# Update on Post COVID-19 Syndrome

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### Disclosures

• None to Report

### Chronic COVID-19

- A multisystem disease, sometimes occurring after a relatively mild acute illness
- Affects approximately 10-30% of those who survive COVID-19
- Etiology is not known

Geddes L.Why strange and debilitating coronavirus symptoms can last for months. New Scientist 2020

# Chronic COVID-19



Fig. 1 | Timeline of post-acute COVID-19. Acute COVID-19 usually lasts until 4 weeks from the onset of symptoms, beyond which replication-competent SARS-CoV-2 has not been isolated. Post-acute COVID-19 is defined as persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms. The common symptoms observed in post-acute COVID-19 are summarized.

Nalbandian et al. Post-acute COVID-19 syndrome. https://doi.org/10.1038/s41591-021-01283-z

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# Post-Acute Chronic COVID-19 Symptoms and Findings



\* persistence of at least one clinically relevant symptom, or abnormalities in spirometry or chest radiology

Moreno-Pérez et al. Post-acute COVID-19 Syndrome. Incidence and risk factors: a Mediterranean cohort study. Journal of Infection, 2021.

### Possible Risk Factors for Post-Acute Chronic COVID-19



**Fig. 1.** An overview of the pathophysiology, symptoms, and potential treatments involved in longhaul COVID-19. Note: Dashed lines represent areas where evidence is relatively lacking compared to non-dashed lines. (Color online only)

Yong, S.J. Long-Haul COVID-19: Putative Pathophysiology, Risk Factors, and Treatments. Preprints 2020, 2020120242 (doi: 10.20944/preprints202012.0242.v1)

# Post-Acute Chronic COVID-19 Symptoms

- Most common: cough, low-grade fever and fatigue, all of which may relapse and remit.
- Other reported symptoms: shortness of breath, chest pain, headaches, neurocognitive difficulties, muscle pains and weakness, gastrointestinal upset, rashes, metabolic disruption (such as poor control of diabetes), thromboembolic conditions, and depression and other mental health conditions
- Skin rashes can take many forms including vesicular, maculopapular, urticarial, or chilblain-like lesions on the extremities (so-called Covid toe)

Assaf G, Davis H, McCorkell L, et al. An analysis of the prolonged COVID-19 symptoms survey by Patient-Led Research Team. Patient Led Research, 2020

### Respiratory Injury Associated with SARS-CoV-2 Infection



### Temporal lung changes on thin-section CT in patients with COVID-19 pneumonia.



Zhang Z, et al; Sci Rep 10:19649(2020)

### Post COVID-19 Symptoms in Critically III

- Similar to those in non-COVID-19 critical illness
- 85% develop long-term neurocognitive deficits
- PTSD
- Airway complications (tracheomalacia, stenosis)
- Dysphagia and aspiration
- Impairment of gas exchange
- Pulmonary fibrosis



#### JAMA | Original Investigation

### Four-Month Clinical Status of a Cohort of Patients After Hospitalization for COVID-19

The Writing Committee for the COMEBAC Study Group Ta

Published Online 3/17/21

Fatigue was the most common complaint, whether intubated or not

able 2. Results of the Telephone Assessment in Nonintubated and Intubated Patients				
	No./total (%)			
	All patients (n = 478)	Nonintubated (n = 405)	Intubated (n = 73)	
ime from hospital discharge o telephone assessment, nedian (IQR), d [No.]	113 (94-128) [442]	121 (104-131) [375]	93 (77-110) [67]	
Declared symptoms <sup>a</sup>				
Dyspnea	78 (16.3)	53 (13.1)	25 (34.2)	
Cough	21/420 (5)	16/358 (4.5)	5/62 (8.1)	
Chest discomfort/pain	34/418 (8.1)	25/356 (7)	9/62 (14.5)	
Fatigue	134/431 (31.1)	110/368 (29.9)	24/63 (38.1)	
Anorexia	34/436 (7.8)	25/370 (6.7)	9/66 (13.6)	
Weight loss >5% baseline weight	31/342 (9.1)	30/281 (10.7)	1/61 (1.6)	
Anosmia	25/419 (6.0)	19/357 (5.3)	6/62 (9.7)	
Headaches	23/420 (5.5)	22/358 (6.2)	1/62 (1.6)	
Paresthesia	51/421 (12.1)	40/359 (11.1)	11/62 (17.7)	
Cognitive testing Q3PC questionnaire) <sup>a,b</sup>				
Memory difficulties	73/416 (17.5)	63/354 (17.8)	10/62 (16.1)	
Mental slowness	42/415 (10.1)	38/353 (10.8)	4/62 (6.5)	
Concentration problems	41/412 (10.0)	35/351 (10.0)	6/61 (9.8)	

Table 3. Results of the In-Person Outpatient Clinic Visit in Nonintubated and Intubated Patients

