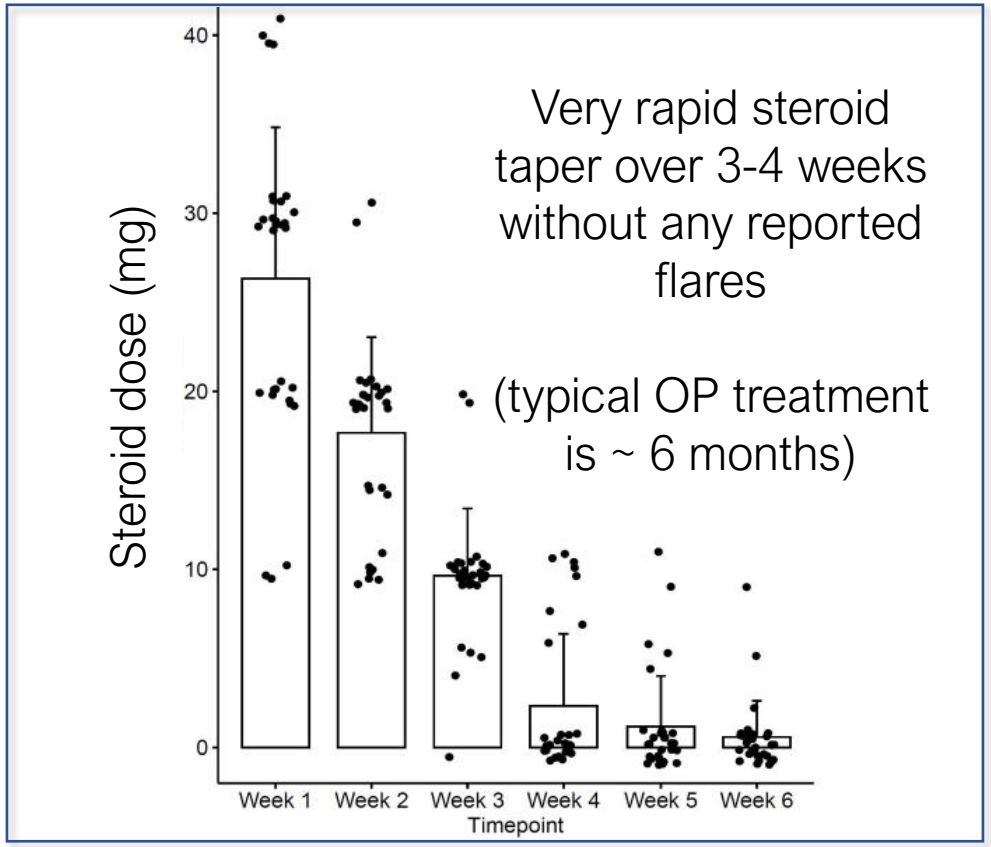
Follow up HRCT

Organizing Pneumonia

Case series of patients (n=837) post-COVID-19 with 35 (4.8%) found to have organizing pneumonia and 30 (3.6%) treated with 0.5 mg/kg prednisone



FVC, TLC, and D_LCO improved with treatment c/w improved restriction and gas exchange

