

POST-ICU COVID-19



DR. MARY SUCHYTA PULMONARY DIVISION INTERMOUNTAIN HEALTH CARE SALT LAKE CITY, UTAH

No disclosures

LEARNING OBJECTIVES

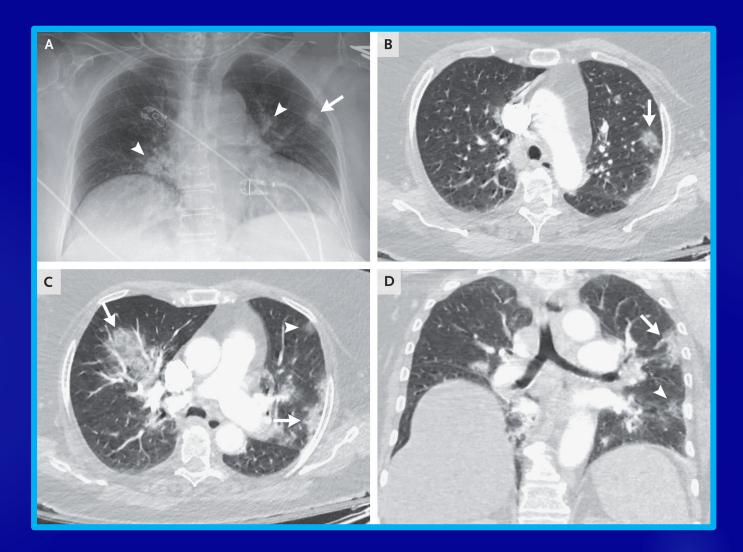
- Objective #1: Understand the severity of COVID ICU illnesses
- Objective #2: Understand that the majority of patients with COVID have ARDS & as such have a similar yet different course as other patients with ARDS

Objective #3: Understand Post ICU syndromes & possible rehab for these patients

CASE PRESENTATION

A 45 year-old female presented to ER w/ SOB & cough. She had viral s/s for 7 days. Temperature 38°C, HR 110, BP 102/70 & RR 26 w/saturation 85%. CXR w/ground glass opacities. Labs: CBC 4,500 w/lymphopenia, normal electrolytes. **Oximetry improved to 95% on 4L/NC. IV fluids** administered; she was admitted to the floor. PCR was positive for SARS-CoV-2. She required increasing oxygen & was transferred to the ICU.

IMAGING



CASE PRESENTATION

She spent 66 days in the ICU (30 days ventilated) & was admitted to acute rehabilitation for 6 weeks. She was discharged to home, but her family was distressed at her level of functioning.

WHAT HAPPENS TO COVID PATIENTS WITH EXTENDED ICU STAYS?

SEVERE COVID-19

- **> Wu et al (2020)**
 - **Dyspnea**
 - ▶ RR >=30
 - Oxygen saturation <= 93%</p>
 - Pao₂:Fio₂ < 300 mm Hg, OR infiltrates > 50% of the lung field within 24 to 48 hours from the onset of symptoms
- ~5% with severe disease
 - Mortality ~25-50%

SEVERE COVID-19

- Age > 65 yrs.Men > women
- Ethnicity: Hispanic, African American, Polynesian, Native American
- Underlying diseases: CVD, DM, Obesity, Htn, Chronic lung disease

ORGAN INVOLVEMENT

Many of manifestations due to cytokinerelease syndrome

Pulmonary

ARDS, respiratory failure

Hematology

Arterial & venous thromboses

Renal

>5% require renal replacement

ORGAN INVOLVEMENT Cardiac Myocarditis, CHF, arrhythmia, AMI **Neurologic CVA**, encephalitis, polyneuropathy, anosmia, GBS Gastrointestinal Diarrhea, nausea, transaminitis, ischemic bowel

LONGTERM CHRONIC DX

- Severe ARDS survivors may suffer from chronic disease
- **Physical**
 - Critical illness polyneuropathy (CIP)
 Critical illness myopathy (CIM)
 - Mononeuritis multiplex
 - Chronic Fatigue & other

LONGTERM CHRONIC DX

Pulmonary Post intensive care syndrome **Neurologic** Cognitive dysfunction Anxiety Depression **PTSD**