### 4 months follow-up

- 15% of nonintubated patients had persistent cough
- 58% of non-intubated patients still had CT scan abnormalities
  - 37% had persistent ground glass
  - 12% had fibrotic lesions
- Lung function (nonintubated)
  - Median FEV1, FEV1/FVC and TLC normal
  - 15% had DLCO < 70% predicted</li>
  - Lung function was worse in survivors who were intubated

	No./total (%)		
	All patients (n = 177)	Nonintubated (n = 126)	Intubated (n = 51)
Time from hospital discharge to outpatient clinic, median (IQR), d [No.]	125 (107-144) [157]	134 (116-150) [107]	105 (90.2-119) [50]
Respiratory assessment			
mMRC scale score for dyspnea, median (IQR) [No.] <sup>a</sup>	2 (2-3) [115]	2 (2-3) [80]	2 (1.5-3) [35]
Persistent cough	23/172 (13.4)	19/123 (15.4)	4/49 (8.2)
6-Minute walk test, median (IQR), m [No.]	462 (380-507) [161]	464 (382-502) [112]	462 (380-523) [49]
Abnormal lung CT scan result	108/171 (63.2)	71/122 (58.2)	37/49 (75.5)
Persistent ground-glass opacities	72/170 (42.4)	45/121 (37.2)	27/49 (55.1)
Lung fibrotic lesions	33/170 (19.4)	15/121 (12.4)	18/49 (36.7)
FEV <sub>1</sub> (expressed as % of theory), median (IQR) [No.]	92 (80-102) [157]	92 (79-103) [108]	90 (80-102) [49]
FEV <sub>1</sub> /FVC, median (IQR) [No.]	83 (79-87) [157]	81 (78-86) [108]	84 (82-87) [49]
TLC (expressed as % of theory) [No.]	83 (15) [49]	86 (15) [104]	76 (14) [45]
DLCO <70%	33/152 (21.7)	16/105 (15.2)	17/47 (36.2)
Echocardiography assessment			
RV dilatation on echocardiography	20/79 (25.3)	11/35 (31.4)	9/44 (20.5)
LVEF 40%-50% on echocardiography <sup>b</sup>	10/83 (12.0)	2/38 (5.3)	8/45 (17.8)
Neurologic and psychological assessment <sup>a,c</sup>			
Cognitive complaint (impaired McNair score, reported cognitive symptoms, or both)	79/159 (49.7)	55/109 (50.5)	24/50 (48.0)
Cognitive impairment (impairment of either MoCA or d2-R score)	61/159 (38.4)	40/109 (36.7)	21/50 (42.0)
Symptoms of anxiety (HADS-Anxiety)	53/169 (31.4)	40/119 (33.6)	13/50 (26.0)
Symptoms of depression (BDI test)	35/170 (20.6)	26/120 (21.7)	9/50 (18.0)
Insomnia (ISI score)	90/168 (53.6)	68/118 (57.6)	22/50 (44.0)
Symptoms of PTSD (PCL-5 score)	24/169 (14.2)	19/119 (16.0)	5/50 (10.0)

# Symptoms in Mild to Moderate (not hospital)

- Two-thirds are asymptomatic 14 days after onset
- 90% are symptom-free by 21 days
- Dyspnea
- Cough
- Lung burn
- Chest pain (musculoskeletal)
- Breathlessness
- Exercise intolerance
- Exaggerated heart rate response to activity

# Post COVID-19 Cough

- Multiple mechanisms
- Direct effect of virus on airway cough receptors
- Post-infectious bronchospasm
- GERD
- Upper airway cough receptors
- Responds poorly to bronchodilators
- Trial of inhaled steroids?



# Post COVID-19 Dyspnea

- 26% of patients report
- Generalized physical deconditioning after viral illness
- Breathing pattern altered with reduced diaphragmatic movement and greater use of neck and shoulder accessory muscles
- Inefficient breathing pattern, which results in higher energy expenditure
- Responds best to structured breathing techniques and modest exercise

### **Evaluation**

- Pulse oximeter. SpO2 >92% on RA.
- 6-minute walk test
- Imaging generally not necessary unless hypoxic
- Incidence of post-COVID-19VTE in patients recovering from mild to moderate disease not known but probably not high risk
- Reassurance with recommendation for modest exercise, breathing techniques and adequate sleep. Recovery generally the rule, but time course prolonged (weeks to months)



# **Breathing Exercises**

- Concentrate on diaphragmatic breathing
- Breathe in and out slowly
- Relax neck and shoulders and allow tummy to rise
- Insp/exp ratio 1:2
- Use frequently 5-10 minutes at a time