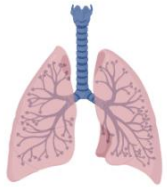


Very rapid steroid taper over 3-4 weeks without any reported flares

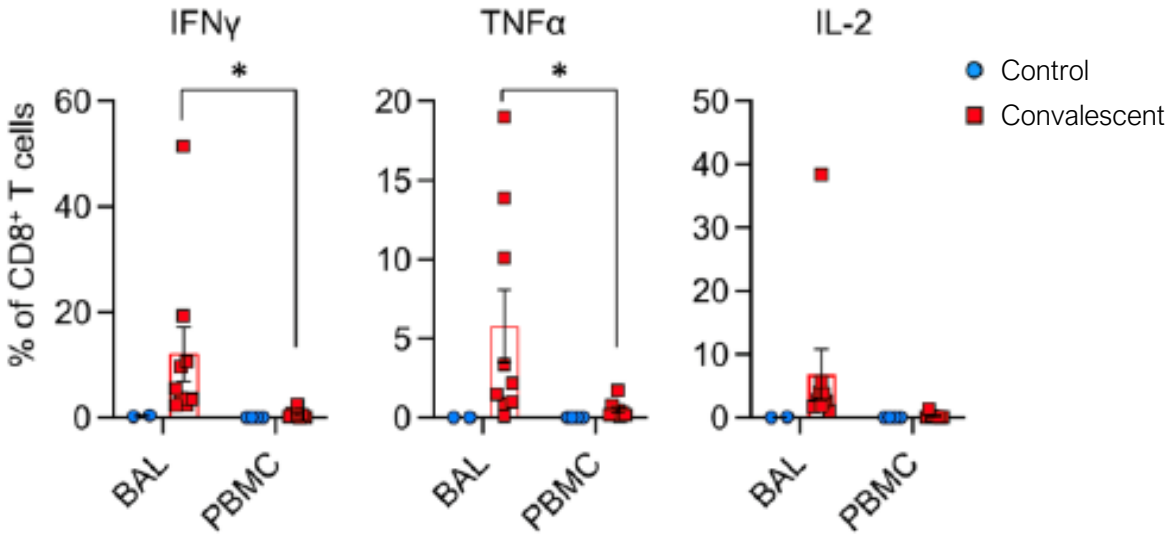
(typical OP treatment is ~ 6 months)

Myall et al. Ann Am Thorac Soc. 2021. doi:10.1513/AnnalsATS.202008-1002OC.

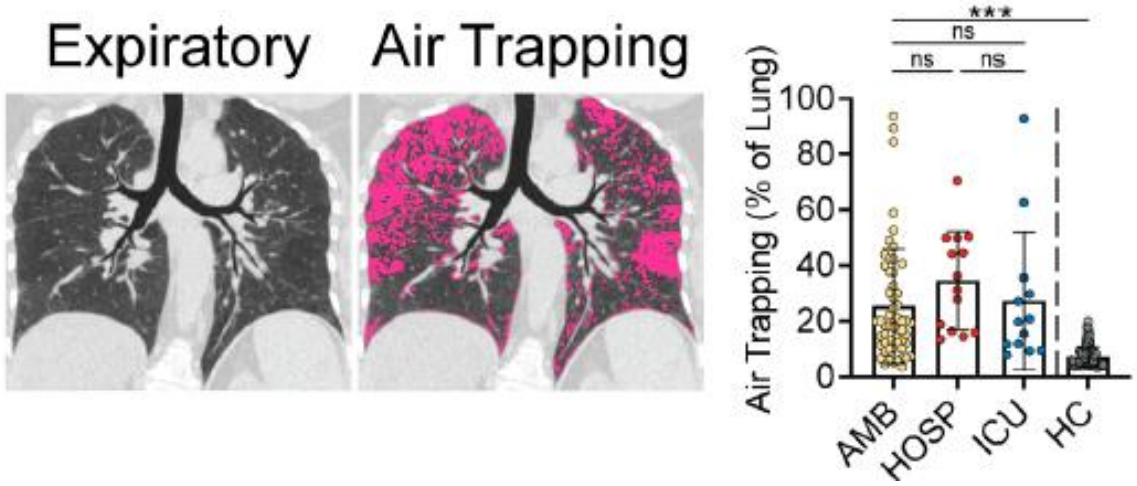
Pathobiology of Post COVID Lung Disease



- Acute systemic inflammation resolves during convalescence but ↑ **lung tissue-resident CD8⁺ T cells associated with impaired lung function**

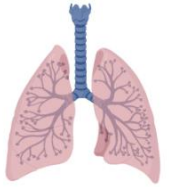


- More severe disease results in more interstitial parenchymal Δs, but **air trapping (small airways disease)** seen in ~25% of *all* convalescent cases not detectable by PFTs



Cheon IS et al. Sci Immunol. 2021 Sep 30;eabk1741. doi: 10.1126/sciimmunol.abk1741.
Cho JL et al. https://www.medrxiv.org/content/10.1101/2021.05.27.21257944v1.full

