The Daily COVID-19 Literature Surveillance Summary

June 8, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Climate:

- Researchers with the European Monitoring Centre for Drugs and Drug Addiction report a 27% increase in online cannabis sales and a paradoxical 17% decrease in estimated revenue from January to March 2020 due to a suspected shift in cannabis purchasing towards "dark net" drug sales.
- Public health officials in Singapore and the United Kingdom draw parallels regarding the stigma seen in the HIV and COVID-19 pandemics stating that stigma may hinder individuals from coming forward to be tested for COVID-19, leading to further spread.

Epidemiology:

- A retrospective cohort study utilizing the data from the 17.4 million patients in the National Health Service in the United Kingdom determined that male sex, older age and deprivation, uncontrolled diabetes, severe asthma, along with both black and Asian ethnicity were associated with a higher chance of in-hospital death in people with confirmed COVID-19.
- Investigators in Pittsburgh utilized Bayesian statistics to support the notion that when a patient has a high RT-PCR pretest probability of COVID-19, such as an emergency room nurse who has evaluated several positive patients, a negative test result may not be sufficient to rule out infection.
- An observational study in Italy found a moderate to strong negative correlation between people over the age of 65 who received the influenza vaccine and COVID-19-related deaths in Italy leading experts to call for experimental studies to investigate potential causal links.
- A systematic review of literature found that of 92 pregnant persons diagnosed with COVID-19 via RT-PCR or CT, 64% were symptomatic, 76.6% of RT-PCR tests were positive, 8.7% had pneumonia diagnosed with CT, and there were no reports of maternal mortality or confirmed vertical transmission supporting that mothers and neonates are at relatively low risk of severe infection.

Transmission and Prevention:

- An author from Oxford argues that two recent publications that indicate low effectiveness of public mask-wearing fail to take into account the source control that masks provide by preventing large droplet aerosolization by the user.
- A group of American physicians points out that well-established vaccines against pathogens such as respiratory syncytial virus (RSV), streptococcus species, and seasonal influenza only have modest efficacies around 60-70% and explain that an initial SARS-CoV-2 vaccine will likely be less effective due to our naive immune systems.
- A cohort study of 14,000 people in Vietnam who were tested for SARS-CoV-2 via RT-PCR found that 43% of the 30 who tested positive were completely asymptomatic and would otherwise not have been identified as infected with the virus.
- A retrospective study of data in the states of Colorado, Minnesota, Ohio, and Virginia from seven consecutive days before and 17 consecutive days after the implementation of stay-at-home orders revealed that these efforts were effective in preventing hospitalizations from growing at an exponential rate.

Management:

- Guidelines and recommendations for management of COVID-19 patients include:
  - The role of imaging in the COVID-19 pandemic
  - Delivering care in patients with heart failure
- A group of pulmonary and critical care specialists discuss the current data on the utility of noninvasive ventilation techniques for management of acute hypoxemic respiratory failure and indicate that these approaches may prevent the need for intubation in some patients.
- A case series of 85 asymptomatic cancer patients found that seven were positive for COVID-19 on nasopharyngeal RT-PCR. Their findings suggest that universal screening of immunocompromised patients, especially patients on anti-cancer therapy, may be beneficial in mitigating progression to severe disease and preventing further transmission of SARS-CoV-2.

Adjusting Practice

- Guidelines and recommendations for adjusting practice during the COVID-19 pandemic include:
  - Reopening hospitals and maintaining patient safety
  - Motility and functional disorder-related procedures
  - Management of gynecologic malignancies and patients with acute stroke
- A cohort study found that neck circumference was significantly associated with risk for invasive mechanical ventilation (95% CI:1.120-1.417; $p<0.001$), when adjusted for age, sex, diabetes, hypertension, COPD, and BMI, suggesting that neck circumference may be a useful independent predictor upon admission for invasive mechanical ventilation in COVID-19 patients.
- In a survey, 88 of 106 academic orthopedic institutions in the US using telehealth services stated that COVID-19 was a major factor in implementing the services and the geographic location of the programs providing substantially increased telehealth services was positively correlated with COVID-19 disease burden, indicating the "impressive measures" needed in these areas to provide quality care for their orthopedic surgery patients.

R&D: Diagnosis and Treatment

- A systematic review including 4 randomized controlled trials, 10 cohort studies, and 9 case series found that evidence was conflicting and insufficient regarding the use of hydoxychloroquine and chloroquine in decreasing mortality, disease progression, clinical symptoms, and viral clearance in patients with COVID-19.
- A pilot randomized controlled trial analyzed the effect of 3 months of colchicine on 35 COVID-19 patients with characteristics of high BMIs (over 30 kg/m^2), metabolic syndrome, and no significant chronic medical conditions. Findings were a significant decrease in concentration of 26 molecules associated with neutrophil function and the innate immune system (including IL-6) and an increase in 8 molecules associated with metabolism and tissue repair.

Mental Health and Resilience Needs

- A cohort study evaluated the efficacy of social media-based counseling via two daily face-to-face sessions on WeChat for 63 patients hospitalized with suspected COVID-19 during hospital quarantine and found a significant reduction in both anxiety and depression among the 15 qualified patients (initial score of 8 or higher on the Hospital Anxiety and Depression Scale [HADS]) two weeks after the first intervention.

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CLIMATE

WILL THE CURRENT COVID-19 PANDEMIC IMPACT ON LONG-TERM CANNABIS BUYING PRACTICES?

Groshkova T, Stoian T, Cunningham A, Griffiths P, Singleton N, Sedefov R.. J Addict Med. 2020 May 29. doi: 10.1097/ADM.0000000000000698. Online ahead of print.
Level of Evidence: Other

BLUF

Researchers with the European Monitoring Centre for Drugs and Drug Addiction report a 27% increase in online cannabis sales and a paradoxical 17% decrease in estimated revenue from January to March 2020, at the onset of the COVID-19 pandemic. They suspect a shift in cannabis purchasing from online marketplace sales to one-on-one encrypted sales, prompting concern over decreased government ability to oversee and track these "darknet" drug sales.

ABSTRACT

The COVID-19 pandemic and the response to have resulted in an increase in sales activity levels on darknet markets during the first three months of 2020, mainly related to cannabis products. One key question is whether more people will become used to this form of purchasing their drugs and will they continue with it post COVID-19 lockdown. As one-to-one encrypted communication services or social media apps are increasingly being used, monitoring and interdiction will become much more challenging.

AFFECTING THE HEALTHCARE WORKFORCE

"THE STORM HAS ARRIVED": THE IMPACT OF SARS-COV-2 ON MEDICAL STUDENTS

Klasen JM, Vithyapathy A, Zante B, Burm S.. Perspect Med Educ. 2020 May 26. doi: 10.1007/s40037-020-00592-2. Online ahead of print.
Level of Evidence: Other

BLUF

A multinational group of medical students, physicians, and scientists convened to discuss medical student clinical education during the COVID-19 pandemic. Many medical students are eager to be of assistance in healthcare during this time, while many others are faced with the dilemma between fulfilling their clinical duties and protecting at risk populations they may live with. The authors recommend the following:

1. Students must know and recognize the symptoms of the disease as well as how to protect patients and themselves.
2. The assignment of students can be rescheduled at any time if there is an increase in knowledge or a redistribution of resources; there should be a constant re-evaluation by the supervising authority.
3. An introduction to the corresponding tasks must not be neglected; briefing and debriefing activities should take place regularly.
4. We suggest creating and maintaining the best possible conditions if we seek to deploy medical students during such a crisis while mentoring them.
5. We do not know exactly what and how students learn in such crisis situations and what coping strategies they have, so we as educators have to be aware of the need to support them even more than usual during such uncertain times. Prioritizing medical students' safety and wellbeing is essential."

ABSTRACT

In a few weeks, the global community has witnessed, and for some of us experienced first-hand, the human costs of the COVID-19 pandemic. There is incredible variability in how countries are choosing to thwart the disease's outbreak, sparking intense discussions around what it means to teach and learn in the era of COVID-19, and more specifically, the role medical students play in the midst of the pandemic. A multi-national and multi-institutional group made up of a dedicated medical student from Austria, passionate clinicians and educators from Switzerland, and a PhD scientist involved in Medical Education from Canada, have assembled to summarize the ingenious ways medical students around the world are contributing to emergency efforts. They argue that such efforts change COVID-19 from a "disruption" to medical students learning to something more tangible, more important, allowing students to become stakeholders in the expansion and delivery of healthcare.

REPLY TO RE: COVID-19 AND THE UROLOGY MATCH: PERSPECTIVES AND A CALL TO ACTION

Gabrielson AT, Kohn TP, Clifton MM.. J Urol. 2020 May 27:101097JU0000000000001146. doi: 10.1097/JU.0000000000001146. Online ahead of print.
Level of Evidence: Other

BLUF

Authors from the James Buchanan Brady Urological Institute at Johns Hopkins University School of Medicine advocate for setting a limit on the number of applications medical students may submit to urology residency programs in light of in-person visit days and interviews being canceled by COVID-19. They also suggest that residency programs cap the number of interviews offered and call for more transparency from residency programs so students are able to better apply to programs where they may be seriously considered for an interview.

EPIDEMIOLOGY

RISK FACTORS FOR DEATH FROM COVID-19

Selvan ME.. Nat Rev Immunol. 2020 May 27. doi: 10.1038/s41577-020-0351-0. Online ahead of print.
Level of Evidence: Other

BLUF

A retrospective cohort study conducted by a multidisciplinary group of researchers in the United Kingdom analyzed the health record data of 17.4 millions patients from the national health service (NHS) and determined that male sex (HR 1.99, 95%CI 1.88-2.10), older age and deprivation (with a strong "dose" response), uncontrolled diabetes (HR 2.36 95%CI 2.18-2.56), severe asthma (HR 1.25 95%CI 1.08-1.44), and various other prior medical conditions, along with both black (age-sex adjusted HR 2.17 95% CI 1.84-2.57; fully adjusted HR 1.71 95% CI 1.44-2.02) and asian ethnicity (age-sex adjusted HR 1.95 95% CI 1.73-2.18; fully adjusted HR 1.62 95% CI 1.43-1.82) were associated with a higher chance of in-hospital death in people with confirmed COVID-19 (Figure 3). Clinicians must pay special attention to patients with the listed characteristics in order to provide the highest quality care while continuing to investigate the cause of such disparities.

MODELING

INTERPRETING COVID-19 TEST RESULTS: A BAYESIAN APPROACH

Good CB, Hernandez I, Smith K.. J Gen Intern Med. 2020 Jun 3. doi: 10.1007/s11606-020-05918-8. Online ahead of print.
Level of Evidence: 5

BLUF

The authors address the problem of false-negative test results for COVID-19 by RT-PCR through the application of Bayesian statistics. They performed statistical analyses of the false negative probability on simulated cases of COVID-19 in cases of either high or low pretest probability of COVID-19 (Table 1). They show that when a patient has a high pretest probability, such as an emergency room nurse who has evaluated several patients with COVID-19, a negative test result cannot rule out infection and conclude these patients should undergo further workup and repeat testing.

FIGURES

Clinical Scenarios	Pre-test probability (%)	PCR assay sensitivity (%)	Post-test probability of acute COVID-19 infection	
			Positive test (%)	Negative test (%)
Patient 1: high pre-test probability	70	70	100	41.2
		90	100	18.9
	90	70	100	73.0
		90	100	47.4
Patient 2: low pre-test probability	5	70	97.4	1.6
		90	97.9	0.5
	10	70	98.7	3.2
		90	99.0	1.1

Table 1. Estimates for Post-Test Probability of Acute COVID-19 Infection for Simulated Patient Scenarios

PREDICTING INTERVENTION EFFECT FOR COVID-19 IN JAPAN: STATE SPACE MODELING APPROACH

Kobayashi G, Sugasawa S, Tamae H, Ozu T.. Biosci Trends. 2020 May 28. doi: 10.5582/bst.2020.03133. Online ahead of print.
Level of Evidence: Other

BLUF

Researchers in Japan conducted statistical modeling with state spate models combined with a susceptible-infected recovered (SIR) model, using data from March 1 to April 22, 2020 in order to evaluate rates of COVID-19 infection (figures 3-6). They

found that the state of emergency likely reduced the infection rate in Japan, and suggest that reduction of the reproduction number could reduce the eventual epidemic peak.

ABSTRACT

Japan has observed a surge in the number of confirmed cases of the coronavirus disease (COVID-19) that has caused a serious impact on the society especially after the declaration of the state of emergency on April 7, 2020. This study analyzes the real time data from March 1 to April 22, 2020 by adopting a sophisticated statistical modeling based on the state space model combined with the well-known susceptible-infected-recovered (SIR) model. The model estimation and forecasting are conducted using the Bayesian methodology. The present study provides the parameter estimates of the unknown parameters that critically determine the epidemic process derived from the SIR model and prediction of the future transition of the infectious proportion including the size and timing of the epidemic peak with the prediction intervals that naturally accounts for the uncertainty. Even though the epidemic appears to be settling down during this intervention period, the prediction results under various scenarios using the data up to May 18 reveal that the temporary reduction in the infection rate would still result in a delayed the epidemic peak unless the long-term reproduction number is controlled.

