April 1, 2020 COVID-19 Update

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Contents include:

Brief summary:

- Heart Failure Collaboratory Statement on Clinical Trials in the Landscape of COVID-19 (JACC)

Articles reviewed:

- Covid-19 in Critically Ill Patients in the Seattle Region — Case Series (NEJM)
- Renin–Angiotensin–Aldosterone System Inhibitors in Patients with Covid-19 (NEJM)

Heart Failure Collaboratory Statement on Clinical Trials in the Landscape of COVID-19 (JACC)

- Patient and health care team safety should be top priorities
- Continuing clinical research is ethically important out of respect to prior and current participants
- Telehealth should be utilized whenever possible along with delaying in-person visits and procedures
- Statistical considerations will need to be made to account for changes in enrollment and asymmetric recruitment
- Although enrollment will likely slow, systems for patient recruitment should be maintained to ramp up when safe to do so


<table>
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<tr>
<th>Article Title:</th>
<th>Covid-19 in Critically Ill Patients in the Seattle Region — Case Series</th>
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<tr>
<td>Authors:</td>
<td>Bhatraju PK, Ghassemiah BJ, Nichols M et al</td>
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Study Question:

What were the clinical characteristics of a series of patients admitted to the ICU with confirmed SARS-CoV-2?

Methods:

Case-series including 24 adults in 9 Seattle-area ICUs with PCR-confirmed COVID-19 admitted in Feb/March 2020 (first 3 weeks of Seattle outbreak) with data obtained by EMR review.

Results:

- Mean age was 64y (SD 18, range 23-97); 63% men; 6 (25%) patients admitted from SNF
- Most had underlying comorbidity with 33% having multiple; DM was most common (58%), also CKD, COPD, asthma, OSA
- Mean duration of symptoms prior to ICU admission was 7±4 days
- Shortness of breath and cough were most common presenting sx (88% each)
- None had travel exposure and only 50% had known sick contact (any illness, not COVID specifically)
- None had coinfection with any bacterial or viral pathogen, including 23/24 tested for flu/RSV
- 17/24 required pressors, 18/24 required intubation
- Median duration of mechanical ventilation 10 days (IQR 7-12) – likely underestimate with 3 pts still ventilated 3/23/20
- While intubated, vent settings needed are similar to classic ARDS – prolonged course needed, with shortest time to extubation 8 days; successful extubations were performed in patients aged 23-88
- Patients requiring pressors for hypotension usually had normal ventricular function on echo
- 12 (50%) died in hospital, 5 (21%) discharged home, others remained hospitalized as of 3/23/20
- Patients over 65 were more likely to have died (62% vs 37%)
- Median hospital stay 17 days (IQR 17-24)
- Median ICU stay for survivors 14 days (IQR 4-17)
Conclusions:

- Most common reasons for ICU admission in patients with COVID-19 were hypoxemic respiratory failure needing intubation and/or hypotension needing pressors.
- When needed, mechanical ventilation was prolonged (min 8 days) with ventilatory requirements similar to ARDS.
- Some patients did recover, but they often required prolonged ICU and hospital LOS.
- Fatality rate for patients admitted to the ICU was high - 50% - and higher in those >65y.

Perspective:

This is the first multicenter paper looking at COVID-19 patients in the US. Focusing on a small series of ICU patients allowed for granular description of clinical and ventilatory characteristics, but is likely not fully generalizable to all COVID-19 infected patients. Of note, the authors suggest that their mortality rate for the ICU cohort is a ‘case fatality rate’ – this use of the phrase is inaccurate, as all cases of COVID-19 and not just those in the ICU should be included. One key finding is how long patients require mechanical ventilation and ICU-level care prior to recovery – while it is promising that recovery is possible even when illness is critical, it highlights the huge amount of resources which will be needed across the country in order to optimally support patients during the pandemic.

Summary written by: Katherine B. Salciccioli MD
Topic Areas: COVID-19, intensive care, mechanical ventilation
Key points to remember:

- ACE2 is the functional receptor for SARS-CoV-2 – physiologically, the receptor’s purpose is to counter RAAS activation
- No studies have evaluated effects of RAAS inhibition in COVID-19, but clinical trials are currently underway
- The concern for upregulation of ACE2 in patients taking RAAS inhibitors is based on preclinical studies – the concern that this upregulation could be harmful in COVID-19 is purely hypothetical
- Mechanistically, it is reasonable to hypothesize that RAAS inhibition could be helpful in COVID-19: once the virus has bound ACE2 and entered the cell, it downregulates ACE2 and this dysregulation may play a key role in lung injury
- Abrupt withdrawal of RAAS modulating medications in high-risk patients (i.e., HF or s/p MI) may result in instability or other acute adverse health outcomes
- Final recommendation: pending further data, continue RAAS inhibitors in patients who are already taking them, regardless of whether they are being evaluated for or treated with COVID unless a contraindication (i.e., hypotension)

Summary written by: Katherine B. Salciccioli MD

Topic Areas: COVID-19, renin-angiotensin-aldosterone system