Johns Hopkins Medicine Breathing Exercises: <u>https://bit.ly/3w0wXAK</u>



### Cardiac Complications Post-COVID-19

- 20% of patients admitted to hospital for COVID-19 have significant cardiac involvement. Occult involvement more common?
- Myocarditis
- Pericarditis
- Myocardial infarction
- Dysrhythmias
- Pulmonary embolism
- May present several weeks post-COVID-19

# Pathophysiology

- Viral infiltration
- Inflammation
- Microthrombi
- Down regulation of ACE-2 receptors



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Cardiovascular Magnetic Resonance Findings in Competitive Athletes Recovering From COVID-19 Infection

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**COVID-19 Resource Center** 

Found Evidence for Myocarditis in 15%

More recent study from Vanderbilt found incidence to be 3% (Clark, D; Circulation in press)

### Athlete with myocardial inflammation on Cardiac Magnetic Resonance Imaging



### From left to right :

- A: T 2 mapping in short axis plane with elevated T2 signal in inferolateral wall suggestive of edema
- B: SSFP Cine in short axis showing contrast uptake in inferolateral wall
- C: Late gadolinium enhancement in inferolateral wall in short axis
- D: Late gadolinium enhancement in inferolateral wall in long axis view

### Post-COVID-19: Pericarditis: Athlete – Return to play 9 days after COVID-19 infection. Developed chest pain during basketball practice.



A: ST elevation suggestive of pericarditis B: Changes of ST elevation resolved after 2-week treatment with high-dose NSAIDs for pericarditis.

# Conditions Needing F/U after COVID-19

- Exacerbation of pre-existing cardiac disease
- Patients who experienced (hospitalized): stroke, PE, troponin elevation, myocarditis, myocardial infarction
- Persistent chest pain, especially with exertion
- Resting tachycardia
- Palpitations

### **Dysautonomia and POTS**

- Autonomic nervous system controls blood pressure, temperature regulation and digestion
- Etiology not clear (direct effect of virus, triggers autoimmune disease)
- Similarities to ME/CFS, post-treatment Lyme disease syndrome and Ehlers-Danlos
- Treatment approaches: very gentle rehab, compression garments, salt, hydration, beta-blockers

### Athletes and Return to Exercise Post-COVID-19

- After full recovery from mild illness: I week of low-level stretching before targeted cardiovascular sessions
- If remains symptomatic (very mild): limit activity to slow walking or equivalent. Increase rest periods if symptoms worsen. Avoid highintensity training
- Persistent symptoms (fatigue, cough, breathlessness, fever): limit activity to 60% HRmax until 2-3 weeks after symptoms resolve

Barker-Davies RM et al; Br J Sports Med 2020; bjsports-2020-102596

### Tests for Initial Assessment

- Chest pain or heaviness at rest or exertion: hs troponin +/- echocardiogram
- Shortness of breath: hs troponin +/- echo, +/- CTPE
- Palpitations: hs troponin +/- echo +/- Holter monitor

# Criteria for Cardiology Specialty Visit

- Persistent chest pain
- Resting tachycardia or tachycardia with minimal levels of exercise
- Persistent shortness of breath
- Palpitations

"Some long-haul covid-19 patients say their symptoms are subsiding after getting vaccines"- Washington Post 3/16/2021

- Online group ("Survivor Corps") of patients with COVID-19 long-term symptoms
  - 216 felt no different
  - 171 said conditions improved
  - 63 reported they were worse
  - Placebo effect? T-cells boosted by vaccine? Divert autoimmune cells?

# Post-Acute Chronic COVID-19 Management Considerations in Primary Care



### Post-Acute Chronic COVID-19 Management Considerations in Primary Care

#### Investigations

Clinical testing is not always needed, but can help to pinpoint causes of contiuing symptoms, and to exclude conditions like pulmonary embolism or myocarditis. Examples are provided below:

#### **Blood tests**

Full blood count Electrolytes				
Liver and renal function Troponin				
C reactive protein Creatine kinase				
D-dimer Brain natriuretic peptides				
Ferritin – to assess inflammatory and prothrombotic states				

#### Other investigations

Chest x ray Urine tests

12 lead electrocardiogram

# Refer to Rehabilitation if unable to return to ADLs in COVID-19 Recovery Period



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# Approach to Therapeutics

- Risk: Benefit analysis
  - PT, Pulmonary Rehab, CBT
- Listen Intently
  - Validation of concerns
- Remain open to other diagnostic considerations
  - Avoid Anchor bias especially with prolonged symptoms
- Consider Palliative approach when appropriate

# Summary of Integration of Learning

- Post Acute COVID-19 symptoms may impact a majority of patients
  - Especially Fatigue, headache, mental health disorders
- Similarities to other post-viral syndromes are common
- Given the breadth of possible symptoms, many diagnostics, referrals, and therapeutic options are available
  - Careful consideration of benefit is critical
- Time is likely to lead to improvement
- Active research of Post Acute COVID-19 will lead to better understanding