Emergency Medicine Journal COVID-19 monthly top five

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Introduction

Following from the successful 'RCEM weekly top five' series starting in April 2020, this is the fifth of a monthly format for *Emergency Medicine Journal* (EMJ) readers. We have undertaken a focused search of the PubMed literature using a standardised COVID-19 search string. Our search between 1 March and 31 March 2021 returned 2613 papers limited to human subjects and English language. We also searched high-impact journals for papers of interest.

Our team have narrowed down the most interesting, relevant and important of the papers and provided a critical snapshot of five of those we felt most deserved EMJ reader attention. Importantly, we have highlighted not only the main findings from the papers but key limitations and considerations for emergency medicine (EM) clinicians when interpreting the work. In doing so, we have created an accessible window into pertinent research findings for our busy colleagues during this fast-paced and ever-changing COVID-19 landscape.

The papers are ranked in one of three categories, allowing 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 could/should change practice.

This month's searches were undertaken by the team in Plymouth and the Academic Department of Military Emergency Medicine. Next month we cross to Cork, Ireland.

Seroprevalence of SARS-CoV-2 infection in healthcare workers in a large teaching hospital in the North West of England: a period prevalence survey

Topic: transmission

Rating: head turner

In this paper, Shorten *et al* present the results of a COVID-19 antibody screening programme and a COVID-19 symptom survey among staff in a large UK hospital.[1]

Overall, 17.4% of staff were seropositive for COVID-19 and there were several statistically significant findings within this group. Older staff were less likely to be seropositive than younger staff, as were staff of white ethnicity compared with those of black or Asian ethnicity. Rates of seropositivity among staff increased as patients with COVID-19 spent longer in each location (COVID-19 bed-days). Clinical staff had higher rates of seropositivity than those with non-clinical roles; but interestingly for emergency department (ED) and critical care staff, seropositivity was not significantly different between clinical and non-clinical staff. Of all staff who were seropositive, 25.2% were asymptomatic and were not aware of having been infected with SARS-CoV-2.

The overall rate of seropositivity and the trends in relation to ethnicity are compatible with similar studies within the UK.[2 3] It is intuitive that clinically facing staff are more at risk of catching COVID-19 than those who are not, although it is interesting that this was not the case in the ED or critical care.

The major limitation of this study is its reliance on the antibody result as the gold standard. We know that antibody titres take time to reach detectable levels (most sensitive after 21 days following infection) and that they wane after a time, again impacting detectability and potentially resulting in some false-negative results.

Bottom line

The high rate of asymptomatic infection is concerning and provides the take-home message from this paper, which is that staff must ensure adherence to social distancing guidelines, and personal protective equipment use should be exemplary to protect both patients and colleagues.

Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study

Topic: prognosis

Rating: head turner

In October 2020, a new SARS-CoV-2 variant of concern (VOC) B.1.1.7 (202012/1), was identified in South East England by genomic sequencing.[4] One feature of the variant is the absence of the gene coding for the spike glycoprotein of SARS-CoV-2 (S gene) on PCR testing. This study examines the effect of the new variant on death within 28 days of a positive test in the community.[5] A matched cohort design was used to control for the effects of age, ethnicity, date of test, location and index of multiple deprivation. A total of 54 906 matched pairs were identified in the 4 months from 01 October 2020, and outcomes were compared according to the S gene status on positive PCR tests. The new variant was associated with increased mortality in this comparatively low-risk group from 2.5 to 4.1 per 1000 detected cases, with amortality hazard ratio of 1.64 (95% CI 1.32 to 2.04).

The assumption that S gene negativity was indicative of the VOC is a possible limitation; however, the association has been found to be robust in the study population.[4]

Although this observational cohort study cannot prove causation, this study suggests that the new VOC is between 32% and 104% more deadly. Especially in light of previous findings that this new variant is more transmissible, this has important ramifications for local and national policy.

Bottom line

B.1.1.7 appears to be associated with both a higher transmissibility and a higher mortality rate.

Interleukin-6 blocking agents for treating COVID-19: a living systematic review

Topic: treatment

Rating: head turner

This 'living' systematic review looks at the use of biological agents targeting interleukin-6 (IL-6),[6] a pro-inflammatory cytokine that could be a major player in COVID-19-induced cytokine storm.

Forty-nine relevant randomised trials in publication or preprint were identified, of which 10 had published results and

were subject to analysis. The 10 studies encompassed 6896 admitted patients with either suspected or confirmed mild to severe COVID-19. The intervention was either tocilizumab or sarilumab against the control of placebo or standard care. Administration of tocilizumab reduced all-cause mortality at 28 days (risk ratio 0.89 (95% CI 0.82 to 0.97), which in practical terms could represent 32 lives saved per 1000 treated patients. Although sarilumab did not seem to cause more unwanted side-effects than placebo treatment, the effects on mortality and other clinical outcomes were uncertain.