FIGURES

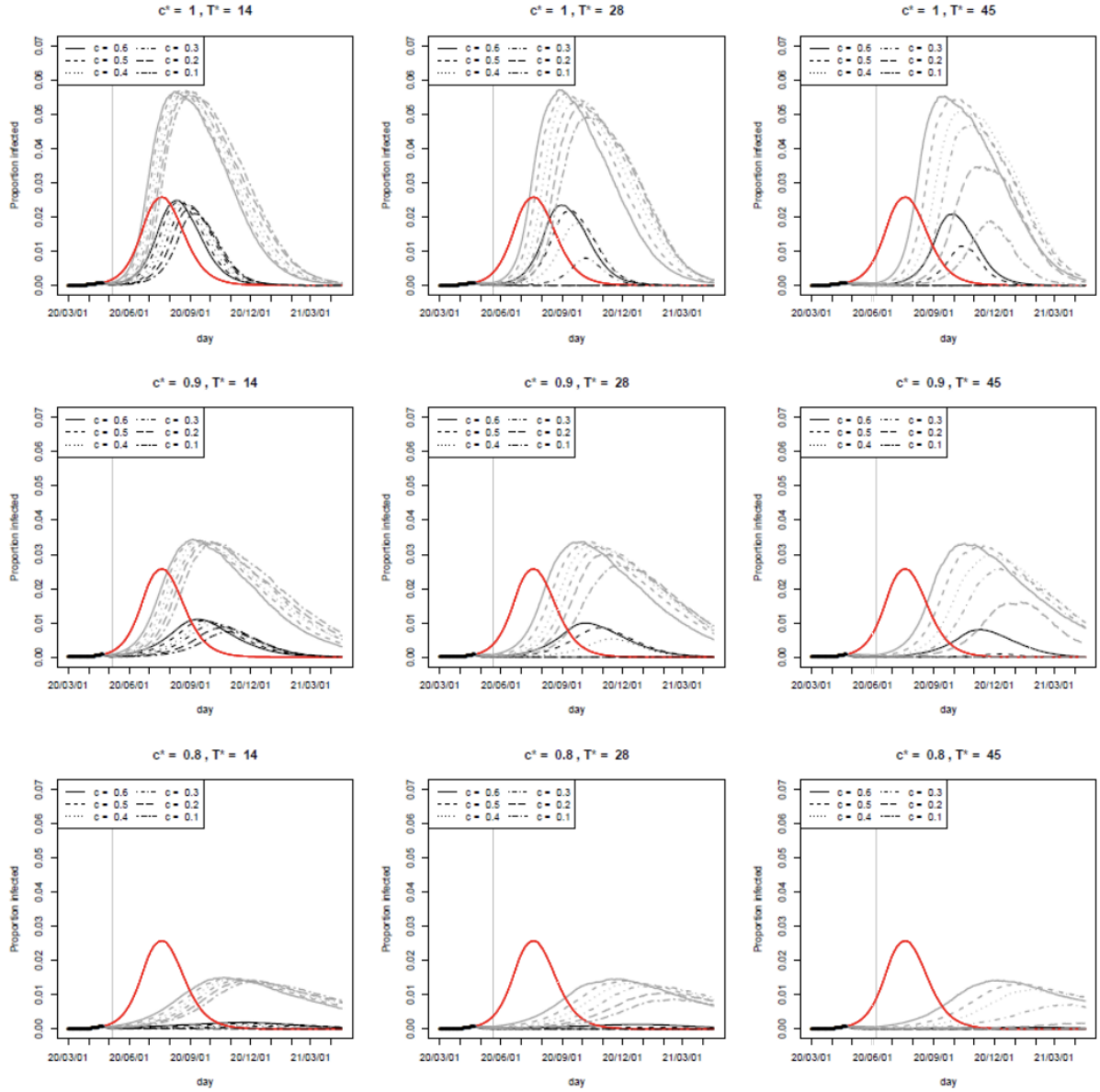

Figure 3. Future prediction under the nine combinations of T^* (the period of the intervention) and c^* (the multiplier for β after the intervention) for $p = 0.1$. The red, black and grey curves respectively represent the future point prediction without intervention shown in Figure 2, point prediction under each scenario and upper bounds of the 95% prediction intervals. The black circles represent the observed data points. The grey vertical lines indicate the dates on which there is a change in the infection rate represented by c^*.

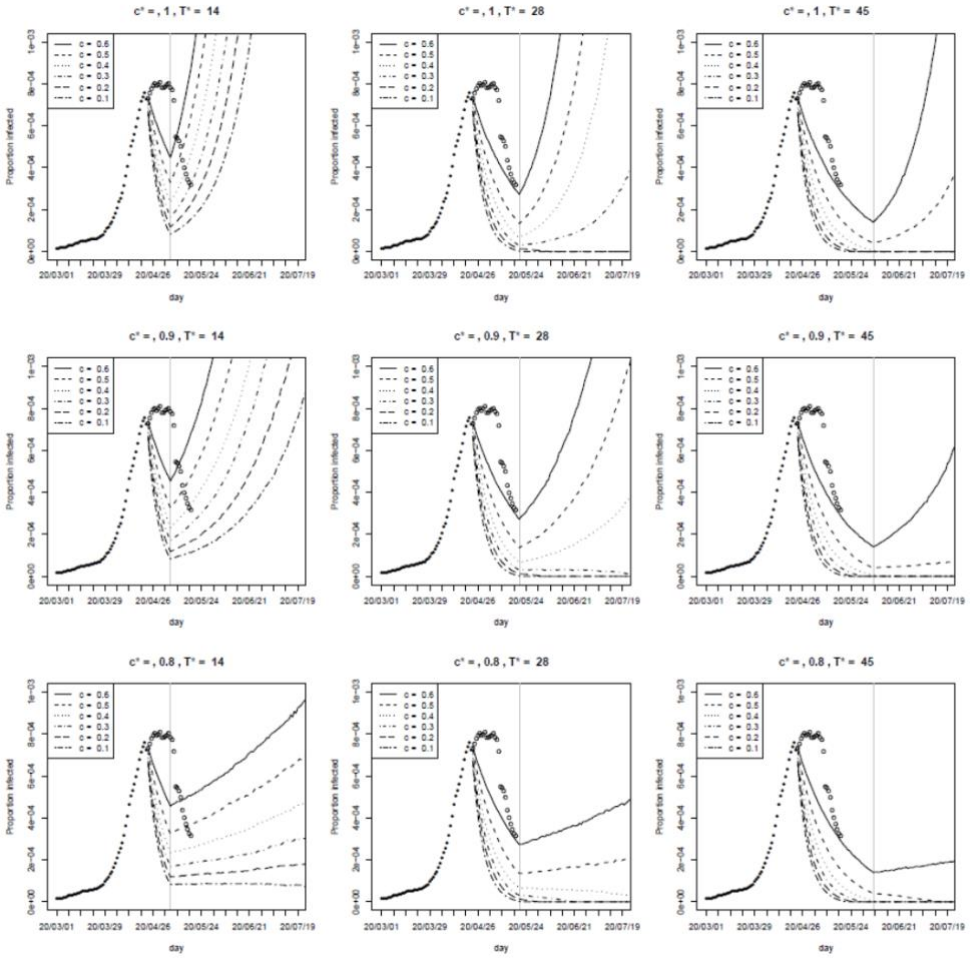

Figure 4. Details Figure 3. around the dates on which the infection rate changes according to c^*. The curves represent the future point prediction. The black circles are the observed data points up to April 22 and white circles are the observed data points additionally obtained after April 22 up to May 18. The grey vertical lines indicate the dates on which there is a change in the infection rate represented by c^*.

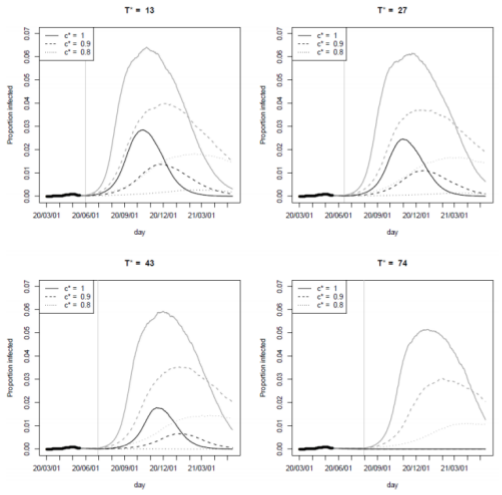

Figure 5. Future prediction under the combinations of T^* (the period of the intervention) and c^* (the multiplier for β after the intervention) for p = 0.1 using the extended dataset. The black and grey curves respectively represent the future point prediction under each scenario and upper bounds of the 95% prediction intervals. The grey vertical lines indicate the dates on which there is a change in the infection rate represented by c^*.

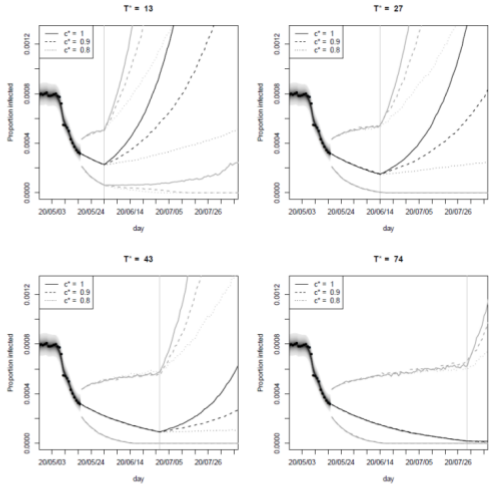

Figure 6. Details Figure 5 around the dates on which the infection rate changes according to c^*. The black and grey curves respectively represent the future point prediction and 95% prediction intervals. The black circles represent the observed data points along with the 95% credible intervals. The grey vertical lines indicate the dates on which there is a change in the infection rate represented by c^*.

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

EPIDEMIOLOGICAL EVIDENCE FOR ASSOCIATION BETWEEN HIGHER INFLUENZA VACCINE UPTAKE IN THE ELDERLY AND LOWER COVID-19 DEATHS IN ITALY

Marín-Hernández D, Schwartz RE, Nixon DF.. J Med Virol. 2020 Jun 4. doi: 10.1002/jmv.26120. Online ahead of print.
Level of Evidence: 3

BLUF

This observational study conducted in Italy by experts from Cornell University found a moderate to strong negative correlation through a Pearson product-moment correlation between the number of people over the age of 65 who received the influenza vaccine and the number of COVID-19-related deaths in Italy [r= -0.5874, n= 21, p= 0.0051]. Further experimental studies are needed to investigate a possible causal link between the influenza vaccine and reduced COVID-19 mortality.

ABSTRACT

The Italian COVID-19 epidemic may finally be slowing, although the virus has spread from the North in Lombardy throughout the rest of the country. While there have been more than 233,000 confirmed cases, and a mortality rate estimated around 14%, Italy will now navigate an exit from lockdown with continued testing, monitoring, and contact tracing of any new infections.

PANCREATIC INJURY IN THE COURSE OF CORONAVIRUS DISEASE 2019 (COVID-19): A NOT-SO-RARE OCCURRENCE

Bruno G, Fabrizio C, Santoro CR, Buccoliero GB.. J Med Virol. 2020 Jun 4. doi: 10.1002/jmv.26134. Online ahead of print.
Level of Evidence: 4

BLUF

A case series conducted at San Giuseppe Moscati Hospital in Taranto, Italy between February 25 and May 10, 2020 by the Infectious Diseases Unit found pancreatic abnormalities in 6 out of 70 COVID-19 patients (8.5%); the abnormalities regressed completely by discharge in the 5 surviving patients. The authors conclude management of COVID-19 should include close monitoring of pancreatic parameters.

ABSTRACT

Despite respiratory symptoms are typically found during the course of coronavirus disease 2019 (COVID-19), gastrointestinal manifestations are increasingly described. However, data regarding COVID-19-associated pancreatic injury are still limited, as well as the mechanisms underlying COVID-19 induced-pancreatic damage have not been completely clarified. Herein, we described pancreatic abnormalities in six (8.5%) out of 70 patients with COVID-19 hospitalized in our unit from February 25, 2020 to May 10, 2020. We hypothesized that pancreatic damage may be associated with several factors including direct effect of SARS-CoV-2, inflammatory cascade, dehydration and multiple organ dysfunction.

GUILLAIN-BARRÉ SYNDROME IN A PATIENT WITH MINIMAL SYMPTOMS OF COVID-19 INFECTION

Oguz-Akarsu E, Ozpar R, Mirzayev H, Acet-Ozturk NA, Hakyemez B, Ediger D, Karli N; Pandemic Study Team.. Muscle Nerve. 2020 Jun 4. doi: 10.1002/mus.26992. Online ahead of print.
Level of Evidence: 5

BLUF

In a case report, authors from Uludag School of Medicine, Bursa, Turkey describe a patient with Guillain–Barré Syndrome (GBS), in whom imaging showed incidental findings consistent with COVID-19. Subsequent testing for SARS-CoV-2 was positive by RT-PCR, highlighting the importance of considering COVID-19 in patients with GBS.

SUMMARY

A 53-year old female patient presented with 3 days of progressive weakness and numbness. GBS was considered the most likely diagnosis. In the work-up of GBS, MRI of the brachial plexus revealed incidental findings indicative of COVID-19 pneumonia. Follow- up CT revealed bilateral peripheral consolidations and ground-glass opacities in both lungs. The patient had high C-reactive protein levels and a positive RT-PCR for SARS-CoV-2, but did not have any other symptoms typically associated with COVID-19. The patient was placed in isolation and received hydroxychloroquine and azithromycin. Two weeks later, the patient showed improvement in neurologic findings. The authors conclude that attention must be paid to the subtle clinical findings of COVID-19 in newly diagnosed patients with GBS.

PSYCHOPHYSICAL OLFACTORY TESTING IN COVID-19: IS SMELL FUNCTION REALLY IMPAIRED IN NEARLY ALL PATIENTS?