LONGTERM CHRONIC DX

Pathology & course of severe **COVID-19** similar to severe ARDS **Likely similar issues** Improvement up to >=1 year post ICU D/C for ARDS survivors



Critical Illness Polyneuropathy Symmetrical weakness Proximal>distal Muscle atrophy **Distal sensory loss**



Critical Illness Myopathy Associated w/exposure to Steroids, paralytics, sepsis Symmetrical weakness Proximal>distal Muscle atrophy **Sensory preservation**

MONONEURITIS MULTIPLEX

- Needham et al (2021)
- 11/69 patients w/severe ARDS
- Initially diagnosed as critical illness myopathy
- Focal neurologic deficits
 - Upper & lower extremities
- EMG not c/w diffuse myopathy

PHYSICAL IMPAIRMENTS

Proning

- Shoulder injuries (subluxation)
- Brachial Plexus Injuries
- Prolonged intubation
 - Laryngeal injury
 - Dysphagia
 - Diaphragm dysfunction
- Long term fatigue

POSTINTENSIVE CARE SYNDROME

Restrictive PFTs Reduced inspiratory muscle strength Poor upper extremity grip strength Low functional capacity

COGNITIVE IMPAIRMENTS

- Prolonged ventilation = Prolonged delirium
- Most Prominent Deficits in
 - Memory
 - **Executive Function**
 - Attention Deficits

MENTAL IMPAIRMENTS

Not related to severity of illness
 Isolation has >risk for mental disorders

- **Anxiety**
- Depression
- **PTSD**
- **Survivor guilt**

LONGTERM ORGAN DYSFUNCTION

Organ systems w/different involvement than other etiologies of ARDS Cardiac-AMI, myocarditis Renal-AKI Pulmonary-risk for interstitial fibrosis **Neuro-CVA** in young patients

Hematologic-thromboses, coagulopathy

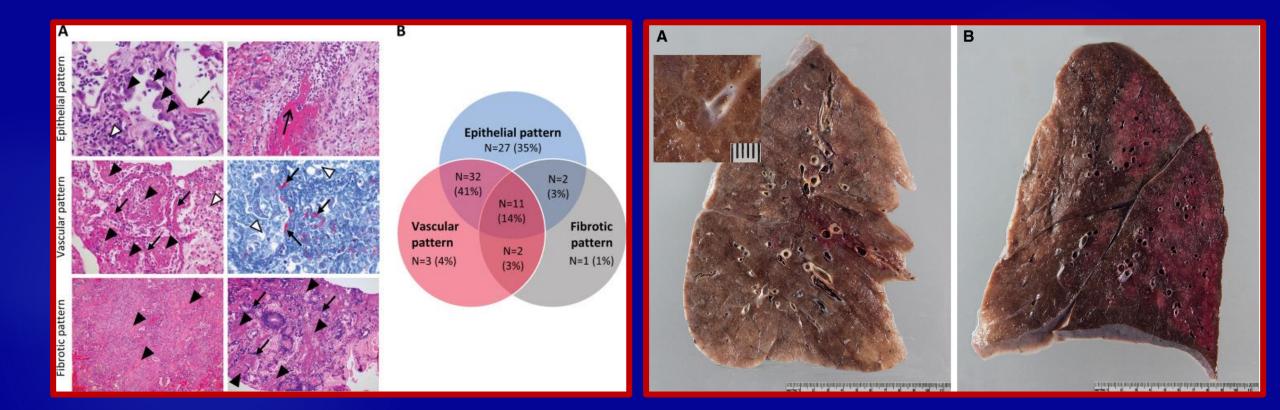
LONGTERM ORGAN DYSFUNCTION

Many patients have significant preexisting co-morbidities May interplay with organ injury & organ failures Older patients may have significant frailty May interplay with mortality, morbidity, recovery

LONGTERM PULMONARY

- Lung is most frequently devastated organ in severe COVID-19
- Degree of lung improvement unknown
 - Severe ARDS survivors may have moderate to severe residual disease
 - **►**Torres-Castro et al (2021)
 - Meta-analysis COVID survivors
 - ▶N=380
 - Restrictive, obstructive and DLCO defects
- Severe injury seen in COVID-19 pathology
 - DAD, hemorrhage, fibrosis

