COVID-19 Evidence Accelerator Collaborative

Lab Meeting # 40

Thursday, September 2nd, 2021, 3 - 4:00 pm ET

Call Summary

Overview of Lab Meeting 40

Lab Meeting 40 featured two presentations on understanding and caring for post-acute sequelae of SARS-CoV-2 (PASC). First, Dr. Manesh Patel of Duke University discussed his experience treating PASC and provided an overview of ongoing studies of athletes experiencing long-term cardiovascular symptoms of COVID. Next, Dr. Ethan Berke of UnitedHealth Group discussed how to approach defining PASC and adapting models of care to ensure care for PASC is accessible, sustainable, and respectful. Finally, we saw this week's data visualization of the week which shows the wide array of symptoms reported by patients with PASC.

Evaluation Post-Acute COVID Infection

Dr. Manesh Patel, Duke University

Overview & Context

- Duke Health touches ~800k patients across 3 hospitals
- Duke Heart Affiliations with Lifepoint Health system (7 hospitals)
- 95 cardiologists across Virginia/ North Carolina, ~40 cardiologist fellows

Patient Examples

- **Patient #1**
  - **January 2021:** 53-year-old male admitted with COVID pneumonia, 13-day hospital stay (5-day ICU stay), never intubated, no cardiovascular (CV) or neurology complications
  - **March 2021:** Pulmonary appt. for shortness of breath, examined lung function & volume
  - **May 2021:** Fatigue on activity, abnormal EKG, ordered stress echo
  - **June 2021:** Heart catheterization, multi-vessel occlusions, three vessel disease, underwent by-pass surgery
  - **August 2021:** Symptoms improved, normal LV function
- **Patient #2**
  - **October 2020:** 19-year-old female student infected with COVID, lost taste/smell
  - **November 2020 – December 2020:** Starts getting fatigued/lightheaded
  - **February 2021:** 2-3 episodes of passing out/ "syncope" upon standing or moving
  - **April 2021:** Cardiology evaluation, normal Echo, reportedly had orthostatic hypotension (POTS) diagnosed outside of Duke, placed on metoprolol
  - **May 2021**: Evaluated at Duke, orthostatic + tachycardic, put on a hydration protocol, negative pregnancy test, switched to ivabradine
  - **June 2021:** Cardiac MRI without fibrosis or myocarditis inflammation

    - **July 2021:** Symptoms vastly improved
- Both patients may or may not have had conditions (three vessel disease/ POTS) prior to COVID – difficult to ascertain whether these conditions are COVID-related or part of individuals' natural history.

Clinical Questions

1. What are the CV manifestations of COVID – both in the acute and post-COVID phase?
2. What should be our simple post-COVID evaluation?
3. How are we continuing to learn?

Myocardial Injury: Mechanisms

- Localized in myocardial tissue to pericytes (surround endothelial cells)
- Responsible for presentation with pericarditis or myocarditis?
- Variety of mechanisms & therapeutics that could be responsible for myocardial injury (cytokines --> oxidative stress, immunomediated injury, endothelial dysfunction plaque instability)

Clinical Strategy to Understand COVID CV Complications & Long-Term Issues

- Study young adults – lower likelihood of prior CV disease, increased ability to distinguish changes in functional status
- College Athletes – national and collegiate interest and protocols being formed to evaluate, also an increased interest in staying in sports
    - Studied college athletes at 42 colleges/universities in 23 states to examine COVID cardiac involvement.
    - CV testing starting at 30 days after COVID infection 95% of tests "normal," 5% abnormal, .7% had possible, probable, or definitive myocarditis

Hearts of Athletes Program: Evaluation of CV System in Athletes

- Research building off prior study
- 300 athletes (200 athletes COVID+, 100 control athletes who were COVID-)
- Cardiac workup (ECG, echocardiogram, troponin, Cardiac MRI)
- Follow-up 30-days – symptoms, athletic activity questions, entered by participants
- Study Proposal
    1. All athletes will get ECG, Troponin and BNP, Echocardiogram
    2. If any abnormalities on #1 then clinically indicated CMR with delayed enhancement (standardized protocol)
    3. If no abnormalities on #1 then research CMR with delayed enhancement (standardized protocol)
    4. All CMRs de-identified and read in a core lab
- Status of Study: IRB approved, actively enrolling, also now capturing athletes who had COVID 6-months ago

Current Practice/ Evaluation

- Follow-up visit 30-90 days after discharge for patients with COVID

- Symptom screening, mini mental status exam, physical exam (orthostatic BP in both arms), peripheral neuropathy, chest x-ray, ECG, and chemistry panel
- For cardiac concerns:
    - ECG and if abnormal discussion around CMR
    - Pulmonary function tests for symptoms
    - US for continued limb fatigue swelling
- Referral for neuro-cognitive exam if continued "fog" symptoms
- Extreme fatigue (prevents return to play), exercise testing (6-minute walk testing, pulmonary-cardio testing) to understand what the cause is