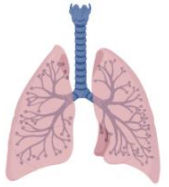
Pulmonary Sequelae of COVID-19



- Typical post-ARDS sequelae
  - At 5 years, 75% will have residual parenchymal abnormalities
- Chronic organizing pneumonia pattern
  - Based on reported literature, ~5% of patients following SARS-CoV-2 pneumonia
- Mild mosaic attenuation and air trapping on HRCT expiratory views
  - Suggestive of small airways inflammation (bronchiolitis)
- Airway complications (related to intubation and tracheostomy)
  - Incidence in the literature anywhere from 1-10%
- Venous thromboembolism
  - Acute macro- and micro-thromboses observed in ~15-20% of patients with acute COVID-19
  - However, in the post-acute setting < 5% incidence

Chiumello et al. Respir Care 2016.
Thille et al. Lancet Respir Med 2013.
Nalbandian et al. Nat Med. 2021. doi:10.1038/s41591-021-01283-z.

Evaluation of Pulmonary Sequelae



- Understand their initial disease severity and clinical course
  - Disease severity, complications of illness and hospitalization, and interventions inform post-acute sequelae
- Identify objective signs of abnormal pulmonary function to guide workup
  - Full pulmonary testing including spirometry, lung volumes, and D_LCO
  - Exertional oximetry to detect occult hypoxemia
- Refer to pulmonary specialist or dedicated post-COVID clinic
  - For consideration of additional imaging, testing (e.g., cardiopulmonary exercise testing), or treatments

Bai C, Chotirmall SH, Rello J, Alba GA, Ginns LC, et al. Eur Respir Rev. 2020 Oct 5;29(157):200287.
Alba GA et al. EClinicalMedicine. 2021 Aug 28;39:101066. doi: 10.1016/j.eclinm.2021.101066.

Case 3

38-year-old nurse with migraines with mild COVID-19 with > 6 months of multiple symptoms including exercise intolerance, post-exertional malaise, insomnia, and cognitive impairments out of work on disability

Normal PFTs and HRCT

Abnormal tilt table testing

Cardiopulmonary exercise test (CPET) with low peak oxygen consumption (VO_2) and evidence of postural orthostatic tachycardia syndrome (POTS)

Case 3

What is the most likely cause of this patient's shortness of breath?

A) Persistent SARS-CoV-2 infection
B) Organizing pneumonia
C) Tracheal stenosis
D) Deconditioning
E) Pulmonary fibrotic sequelae of ARDS
F) None of the above

Case 3

What is the most likely cause of this patient's shortness of breath?

A) Persistent SARS-CoV-2 infection
B) Organizing pneumonia
C) Tracheal stenosis
D) Deconditioning
E) Pulmonary fibrotic sequelae of ARDS
F) None of the above

Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS)

Clinical syndrome defined by having 3 symptoms:

1. >6 months of fatigue and inability to participate in routine activities that were possible before becoming ill
2. Post-exertional malaise
3. Unrefreshing sleep

Plus at least 1 of the following:

1. Impaired memory or ability to concentrate
2. Orthostatic intolerance

Our patient met all clinical criteria for ME/CFS

Has been associated with several infectious diseases but pathobiology is unclear

There is no specific treatment

CDC. https://www.cdc.gov/me-cfs/index.html.
Clayton EW. JAMA. 2015;313(11):1101-2.

Dysautonomia / small fiber neuropathy

Two primary pathophenotypes emerge on invasive CPET in ME/CFS patients

1. "Preload failure" with low right atrial pressure / low cardiac output
2. "Peripheral shunt" with impaired peripheral O_2 extraction

In a cohort of ME/CFS patients (n=160), 50 (31%) had biopsy-proven small fiber neuropathy (SFN)

In post-COVID-19 cohorts, ~ 30% have abnormal autonomic testing (F>M)

