

This week's flash update comes from the King's College Hospital ED research group. Spearheaded by Dr Fleur Cantle, we consist of three clinical research fellows, along with a group of dedicated junior doctors and medical student colleagues. Our team philosophy is focussed on the need for collaboration in research, we work closely with the anaesthetic, critical care, emergency medicine and trauma (ACET) research delivery team on a variety of portfolio and local departmental, patient-focused projects. We are very proud of our local research community, through which we have built a small network of clinical researchers across grades and stages of training. This allows us to ensure peer support and to allow research ideas and projects to become a reality in order to add to the evidence base for emergency medicine



We have sorted through 910 papers this week, and here are the papers that deserve your attention. As in previous weeks, these have been split into 3 categories that will allow you to focus on the papers 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

COVID-19 and Cardiovascular Disease by Mai et al ¹

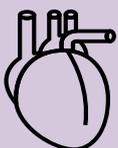
Topic: Cardiovascular review

Rating: Head Turner

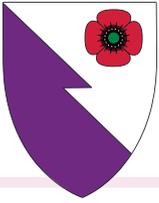
Scout: Andrew Brookes and Emma Backhurst

We have seen previous reviews of the cardiovascular system in COVID-19 rated as head turners and this review, by Mai, Del Pinto and Ferri from University of L'Aquila in Italy is among the best. In our research group at King's College Hospital, we love a "one sider" (a summary of our research/proposal fitting on to one sheet of A4 paper) and this review does exactly that. Mai et al. cover four key topics; cardiovascular disease, hypercoagulability, renin-angiotensin-aldosterone system inhibitors and electrocardiography in COVID-19. Within each review the key epidemiological features and pathophysiology, along with an evaluation of the WHO recommendations, are discussed.

The key points of this article highlight the "cytokine storm" featured in the latter stages of the COVID-19 disease process. Acknowledging the negative impact pre-existing cardiovascular disease, and COVID induced acute cardiovascular events have on mortality. Along with the need to focus on both local and systemic thrombotic manifestations and to be mindful of the much dreaded QT prolongation on patients' ECGs. Finally, providing us advice to continue ARBs and ACEIs until there is greater evidence on their interaction with the disease process.



This review article is a compact, comprehensive summary of cardiovascular disease in COVID-19. It is for the busy emergency physician, who wants to learn the key information needed, but doesn't have the time to sit down and trawl the literature.



Recovery of severely ill COVID-19 patients by intravenous immunoglobulin T (IVIG) treatment: A case series by Mohtadi et al ²

Topic: Treatment

Rating: Head Turner

Scout: Inbar Aberman and Nicole Minta

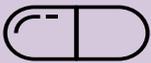


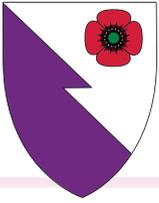
This paper, published in Virology by Mohtadi et al., demonstrates that IVIG in deteriorating COVID-19 patients may dramatically improve clinical respiratory symptoms. It outlines five COVID-19 case presentations in an Iranian hospital with severe treatment-resistant symptoms – in which early administration of IVIG prevented progression of the disease and allowed quick subsequent discharge.

Patients were aged 50-70, and four had multiple co-morbidities associated with increased mortality risk. All patients received treatment as per the Iran Ministry of Health COVID-19 protocol, but had descending or low O₂ saturation (as low as 82% on oxygen, 62% on air) as well as continually progressing pulmonary lesions on HRCT scans.

Patients were administered 0.3-0.5g/kg IVIG for 5 days (alongside supplementary treatment), following the protocol successfully implemented by Cao et al. (2020) in China. All patients were discharged 1-5 days post-treatment with stable vital signs (O₂ saturation >93%) and pleural imaging improvements. It is of note that the supplementary interventions may have also assisted quick patient recovery, and so further studies should aim to remove confounding factors where possible.

Although this study was a case series and had only five patients, it provides support to the current clinical evidence that IVIG has potential for treating deteriorating COVID-19 patients.





COVID-19 Preliminary Case Series: Characteristics of Emergency Medical Services (EMS) encounters with linked hospital diagnoses by Fernandez et al³

Topic: Prehospital emergency care

Rating: Head Turner

Scout: Raesa Jina

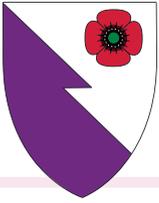


This report describes 84,540 prehospital encounters from 1st March to 19th April 2020 for patients with a COVID-19 hospital diagnosis or EMS suspicion versus those with neither a hospital diagnosis nor EMS suspicion of the disease. The standout message in this paper is that EMS suspicion for COVID-19 showed only a 20% positive predictive value and 78% sensitivity when compared to hospital diagnosis of COVID-19. This should ring warning bells for ED clinicians as many decisions regarding risk stratification, patient location and PPE utilisation are made based on EMS findings.

Demographic and clinical findings unsurprisingly echoed the results of many previous studies. Interestingly, 'stroke' was a common presentation in patients who weren't suspected of COVID-19 but went on to have a positive hospital diagnosis. This supports emerging reports of COVID-19 patients who manifest stroke features. There is a need for further research on this topic to appropriately incorporate it in to clinical practice. After finding inconsistent practices in PPE use, the authors raise important points regarding diversity in PPE policies, availability, compliance and documentation accuracy. In 20% of suspected cases, EMS providers didn't document the use of a mask. This has consequences on provider and patient safety as well as inventory management.

Often the first line of healthcare response, EMS providers play a key role in identifying COVID-19 patients. Their findings often have compounding effects on patient care. This study raised important action points, while serving as a reminder of the need for information sharing, accurate documentation and good communication between ED and EMS staff.