An Effective and Sustainable Response to PASC

Dr. Ethan Berke, UnitedHealth Group

Defining PASC

- V.1 definition based on literature to-date
- Acute COVID Phase: day 0 – 30, Chronic COVID Phase: day 31+
- Claims data from acute phase not considered
- PASC Cohort Inclusion:
    - At least 2 distinct service dates for any combination of PASC-qualified diagnoses in the 4-month post-COVID period
    - PASC-qualified diagnosis(es) seen in the post-COVID period cannot be detected in the 6 months prior to the first COVID diagnosis date

Scope of the Condition: Impact, Length, & Resources

- PASC Qualified Diagnoses
    - Top CCSRs with >= 2% of suspected PASC members (n=175,979)
    - A lot of variation in conditions observed in claims data – includes musculoskeletal pain, respiratory signs/symptoms, abdominal pain and other digestive/abdomen signs/symptoms, circulatory signs/symptoms, mental health issues, etc.
    - Musculoskeletal, respiratory, and abdominal symptoms most common diagnoses regardless of the number of CCSRs -- requires a multidisciplinary approach
- Suspected PASC vs. Non-PASC
    - Gender: 60% female suspected PASC vs. 50% female non-PASC
    - Percent developing suspected PASC based on hospitalization history: 51.2% of those hospitalized for COVID fall into suspected PASC group vs. 19.2% of those not hospitalized for COVID

Adapting the Health System to Care for PASC Patients

- Not a rare condition and should not be treated like one
    - Care model needs to be accessible, sustainable, inclusive, respectful, and have demonstrable efficacy
    - Care should be coordinated and multidisciplinary involving PASC centers (multidisciplinary center or center of excellence, specialty care for PASC not available elsewhere), specialty engagement, primary care, and facilitated self-care

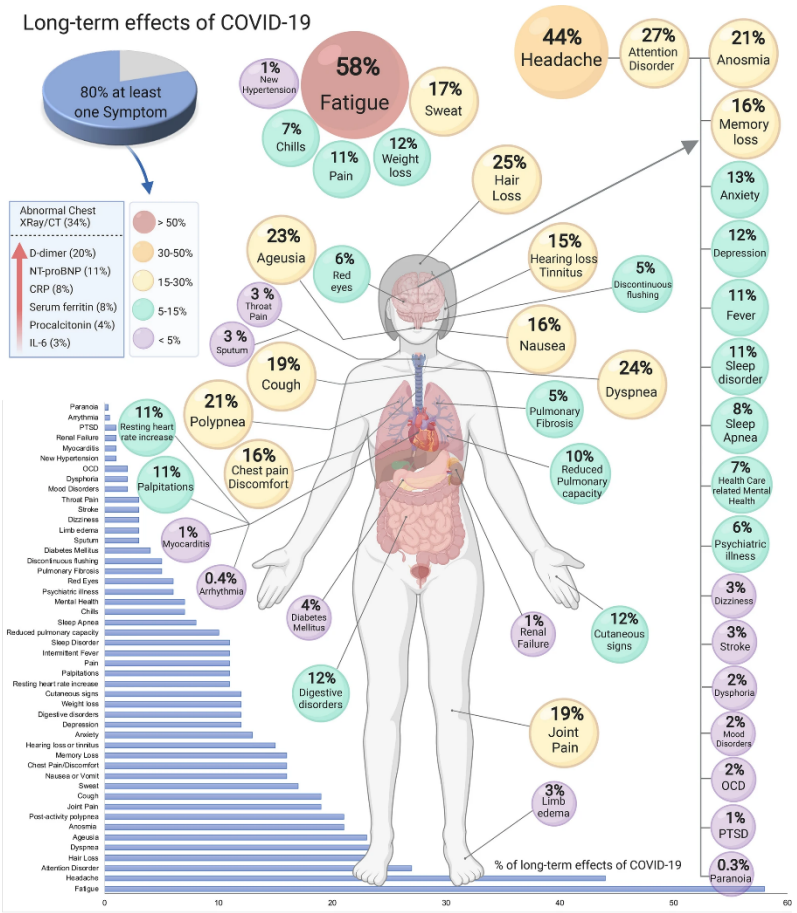
    - Leveraging care tools such as multimedia, telehealth, E-Consults, in person care, shared decision making, integrated behavioral health, and rehabilitation services
- Evaluation, PASC Program Metrics
    - PCPs – clinical measures for quality, provider engagement/communication, accessibility to resources, provider satisfaction training
    - Patient experience – health outcomes, patient satisfaction, quality of life measures, return to work measures
    - PASC Resources – experience of care measures (e.g., average time to appt.), clinical measures for quality, treatment outcomes by specialty
    - Program Level – case volumes & trends, performance of identification stratification algorithms, case management metrics, performance of tools, performance of case management systems, program training

Summary

- Need to be thoughtful about how we identify PASC cases – varying definitions
- Continued understanding of the natural course and scope of PASC – will be a common condition and has many unique presentations
- Health systems need clinical strategies that are accessible to all, and leverage self-care, primary care, and specialty care resources at the appropriate moment in the patient journey

Data Visualization of the Week

- Diagram illustrating more than 50 long-term effects of COVID (symptoms of PASC).



Source: Lopez-Leon, S., Wegman-Ostrosky, T., Perelman, C. et al. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. Sci Rep 11, 16144 (2021). https://doi.org/10.1038/s41598-021-95565-8