Northwestern Medicine®
Feinberg School of Medicine

Department of Medicine
Medical Grand Rounds Webinar: COVID-19 Updates
April 14, 2020
7:30 a.m. to 8:30 a.m.

Questions submitted by participants during webinar

The answers provided are relative to a specific point in time and are subject to change as the management and care for COVID-19 patients continues to evolve

1. **What is the percentage of survivors among patients who require intubation and what is the median duration of intubation?**
   Answer from Dr. Cuttica: As of 4/12/2020 - 115 confirmed COVID positive patients admitted through the COVID MICU since it opened around 3/12/2020. 75% (86/115) required mechanical ventilation. Average Time on vent 6.67 days. 53% (61/115) have been discharged from the COVID MICU Average ICU LOS 8.13 days. 62% (38/61) patients discharged from the COVID MICU had required mechanical ventilation 47.5% (29/61) of patients discharged from the COVID ICU have been discharged home.

2. **Are there data on coagulation studies with Covid (protein C/S, AT-3, antiphospholipids, etc.)?**
   Answer from Dr. Cuttica: Limited data – there was the NEJM report of 3 patients in China with anti-phospholipid antibodies, COVID19 infection, and multiple infarcts (all cerebral infarcts) but it is impossible to know if the antiphospholipid antibodies were covid specific vs transiently elevated due to critical illness or even if the antibodies had any relation at all to the infarcts. The difficulty in teasing out what are COVID specific issues (clotting and otherwise) vs issues that arise due to critical illness all the time that we just don't routinely look for (i.e. we do not routinely trend d-dimer in critically ill patients or check antiphospholipid antibodies in septic patients that have strokes) in the non-COVID world highlights the importance of focusing our clinical efforts on proven evidence based practices and doing them well. Everything else should be approached as clinical research worthy of exploring but not of routine implementation in clinical practice.

3. **What scenario should lead one to test for a PE? Have you seen a sudden rise in D-Dimer out of proportion to other inflammatory markers to be a sign of PE/DVT?**
   Answer from Dr. Cuttica: This is just my opinion but I think empiric screening for PE based on D-dimer alone in the setting of critical illness is not warranted and given that acute kidney injury, as outlined in Dr. Quaggin's talk, is probably the second most common organ involvement in acute COVID infection is potentially dangerous. That being said we can't ignore the data suggesting possible increased thrombosis risk (either COVID 19 driven or driven by the degree of critical illness) so perhaps a sudden rise in the D-dimer accompanied by clinical suspicion for PE/DVT (unilateral leg swelling, increased oxygen needs, persistent/new tachycardia, etc.) should be the threshold to trigger testing.

4. **I know we are not currently switching patients off ACE-I and ARBs, but are there any studies ongoing (even observational) looking at the risks or benefits of being on these medications?**
Answer from Dr. Feinstein: Some of what we learn will be from observational data, but there is actually one new randomized trial initiated at Penn investigating stopping ACE-I or ARB therapy in patients hospitalized with COVID (called the REPLACE COVID trial). The primary endpoints are time to death and illness severity-related measures. A concern with the observational data is the potential for confounding by indication of therapy as well as by illness (e.g., ACEi being stopped due to a patient becoming increasingly hypotensive); in practice, many of these medications are being stopped as patients become sicker and require ICU-level care including potential pressor support. The randomized nature of the trial should help get at this question in a more rigorous way, but there of course remains major potential for the "non-stopping" group to have to stop ACEi/ARB therapy due to clinical deterioration, which could affect planned intention-to-treat or as-treated analyses.
See this great resource: http://www.nephjc.com/news/covidace2 Lists all trials, evidence in one spot

5. **Is there any work going on to discover an inhibitor to the viral spike protein to prevent it from docking on to the ACE-2 receptor?**
Answer from Dr. Quaggin: Yes - there are studies to determine if blocking ACE2 binding with a 'decoy' soluble ACE2 is beneficial and inhibiting the coreceptor TMPRSS2 – clinical grade drugs available. Two recent Cell publications showing support for blocking binding to soluble ACE2 or inhibiting the co-receptor TMPRSS2

