

This week's top 5 flash update continues the COVID-19 evidence journey. The team have sorted through approximately 1,500 papers this week, and here are the ones that deserve your attention. If you have the headspace for ten more fantastic papers check out the Director's Cut. If an interactive live journal club captures your interest, keep your eye out on social media for our next webinar. Finally, change is afoot as you'll notice in the coming weeks. We're looking forward to a wider team of EM colleagues from across the country bring their expertise into the mix.



The following papers have been split into 3 categories that will allow you to focus on those that are most vital to your practice.

- Worth a peek: interesting, but not yet ready for prime time
- Head Turner: new concepts
- Game Changer: this paper should change practice

Association of Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker Use With COVID-19 Diagnosis and Mortality by Fosbøl et al¹

Topic: Treatment / Prognosis

Rating: Head turner

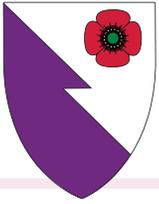
Scout: Govind Oliver / Anisa Jafar



Here we have a study within a study. On the one hand it is a retrospective cohort study of 4,480 patients with COVID-19. Following adjustment for age and medical history, the hazard ratio for being on ACEI/ARB for 30-day mortality was 0.83 (95% CI 0.67 - 1.03), severe COVID-19 was 1.15 [95% CI, 0.95-1.41] and 30-day death OR severe COVID-19 was 1.04 (95% CI 0.89 - 1.23).

On the other, it is also a nested case-control study of susceptibility of developing COVID-19 in which they matched for age and sex in a 10:1 ratio of controls to cases and adjusted for chronic obstructive pulmonary disease, diabetes, cancer, myocardial infarction, and cerebrovascular disease. In the latter study they found that in comparison with those on other antihypertensives, ACEI/ARB use was not significantly associated with developing COVID-19 in the first place (adjusted HR, 1.05 [95% CI, 0.80-1.36]). Overall this adds weight to the argument that being on ACEIs/ARBs is not something we need to be unduly concerned about in our patients during the COVID-19 pandemic. The authors do highlight several complex limitations to a study of this nature and remain sage and simple in their conclusions rather than signaling the end of any need to question this further.





Utility of Lung Ultrasound in COVID-19: A Systematic Scoping Review ²

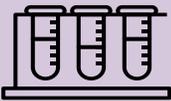
Topic: Diagnosis

Rating: Game changer

Scout: Anisa Jafar



Hands up for a one-stop shop for the current evidence behind lung ultrasound (LUS) in COVID-19? Well here it is (we must add, it's still only pre-print): or as close to it as we've seen in the past few months. The authors have done a thorough job seeking out the available data and instead of befuddling us with the numbers from very heterogeneous studies; they've gone for a scoping review approach. Hats off to that. We know that in theory LUS is the perfect test for COVID-19 pneumonitis: it's quick to perform, gives immediate results, causes no radiation and assesses the peripheral lung in great detail... but how useful is it? This review identified 33 studies that looked at the utility of LUS in COVID-19. Despite the quality of the included studies being relatively low, the authors concluded that LUS appears to be highly sensitive in all ages, and in pregnancy, and is almost certainly more sensitive than CXR. Specificity appears to be more complicated and will depend on, for example, the presence of underlying cardiorespiratory disease. Yes, we need more research, but given that we've gear-shifted towards protecting vulnerable patients from nosocomial COVID-19, as opposed to early in the pandemic when it was more "COVID-19 until proven otherwise", we can use this summary to help guide what we are doing right now. Read it, digest it, tell your friends.



Early Safety Indicators of COVID-19 Convalescent Plasma in 5,000 Patients by Joyner et al ³

Topic: Treatment

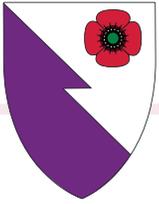
Impact rating: Head turner

Scout: Govind Oliver



Treating with convalescent plasma has both historical evidence and biological plausibility, but can we use this strategy with COVID-19? The data presented in this study show that at least it appears safe to try. This is an observational study and has not been designed to assess the efficacy of convalescent plasma. But, in 5,000 hospitalised adults with severe or life-threatening COVID-19 that were treated with ABO-compatible human COVID-19 convalescent plasma as part of the US FDA Expanded Access Program, the rate of serious adverse event (SAE) after transfusion in the first four hours after transfusion was <1% and the mortality rate was 0.3%. Of 36 SAEs, 2 were attributed to the convalescent plasma transfusion, 7 to transfusion related circulatory overload, 11 to transfusion associated lung injury and 3 to severe allergic reaction. The seven-day mortality rate within the study was 14.9% but this cohort included 66% of patients on ICU, a figure consistent with or lower than figures reported elsewhere for similar patient groups. This study is very reassuring from a safety perspective and the author's conclusion that it is safe to treat severely and critically unwell COVID-19 patients with convalescent plasma is justified. Further trial evidence is needed to establish actual clinical efficacy of this potentially promising treatment.





Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study by Stringhini et al⁴

Topic: Epidemiology

Impact rating: Worth a peek

Scout: Gaby Prager



How widely has COVID-19 spread within the population? Stringhini et al show their results of the first 5 of 12 consecutive weeks of SARS-Cov-2 antibody testing on randomly selected individuals and their households from the previous Bus Santé study in Geneva, Switzerland. They included 2,766 individuals from 1,339 households, of which 219 had a positive antibody test at some point. They started April 6th ending May 9th. The first COVID-19 case in Geneva was February 26th. They found the seroprevalence was 4.8% in week 1 and 10.8% in week 5, with no significant difference in results from week 2 to week 5. There were approximately 10.32 'confirmed cases' per 1000 in Geneva by May 9th. Cases were clustered in households. They saw lower seroprevalence in those aged 5-9 (RR 0.32) and those aged >65 RR 0.5 in comparison to those 20-49 years old. As Geneva is approaching the end of this potential 'first wave', it appears a higher number of individuals have been infected than confirmed cases over the same time. This is early data and the majority of the population has yet to be tested. The study population was not completely randomised and also had less relative representation from those over 70, non-Swiss nationals and over representative of those with tertiary education. Nonetheless, in an area in Europe that was heavily affected by COVID-19, it provides further evidence that there are likely a higher number of cases in the community than have been accounted for but this number is still small, important to bear in mind as lockdown policies are lifted.



Electrocardiographic Findings in COVID-19: Insights on Mortality and Underlying Myocardial Processes by McCullough et al⁵

Topic: Observational

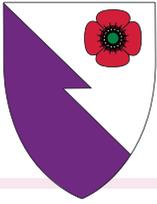
Impact rating: Worth a peek

Scout: Daniel Darbyshire



This retrospective cohort study looked at 756 consecutive patients who tested positive for COVID-19 and had an ECG at or near to admission to hospital. They found, using multivariable logistic regression that included age, ECG, and clinical characteristics, that patients with ECG findings have higher odds of death. The odds ratio for each feature varied from 2.31 (95% CI 1.27-4.21) for repolarisation abnormalities to 3.49 (95% CI 1.56-7.80) for ischaemic t-wave inversion. The study does not attempt to identify if the ECG changes were new and we would expect that someone with either pre-existing cardiovascular disease or cardiovascular complication of acute illness would fare worse than someone without these problems. The study has the similar weaknesses to many similar pieces of work in that it is single centre and retrospective, and the number of patients with specific abnormalities such as ST-elevation was too small to meaningfully analyse. However, as most patients getting admitted will have an ECG it helpful for us to be able to contextualise any changes we might identify for a patient with COVID-19.





Game changer summary

Trauer et al. conclude that lung US is highly sensitive for COVID-19 ²



In summary

Fosbøl et al. reassure us that ACEIs/ARBs do not increase COVID-19 risk ¹
Joyner et al. find that treatment with convalescent plasma is safe ³
Stringhini et al. discover population antibodies levels have only risen modestly ⁴
McCullough et al. show that odds of death are higher with ECG findings in COVID-19 ⁵



References

- 1) Fosbøl EL, Butt JH, Østergaard L, et al. Association of Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker Use With COVID-19 Diagnosis and Mortality [published online ahead of print, 2020 Jun 19]. *JAMA*. 2020;10.1001/jama.2020.11301. doi:10.1001/jama.2020.11301
- 2) Trauer M, Matthies A, Mani N, McDermott CB, Jarman R. Utility of Lung Ultrasound in COVID-19: A Systematic Scoping Review. *medRxiv* 2020:2020.06.15.20130344
- 3) Joyner MJ, Wright RS, Fairweather D, et al. Early safety indicators of COVID-19 convalescent plasma in 5,000 patients [published online ahead of print, 2020 Jun 11]. *J Clin Invest*. 2020;140200. doi:10.1172/JCI140200
- 4) Stringhini S, Wisniak A, Piumatti G, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study [published online ahead of print, 2020 Jun 11]. *Lancet*. 2020;S0140-6736(20)31304-0. doi:10.1016/S0140-6736(20)31304-0
- 5) McCullough SA, Goyal P, Krishnan U, Choi JJ, Safford MM, Okin PM. Electrocardiographic Findings in COVID-19: Insights on Mortality and Underlying Myocardial Processes [published online ahead of print, 2020 Jun 13]. *J Card Fail*. 2020;S1071-9164(20)30605-9. doi:10.1016/j.cardfail.2020.06.005