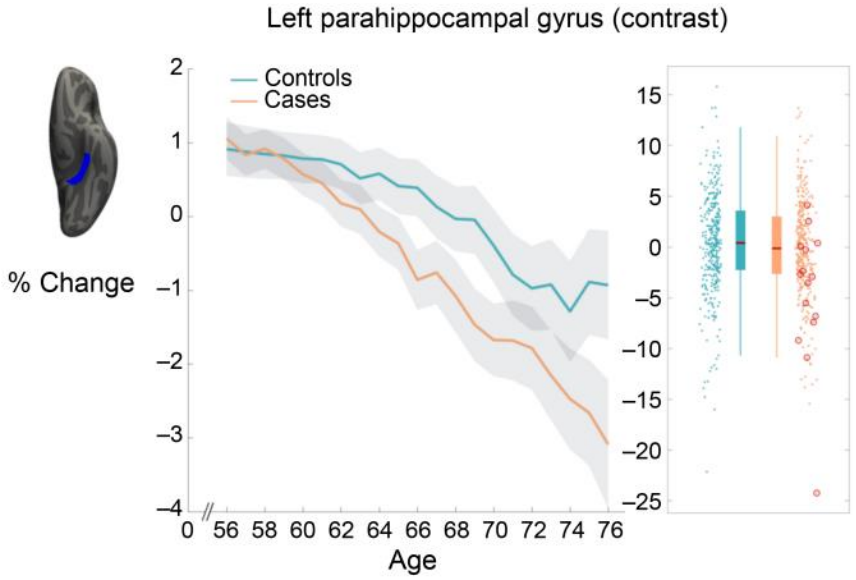
- If dysautonomia present, ~80% have biopsy-proven SFN and ~50% have auto-antibodies (e.g., anti-TS-HDS, component of peripheral nerve sites)

Joseph et al. Chest 2021 Aug;160(2):642-651.
Shouman K et al. Clin Auton Res 2021 Jun;31(3):385-394.
Novak P et al. Ann Neurol 2022;91:367-379.

Pathobiology of neurologic sequelae in PASC

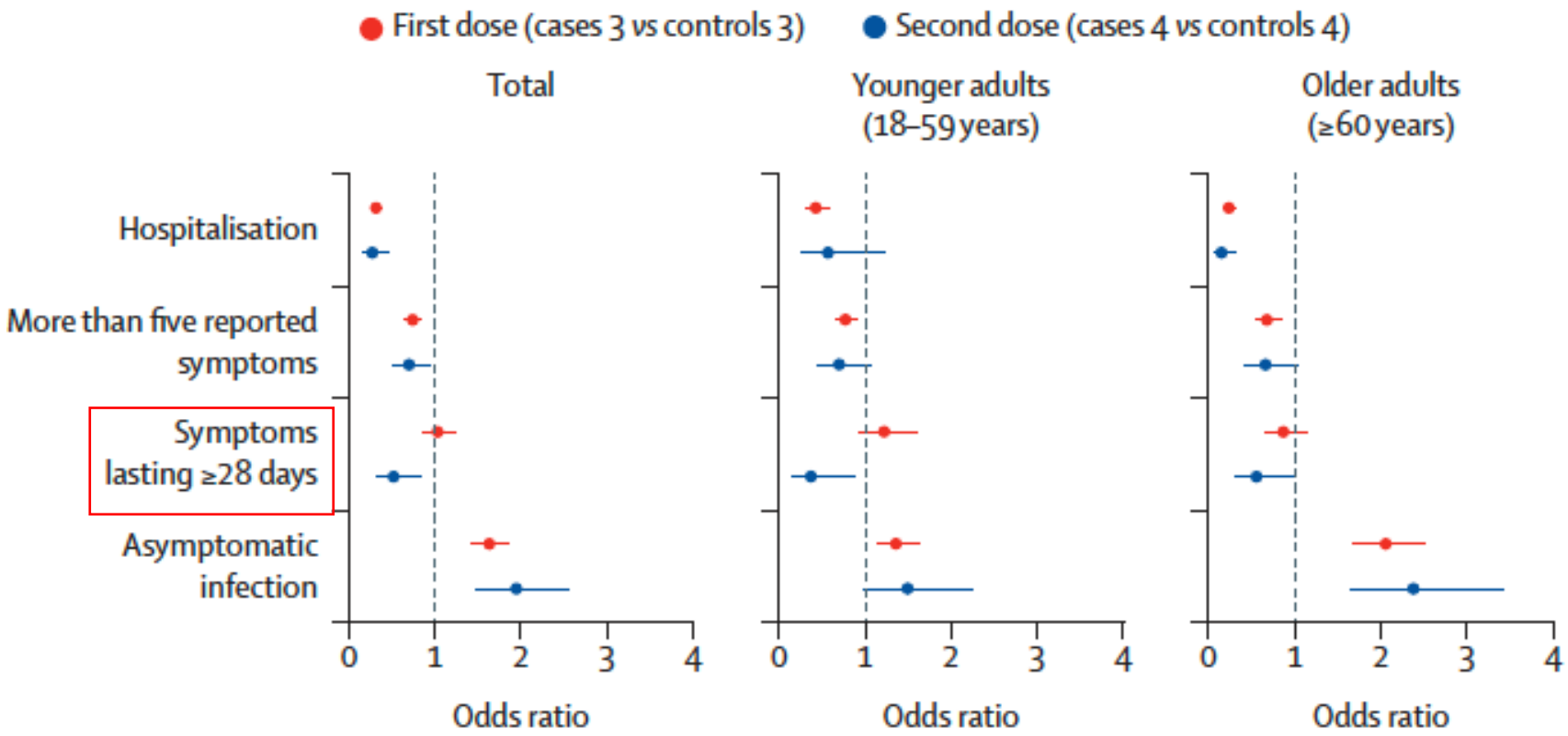
- No evidence of direct brain tissue infiltration of virus but there is evidence of response to peripheral inflammation and peripheral T cell infiltration with transcriptional changes that overlap with neurodegenerative diseases