Mariño-Sánchez F, Santamaría A, de Los Santos G, Alobid I, Mullol J.. Int Forum Allergy Rhinol. 2020 Jun 4. doi: 10.1002/alr.22639. Online ahead of print.
Level of Evidence: Other

BLUF

Since previous studies have shown that the University of Pennsylvania Smell Identification Test (UPSIT) produces inadequate results in Iranian populations due to cultural differences, authors from Spain challenge [Moein et al. 2020's](https://pubmed.ncbi.nlm.nih.gov/32301284/) conclusion that 98% of Iranian COVID-19 positive patients had anosmia as measured by the UPSIT. The authors note that while olfactory dysfunction commonly occurs in viral infections, clinicians should account for cultural and regional differences in olfactory differentiation when using the UPSIT to clinically test for anosmia in suspected COVID-19 cases.

PREGNANT PERSONS

MATERNAL AND NEONATAL OUTCOMES ASSOCIATED WITH COVID-19 INFECTION: A SYSTEMATIC REVIEW

Smith V, Seo D, Warty R, Payne O, Salih M, Chin KL, Ofori-Asenso R, Krishnan S, da Silva Costa F, Vollenhoven B, Wallace E.. PLoS One. 2020 Jun 4;15(6):e0234187. doi: 10.1371/journal.pone.0234187. eCollection 2020.
Level of Evidence: 2

BLUF

Researchers in Victoria, Australia conducted a systematic review across Pubmed, Ovid Medline, and EMBASE from 11/1/2019 - 3/28/2020. A total of 73 articles were identified with 9 meeting the inclusion criteria (n=92 COVID-19 positive women) (Figure 1). The authors found that of pregnant mothers with COVID-19, 64% were symptomatic, 76.6% of RT-PCR tests were positive, 8.7% had pneumonia diagnosed with CT, and there were no reports of maternal mortality or confirmed vertical transmission (Table 2). Results further suggest that in cases of COVID-19 maternal and neonate mortality rates are low, mothers may present with fewer symptoms, and the incidence of pre-term birth, low birth weight, C-section, and NICU may be increased (Figure 3).

ABSTRACT

BACKGROUND: COVID-19 has created an extraordinary global health crisis. However, with limited understanding of the effects of COVID-19 during pregnancy, clinicians and patients are forced to make uninformed decisions.
OBJECTIVES: To systematically evaluate the literature and report the maternal and neonatal outcomes associated with COVID-19.
SEARCH STRATEGY: PubMed, MEDLINE, and EMBASE were searched from November 1st, 2019 and March 28th, 2020.
SELECTION CRITERIA: Primary studies, reported in English, investigating COVID-19-positive pregnant women and reporting their pregnancy and neonatal outcomes.
DATA COLLECTION AND ANALYSIS: Data in relation to clinical presentation, investigation were maternal and neonatal outcomes were extracted and analysed using summary statistics. Hypothesis testing was performed to examine differences in time-to-delivery. Study quality was assessed using the ICROMS tool.
MAIN RESULTS: Of 73 identified articles, nine were eligible for inclusion (n = 92). 67.4% (62/92) of women were symptomatic at presentation. RT-PCR was inferior to CT-based diagnosis in 31.7% (26/79) of cases. Maternal mortality rate was 0% and only one patient required intensive care and ventilation. 63.8% (30/47) had preterm births, 61.1% (11/18) fetal distress and 80% (40/50) a Caesarean section. 76.92% (11/13) of neonates required NICU admission and 42.8% (40/50) had a low birth

weight. There was one indeterminate case of potential vertical transmission. Mean time-to-delivery was 4.3+-3.08 days (n = 12) with no difference in outcomes (p>0.05).
CONCLUSIONS: COVID-19-positive pregnant women present with fewer symptoms than the general population and may be RT-PCR negative despite having signs of viral pneumonia. The incidence of preterm births, low birth weight, C-section, NICU admission appear higher than the general population.

FIGURES

Descriptive statistics	(n)/N, summary statistic
Age, yr (mean;SD)	(36) 30.31 ± 3.80
Gestational age at presentation	(27) 35.39 ± 3.51
Stage of pregnancy	(27)
1st trimester	0
2nd trimester	2 (7.41%)
3rd trimester	25 (92.59%)
Symptomatic on presentation	(92) 62 [67.4%]
Fever on admission	(92) 57 [61.96%]
Cough	(92) 35 (38.04%)
Dyspnoea	(83) 10 [12.05%]
Malaise/fatigue	(82) 25 [30.49%]
Myalgia	(28) 6 [21.43]
Sore throat	(50) 6 [12.0%]
Nasal congestion	(4) 2 [50%]
Diarrhoea	(38) 4 [10.43%]
Lymphopenia	(69) 46 [66.67%]
Maternal Investigations	
CRP, mg/L (median; SD)	(10) 18.39 (±9.46)
RT-PCR performed	(92) 84 [91.3%]
RT-PCR result positive	(84) 66 [78.6%]
Imaging CT performed	(79) 79 [100%]
Pneumonia found from CT	(79) 78 [98.73%]
Maternal Outcomes	
Gestation at delivery, weeks	(13) 37.47 (±1.45)
Pre-term delivery*	(47) 30 [63.83%]
<37 weeks	(13) 6 (46.15%)
<34 weeks	(0) 0 (0%)
Days between symptom and delivery	(12) 4.33 (± 3.08)
ICU admission	(23) 1 (4.35%)
Mode of delivery	(50)
Caesarean section	40 [80.0%]
Vaginal	3 [6.0%]
On-going pregnancy	7 [14.00%]
Symptomatic post-delivery	(72) 28 [38.89%]
Fetal distress (4 ongoing pregnancy)	(18) 11 (61.11%)
Perinatal mortality	(51) [3.92%]
Neonatal Outcomes	
Birthweight (mean, SD)	(21) 2743.81 (± 676.34)
Birthweight <2500gm	(21) 9 (42.86%)
APGAR recorded*	(33) 32 (96.97%)
APGAR 1 min*, (median, 25th to 75th)	(32) 9 (8–10)
Apgar <7 at 1 min	0
APGAR 5 min*, (median, 25th to 75th)	(23) 10 (9–10)
Apgar <7 at 5 min	0
NICU admission *	(13) 11 (76.92%)
Neonate symptomatic of D1*	(23) 12 (52.17%)
Diagnosed with COVID-19*	(21) 1 (4.76%)

NA–Not available.

*ongoing pregnancy excluded, n—number of cases, N—total numbers of pregnancies in analysis

https://doi.org/10.1371/journal.pone.0234187.t002

Table 2. Summary statistical analyses and outcome measures.

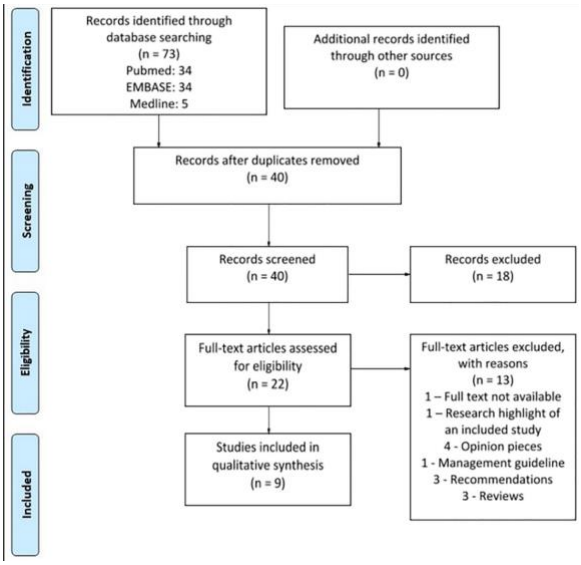

Figure 1: PRISMA Flow Diagram

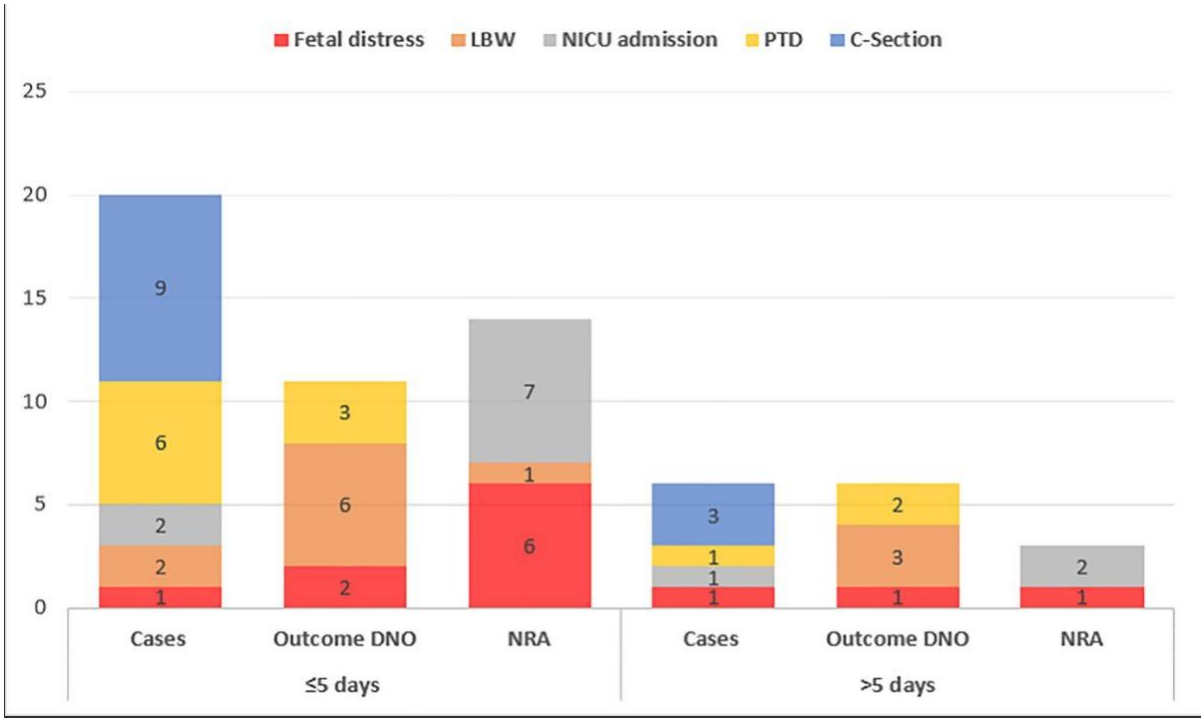

Figure 1: PRISMA Flow Diagram

PEDIATRICS

INCIDENCE OF COVID-19 IN PEDIATRIC SURGICAL PATIENTS AMONG 3 US CHILDREN'S HOSPITALS

Lin EE, Blumberg TJ, Adler AC, Fazal FZ, Talwar D, Ellingsen K, Shah AS.. JAMA Surg. 2020 Jun 4. doi: 10.1001/jamasurg.2020.2588. Online ahead of print.
Level of Evidence: 3

BLUF

This retrospective study performed by researchers from three pediatric hospitals in the United States analyzed the incidence of COVID-19 detected during pre-operative screening of 1,295 pediatric surgical patients. They determined that the overall incidence was 0.93%, there was great variability in the case rate between the hospitals, and that half of the those testing positive for SARS-CoV-2 were asymptomatic (Table 2).

Characteristic	RT-PCR, No./total No. (%)		*P* value
	Positive (n = 12)	Negative (n = 1283)	
Age, mean (SD), y	11.25 (6.39)	7.32 (5.98)	.03
Male	8/12 (66.67)	708/1282 (55.23)	.43
Race			
White	9/12 (75.00)	831/1282 (64.82)	.76
Black	1/12 (8.33)	148/1282 (11.54)	
Other[a]	2/12 (16.67)	303/1282 (23.63)	
Hispanic	2/12 (16.67)	334/1236 (27.02)	.42
ASA physical status classification system			
1	1/10 (10.00)	282/1268 (22.24)	.78
2	5/10 (50.00)	409/1268 (32.26)	
3	3/10 (30.00)	460/1268 (36.28)	
4	1/10 (10.00)	114/1268 (8.99)	
5	0	3/1268 (0.24)	
ASA emergent	6/12 (50.00)	179/1283 (13.95)	.001
Inpatient[b]	3/12 (25.00)	341/1261 (27.04)	.87
Preoperative symptoms[c]			
Any symptom	6/12 (50)	157/1283 (12.24)	.001
Cough	1/12 (8.33)	51/1186 (4.30)	.41
Fever	3/12 (25.00)	72/1077 (6.69)	.04
Rhinorrhea	2/12 (16.67)	34/1204 (2.82)	.047
Diarrhea	1/12 (8.33)	34/689 (4.93)	.46
Conjunctivitis	0/12 (0.00)	3/989 (0.30)	.96
Travel outside US	0	6/740 (0.81)	.76
Travel outside region	0	10/320 (3.13)	.59
Known exposure to COVID-19	2/10 (20.0)	12/715 (1.68)	.001

Table 2. Abbreviations: ASA, American Society of Anesthesiologists; COVID-19, coronavirus disease 2019; RT-PCR, reverse transcriptase–polymerase chain reaction. Footnotes: a - The other category included Asian, Native Hawaiian or other Pacific Islander, American Indian or Alaska Native, other, or declined to answer. b - Inpatient defined as having been admitted to the hospital 2 or more days before surgery. c - Patient may have more than 1 symptom. If symptom was not explicitly mentioned, this was treated as missing data.