PULMONARY PATHOLOGY



LONGTERM CARDIAC

Cardiovascular damage that persists after recovery

CV dysfunction affects ~20% of patients admitted to the hospital w/COVID-19

When heart damage present

Increased risk for ventilatory support

Increased risk of dying from COVID-19

CARDIAC DYSFUNCTION

- Kirk Knowlton MD (Journal of Molecular & Cellular Cardiology, August 2020)
 - Examined >100 published studies related to COVID-19 & its effects on the heart.
- Rajpal et al
 - >26 athletes at Ohio State (27% had s/s during COVID)
 - **CMR** imaging
 - ▶15% had myocarditis
 - ► 30% w/findings suggestive of prior myocardial injury

RENAL DYSFUNCTION

Gupta et al (2020) N=3099 ▶ 67 hospitals in US ▶21% w/AKI-RRT within 14 days of ICU admission Mortality >60% ▶ 39 (18.1%) RRT dependent 60 days after ICU admission

PUBLISHED DATA

COVID ICU Group (2021)

- N=4643 (4244 w/90-day post ICU available)
- ▶ 138 hospitals in US
- **February 25-May 4, 2020**
- SAPS III 37
- 80% Ventilated
- Mortality 31%
 - Decreased from 42 to 25% over the time frame
- Mortality was higher in older, diabetic, obese & severe ARDS patients

Ahmed et al (2020)

- SARS and MERS patients
- Literature search
- > 28 articles (26 SARS, 2 MERS)
- ► HRQoL
 - Measured using SF-36
 - Reduced in survivors at 6 months post admission
- Reduction in DLCO may still be present in 11–45%
- ~30% w/ anxiety, depression, PTSD
- Did not distinguish between ICU & non ICU survivors

Musheyev et al (2021) N=118

Retrospective in US
 Calculated Barthel Index, modified Mental Status, ICU Mobility Scale
 Analysis at hospital DC

Musheyev et al (2021)

Worse functional status at hospital discharge **Longer IMV duration** Older age Male sex Higher number of comorbidities Hypertension, diabetes, COPD, immunosuppression

Medrinal et al (2021)

►N=23 ▶ 2 ICU, 60 beds Retrospective; 30 days post DC No standardized testing ▶ 69% limb muscle weakness ► 26% limb & respiratory weakness ► 44% unable to walk 100 m 30 days post DC Halpin et al (2021) ▶ N=100 (sample; 32 ICU) ▶ 32 ICUs in US ▶ **Prospective** Screened 4-8 weeks post DC **Fatigue, breathlessness, psychological** distress ICU >> Ward **EQ5D** dropped significantly in 68% of ICU vs 45% Ward

Taboada et al (2021)

- ▶ N=183 (32 in ICU)
- Prospective, 32 ICUs
- ▶ 6 month FU
- Functional status: post-COVID-19 functional status scale (PCFS)
- ICU patients had significant limitations in every day life compared w/non-ICU
- Female sex, age, length of hospital stay, mechanical ventilation, and ICU admission were associated with limitations in the functional status (grade II-IV PCSF)

Puchner et al (2021)

►N=23

Prospective observational study w/individualized rehab High percent of patients Post intensive care syndrome Diminished PFTs **Cognitive** issues Decreased 6 minute walk time

Puchner et al (2021) At D/C from rehab Residual diffusion deficits **Cognitive** issues Abnormal 6 minute walk time

Rousseau at el (2021)

- ▶ N=32 (80% of survivors)
- Prospective, 3 month evaluation
- 60 bed ICU; March 2020-July 2020 in Belgium
- Testing
 - Health-related quality of life (EQ-5D-3L)
 - Sleep disorders (PSQI)
 - Physical status (Barthel index, handgrip and quadriceps strength)
 - Mental health disorders (HADS and IES-R)
 - Cognitive impairment (MoCA)
 - Biological parameters
 - ▶ CRP, Cr

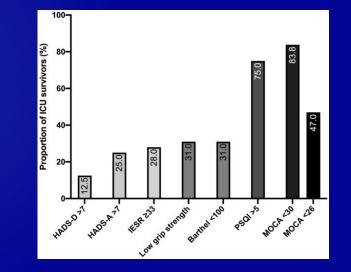
Rousseau at el (2021)