The effect of smoking on COVID-19 severity: a systematic review and meta-analysis by Reddy and Charles ⁴

Topic: Smoking

Rating: Worth a peek

Scout: Carole Reid and Aidan Beaumont

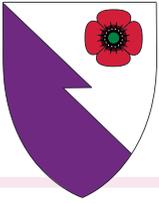


It wouldn't be a stretch to assume smoking is a major risk factor for COVID-19 severity, but prior to this article, peer-reviewed data surrounding its impact has been limited and controversial; one preliminary study going so far as to say active smoking was not significantly associated with increased risk of severe disease. Some non-peer-reviewed articles even suggested it may be a protective factor. Alas, studies have been small, and methodology regarded as poor. This paper aims to up the game by analysing a larger number of studies (47) and considers a much more impressive sample size (32,849 patients), to give us more robust and definitive answers.

The bottom line? Current smokers have an increased risk of presenting to hospital with severe COVID-19 (RR 1.31) and are almost twice as likely to experience severe or critical disease as former or never smokers. (RR 1.98)

As emergency physicians dealing with acutely unwell patients, smoking history can be low on the priority list and is often an afterthought in ED clerking. This article definitively reinforces the importance - not only for good triage of vulnerable patients but also to support further research efforts in this ongoing pandemic, which as we're all aware, is unlikely to be going anywhere anytime soon. So, in addition to front lining those risk factors we've all become so familiar with, "older age, male sex, hypertension, cardiovascular disease, diabetes and respiratory disease" - we should also be considering patient smoking history.





Risk of severe COVID-19 disease with ACE inhibitors and angiotensin receptor blockers: cohort study including 8.3 million people by Hippisley-Cox et al ⁵

Topic: Medication

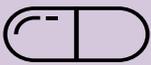
Rating: Worth a peek

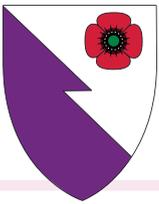
Scout: Ruth Snee



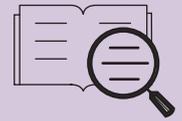
At the beginning of the pandemic, concerns were raised about the possible increased risk of (severe) COVID-19 from ACE-inhibitors and ARB drugs, leading to people en masse stopping their medication. This study focuses, unlike previous admission orientated studies, on the general population. Hippisley-Cox et al. used the largest GP practice research database in combination with the national registry of COVID-19 test positive results and the ICNARC database. This leads to an impressive cohort of 8.3 million people of which 19486 had a COVID-19 RT-PCR positive test and 1286 a ICU admission.

Similar risk factors of severe COVID-19 were identified as in previous studies, but the most interesting finding was that the use of ACEI/ARBs were associated with a significantly reduced risk of COVID-19, without any change in the risk of ICU care. The effect remained after adjusting for severity of hypertension and restricting analysis to patients with hypertension or congestive cardiac failure. However, there was significant interaction between ethnicity and ACEI/ARBs. The authors suggest there is a possible ethnic-specific effect of these medications. Considering the volume of information the authors provide and how rigorously the analysis is done, it is surprising there is no clear baseline table of the two groups they actually tried to compare: ACEI/ARB-users versus no ACEI/ARB-users. This makes it difficult to identify possible confounders. The impressive number of characteristics reviewed are definitely worth a peek though (for instance: the differences between region in risk of ICU admission) and create yet more interesting research questions.





In summary



Mohtadi et al demonstrate that IVIG can improve respiratory symptoms in COVID-19 patients ¹

Mai et al summarise cardiovascular disease in COVID-19 patients ²

Fernandez et al. raise important action points for the ED regarding risk stratification and emergency medical services assessment ³

Reddy and Charles reiterate the clinical significance of patients smoking history during triage ⁴

Hippisley-Cox et al observe the decline in ACEI/ARBs use in the general population and its positive association with contraction of COVID-19 ⁵

References



1) Mai. F, Del Pinto. R, Ferri. C, 2020, COVID-19 and cardiovascular diseases, *Journal of Cardiology*. [journal-of-cardiology.com/article/S0914-5087\(20\)30254-9/fulltext](https://journal-of-cardiology.com/article/S0914-5087(20)30254-9/fulltext) [accessed 11/08/20]

2) Mohtadi. N, Ghaysouri. A, Shirazi. S, Ansari. S, Shafiee. E, Bastani. E, Kokhazadeh. T, Tavane. H, 2020, Recovery of severely ill COVID-19 patients by intravenous immunoglobulin (IVIG) treatment: A case series, *Virology*, volume 548, pp 1-5. sciencedirect.com/science/article/pii/S0042682220300933?via%3Dihub [accessed 11/08/20]

3) Fernandez. AR, Crowe. RP, Bourn. S, Matt. SE, Brown. AL, Hawthorn. AB, Myers. JB, 2020, COVID-19 Preliminary Case Series: Characteristics of EMS Encounters with Linked Hospital Diagnoses, *Prehospital Emergency Care*. doi.org/10.1080/10903127.2020.1792016 [accessed 11/08/20]

4) Reddy. RK, Charles. WN, Sklavounos. A, Dutt. A, Seed. PT, Khajuria. A, 2020, The effect of smoking on COVID-19 severity: a systematic review and meta-analysis, *Journal of Medical Virology*. doi.org/10.1002/jmv.26389 [accessed 11/08/20]

5) Hippisley-Cox. J, Young. D, Coupland. C, Channon. KM, Tan. PS, Harrison. DA, Rowan. K, Aveyard. P, Pavord. ID, Watkinson. PJ, Risk of severe COVID-19 disease with ACE inhibitors and angiotensin receptor blockers: cohort study including 8.3 million people, *Heart*. doi.org/10.1136/heartjnl-2020-317393 [accessed 11/08/20]