UNDERSTANDING THE PATHOLOGY

MYOCARDITIS DETECTED AFTER COVID-19 RECOVERY

Sardari A, Tabarsi P, Borhany H, Mohiaddin R, Houshmand G.. Eur Heart J Cardiovasc Imaging. 2020 May 27:jeaa166. doi: 10.1093/ehjci/jeaa166. Online ahead of print.
Level of Evidence: 5

BLUF

Physicians in Iran and the United Kingdom describe a case of myocarditis after clinical and RT-PCR resolution of COVID-19. The patient tested negative for known common causes of myocarditis, such as Coxsackie, Parvovirus B19, Epstein–Barr, and human herpesvirus, suggesting that SARS-CoV-2 infection may be associated with myocarditis.

SUMMARY

Physicians describe the case of a 31-year-old man, discharged 3 weeks prior following COVID-19 pneumonia, who presented with dyspnea on exertion and low-grade fever. He had no other significant past medical history. At previous admission, he tested positive for SARS-CoV-2 (by RT-PCR), with computed tomography (CT) and lab findings supportive of COVID-19 diagnosis. He had a normal high-sensitivity troponin T of <0.03 ng/mL. He was discharged in good condition with 2 negative RT-PCRs and resolution of lung sequelae on CT.

On current presentation, echocardiography and cardiac magnetic resolution revealed findings suggestive of active myocarditis. Vitals, 12-lead ECG, and lab findings, including troponin, were otherwise unremarkable except for 37.8°C axillary temperature. The authors suggest the patient's myocarditis may have been a result of residual inflammation from SARS-CoV-2 infection and that cardiac involvement may be overlooked in COVID-19 pneumonia.

COVID-19 AND RENIN-ANGIOTENSIN SYSTEM INHIBITION - ROLE OF ANGIOTENSIN CONVERTING ENZYME 2 (ACE2) - IS THERE ANY SCIENTIFIC EVIDENCE FOR CONTROVERSY?

Aleksova A, Ferro F, Gagno G, Cappelletto C, Santon D, Rossi M, Ippolito G, Zumla A, Beltrami AP, Sinagra G.. J Intern Med. 2020 May 27. doi: 10.1111/joim.13101. Online ahead of print.
Level of Evidence: Other

BLUF

This is a review of the role of angiotensin converting enzyme 2 (ACE2) in SARS-CoV-2 pathogenesis and the mechanisms of acute lung injury and myocardial injury during COVID-19 infection (figure 1). Given the proven mortality benefit of ACE inhibitors and angiotensin receptor blockers (ARBs) for patients with cardiovascular disease, and the lack of data contraindicating these medications during COVID-19 infection, the authors conclude that these medications should be continued in COVID-19 patients.

ABSTRACT

Renin-angiotensin system (RAS) blockers are extensively used worldwide to treat many cardiovascular disorders, where they are effective in reducing both mortality and morbidity. These drugs are known to induce an increased expression of Angiotensin Converting Enzyme 2 (ACE2). ACE2 acts as receptor for the novel SARS-Coronavirus-2 (SARS-CoV-2) which raising the important issue of possible detrimental effects that RAS blockers could exert on the natural history and pathogenesis of the COronaVIrus Disease 19 (COVID-19) and associated excessive inflammation, myocarditis, and cardiac arrhythmias. We review the current knowledge on the interaction between SARS-CoV-2 infection and RAS blockers and suggest a scientific rationale for continuing RAS blockers therapy in patients with COVID-19 infection.

FIGURES

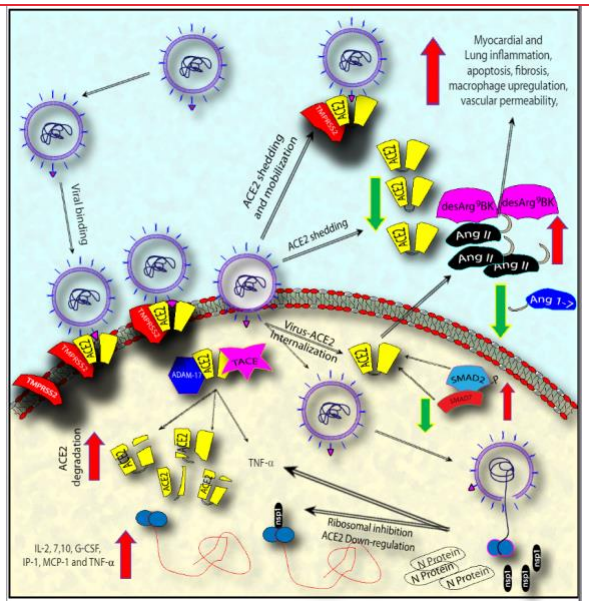

Figure 1. The figure summarizes SARS-CoV, and presumably SARS-CoV-2, confirmed and hypothesized mechanism of viral binding, internalization and shedding via ACE2 interactions, as well as the successive downregulative effect on ACE2 and the resulting pathogenic effect on lung and cardiac tissues.

Abbreviations: Angiotensin converting enzyme 2 (ACE2); Angiotensin (Ang); Angiotensin 1-7 (Ang 1-7); Transmembrane protease, serine 2 (TMPRSS2); ADAM metallopeptidase domain 17 (ADAM-17); Tumor necrosis factor a converting enzyme (TACE); SMAD family member2, 7 (SMAD2, SMAD7); Non structural protein 1 (nsp-1); SARS-CoV nucleocapsid (N) protein (N protein); Interleukin-2, 7, 10 (IL-2, 7,10); Granulocyte colony stimulating factor (G-CSF); Transforming growth factor alpha (TNF-alpha); Monocyte chemoattractant protein 1 (MCP-1).

IN SILICO

MECHANOBIOLOGY PREDICTS RAFT FORMATIONS TRIGGERED BY LIGAND-RECEPTOR ACTIVITY ACROSS THE CELL MEMBRANE

Carotenuto AR, Lunghi L, Piccolo V, Babaei M, Dayal K, Pugno N, Zingales M, Deseri L, Fraldi M.. J Mech Phys Solids. 2020 Aug;141:103974. doi: 10.1016/j.jmps.2020.103974. Epub 2020 May 22.
Level of Evidence: Other

BLUF

Researchers use mathematical modeling to explain the association between activated G-protein-coupled receptors (GPCRs) and thickened areas of the cell membrane by using a mechanobiological approach. Lipid rafts commonly serve as entry points for viruses, so a deeper understanding of the mechanics involved in the formation of these lipid rafts could help to understand the pathology of COVID-19.

ABSTRACT

Clustering of ligand-binding receptors of different types on thickened isles of the cell membrane, namely lipid rafts, is an experimentally observed phenomenon. Although its influence on cell's response is deeply investigated, the role of the coupling between mechanical processes and multiphysics involving the active receptors and the surrounding lipid membrane during ligand-binding has not yet been understood. Specifically, the focus of this work is on G-protein-coupled receptors (GPCRs), the widest group of transmembrane proteins in animals, which regulate specific cell processes through chemical signalling pathways involving a synergistic balance between the cyclic Adenosine Monophosphate (cAMP) produced by active GPCRs in the intracellular environment and its efflux, mediated by the Multidrug Resistance Proteins (MRPs) transporters. This paper develops a multiphysics approach based on the interplay among energetics, multiscale geometrical changes and mass balance of species, i.e. active GPCRs and MRPs, including diffusion and kinetics of binding and unbinding. Because the obtained energy depends upon both the kinematics and the changes of species densities, balance of mass and of linear momentum are coupled and govern the space-time evolution of the cell membrane. The mechanobiology involving remodelling and change of lipid

ordering of the cell membrane allows to predict dynamics of transporters and active receptors -in full agreement with experimentally observed cAMP levels- and how the latter trigger rafts formation and cluster on such sites. Within the current scientific debate on Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) and on the basis of the ascertained fact that lipid rafts often serve as an entry port for viruses, it is felt that approaches accounting for strong coupling among mechanobiological aspects could even turn helpful in better understanding membrane-mediated phenomena such as COVID-19 virus-cell interaction.

IN ANIMAL MODELS

FEATURES OF ENTERIC DISEASE FROM HUMAN CORONAVIRUSES: IMPLICATIONS FOR COVID-19

Cimolai N.. J Med Virol. 2020 May 28. doi: 10.1002/jmv.26066. Online ahead of print.
Level of Evidence: Other

BLUF

A researcher from British Columbia presents a comparative review of enteric coronaviruses in both animal and human models. The author suggests that coronaviruses may have trophism for gastrointestinal cell types across viral species. It was also reported that prolonged stool detection of endemic coronavirus RNA is correlated with mildly increasing patient co-morbidities This study aims to bring attention to the prevalence of all coronaviruses and their enteric sequelae and prompt consideration of these factors when assessing institutional protocols for preventing disease transmission, reinforcing already widely accepted standards of 'universal precautions'. The author suggests that more research is required regarding SARS-CoV-2's enteric trophism in order for specific safety protocols to be changed.

ABSTRACT

Coronaviruses have long been studied in both human and veterinary fields. Whereas the initial detection of endemic human respiratory coronaviruses was problematic, detection of these and newly discovered human coronaviruses has been greatly facilitated with major advances in the laboratory. Nevertheless, technological factors can affect the accuracy and timeliness of virus detection. Many human coronaviruses can be variably found in stool samples. All human coronaviruses have been variably associated with symptoms of gastroenteritis. Coronaviruses can occasionally be cultured from enteric specimens, but most detection is accomplished with genetic amplification technologies. Excretion of viral RNA in stool can extend for a prolonged period. Culture-positive stool samples have been found to exceed a fourteen day period after onset of infection for some coronaviruses. Virus can also sometimes be cultured from patients' respiratory samples during the late incubation period. Relatively asymptomatic patients may excrete virus. Both viable and non-viable virus can be found in the immediate environment of the patient, the health care worker, and less often the public. These lessons from the past study of animal and human coronaviruses can be extended to presumptions for SARS-CoV-2. Already, the early reports from the COVID-19 pandemic are confirming some concerns. This data has the cumulative potential to cause us to rethink some current and common public health and infection control strategies.

TRANSMISSION & PREVENTION

FACE COVERINGS FOR THE PUBLIC: LAYING STRAW MEN TO REST

Greenhalgh T.. J Eval Clin Pract. 2020 May 26:e13415. doi: 10.1111/jep.13415. Online ahead of print.
Level of Evidence: Other

BLUF

In this letter, the author responds to two publications arguing against the effectiveness of laypeople wearing masks, highlighting that much of the research regarding mask-use only addresses protection for the person wearing the mask without considering the “source control” that masks provide by preventing large droplet aerosolization by the user. They also argue that masks should be recommended even in the absence of randomized control trial data on their efficacy, noting that other sources of evidence are often needed to comment on the effectiveness of large scale public health measures.

ABSTRACT

Background This article responds to one by Graham Martin and colleagues, who offered a critique of my previous publications on face coverings for the lay public in the Covid-19 pandemic. Their paper reflects criticisms that have been made of face coverings policies more generally. Method Narrative rebuttal. Results I address charges that my coauthors and I had misapplied the precautionary principle; drawn conclusions that were not supported by empirical research; and failed to take account of potential harms But before that, I remind my critics that the evidence on face coverings goes beyond the contested trials and observational studies they place centre stage. I set out some key findings from basic science, epidemiology, mathematical modelling, case studies, and natural experiments, and use this rich and diverse body of evidence as the backdrop for my rebuttal of their narrowly framed objections. I challenge my critics' apparent assumption that a particular kind of systematic review should be valorised over narrative and real-world evidence, since stories are crucial to both our scientific understanding and our moral imagination. Conclusion I conclude by thanking my academic adversaries for the intellectual sparring match, but exhort them to remember our professional accountability to a society in crisis. It is time to lay straw men to rest and embrace the full range of evidence in the context of the perilous threat the world is now facing.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

ON SETTING EXPECTATIONS FOR A SARS-COV-2 VACCINE

Canaday DH, Gravenstein S.. Clin Infect Dis. 2020 Jun 4:ciaa726. doi: 10.1093/cid/ciaa726. Online ahead of print.
Level of Evidence: Other

BLUF

An expert opinion by American physicians points out that well-established vaccines against pathogens such as respiratory syncytial virus (RSV), streptococcus species, and seasonal influenza only have modest efficacies maxing out at 60-70%. They explain that an initial SARS-CoV-2 vaccine will likely be less effective than those detailed above due to our naive immune systems. An ideal vaccine would not only prevent infection but also mitigate evasion of cell mediated immunity (CMI) and this is difficult to execute given the time-sensitive characteristics of the COVID-19 pandemic, as is seen in the current vaccines approaching clinical trials. Overall, the authors expect vaccine development to continue as an iterative process and believe that a live attenuated vaccine could be optimal if proven to be safe. However, they encourage additional clinical trials to better understand the immunologic response.

ABSTRACT

The global coronavirus pandemic is unlike any other since 1918. A century of dramatic medical advances has produced a public expectation that the medical field will rapidly provide solutions to restore normalcy. In under 6 months, since SARS-CoV-2 was identified, the massive international effort to develop a SARS-CoV-2 vaccine has generated more than 140 vaccines in different stages of development with 9 already recruiting into clinical trials posted on clinicaltrials.gov. The long-term strategy to handle COVID-19 will almost certainly rely on vaccines. But, what type of protection can we realistically expect to achieve from vaccines and when?

SARS-COV-2 HUMAN CHALLENGE TRIALS: TOO RISKY, TOO SOON

Dawson L, Earl J, Livezey J.. J Infect Dis. 2020 Jun 4:jiaa314. doi: 10.1093/infdis/jiaa314. Online ahead of print.