Prolonged MV (ave 21 days)

2/32 tested normal for all parameters

►~50% went to rehab

20% still hospitalized/rehab at 3 months



Van Veenendaal et al (2021)

- 60 survivors/78 family members in Netherlands
- Prospective; questionnaires at 3 & 6 months post ICU D/C
- Physical functioning
 - MOS Short-Form General Health Survey
 - Clinical Frailty Scale
 - Spirometry (including DLCO)
- Social functioning
 - McMaster Family Assessment Device
 - Return to work
- Psychological functioning
 - Hospital Anxiety and Depression Scale

Van Veenendaal et al (2021)

- Physical functioning impaired at 3 & 6 months
 - ▶ 33.3 (IQR 16.7-66.7) & 50 (IQR 16.7-83.3) out of 100
 - ▶90% reported continued impairment > 6 months
- Social function impaired in 90%
- Psychological function impairment patients < family</p>
 - 63% of family w/ongoing impaired well-being
 Family members also couldn't return to work

ICU SURVIVOR LESSONS

RECOVERY OF IADLS RETURN TO WORK FAMILY MEMBER RECOVERY

RECOVERY OF IADLs

- Hopkins et al (2017)
- ICU population systematic review
- 16 studies; 4,723 survivors
- IADLS-Shopping, Housekeeping, Accounting, Food preparation & Telephone/Transportation (SHAFT)
- 11 studies (69%) found that survivors of critical illness had new or worsening IADL dependencies
- Sof 4 longitudinal studies-IADL dependencies decreased over the follow-up period, but did not disappear

RETURN TO WORK

- **Kamdar et al (2020)**
- ICU population systematic review
- 52 studies, 10,015 previously employed survivors
- ~2/3, 2/5 & 1/3 of previously employed ICU survivors are jobless up to 3, 12 & 60 mos. after hospital d/c
- Survivors returning to work often experience
 - Job loss
 - Occupation change
 - Worse employment status

FAMILY MEMBERS

- Johnson et al (2019)
- ICU population systematic review; 40 articles (>5000 w/FU)
- Caregiver experience during ICU STAY
 - Anxiety 0-73%
 - Severe depression 16-42%
 - **PTSD 14-81%**
- Caregiver experience post-ICU
- Anxiety 2-80%
- Depression 4-94%
- **PTSD 3-62%**
- Decreased or unchanged prevalence over time

SO WHAT IS NEXT FOR SEVERE COVID SURVIVORS?

REHABILITATION

Rehab w/multidisciplinary team >PT, OT, ST, PMR, Pulmonary, Cardiology Demonstrated efficacy in patients w/ severe ARDS, other critical illness w/ prolonged ICU stays (Hopkins, Herridge, Needham) Recommendations from Barker-Davies et al (UK) & Curci et al (Italy) are similar to those for ARDS patients

REHABILITATION ISSUES

- COVID may impede rehab, extend rehab times
- Increased frailty due to age, isolation
- More cardiac complications
 Chronic fatigue

REHABILITATION

Early mobilization in ICU

- Cardiac rehab
- **Early & long-term OT/PT/ST**
 - Recognition of syndrome(s) to facilitate targeted therapy

Cognitive testing with rehab, job retraining
 Screening for depression, PTSD, Anxiety

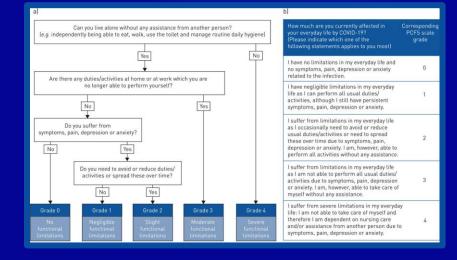
Management of family during & post ICU

EVALUATION-IN OFFICE

- **IHC Pulmonary, Yonter et al**
- Walking pulse oxi/6-minute walk
- Questionnaires & screenings
 - Post Covid-19 Functional Status scale https://bit.ly/3cofGaa
 - GAD-7 anxiety
 - PHQ2/9 depression
 - SBIRT substance use
 - MOCA cognition