- Compared to non-infected controls, COVID+ had:
  - Greater ↓ in grey matter thickness
  - Greater tissue damage in areas connected to olfactory cortex
  - Greater ↓ in global brain size
  - Greater ↓ in cognitive testing



Yang et al. Nature. 2021;595(7868):565-571.
Douaud et al. Nature. 2022. doi: 10.1038/s41586-022-04569-5.
Khan et al. Cell 2021;84(24):5932-5949.

Vaccination Decreases Incidence of “Long COVID”



Odds of symptoms lasting beyond 1 month (i.e., “long COVID”) is **halved** in the fully vaccinated group vs. matched unvaccinated controls

Matta J et al. AMA Intern Med. 2021 Nov 8. doi: 10.1001/jamainternmed.2021.6454.
Antonelli M et al. Lancet Infect Dis. 2021 Sep 1;S1473-3099(21)00460-6.

The NIH is funding research in PASC ($470 million)

RECOVER

Researching COVID to Enhance Recovery

https://recovercovid.org/

Take-home points

Survivors of COVID-19, regardless of disease severity, may manifest with PASC, and protracted symptoms beyond 4-12 weeks is common

PASC is a heterogenous disorder made up of distinct “syndromes” that we are still trying to understand but include common clinical syndromes (e.g., post-intensive care syndrome, organizing pneumonia, bronchiolitis) and rarer clinical syndromes (ME/CFS, dysautonomia, small fiber neuropathy, olfactory dysfunction)

Common themes underlying pathophysiology appear to be dysregulated immune cell responses with organ-specific manifestations

There are no specific, approved therapies for these different PASC phenotypes, but prevention with equitable distribution of vaccination, early post-exposure treatment, or pre-exposure prophylaxis is key

MASSACHUSETTS GENERAL HOSPITAL
DEPARTMENT OF MEDICINE

MASSACHUSETTS GENERAL HOSPITAL
NEUROLOGY

HARVARD MEDICAL SCHOOL

Pulmonary Medicine

Director

Leo Ginns, MD

Associate Director

George Alba, MD

Division of Pulmonary and Critical Care

Kathryn Hibbert, MD
Ben Medoff, MD
Christopher Richards, MD
James Mojica, MD
Corey Hardin, MD
Greg Lewis, MD
David Kanarek, MD

Fiona Gibbons, MD
Robert Hallowell, MD
Jill Clement
Hannah Delorey
Kym Burden
Theresa Kranz
Wanda Rodriguez

Neurology

Brian Edlow, MD

Eric Rosenthal, MD

Haitham Alabsi, DO

Jonathan Rosand, MD

Shibani Mukerji, MD PhD

Anne Oaklander, MD PhD

David Lin, MD

Emily Lewis, BA

RECOVER
Researching COVID to Enhance Recovery

Ingrid Bassett, MD MPH

Bruce Levy, MD

Resources for Patients

Body Politic COVID-19 Support Group:

https://docs.google.com/forms/d/e/1FAIpQLScM2EeJhgisTUdo5Op6euyx1PYu8O-aNeDVYhXuPFa_Gs9PnQ/viewform