Level of Evidence: Other

BLUF

US bioethicists with experience in vaccine challenge trials assert that a SARS-CoV-2 challenge study would be unethical at this time. They are concerned that our current knowledge is inadequate to manage study risks and that participation may inadvertently disadvantage vulnerable groups or select volunteers who underestimate risks. They warn that poor outcomes in a challenge study could undermine public confidence in COVID-19 research and the public health response.

SUMMARY

The authors recommend the following conditions be met to alleviate concern for human SARS-CoV-2 vaccine challenge trials:

- Better characterization of risk factors for severe disease and mortality from SARS-CoV-2 infection to screen out high-risk volunteers
- Availability of a proven effective treatment for COVID-19
- Improved clarity on protective effects of immunity to inform the goal of a vaccine, guiding dosing and endpoint selection
- A public engagement strategy to inform participants of the challenge study and its risks

PREVENTION IN THE COMMUNITY

THE NATURAL HISTORY AND TRANSMISSION POTENTIAL OF ASYMPTOMATIC SARS-COV-2 INFECTION

Chau NVV, Thanh Lam V, Thanh Dung N, Yen LM, Minh NNQ, Hung LM, Ngoc NM, Dung NT, Man DNH, Nguyet LA, Nhat LTH, Nhu LNT, Ny NTH, Hong NTT, Kestelyn E, Dung NTP, Xuan TC, Hien TT, Thanh Phong N, Tu TNH, Geskus RB, Thanh TT, Thanh Truong N, Binh NT, Thuong TC, Thwaites G, Tan LV; OUCRU COVID-19 research group.. Clin Infect Dis. 2020 Jun 4:ciaa711. doi: 10.1093/cid/ciaa711. Online ahead of print.
Level of Evidence: 3

BLUF

This prospective cohort study of 14,000 people, conducted at a quarantine center in Ho Chi Minh City, Vietnam, included 30 subjects who were confirmed to have SARS-CoV-2 with reverse transcriptase (RT)-PCR from nasopharyngeal swabs and saliva samples between 10 March and 4 April 2020 (Table 1). Authors concluded that 13 (43%) of those who tested positive were completely asymptomatic and would not have been identified as infected with SARS-CoV-2 without strict quarantine testing measures, suggesting the importance of isolation, even without symptoms, to reduce transmission during this pandemic.

ABSTRACT

BACKGROUND: Little is known about the natural history of asymptomatic SARS-CoV-2 infection or its contribution to infection transmission.
METHODS: We conducted a prospective study at a quarantine center for COVID-19 in Ho Chi Minh City, Vietnam. We enrolled quarantined people with RT-PCR-confirmed SARS-CoV-2 infection, collecting clinical data, travel and contact history, and saliva at enrolment and daily nasopharyngeal throat swabs (NTS) for RT-PCR testing. We compared the natural history and transmission potential of asymptomatic and symptomatic individuals.
RESULTS: Between March 10th and April 4th, 2020, 14,000 quarantined people were tested for SARS-CoV-2; 49 were positive. Of these, 30 participated in the study: 13(43%) never had symptoms and 17(57%) were symptomatic. 17(57%) participants acquired their infection outside Vietnam. Compared with symptomatic individuals, asymptomatic people were less likely to have detectable SARS-CoV-2 in NTS samples collected at enrolment (8/13 (62%) vs. 17/17 (100%) P=0.02). SARS-CoV-2 RNA was detected in 20/27 (74%) available saliva; 7/11 (64%) in the asymptomatic and 13/16 (81%) in the symptomatic group (P=0.56). Analysis of the probability of RT-PCR positivity showed asymptomatic participants had faster viral clearance than symptomatic participants (P<0.001 for difference over first 19 days). This difference was most pronounced during the first week of follow-up. Two of the asymptomatic individuals appeared to transmit the infection to up to four contacts.
CONCLUSIONS: Asymptomatic SARS-CoV-2 infection is common and can be detected by analysis of saliva or NTS. NTS viral loads fall faster in asymptomatic individuals, but they appear able to transmit the virus to others.

FIGURES

Table 1:Baseline characteristics of the study participants

	All (N=30)	Symptomatic group (N=17)	Asymptomatic group (N=13)
Age in years, median (range)	29 (16–60)	27 (18–58)	30 (16–60)
Gender (female/male), n/n	15/15	9/8	6/7
Arriving in Vietnam from abroad, n(%)	16 (53)	10 (59)	6 (47)
Locally acquired infection, n(%)	14 (47)	7 (41)	7 (53)
Nationality, n(%)			
Vietnamese	19 (63)	12 (71)	7 (53)
Others	11 (37)[#]	5 (29)[^^]	6 (46)[&]
Days from confirmed diagnosis to enrolment, median (range)	2 (2 – 5)	2 (0 – 3)	2 (1 – 5)
Days from admission to enrolment, median (range)	1 (0 – 2)	1 (0 – 2)	1 (0 – 2)
Duration of stay (days)	16 (9-26)	16 (11-26)	15 (9-23)
Laboratory results[$], median (range) /normal range			
White-cell count ($\times 10^3$per µl)	5.16 (3.1–9.9)/(4-11)	5.0 (3.4–8.3)	5.51 (3.15–4.83)
Lymphocyte counts ($\times 10^3$per µl)	1.65 (0.56-2.94)/(1.5-4)	1.47 (0.56-2.94)	1.88 (1.17-2.5)
Hemoglobin ((g/dl)	14.3 (10–17.3)/13-18)	14.4 (11.6–16.8)	14.15 (10–17.3
Hematocrit (%)	35.5 (28.5–42.3)/(37-52)	36.5 (28.5–42.3)	36 (35.78–42.27)
Platelet count (per µl)	257 (130–414)/(150-450)	249 (130–414)	265.5 (174–321)
Glucose (mmol/liter)	85 (6 –340)*/(70-130)	84.2 (68–340)[¥]	101.65 (64–146)[£]
Creatinine (mg/dl)	1.0 (0.9–1.5)^/(0.5-1.2)	1.0 (0.9–12.4)[¢]	1 (0.96–1.54)[£]
Aspartate aminotransferase (U/liter)	22.5 (15.4–56.8)*/(<40)	22.5(17.4–56.8)[¢]	17.4 (15.4–32.4)[£]
Alanine aminotransferase (U/liter)	22.3 (9.7-44.9)/(<37)	24 (10.2–34.8)[¢]	19.15(9.7–44.9)[£]
Clinical signs/symptoms**			
Fever, n(%)	8 (27)	8 (47)	NA
Cough, n(%)	10 (33)	10 (59)	NA
Rhinorrhea, n(%)	3 (10)	3 (18)	NA
Fatigue, n(%)	1 (3)	1 (6)	NA
Diarrhea, n(%)	3 (10)	3 (18)	NA
Sore throat, n(%)	6 (20)	6 (36)	NA
Muscle pain, n(%)	3 (10)	3 (18)	NA
Headache, n(%)	2 (7)	2 (12)	NA
Abdominal pain, n(%)	1 (3)	1 (6)	NA
Lost sense of smell, n(%)	3 (10)	3 (18)	NA
Comorbidity, n(%)	2 (7)	2 (12)[##]	0

ASSOCIATION OF STAY-AT-HOME ORDERS WITH COVID-19 HOSPITALIZATIONS IN 4 STATES

Sen S, Karaca-Mandic P, Georgiou A.. JAMA. 2020 May 27. doi: 10.1001/jama.2020.9176. Online ahead of print.
Level of Evidence: 3

BLUF

This retrospective study evaluated four states (Colorado, Minnesota, Ohio, and Virginia) that had hospitalization data from seven consecutive days before and 17 consecutive days after the implementation of stay-at-home orders, revealing that these efforts were effective in preventing hospitalizations from growing at an exponential rate (Figure). This shows the effectiveness and value of social distancing measures in minimizing the spread of COVID-19.

FIGURES

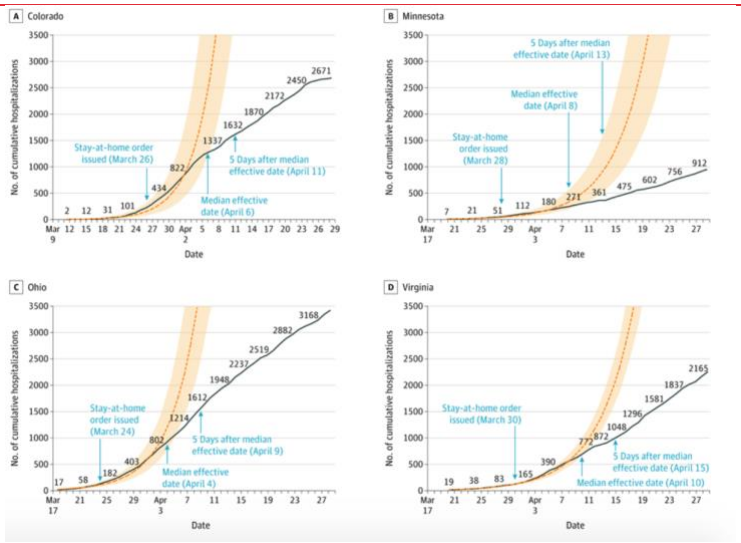

Figure: Projected vs observed COVID-19 hospitalizations before and after stay-at-home orders, March 10 through April 28, 2020

DIGITAL SMARTPHONE TRACKING FOR COVID-19: PUBLIC HEALTH AND CIVIL LIBERTIES IN TENSION

Cohen IG, Gostin LO, Weitzner DJ.. JAMA. 2020 May 27. doi: 10.1001/jama.2020.8570. Online ahead of print.
Level of Evidence: 5

BLUF

This article discusses the trade-off between various tracking strategies used to notify citizens who have come in close contact with a COVID-19 patient, in a public health effort to prevent spread of the disease. Debated approaches include manual contact tracing vs. digital tracing via smart phones, as well as centralized reporting to public health authorities vs. decentralized reporting to the user only who could then choose to share the information with health officials. The authors conclude that what is best for public health is often at odds privacy and autonomy. They state that given the current evidence for these methods, it would be premature to mandate their use and that incentivizing their use is the likely path forward.

MANAGEMENT

ACUTE CARE

GLYCYRRHETINIC ACID AND ITS DERIVATIVES AS POTENTIAL ALTERNATIVE MEDICINE TO RELIEVE SYMPTOMS IN NON-HOSPITALIZED COVID-19 PATIENTS

Ding H, Deng W, Ding L, Ye X, Yin S, Huang W.. J Med Virol. 2020 May 27. doi: 10.1002/jmv.26064. Online ahead of print.
Level of Evidence: Other

BLUF

A non-hospitalized 62-year-old female patient in Wuhan with clinically diagnosed COVID-19 infection (confirmed after recovery with antibody testing) showed improvement in symptoms of fever and shortness of breath with a week long regimen of a diammonium glycyrrhizinate, a steroid-like molecule consisting of a traditional Chinese herb, and Vitamin C. The authors suggest this medication combination may be useful as an alternative treatment for patients who may not have access to traditional hospitals or standard care.

ABSTRACT

SARS-CoV-2 is highly infectious, and infection by this virus results in COVID-19, manifesting predominantly respiratory symptoms in the lower respiratory system. Detection of viral genomic materials by RT-PCR is the gold standard for diagnosis. Suspected COVID-19 patients who had a documented history of exposure and exhibited symptoms, but did not have positive PCR test results, were generally self-quarantined with prescriptions aiming to help attenuate their symptoms. These prescriptions are however neither specific nor highly effective for COVID-19 treatment. Given the rapidly growing pandemic and overwhelmed medical system, the number of self-quarantined patients is increasing. There is an urgent need of alternative medicine to help patients relieve symptoms during self-quarantine, and to potentially help increase their chances of survival and recovery from the infection. We report here a case of COVID-19 that never had a positive PCR test result during disease progression but was confirmed with antibody test post recovery. This patient was self-quarantined and received diammonium glycyrrhizinate, a steroid-like molecule, in combination with Vitamin C as alternative medicine. This patient went through severe COVID-19 but eventually recovered upon the implementation of this treatment regimen, suggesting potential therapeutic effects of diammonium glycyrrhizinate as alternative medicine to help relieve COVID-19 symptoms.

DIAGNOSTIC RADIOLOGY

RECOMMENDATIONS OF THE THORACIC IMAGING SECTION OF THE GERMAN RADIOLOGICAL SOCIETY FOR CLINICAL APPLICATION OF CHEST IMAGING AND STRUCTURED CT REPORTING IN THE COVID-19 PANDEMIC

Vogel-Claussen J, Ley-Zaporozhan J, Agarwal P, Biederer J, Kauczor HU, Ley S, Kühl H, Mueller-Lisse UG, Persigehl T, Schlett CL, Wormanns D, Antoch G, Hamer OW.. Rofo. 2020 May 26. doi: 10.1055/a-1174-8378. Online ahead of print.
Level of Evidence: 4

BLUF

On April 29, 2020, the Thoracic Imaging Section of the German Radiological Society created recommendations for physicians on the use of imaging during the COVID-19 pandemic based on a series of retrospective studies in China and Italy. They describe the role of imaging in the COVID-19 pandemic to include:

- “Support of diagnosis"
- "Assessment of the severity of lung parenchyma changes and monitoring"
- "Detection of complications"
- "Detection of ‘incidental’ COVID-19 pneumonia"
- "Triage in an environment with limited resources.”
- The authors also recommend uniform CT reporting of suspected COVID-19.

They conclude future research is likely to lead to future revisions.