- PSS/IESR/SPTSS PTSD
- Labs CBC, CMP, dimer, TSH, A1C, & EKG





EVALUATION-FU

CT chest

- 3 month follow up if abnormal imaging on diagnosis
- Consider follow up inflammatory markers
 - Ferritin, CRP, trop, CPK, pro-BNP, procalcitonin for persist symptoms
- Ongoing pulmonary symptoms
 - Referral to pulmonary, PFT, chest CT/CTA, ECHO
- Ongoing chest symptoms or abnormal EKG
 - Referral to cardiology, ECHO, cardiac MRI, stress test, Holter monitor

TAKE HOME MESSAGE

Post ICU COVID survivors may need extensive multi team rehab, have remaining deficits & not achieve pre-COVID ICU functional status

Acute Respiratory Distress Syndrome Clinical Network. Mechanical Ventilation protocol summary. http://ardsnet.org/tools.shtml

Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: A literature review. J Clin Neurosci. 2020;77:8-12.

Ahmed H, Patel K, Greenwood DC, Halpin S, Lewthwaite P, Salawu A, Eyre L, Breen A, O'Connor R, Jones A, Sivan M. Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis. J Rehabil Med. 2020 May 31;52(5):jrm00063.

Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med 2020;46:854-887.

Akhmerov A, Marbán E. COVID-19 and the Heart. Circ Res. 2020;126(10):1443-1455.

Azoulay E, Vincent JL, Angus DC, et al. Recovery after critical illness: putting the puzzle together-a consensus of 29. Crit Care. 2017 Dec 5;21(1):296.

Barker-Davies RM, O'Sullivan O, Senaratne KPP, et al. The Stanford Hall consensus statement for post-COVID-19 rehabilitation. Br J Sports Med. 2020;54(16):949-959.

Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med. 2020;10.1056/NEJMcp2009575.

Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of COVID-19: preliminary report. N Engl J Med. Published online May 22, 2020. doi:10.1056/NEJMoa2007764

Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. N Engl J Med. 2020;382(19):1787-1799. doi:10.1056/NEJMoa2001282

Connolly B, O'Neill B, Salisbury L, Blackwood B, Enhanced Recovery After Critical Illness Programme Group Physical rehabilitation interventions for adult patients during critical illness: an overview of systematic reviews. Thorax. 2016 Oct;71(10):881–90.

Cook TM, El-Boghdadly K, McGuire B, et al. Consensus guidelines for managing the airway in patients with COVID-19: guidelines from the Difficult Airway Society, the Association of Anaesthetists the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists. Anaesthesia 2020;75:785-799.

COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. Intensive Care Med. 2021 Jan;47(1):60-73.

Curci C, Pisano F, Bonacci E, Camozzi DM, Ceravolo C, Bergonzi R, De Franceschi S, Moro P, Guarnieri R, Ferrillo M, Negrini F, de Sire A. Early rehabilitation in post-acute COVID-19 patients: data from an Italian COVID-19 Rehabilitation Unit and proposal of a treatment protocol. Eur J Phys Rehabil Med. 2020 Oct;56(5):633-641.

Davis B, Rothrock AN, Svetland S, et al. Viral and atypical respiratory co-infections in COVID-19: A systematic review and metanalysis. JACEP Open; 2020. 1-15.

De Biase S, Cook L, Skelton DA, Witham M, Ten Hove R. The COVID-19 rehabilitation pandemic1. Age Ageing. 2020;49(5):696-700.

Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. Crit Care 2020;24:28-28.

Gattinoni L, Coppola S, Cressoni M, et al. Covid-19 does not lead to a "typical" acute respiratory distress syndrome. Am J Respir Crit Care Med 2020; 15;201(10):1299-1300.

Goldman JD, Lye DCB, Hui DS, et al. Remdesivir for 5 or 10 days in patients with severe COVID-19. N Engl J Med. Published online May 27, 2020. doi:10.1056/NEJMoa2015301

Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy [published online ahead of print, 2020 Apr 6]. JAMA. 2020;323(16):1574-1581.

