



Long-term outcomes in Covid-19 patients

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Game plan

- ▶ Review a recent JAMA article on long-term outcomes among Covid-19 survivors, among both outpatient and hospitalized patients (a summary report, worth your time to read)
- ▶ We will consider some additional related study findings that were not included in the review article

Objectives

- ▶ Recognize that long-term complications from even mild cases can be measured weeks to months post recovery
- ▶ Describe some of the abnormalities among Covid-19 survivors in major organ systems (pulmonary, neurologic, cardiac)...both signs and symptoms
- ▶ Pass a take-home test at the end

Take home messages

- ▶ SARS-CoV-2 affects multiple organ systems and can have long-term consequences..we do not know yet how long they can last, and the true definition of 'long-haulers'
- ▶ Even among mildly ill Covid-19 patients, cardiovascular, neuro, and pulmonary abnormalities can be measured many weeks post recovery...including in asymptomatic young patients
- ▶ A multidisciplinary approach to management of 'long-haulers' may be indicated for your clinic patients..including mental health experts

Introduction

- ▶ Most of the published reports to date have been focused on short term complications post Covid-19
- ▶ Several case reports and case series suggest SARS-CoV-2 affects CV, neuro and pulmonary systems in the 'short haul'
- ▶ Mechanisms proposed for many outcomes: ex: for CV long-term, plaque rupture, stent thrombosis, Increased cardiac output leading to stress of muscle, endothelial cell inflammation
- ▶ 2020 Italian study post Covid-19, only 12.6% of patients were symptom- free after two months
- ▶ 2016 (non-Covid-19) patient ICU survey: 84% reported decrease mental or physical function 6-12 months post hospital discharge

'Long-hauler' article, Del Rio et al, JAMA (review of multiple studies)

- ▶ CDC phone survey, n=292, all 18 years or older
- ▶ All had positive test for SARS-CoV-2
- ▶ 35% reported sub-normal health after 12 weeks
- ▶ Higher percent of abnormalities reported with increasing age
- ▶ Even in youngest group (18 to 34 years), 20% abnormal health at 16 days after the first positive test
- ▶ Most commonly reported symptoms: fatigue, dyspnea, joint pain, chest pain

Pulmonary long-term outcomes

- ▶ Among 55 Covid patients, 2/3 had persistent symptoms and radiographic abnormalities 3 months post discharge (Zhang et al)
- ▶ Among 57 Covid patients in another study, 1/2 had abnormal pulmonary function at one month post d/c
- ▶ 289 Covid-19 pneumonia patients followed 4 months post onset: 17% with pulmonary fibrosis (Li et al). Appears to be reversible in some patients, tho older pts at highest risk for non-reversal
- ▶ For CoV-1 patients, 71 participants followed for 15 years post infection, 38% still had decreased lung function
- ▶ In recent 'long-hauler' surveys, shortness of breath remained one of the most common complaint (up to 7 weeks post acute infection)

Neuro long-term outcomes

- ▶ SARS-CoV-2 can penetrate brain via viremia or direct invasion (like thru olfactory nerve)..thus, neurotropic and neuroinvasive
- ▶ Common long-term neuro symptoms post Covid-19 acute infection: headache, vertigo, decrease in smell, fatigue, difficulty concentrating ('brain fog'), reported months post infection in at least one study
- ▶ Less common neuro outcomes: stroke, encephalitis, seizures, mood swings (Zubair et al)
- ▶ Predictably, poor neuro outcomes more common with older patients for a variety of biologic/physiologic reasons (see Hascup reference for detailed discussion)

BBB deterioration in older adults leaves them more susceptible to neuroinvasion during SARS-CoV-2 infection. After the acute recovery phase, the long-term consequences on accelerated aging and age-related neurodegenerative disorders are unknown. Viral aggravation of underlying neuropathologies has the potential to hasten the onset of or further deteriorate motor and cognitive deficits. Prior to this pandemic, the number of Alzheimer's and Parkinson's disease patients was rapidly rising due to our aging demographic and a lack of disease modifying therapies. When this viral outbreak is managed, our healthcare system could face an increased volume of patients dealing with these and their associated comorbid neurological issues. As such, long-term neurological follow-up in older adults may be needed after severe SARS-CoV-2 infection.

Cardiac long-term effects

- ▶ Among 26 college athletes, all Covid-19 positive with no symptoms, $\frac{1}{2}$ showed cardiac magnetic resonance imaging abnormalities 12-53 days post diagnosis (Rajpal et al)
- ▶ German cohort study showed $\frac{3}{4}$ with a variety of cardiac abnormalities among Covid survivors (two months post d/c)
- ▶ Over $\frac{1}{3}$ of these patients reported continued shortness of breath in the German study after two months (? Cardiac, pulmonary, or mixture of pathologies)

Key cardiac findings, summary

- ▶ Most prevalent signs in Covid-19 survivors were myocardial inflammation in 60%, regional scarring, and pericardial enhancement
- ▶ Even mildly sick Covid-19 survivors had signs of cardiovascular abnormalities, similar to hospitalized Covid survivors earlier
- ▶ Abnormalities persist at least 70 days post recovery (on the average)
- ▶ Perhaps another epidemic of heart diseases will follow Covid-19 among survivors, even those with mild cases

Behavioral health/mental health

- ▶ The JAMA review by Del Rio touches on the importance of this issue for patients and clinicians who care for them
- ▶ Chronic fatigue syndrome is a frequent post-Covid-19 long-term complaint (Nature, 2020)
- ▶ Providers and health care planners may want to start ramping up for this set of outcomes, in addition to long-term physiological clinical management challenges
- ▶ Multidisciplinary clinic in NM with psychiatry, family medicine, and internal medicine practitioners available in the same clinic to meet challenging (non-Covid-19) patients...with some success, tho it was probably expensive
- ▶ A variant of this model in your clinics/hospitals/practices may be worth considering (soon) depending on your Covid load and \$\$

The “COVID-19 Prolonged Symptoms Survey” found the following symptoms to be most common [[3, p. 4](#)] on one particular patient group:

- * mild shortness of breath
- * mild tightness of chest
- * moderate fatigue,
- * mild fatigue,
- * chills or sweats,
- * mild body aches,
- * dry cough,
- * elevated temperature (98.8 to 100 F),
- * mild headache,
- * brain fog/concentration challenges

Ongoing research in this arena

- ▶ Large (10,000) Covid-19 patient cohort now followed in UK with goal of monitoring multiple outcomes for one year
- ▶ Similar but smaller study in US
- ▶ Rhineland Study in Bonn: 5,000 participants...immune system focus related to long-term outcomes in multiple organ systems (genes, environment, behavior considerations). Not all are Covid survivors.
- ▶ Norwegian Mother-child cohort, also immune system focus
- ▶ Iceland genetic studies, immune system focus, 50,000 participants
- ▶ Citizen-Scientist Covid-19 surveys (US and UK)
- ▶ Post hospitalization survey Covid-19 (UK)

Take home test

- ▶ If you wanted to calculate actual incidence rates of long term complications of Covid-19 at the 6 month mark after hospital discharge, what type of study design would you choose?
- ▶ This long-term outcome is the most common symptom reported in most follow-up studies. What is it?
- ▶ True or false: pulmonary fibrosis remains a stable finding on CXR and or CT for months post acute Covid-19 pneumonia infection.
- ▶ True or false: behavioral health issues, including anxiety, depression, substance use disorder, and suicide are likely to increase the further we progress into the Covid-19 pandemic.

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