ABSTRACT

This information provided by the Thoracic Imaging Section of the German Radiological Society is intended to give physicians recommendations on the use of thoracic imaging procedures in the context of the current COVID-19 pandemic. It represents the consensus of the authors based on the previous scientific knowledge and is intended to provide guidance for unified, structured CT reporting if COVID-19 pneumonia is suspected. The recommendations presented correspond to state of knowledge at the time of print and will be updated according to the results of ongoing and future scientific studies. KEY POINTS:: COVID-19. chest imaging. German Radiological Society.
CITATION FORMAT: Vogel-Claussen J, Ley-Zaporozhan J, Agarwal P et al. Recommendations of the Thoracic Imaging Section of the German Radiological Society for clinical application of chest imaging and structured CT reporting in the COVID-19 pandemic. Fortschr Rontgenstr 2020; DOI: 10.1055/a-1174-8378.

CRITICAL CARE

ALTERNATIVES TO INVASIVE VENTILATION IN THE COVID-19 PANDEMIC

Patel BK, Kress JP, Hall JB.. JAMA. 2020 Jun 4. doi: 10.1001/jama.2020.9611. Online ahead of print.
Level of Evidence: 4

BLUF

In this editorial, pulmonary and critical care specialists in Chicago discuss current data on the utility of noninvasive ventilation (NIV) techniques for management of acute hypoxemic respiratory failure (AHRF), including NIV through face masks, helmets, and high-flow nasal cannula. They indicate that these approaches may prevent the need for intubation in some patients and call for additional research to assess the role for these noninvasive strategies in the management of specific AHRF causes.

NEUROLOGY

ACUTE SYMPTOMATIC SEIZURES IN CRITICALLY ILL PATIENTS WITH COVID-19: IS THERE AN ASSOCIATION?

Hepburn M, Mullaguri N, George P, Hantus S, Punia V, Bhimraj A, Newey CR.. Neurocrit Care. 2020 May 28. doi: 10.1007/s12028-020-01006-1. Online ahead of print.
Level of Evidence: 4

BLUF

The authors report two cases of multifocal seizures in COVID-19 patients in Cleveland, Ohio mid-March 2020. These patients had no history of seizure disorder and the authors hypothesize the seizures were caused by blood-brain barrier breakdown from increased cytokine production. They believe this suggests that acute seizures are possible in COVID-19 patients and that these patients may benefit from continuous electroencephalography (EEG) monitoring (figure 2 and 3).

SUMMARY

Two cases of multifocal seizures were reported in hospitalized patients with COVID-19. Neither of these patients had a history of seizures. Case #1 was a 76-year old male who arrived to the hospital with a Glasgow coma scale of 14. An MRI was conducted which revealed an epidural abscess in his spine that was promptly drained. Two days late, he experiences three focal seizures lasting approximately 30 seconds each. The patient was monitored with continuous EEG (figure 2) and ultimately transferred for further ventilator management. Case #2 was an 82-year old intubated male who was put on continuous EEG (figure 3) after right eyelid and facial twitching were observed. His seizures were most often non-convulsive and progressed to status epilepticus after some time. Seizure frequency improved after treatment with levetiracetam, however his family opted to withdraw life-sustaining support after 20 days in the ICU.

ABSTRACT

BACKGROUND: The coronavirus disease of 2019 (COVID-19) emerged as a global pandemic. Historically, the group of human coronaviruses can also affect the central nervous system leading to neurological symptoms; however, the causative mechanisms of the neurological manifestations of COVID-19 disease are not well known. Seizures have not been directly reported as a part of COVID-19 outside of patients with previously known brain injury or epilepsy. We report two cases of acute symptomatic seizures, in non-epileptic patients, associated with severe COVID-19 disease.

CASE PRESENTATIONS: Two advanced-age, non-epileptic, male patients presented to our northeast Ohio-based health system with concern for infection in Mid-March 2020. Both had a history of lung disease and during their hospitalization tested positive for SARS-CoV-2. They developed acute encephalopathy days into their hospitalization with clinical and electrographic seizures. Resolution of seizures was achieved with levetiracetam.
DISCUSSION: Patients with COVID-19 disease are at an elevated risk for seizures, and the mechanism of these seizures is likely multifactorial. Clinical (motor) seizures may not be readily detected in this population due to the expansive utilization of sedatives and paralytics for respiratory optimization strategies. Many of these patients are also not electrographically monitored for seizures due to limited resources, multifactorial risk for acute encephalopathy, and the risk of cross-contamination. Previously, several neurological symptoms were seen in patients with more advanced COVID-19 disease, and these were thought to be secondary to multi-system organ failure and/or disseminated intravascular coagulopathy-related brain injury. However, these patients may also have an advanced breakdown of the blood-brain barrier precipitated by pro-inflammatory cytokine reactions. The neurotropic effect and neuroinvasiveness of SARS-Coronavirus-2 have not been directly established.
CONCLUSIONS: Acute symptomatic seizures are possible in patients with COVID-19 disease. These seizures are likely multifactorial in origin, including cortical irritation due to blood-brain barrier breakdown, precipitated by the cytokine reaction as a part of the viral infection. Patients with clinical signs of seizures or otherwise unexplained encephalopathy may benefit from electroencephalography monitoring and/or empiric anti-epileptic therapy. Further studies are needed to elucidate the risk of seizures and benefit of monitoring in this population.

MEDICAL SUBSPECIALTIES

CARDIOLOGY

CONSIDERATIONS FOR HEART FAILURE CARE DURING THE CORONAVIRUS DISEASE 2019 (COVID-19) PANDEMIC

DeFilippis EM, Reza N, Donald E, Givertz MM, Lindenfeld J, Jessup M.. JACC Heart Fail. 2020 Jun 2:S2213-1779(20)30273-0. doi: 10.1016/j.jchf.2020.05.006. Online ahead of print.
Level of Evidence: Other

BLUF

This literature review conducted by researchers in New York, Pennsylvania, Massachusetts, Tennessee, and Texas summarizes the cardiac effects of COVID-19 infection in patients with and without pre-existing heart failure (HF) (Figures 1 & 2), and the adjustments required for delivering care to HF patients during the current pandemic. The key findings and recommendations are summarized below.

SUMMARY

Acute Heart Failure in COVID-19

- Type I and 2 myocardial infarctions secondary to COVID-19 infections may result in either the development of HF or the decompensation of pre-existing HF.
- 50% of patients who developed HF secondary to COVID-19 did not have a history of cardiovascular disease or hypertension.
- In resource-limited settings, younger patients and healthcare workers should be prioritized for Extracorporeal Membrane Oxygenation (ECMO) support.

Patients with Chronic Heart Failure with COVID-19:

- Continue use of ACEi/ARB/ARNI (Angiotensin Converting Enzyme inhibitor/Angiotensin receptor blocker/Angiotensin receptor neprilysin inhibitor) therapy.
- Monitor for QT prolongation.
- Use anti-coagulation prophylactically and therapeutically for hospitalized patients.

Special Populations:

- More data is needed for adequate management of hypoxemic respiratory failure management in patients on LVAD support.

- Immunocompromised transplant patients may present with atypical COVID-19 symptoms, and differentiation between viral myocardial infection and transplant rejection may be difficult.

Health Care Delivery:

- Telemedicine is recommended for consults, check-ins, and for provision of services if possible.
- Recommend home measurement of blood pressure, weight, and blood oxygenation
- Utilize home COVID-19 testing as available.
- Reduce volume of non-emergent cardiac testing.
- Increase use of palliative care and hospice.

ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has affected the care of patients with HF who contract COVID-19 as well as those without COVID-19 who have been impacted by the restructuring of health care delivery. Patients with HF and other cardiovascular comorbidities are at risk for severe disease and complications of infection. Similarly, COVID-19 has been demonstrated to cause myocarditis and may be implicated in new-onset cardiomyopathy. During this pandemic, special considerations are needed for patients with advanced HF, including those supported by durable left ventricular assist devices (LVADs) and heart transplant recipients. The purpose of this review is to summarize emerging data regarding the development of HF secondary to COVID-19, COVID-19 infection in patients with advanced HF, and the implications of the pandemic on care for non-infected patients with HF.

FIGURES

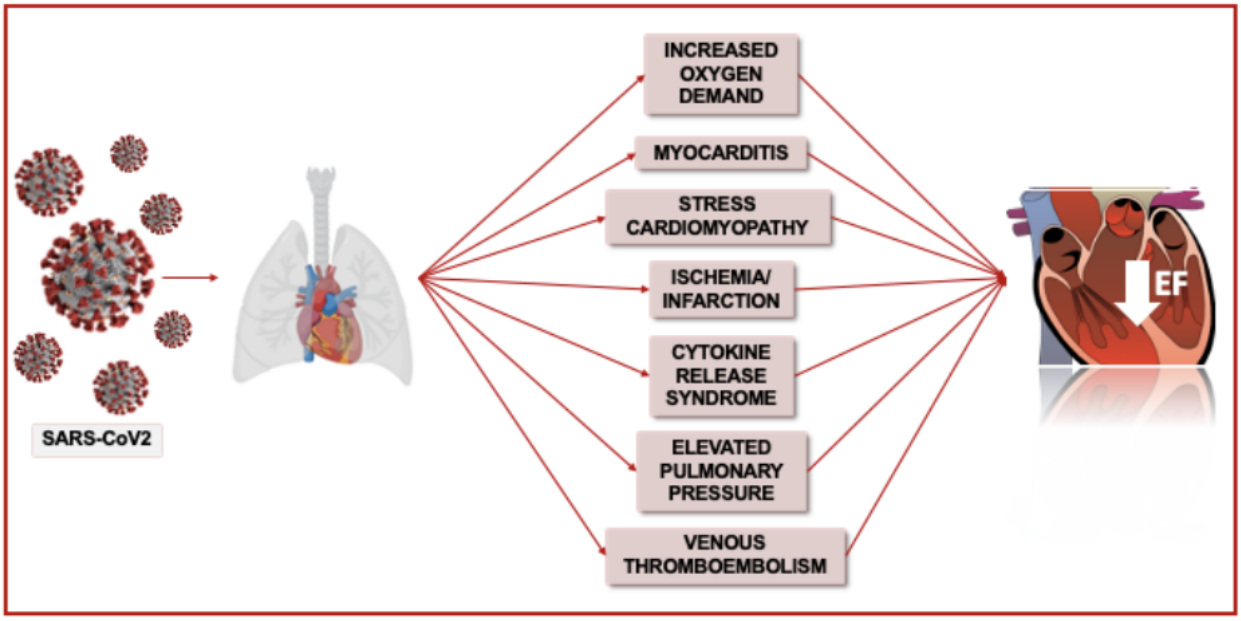

Figure 1. Mechanisms of New or Worsening Heart Failure in Patients with COVID-19
Potential contributing factors and mechanisms of worsening heart failure in patients with COVID-19 include increased oxygen demand, myocarditis, stress cardiomyopathy, ischemia or infarction, cytokine release syndrome, elevated pulmonary pressures, and venous thromboembolism.

HEMATOLOGY AND ONCOLOGY

SCREENING FOR COVID-19 IN ASYMPTOMATIC PATIENTS WITH CANCER IN A HOSPITAL IN THE UNITED ARAB EMIRATES

Al-Shamsi HO, Coomes EA, Alrawi S.. JAMA Oncol. 2020 May 27. doi: 10.1001/jamaoncol.2020.2548. Online ahead of print.
Level of Evidence: 4

BLUF

A case series conducted by physicians at Alzahra Hospital Dubai in the United Arab Emirates, detailed the testing of 85 asymptomatic cancer patients via nasopharyngeal swab polymerase-chain reaction (PCR) and found that seven were positive

for COVID-19. Their findings suggest that universal screening of immunocompromised patients, especially patients on anti-cancer therapy, may be beneficial in mitigating progression to severe disease and preventing further transmission of SARS-CoV-2.

SUMMARY

"Our prospective universal microbiologic screening strategy revealed that 8% (7 of 85) of asymptomatic patients with cancer had COVID-19 at our institution. Asymptomatic cases may not be identified by symptom-based screening, as recommended by the American Society of Clinical Oncology, and such patients may pose particular risk for nosocomial transmission if they are not recognized to have COVID-19. Universal microbiologic screening for SARS-CoV-2 in such high-risk populations may facilitate earlier case identification, and implementation of infection prevention and control strategies. Limitations of this study include a single-center experience, small sample size, and observational design without control group. Further studies are needed to determine the optimal screening frequency for patients undergoing serial anticancer therapy cycles. Universal microbiologic screening for SARS-CoV-2 should be considered in oncology centers for patients undergoing anti-cancer therapy, particularly in regions with a high prevalence of COVID-19."

FIGURES

Characteristic	No. (%)		
	Overall cohort (n = 85)	Asymptomatic with COVID-19 (n = 7)	Asymptomatic without COVID-19 (n = 78)
Age, median (range), y	55 (28-76)	51.6 (40-76)	56 (33-74)
Female	48 (56.5)	5 (71.4)	43 (55.1)
Cancer type			
Breast	25 (29.4)	2 (28.6)	23 (29.5)
Colorectal	22 (25.9)	2 (28.6)	20 (25.6)
Thyroid	10 (11.8)	0	10 (12.8)
Other	28 (32.9)	3 (42.9)	25 (32.1)
Outcomes			
Hospitalization	7 (8.2)	2 (28.6)	5 (6.4)[a]
ICU	2 (2.4)	2 (28.6)	0
Death	1 (1.2)	1 (14.3)	0
Anticancer therapy delay	15 (17.6)	7 (100)	8 (10.3)[a]

Table. Demographic Characteristics and Clinical Outcomes of Patients Screened for COVID-19.