Gupta S, Coca SG, Chan L, Melamed ML, Brenner SK, Hayek SS, Sutherland A, Puri S, Srivastava A, Leonberg-Yoo A, Shehata AM, Flythe JE, Rashidi A, Schenck EJ, Goyal N, Hedayati SS, Dy R, Bansal A, Athavale A, Nguyen HB, Vijayan A, Charytan DM, Schulze CE, Joo MJ, Friedman AN, Zhang J, Sosa MA, Judd E, Velez JCQ, Mallappallil M, Redfern RE, Bansal AD, Neyra JA, Liu KD, Renaghan AD, Christov M, Molnar MZ, Sharma S, Kamal O, Boateng JO, Short SAP, Admon AJ, Sise ME, Wang W, Parikh CR, Leaf DE; STOP-COVID Investigators. AKI Treated with Renal Replacement Therapy in Critically III Patients with COVID-19. J Am Soc Nephrol. 2021 Jan;32(1):161-176.

Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, Walshaw C, Kemp S, Corrado J, Singh R, Collins T, O'Connor RJ, Sivan M. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. J Med Virol. 2021 Feb;93(2):1013-1022.

Herridge MS, Moss M, Hough CL, et al. Recovery and outcomes after the acute respiratory distress syndrome (ARDS) in patients and their family caregivers. Intensive Care Med. 2016;42(5):725-738. doi:10.1007/s00134-016-4321-8

https://www.healthmap.org/covid-19/

Hopkins RO, Suchyta MR, Kamdar BB, et al. Instrumental Activities of Daily Living after Critical Illness: A Systematic Review. Ann Am Thorac Soc. 2017;14(8):1332-1343.

Hopkins RO, Suchyta MR, Beene K, Jackson JC. Critical illness acquired brain injury: Neuroimaging and implications for rehabilitation. Rehabil Psychol. 2016;61(2):151-164. doi:10.1037/rep0000088

Hopkins RO, Suchyta MR, Farrer TJ, Needham D. Improving post-intensive care unit neuropsychiatric outcomes: understanding cognitive effects of physical activity. Am J Respir Crit Care Med. 2012;186(12):1220-1228. doi:10.1164/rccm.201206-1022CP

Hosey MM, Needham DM. Survivorship after COVID-19 ICU stay. Nat Rev Dis Primers. 2020 Jul 15;6(1):60.

Johnson CC, Suchyta MR, Darowski ES, et al. Psychological Sequelae in Family Caregivers of Critically III Intensive Care Unit Patients. A Systematic Review. Ann Am Thorac Soc. 2019;16(7):894-909.

Kamdar BB, Suri R, Suchyta MR, et al. Return to work after critical illness: a systematic review and metaanalysis. Thorax. 2020;75(1):17-27. doi:10.1136/thoraxjnl-2019-213803

Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020;7(6):e438-e440. doi:10.1016/S2352-3026(20)30145-9

Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020;77(6):1-9. doi:10.1001/jamaneurol.2020.1127

Medrinal C, Prieur G, Bonnevie T, Gravier FE, Mayard D, Desmalles E, Smondack P, Lamia B, Combret Y, Fossat G. Muscle weakness, functional capacities and recovery for COVID-19 ICU survivors. BMC Anesthesiol. 2021 Mar 2;21(1):64.

Menter T, Haslbauer JD, Nienhold R, et al. Postmortem examination of COVID-19 patients reveals diffuse alveolar damage with severe capillary congestion and variegated findings in lungs and other organs suggesting vascular dysfunction. Histopathology. 2020;10.1111/his.14134. doi:10.1111/his.14134.

Musheyev B, Borg L, Janowicz R, Matarlo M, Boyle H, Singh G, Ende V, Babatsikos I, Hou W, Duong TQ. Functional status of mechanically ventilated COVID-19 survivors at ICU and hospital discharge. J Intensive Care. 2021 Mar 31;9(1):31.

Needham E, Newcombe V, Michell A, Thornton R, Grainger A, Anwar F, Warburton E, Menon D, Trivedi M, Sawcer S. Mononeuritis multiplex: an unexpectedly frequent feature of severe COVID-19. J Neurol. 2021 Aug;268(8):2685-2689.