Methodological limitations of included studies consisted of inadequate reporting of treatment concealment method, differences in rates of steroid administration between groups and incomplete reporting of other co-interventions. In one study, 17% of patients scheduled to receive tocilizumab did not, while in another 23% of participants in the standard care arm ultimately received tocilizumab, due to clinical deterioration.

Although the potential for a mortality benefit from tocilizumab in COVID-19 is promising, uncertainty remains regarding additional clinical benefits and the effectiveness of other IL-6 blocking agents. As further results from the REMAP-CAP and RECOVERY trials are published, this living review will be updated to further clarify the role of this treatment in specific patient groups.

Bottom line

Tocilizumab may reduce mortality among patients with severe COVID-19 infection. Further research is needed to determine whether there are any associated benefits, the role of other IL-6 blocking agents and whether early administration in the ED is desirable.

Chest CT in COVID-19 at the ED: validation of the COVID-19 Reporting and Data System and CT Severity Score: a prospective, multicentre, observational study

Topic: investigations

Rating: worth a peek

For the diagnosis of COVID-19, CT scans are reported to have improved sensitivity over plain chest radiographs but with no universal agreement on reporting COVID-19 CT abnormalities, their diagnostic utility in COVID-19 remains subjective.[7] This study from the Netherlands aimed to prospectively validate a 5-point CT scan scoring system named COVID-19 Reporting and Data System (CO-RADS).[8] The authors examined the diagnostic characteristics of CO-RADS for the detection of COVID-19, using PCR as the reference standard. This study also validated a prognostic score, the CT Severity Score (CTSS). The outcomes of interest for CTSS were patient disposition from ED and 30-day mortality.

A total of 741 consecutive patients, from two centres, were included in the analysis, between March and May 2020. Patients were included if they received both a PCR and a CT scan, performed according to local protocol, and usually in the presence of moderate to severe symptoms.

The key finding was that a CT with a CO-RADS score of ≥4 was a good discriminator for COVID-19. The area under the curve was 0.91 (95% CI 0.89 to 0.94), with a positive predictive value of 76.4% (95% CI 71.9% to 80.3%) and a negative predictive value of 94.6% (95% CI 92.4% to 96.2%).

The CTSS was performed on all patients with a CO-RADS score of ≥3. Patients were categorised into three groups according to disposition: home from ED, hospital admission or intensive care unit (ICU) admission. Logistic regression demonstrated a significant positive association between CTSS (per point increase) with hospital admission, ICU admission and 30-day mortality.

There are some study limitations specifically relevant to EM. Only ED patients deemed to have moderate to severe symptoms were included. Additionally, this study took place during a period of high prevalence. Both of these factors could limit generalisability particularly for departments seeing lower acuity cases or following an overall population reduction in prevalence.

Bottom line

Both the CO-RADS and CTSS could be useful tools for diagnosing COVID-19 and assisting with disposition; however, utility will be limited as few patients with COVID-19 undergo chest CT while in the ED.

SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study

Topic: transmission

Rating: head turner

This retrospective cohort study from Singapore determined clinical attack rates and risk factors for transmission among close contacts of confirmed cases of COVID-19.[9] Hospitalisation of all COVID-19 cases, and legally enforced quarantine and extensive contact tracing by the Ministry of Health, provided the ideal opportunity for highly accurate data to be analysed with a completion rate of 97%.

Between 3 January and 3 April 2020, 1114 PCR-confirmed index cases were identified, generating 7770 close contacts (1863 household contacts, 2319 work contacts and 3588 social contacts). Close contacts were defined as being within 2 m of each other for ≥30 min. The major novel findings from this study were that verbal interaction for 30 min or greater, sharing a vehicle and having close contact with more than one index case were positively associated with transmission.

However, rates and risk factors were different between household and non-household contacts. The clinical attack rate was 5.9% for household contacts, 1.3% for work contacts and 1.3% for social contacts. Within a household, sharing a bedroom (p=0.0023) and being spoken to by an index case for ≥30 min (p<0.0001) were positively associated with transmission. Among non-household contacts, exposure to more than one case (p<0.001) and sharing a vehicle (p=0.0013) were associated with transmission. Notably, using the same bathroom or sharing food were not found to be predictors of transmission.

Study limitations: not all participants underwent testing and only individuals with symptoms were tested. Overall rates of transmission could therefore be higher, or the tendency to report symptoms may be different between types of contacts.

Bottom line

This study confirms other data that household rates of transmission are higher than for non-household contacts. It also provides data for which behaviours are really the riskiest.

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