ADJUSTING PRACTICE DURING COVID-19

OPENING HOSPITALS TO MORE PATIENTS DURING THE COVID-19 PANDEMIC-MAKING IT SAFE AND MAKING IT FEEL SAFE

Asch DA.. JAMA Intern Med. 2020 May 27. doi: 10.1001/jamainternmed.2020.2626. Online ahead of print.
Level of Evidence: Other

BLUF

A perspective article from a single clinician at the University of Pennsylvania argued that in order to effectively open up elective clinical procedures, healthcare systems must make patients feel emotionally safe and secure. Key points include:

1. Clinical services that were in demand prior to the pandemic may not be the same ones patients feel they need in a post-pandemic world. Hospitals should be aware of this and react to patient desires.
2. Hospitals cannot take for granted that patients will believe that the hospital or clinical process is safe. Hospitals must be proactive in showing patients that they will be safe, even before patients arrive.
3. Patients have never felt in control in the healthcare setting, and the pandemic has only exacerbated that feeling. Hospitals must actively provide that sense of control to patients, which in large part depends on letting patients know what will happen to them and when.
4. Hospitals must make patients feel safe in a way that is not alarming, depending on the context of each clinical setting. Hospitals must be self-aware of their precautions and safety mechanisms to provide a comforting environment for patients.

SUMMARY

"Hospitals around the US are eager to reopen as the coronavirus 2019 (COVID-19) pandemic runs its course. Having curtailed the services that used to support their narrow margins, many now face financial trouble. For example, the Mayo Clinic announced furloughs and hour reductions for 30 000 workers to stem a projected $3 billion loss.1 And of course hospitals are fundamentally in the business of serving the health care needs of their communities. Those needs did not press the pause button just because hospitals did.

Outside of health care, discussions about reopening the economy focus on how to return to work. However, the real engines of the economy are not the producers of goods and services but the consumers of them. Stories from hospitals trying to restart clinical services suggest that many patients do not yet feel that it is safe to come back. And so the need to make clinical services safe is matched by the equally critical need to make them feel safe."

ACUTE CARE

NECK CIRCUMFERENCE AS RELIABLE PREDICTOR OF MECHANICAL VENTILATION SUPPORT IN ADULT INPATIENTS WITH COVID-19: A MULTICENTRIC PROSPECTIVE EVALUATION

Di Bella S, Cesareo R, De Cristofaro P, Palermo A, Sanson G, Roman-Pognuz E, Zerbato V, Manfrini S, Giacomazzi D, Dal Bo E, Sambataro G, Macchini E, Quintavalle F, Campagna G, Masala R, Ottaviani L, Del Borgo C, Ridola L, Leonetti F, Berlot G, Luzzati R.. Diabetes Metab Res Rev. 2020 Jun 2:e3354. doi: 10.1002/dmrr.3354. Online ahead of print.
Level of Evidence: 3

BLUF

A cohort study conducted by a group of physicians at Azienda Sanitaria Universitaria Giuliano Isontina and Santa Maria Goretti Hospital in Italy involving patients with COVID-19 enrolled between 25 March and 7 April 2020, found that neck circumference was significantly associated with risk for invasive mechanical ventilation (95% CI:1.120-1.417; p<0.001), when adjusted for age, sex, diabetes, hypertension, COPD, and even BMI, suggesting that neck circumference may be a useful independent predictor upon admission for invasive mechanical ventilation in COVID-19 patients.

ABSTRACT

AIMS: COVID-19 is especially severe for elderly subjects with cardio-metabolic and respiratory comorbidities. Neck circumference (NC) has been shown to be strongly related to cardiometabolic and respiratory illnesses even after adjustment

for body mass index (BMI). We performed a prospective study to investigate the potential of NC to predict the need for invasive mechanical ventilation (IMV) in adult COVID-19 inpatients.
MATERIALS AND METHODS: we prospectively and consecutively enrolled COVID-19 adult patients admitted to dedicated medical wards of two Italian hospitals from March 25th to April seventh 2020. On admission, clinical, biochemical and anthropometric data, including BMI and NC were collected. As primary outcome measure, the maximum respiratory support received was evaluated. Follow-up time was 30 days from hospital admission.
RESULTS: we enrolled 132 subjects (55.0-75.8 years, 32% female). During the study period, 26 (19.7%) patients underwent IMV. In multivariable logistic regression analyses, after adjusting for age, sex, diabetes, hypertension and COPD, NC resulted independently and significantly associated with IMV risk (adjusted OR 1.260 - per 1 cm increase 95% CI:1.120-1.417; P < 0.001), with a stronger association in the subgroup with BMI <=30 Kg/m2 (adjusted OR 1.526; 95% CI:1.243-1.874; P < 0.001). NC showed a good discrimination power in predicting patients requiring IMV (AUC 0.783; 95% CI:0.684-0.882; P < 0.001). In particular, NC > 40.5 cm (>37.5 for females and > 42.5 for males) showed a higher and earlier IMV risk compared to subjects with lower NC (Log-rank test:P < 0.001).
CONCLUSIONS: NC is an easy to measure parameter able to predict the need for IMV in adult COVID-19 inpatients.

EMERGENCY MEDICINE

AIRWAY MANAGEMENT TEAM FOR PATIENTS WITH COVID-19: A NEW ROLE FOR EMERGENCY MEDICINE PHARMACISTS

Faine BA, Carroll E, Decleene J, Zepeski A.. Am J Health Syst Pharm. 2020 May 28:zxaa129. doi: 10.1093/ajhp/zxaa129. Online ahead of print.
Level of Evidence: Other

BLUF

Emergency medicine pharmacists have been incorporated on the airway management teams caring for COVID-19 patients at the University of Iowa Hospitals and clinics. These professionals have valued pharmaceutical expertise and emergency medicine training that facilitates the care of critically ill patients in the emergency department during the ongoing pandemic.

SUMMARY

In the midst of the ongoing pandemic, emergency medicine pharmacists have adapted their roles to serve among multidisciplinary teams responsible for airway management in patients with COVID-19. At the University of Iowa Hospitals and Clinics, emergency medicine pharmacists have been made responsible for the following roles on the airway management teams: documenting, developing a medication kit, delivering medications to the bedside, evaluating patients' past medical history and vital signs to advise appropriate drug therapy, and advising recommendations for medications and hemodynamic support. Although integrating emergency medicine pharmacists into the airway management team may come with challenges, these members should facilitate patient care during emergency situations.

NEUROLOGY

COVID-19 POLYRADICULITIS IN 24 PATIENTS WITHOUT SARS-COV-2 IN THE CEREBRO-SPINAL FLUID

Finsterer J, Scorza FA, Ghosh R.. J Med Virol. 2020 Jun 4. doi: 10.1002/jmv.26121. Online ahead of print.
Level of Evidence: Other

BLUF

A literature review conducted by an international group of researchers aimed to summarize the current knowledge of COVID-19-associated Guillain-Barre syndrome (GBS) and found that there have been 24 reported COVID-19 patients with GBS, including 15 of whom had CSF testing for SARS-CoV-2 (all were negative) and 22 patients who received IVIG treatment. These results strongly suggest that SARS-CoV-2 can cause GBS and that the clinical presentation, course, and treatment seems to be similar to other GBS triggers.

ABSTRACT

OBJECTIVES: to summarise and discuss current knowledge about COVID-19-associated Guillain-Barre syndrome (GBS).
METHOD: literature review
RESULTS: altogether 18 articles were found, which reported 23 patients with COVID-19-associated GBS. A further patient came to our attention by personal communication. Among these 24 included patients age ranged from 20 to 76y. There was male preponderance. Fourteen patients presented with acute inflammatory demyelinating polyneuropathy (AIDP), 4 with acute motor axonal neuropathy (AMAN), 3 with Miller-Fisher syndrome (MFS), and 2 with acute motor and sensory axonal neuropathy (AMSAN). In one patient the subtype was not specified. The cerebrospinal fluid (CSF) was tested for SARS-CoV-2 in 15 patients but was negative for the virus in all of them. Seven patients required artificial ventilation. Twenty-one patients received intravenous immunoglobulines (IVIG). Thirteen patients recovered, 6 did not, and 2 patients died.
CONCLUSIONS: SARS-CoV-2 can cause GBS. SARS-CoV-2-associated GBS occurs in the absence of the virus in the CSF. Clinical presentation, course, response to treatment, and outcome do not vary between SARS-CoV-2-associated GBS and GBS due to other triggers.

STROKE INTEGRATED CARE PATHWAY DURING COVID-19 PANDEMIC

Frisullo G, De Belvis AG, Marca GD, Angioletti C, Calabresi P.. Neurol Sci. 2020 Jun 3. doi: 10.1007/s10072-020-04480-9. Online ahead of print.
Level of Evidence: Other

BLUF

The authors of this letter describe the guidelines set in place at Gemelli University Hospital in Rome to care for COVID-19 patients with acute stroke while minimizing the risk of transmission to other patients and healthcare workers (Figure 1), which is important for patients that present with acute stroke as they tend to be an older population that is susceptible to severe COVID-19.

SUMMARY

The Gemelli University Hospital in Rome, Italy was dedicated as a COVID-19 positive hospital in March 2020, meaning that guidelines had to be set in place to isolate COVID-19 positive patients, presenting problems for COVID-19 patients with acute stroke who required specialized neurological care. Here the authors discuss their experience in an integrated care pathway (ICP) focused on ischemic stroke patients. Patients with confirmed COVID-19 and patients that presented with either fever, respiratory symptoms, or evidence of interstitial infiltrates on chest x-ray were entered into an ICP that was separated from the non-COVID-19 patients at every step (Figure 1) and included separate rooms for evaluation, CT scans, and for interventional procedures such as intravenous thrombolysis. This approach allows for proper precautions to prevent COVID-19 spread from positive patients without sacrificing the specialized neurological care that patients with COVID-19 and acute stroke require.

FIGURES

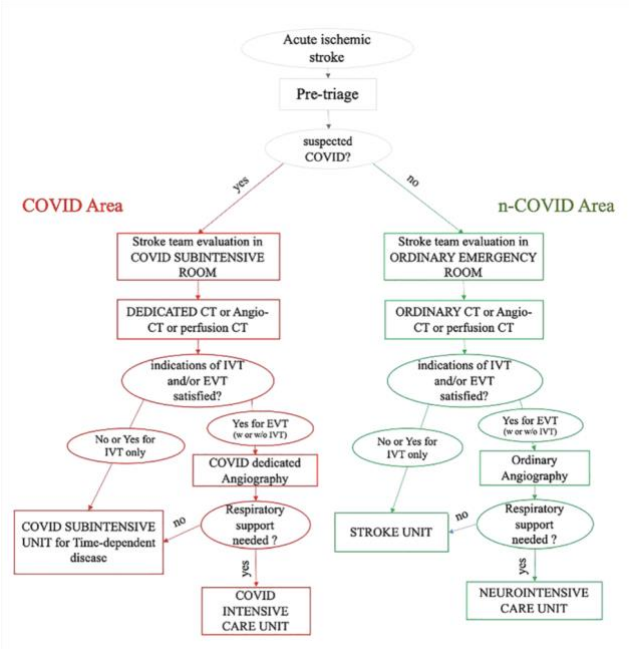

Figure 1: Stroke integrated care pathway (ICP) during COVID-19 pandemic.

GASTROENTEROLOGY

A SURVEY ON THE IMPACT OF THE COVID-19 PANDEMIC ON MOTILITY AND FUNCTIONAL INVESTIGATIONS IN EUROPE AND CONSIDERATIONS FOR RECOMMENCING ACTIVITIES IN THE EARLY RECOVERY PHASE

Tack J, Schol J, Geeraerts A, Huang IH, Mori H, Scarpellini E, Sinonquel P, Carbone F, Colomier E, Geysen H, Jandee S, Moonen A, Pannemans J, Timmermans L, Van den Houte K, Verbeure W, Wauters L, Bisschops R, Hoffman I, Roelandt P, Rommel N, Simren M, Suzuki H, Tornblom H, Verbeke K, Vanuytsel T.. Neurogastroenterol Motil. 2020 Jun 1:e13926. doi: 10.1111/nmo.13926. Online ahead of print.
Level of Evidence: Other

BLUF

A survey conducted by researchers in Belgium, Sweden, and Japan reviews the impact of COVID-19 on motility and functional disorder-related procedures in 39 European centers. The authors found that as of March 16, 2020, almost all centers majorly reduced or stopped performing esophageal manometry (35/38), catheter-based pH monitoring studies (36/39), wireless pH-capsule testing (13/15), anal manometry (28/31 centers), and breath tests (26/30). Furthermore, the authors recommend the following guidelines for motility and functional disorder-related procedures.

SUMMARY

Figure 1 outlines the workflow to assess a patient's risk of infection and the allocated procedures.

- Most motility and function tests can be postponed and only need to be considered in the late recovery phases of the pandemic EXCEPT in the presence of dysphagia associated with aspiration or intractable vomiting with electrolyte imbalances or weight loss.
- Upper GI function tests that involve the positioning of a catheter through the nasopharynx are considered high risk given the risk of aerosol formation.
- Manometry and pH-MII monitoring should only be performed in low-risk patients.
- Anorectal manometry is hardly ever urgent and should be restricted to low-risk patients.
- For esophageal manometry and pH, pH-MII and wireless pH-capsule monitoring, adjust height of bed so that the upper part of the patient's head is under the chin of the nurse or technician.
- For esophageal manometry:
    - Apply lubricating gel containing a local anesthetic on the catheter.
    - Avoid use of sprays with local anesthetic due to risk of aerosol formation.
    - During insertion of catheter, mask should still be worn over the mouth, exposing the nose only.
- For anorectal manometry: "as defecation is considered an aerogenic process and SARS-CoV-2 particles can potentially be shed via feces, a toilet in a separate room is preferred over in-room commode seat."