Ohtake PJ, Lee AC, Scott JC, Hinman RS, Ali NA, Hinkson CR, Needham DM, Shutter L, Smith-Gabai H, Spires MC, Thiele A, Wiencek C, Smith JM. Physical impairments associated with post-intensive care syndrome: systematic review based on the World Health Organization's International Classification of Functioning, Disability and Health Framework. Phys Ther. 2018 Aug 01;98(8):631–645.

Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med. 2020;288(2):192-206.

Polak SB, Van Gool IC, Cohen D, et al. A systematic review of pathological findings in COVID-19: a pathophysiological timeline and possible mechanisms of disease progression [published online ahead of print, 2020 Jun 22]. Mod Pathol. 2020;1-11.

https://www.sccm.org/ICULiberation/Guidelines

Puchner B, Sahanic S, Kirchmair R, Pizzini A, Sonnweber B, WÖll E, MÜhlbacher A, Garimorth K, Dareb B, Ehling R, Wenter J, Schneider S, Brenneis C, Weiss G, Tancevski I, Sonnweber T, LÖeffler-Ragg J. Beneficial effects of multi-disciplinary rehabilitation in post-acute COVID-19 - an observational cohort study. Eur J Phys Rehabil Med. 2021 Jan 15.

Rajpal S, Tong MS, Borchers J, et al. Cardiovascular Magnetic Resonance Findings in Competitive Athletes Recovering From COVID-19 Infection. JAMA Cardiol. Published online September 11, 2020. doi:10.1001/jamacardio.2020.4916

Richardson S, Hirsch JA, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area JAMA. 2020;323(20):2052-2059.

Rousseau AF, Minguet P, Colson C, Kellens I, Chaabane S, Delanaye P, Cavalier E, Chase JG, Lambermont B, Misset B. Post-intensive care syndrome after a critical COVID-19: cohort study from a Belgian follow-up clinic. Ann Intensive Care. 2021 Jul 29;11(1):118.

Sheehy LM. Considerations for Postacute Rehabilitation for Survivors of COVID-19. JMIR Public Health Surveill. 2020;6(2):e19462.

Spruit MA, Holland AE, Singh SJ, Tonia T, Wilson KC, Troosters T. COVID-19: Interim Guidance on Rehabilitation in the Hospital and Post-Hospital Phase from a European Respiratory Society and American Thoracic Society-coordinated International Task Force. Eur Respir J. 2020 Aug 13;56(6):2002197.

Taboada M, Cariñena A, Moreno E, et al. Post-COVID-19 functional status six-months after hospitalization. J Infect. 2021;82(4):e31-e33. doi:10.1016/j.jinf.2020.12.022

Toniati P, Piva S, Cattalini M, et al. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy. Autoimmun Rev. 2020;19(7):102568.

Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, Vilaró J. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology. 2021 Jul-Aug;27(4):328-337.

Tsivgoulis G, Palaiodimou L, Katsanos AH, et al. Neurological manifestations and implications of COVID-19 pandemic. Ther Adv Neurol Disord. 2020;13:1756286420932036. van Veenendaal N, van der Meulen IC, Onrust M, Paans W, Dieperink W, van der Voort PHJ. Six-Month Outcomes in COVID-19 ICU Patients and Their Family Members: A Prospective Cohort Study. Healthcare (Basel). 2021 Jul 8;9(7):865.

Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. JAMA 2020; 10.1001/jama.2020.12839. Wilcox ME, Brummel NE, Archer K, et al. Cognitive dysfunction in ICU patients: risk factors, predictors, and rehabilitation interventions. Crit Care Med. 2013 Sep;41(9 Suppl 1):S81-98.

Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020; Feb 24.

Yang T, Li Z, Jiang L, Wang Y, Xi X. Risk factors for intensive care unit-acquired weakness: A systematic review and meta-analysis. Acta Neurol Scand. 2018 Aug;138(2):104-114.

Yonter SJ, Alter K, Bartels MN, Bean JF, Brodsky MB, González-Fernández M, Henderson DK, Hoenig H, Russell H, Needham DM, Kumble S, Chan L. What Now for Rehabilitation Specialists? Coronavirus Disease 2019 Questions and Answers. Arch Phys Med Rehabil. 2020 Dec;101(12):2233-2242.

Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-1062.

VENTILATOR