Hoffmann et al., SARS-CoV2-2 Cell Entry Depends on ACE2 and TMPRSS2 and is Blocked by a Proven Protease Inhibitor (CELL, 2020)

Monteil, V. et al., Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2

2 NM investigators – D. Batlle and J. Jing are developing 'better' versions of soluble ACE2 and have published on these

6. **Since more COVID inpatients are being treated with hydroxychloroquine, do we have any data on COVID patients going into TdP?**
Answer from Dr. Feinstein: Not that I'm aware of, though this is rapidly evolving and I would not be surprised if case reports of TdP begin to emerge in these patients, who are often taking several QT prolonging medications simultaneously and have underlying hemodynamic and electrolyte instability, all of which can be a set up for further susceptibility to TdP. The Brazilian chloroquine trial that was stopped after 81 patients cited arrhythmia risk and noted that 2 patients died from VT, though the initiator here (and whether it was TdP->VF) was not clear from my reading. In any case, especially in sicker patients on multiple QT prolonging medications, this is a real concern that will require monitoring.

7. **NM has a stable supply of PPE - but what about Austin & Englewood who need it more? And shouldn't we track this on our NM "By the Numbers" daily updates?**
Answer from Dr. Gates: PPE is a small part of this much larger picture. NM must ensure that healthcare workers have appropriate PPE. The larger issues to address acutely is getting appropriate testing in these communities. For instance, drive thru testing was just made available in the Roseland community last week, an entire month into this pandemic. There are additional reports of members

of these communities being turned away for testing. The initially screening questions used to determine testing such as recent travel to specific areas overseas like China and Italy, when community spread was known, also negatively impacted these communities, allowing for under diagnosis and propagation of SARS-COV2. There are larger structural issues that must be addressed. Acutely, offering increased access to testing, housing alternatives, PPE etc. will be key in the attempt to decrease the deadly impact of COVID-19 on these communities.

8. **How does Chicago's doubling time compare to other major outbreaks in the world?**
Answer from Dr. Kho: Doubling times change over time. In Chicago (as in much of the United States) after an initial rapid rise with doubling times oftentimes close to 2 days, rates of rise of cases have slowed. As of the most recent numbers on 4/16, we are now over 10 days doubling time in Chicago and approximately 12 days doubling time in the U.S.
For interactive charts please see: https://ourworldindata.org/coronavirus

9. **Any reason to suspect ARBS are better than ACEIs?**
Answer from Dr. Feinstein: It is difficult to know. Both ACEIs and ARBs have been shown to increase ACE-2 expression in experimental models, but these findings are not necessarily consistent across studies. It is not clear if there is a substantial difference between these two. Furthermore, it is possible that ACEI and ARB therapy actually protects against hyper-inflammatory syndromes in part by reducing angiotensin II activity, so these may be as likely to be beneficial as harmful in the setting of SARS-CoV-2.

Practically, I have not been switching stable patients between ACEI and ARB therapy due to this, though when initiating therapy on outpatients (with COVID or not) I have since the onset of COVID tended to prefer ARBs due to lower risk of dry cough than with ACEI and potential for this to be confused with COVID-related symptomatology.

Answer from Dr. Quaggin: no – not at this point, some theoretical reasons proposed but ***no*** *evidence. Terrific resource on all things renin-angiotensin and COVID-19: http://www.nephjc.com/news/covidace2*

10. **Do the disparities in heart and kidney disease explain a large portion of the disparities with the pandemic?**
Answer from Dr. Gates: The disparities in heart and kidney disease are a direct result of persistent health disparities in healthcare. Social determinants of health are key factors that drive increased rates of diabetes, hypertension, obesity, asthma etc. in African-American communities. There are various structural and personal factors that have interplay in these diseases. Now given their inflammatory response in SARS-COV2 and the known physiologic outcomes of patients with underlying heart and kidney disease in any viral illness, these patients remain at increased risk of morbidity and mortality. What I am encouraging us to consider it that persistent healthcare disparities have caused the disparities in heart and kidney disease. COVID-19 has simply amplified this.