Body Politic COVID-19 Resources:

https://www.wearebodypolitic.com/resources

Survivor Corps Research Opportunities:

https://www.survivorcorps.com/

End Coronavirus Additional Resources:

https://www.endcoronavirus.org/long-covid

Diaphragmatic Breathing Exercises:

https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/coronavirus-recovery-breathing-exercises

References

1. Nalbandian A et al. Post-acute COVID-19 Syndrome. Nat Med. 2021 Apr;27(4):601-615.
2. Al-Aly Z et al. High-dimensional characterization of post-acute sequelae of COVID-19. Nature. 2021 Jun;594(7862):259-264.
3. Post-COVID Conditions: Information for Healthcare Providers. Centers for Disease Control and Prevention. Last Updated July 9, 2021. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html
4. Oran et al. Ann Int Med. 2020;173(5):362.
5. Wu et al. JAMA. 2020;323(13):1239.
6. NIH.gov (https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/)
7. World Health Organization. October 6, 2021. WHO/2019-nCoV/Post_COVID-19_condition/Clinical_case_definition/2021.1
8. Sudre et al. Nat Med. 2021. doi:10.1038/s41591-021-01292-y
9. Needham et al. Crit Care Med 2012.
10. Griffiths et al. Crit Care 2013.
11. Kamdar et al. AJRCCM 2017.
12. Chiumello et al. Respir Care 2016.
13. Thille et al. Lancet Respir Med 2013.
14. Ong et al. Eur Respir J 2004.
15. Spagnolo et al. Lancet Respir Med 2020.
16. Mo et al. Eur Respir J 2020.
17. Myall et al. Ann Am Thorac Soc. 2021. doi:10.1513/AnnalsATS.202008-1002OC.
18. CDC. https://www.cdc.gov/me-cfs/index.html.
19. Clayton EW. JAMA. 2015;313(11):1101-2.
20. Cheon IS et al. Sci Immunol. 2021 Sep 30;eabk1741. doi: 10.1126/sciimmunol.abk1741.
21. Cho JL et al. https://www.medrxiv.org/content/10.1101/2021.05.27.21257944v1.full
22. Maley et al. PM R. 2022 Jan;14(1):77-95.

ON

BRAIN AND NERVE EXHAUSTION (NEURASTHENIA),

AND ON THE

NERVOUS SEQUELÆ OF INFLUENZA.

BY

THOMAS STRETCH DOWSE, M.D., F.R.C.P. ED.,

LATE PHYSICIAN SUPERINTENDENT CENTRAL LONDON SICK ASYLUM; LATE PRESIDENT NORTH LONDON MEDICAL SOCIETY; LATE MEMBER OF COUNCIL AND SECRETARY FOR FOREIGN CORRESPONDENCE MEDICAL SOCIETY OF LONDON; FORMERLY PHYSICIAN TO THE NORTH LONDON HOSPITAL FOR CONSUMPTION AND DISEASES OF THE CHEST, TO THE NORTH-WEST LONDON HOSPITAL, AND TO THE WEST-END HOSPITAL FOR EPILEPSY AND DISEASES OF THE NERVOUS SYSTEM; ASSOCIATE MEMBER OF THE NEUROLOGICAL SOCIETY OF NEW YORK, ETC.

FOURTH EDITION.

LONDON:
BAILLIÈRE, TINDALL AND COX,
20 & 21, KING WILLIAM STREET, STRAND.
1894.

THE

BOSTON MEDICAL AND SURGICAL JOURNAL.

NEW SERIES.] THURSDAY, APRIL 29, 1869. [VOL. III.—No. 13.

Original Communications.

NEURASTHENIA, OR NERVOUS EXHAUSTION.

By GEORGE BEARD, M.D., Lecturer on Nervous Diseases in the University of New York.

in the habit of employing the term *neurasthenia* to express the morbid state that is commonly indicated by the indefinite phrase nervous exhaustion.

This nomenclature would seem to be justified by philological analogy, by scientific convenience, and by actual necessity.

The derivation of the term *neurasthenia*