ABSTRACT

BACKGROUND: The COVID-19 pandemic, declared by WHO on March 13th 2020, had a major global impact on the health care system and services. In the acute phase, the presence of the SARS-CoV-2 virus in the aerodigestive tract limited activities in the gastroenterology clinic and procedures to emergencies only. Motility and function testing was interrupted and as we enter the recovery phase, restarting these procedures requires a safety-focused approach with adequate infection prevention for patients and healthcare professionals.
METHODS: We summarized knowledge on the presence of the SARS-CoV-2 virus in the aerodigestive tract and the risk of spread with motility and functional testing. We surveyed 39 European centers documenting how the pandemic affected activities and which measures they are considering for restarting these measurements. We propose recommendations based on current knowledge as applied in our center.
RESULTS: Positioning of catheters for gastrointestinal motility tests carries a concern for aerosol-borne infection of health care workers. The risk is low with breath tests. The surveyed centers stopped almost all motility and function tests from the second half of March. The speed of restarting and the safety measures taken varied highly.
CONCLUSIONS AND INFERENCES: Based on these findings, we provided recommendations and practical relevant information for motility and function test procedures in the COVID-19 pandemic era, to guarantee a high-quality patient care with adequate infection prevention.

ORTHOPEDICS

TELEHEALTH UTILIZATION IN RESPONSE TO THE NOVEL CORONAVIRUS (COVID-19) PANDEMIC IN ORTHOPAEDIC SURGERY

Parisien RL, Shin M, Constant M, Saltzman BM, Li X, Levine WN, Trofa DP.. J Am Acad Orthop Surg. 2020 Jun 1;28(11):e487-e492. doi: 10.5435/JAAOS-D-20-00339.
Level of Evidence: 3

BLUF

This research conducted by a group of authors from various US medical schools and hospitals examined the impact of COVID-19 on use of telehealth services in the US by surveying 175 academic orthopedic institutions via telephone. With a 96% response rate, 88 of 106 institutions using telehealth services stated that COVID-19 was a major factor in implementing the services. The geographic location of the programs providing substantially increased telehealth services was positively correlated with COVID-19 disease burden (Figure 1 &2), indicating the "impressive measures" needed in these areas to provide quality care for their orthopedic surgery patients.

ABSTRACT

INTRODUCTION: The purpose of this investigation is to assess the current utilization of telehealth capabilities at academic orthopaedic departments in the United States and to determine how practice patterns have been directly influenced by the coronavirus disease 19 (COVID-19) pandemic.
METHODS: Orthopaedic surgery programs participating in the Electronic Residency Application Service were identified. One hundred seventy-five (175) programs were presented with a seven-item questionnaire addressing whether each program is using telehealth services in response to the COVID-19 pandemic.
RESULTS: Of the 175 Electronic Residency Application Service participant orthopaedic programs, 168 responded for a total response rate of 96%. Of the 106 institutions using telehealth services, 88 (83%) cited the COVID-19 pandemic as the impetus for implementation of telehealth services. Institutions located in the Northeast and South regions were markedly more likely to offer telehealth services. Heat map analysis demonstrates an associative overlap of regional "hot spots" with direct comparison of COVID-19 cases in the United States and orthopaedic departments providing telehealth services.
DISCUSSION: This study demonstrates the impressive measures academic orthopaedic institutions are taking to meet the needs of our patients by identifying a notable increase in new telehealth offerings throughout the United States with a positive correlation with COVID-19 disease burden.

FIGURES

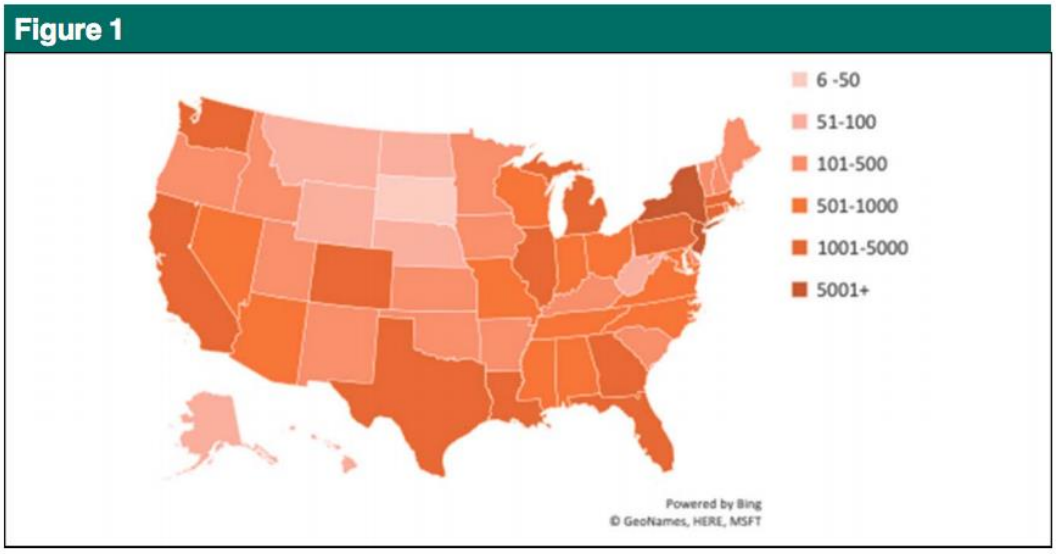

Figure 1. Chart showing the number of COVID-19 cases in the United States as of March 26, 2020.

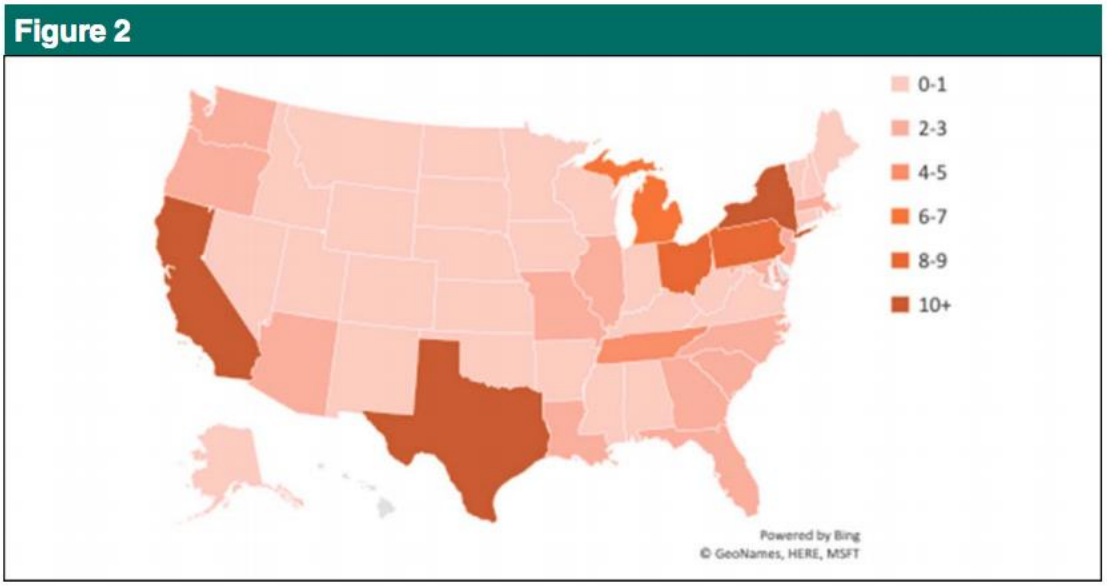

Figure 2. Chart showing the number of orthopaedic departments providing telehealth services as of March 26, 2020.

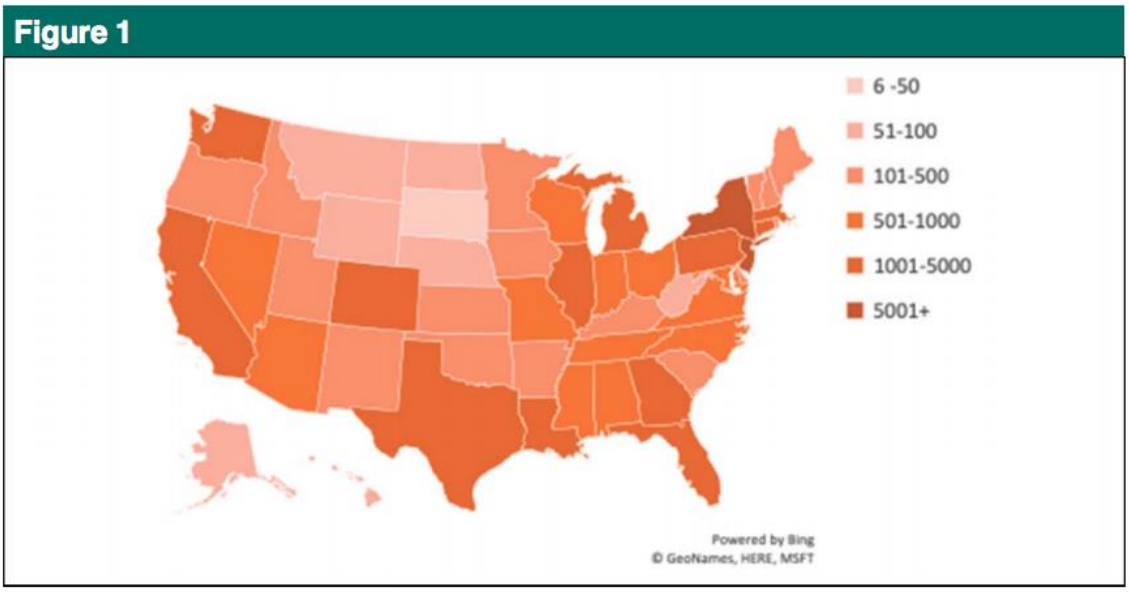

Figure 2. Chart showing the number of orthopaedic departments providing telehealth services as of March 26, 2020.

OBGYN

RECOMMENDATIONS ON MANAGEMENT OF GYNECOLOGICAL MALIGNANCIES DURING THE COVID-19 PANDEMIC: PERSPECTIVES FROM CHINESE GYNECOLOGICAL ONCOLOGISTS

Wang Y, Zhang S, Wei L, Lin Z, Wang X, Wang J, Hua K, Cui M, Wang J, Wang S, Di W, Wang Y, An R, Xi M, Guo R, Zhou Q, Xie X, Xue F.. J Gynecol Oncol. 2020 May 27. doi: 10.3802/jgo.2020.31.e68. Online ahead of print.
Level of Evidence: Other

BLUF

This paper outlines recommendations by Chinese gynecological oncologists for the management of patients with gynecologic malignancies during the COVID-19 pandemic.

SUMMARY

The authors' recommend the following:

- Establishment of a COVID-19 containment team
- Establishment of a multidisciplinary physician team including two gynecology oncologists and an infectious disease specialist
- Education of patients and their families on COVID-19 prevention
- Establishment of a patient triage system
- Screening before outpatient and inpatient visits
- Continuation of emergent surgeries if patient is COVID-19 negative
- Delay all elective surgeries and screen by a multidisciplinary team when delay is not possible
- Ruling-out COVID-19 infection as cause of post-op fever
- Screening for COVID-19 before radio- and chemotherapy and thoroughly disinfect treatment rooms
- Patients with suspected or confirmed COVID-19 should be managed by a multidisciplinary team that includes gynecology oncologists, respiratory physicians, infectious disease specialists, ICU specialists, and anesthesiologists
- If patient is COVID-19 positive and emergent surgery is required, perform surgery with appropriate PPE, in a negative-pressure OR and with proper disposal systems in place
- Telemedicine when feasible for follow-up appointments

ABSTRACT

The outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 has rapidly spread globally. Cancer patients are at a higher risk of being infected with the coronavirus and are more likely to develop severe complications, as compared to the general population. The increasing spread of COVID-19 presents challenges for the clinical care of patients with gynecological malignancies. Concerted efforts should be put into managing gynecological malignancies in an orderly manner by strictly implementing the measures that are specifically developed for controlling the spread of COVID-19. We have drafted Recommendations on Management of Gynecological Malignancies during the COVID-19 Pandemic based on our experience on controlling COVID-19 pandemic in China. We recommend that patients with gynecological malignancies should be managed in hierarchical and individualized manners in combination with local conditions related to COVID-19. Medical care decision should be balanced between controlling COVID-19 pandemic spread and timely diagnosis and treatment for gynecologic oncology patients.

OPHTHALMOLOGY

SANITIZER AEROSOL-DRIVEN OCULAR SURFACE DISEASE (SADOSD)-A COVID-19 REPERCUSSION?

Shetty R, Jayadev C, Chabra A, Maheshwari S, D'Souza S, Khamar P, Sethu S, Honavar SG.. Indian J Ophthalmol. 2020 Jun;68(6):981-983. doi: 10.4103/ijo.IJO_1308_20.
Level of Evidence: Other

BLUF

This expert opinion by authors affiliated with the Narayana Nethralaya Eye Institute in India shares recommendations on how to use hand sanitizer (Figure 1) in order to reduce sanitizer aerosol-driven ocular surface diseases (SADOSD) as the use of alcohol-based hand rubs (ABHRs) is increasing during the COVID-19 pandemic along with increasing complaints of conjunctivitis in teleophthalmology.

SUMMARY

The authors recommend responsible use of hand sanitizer and the following to reduce direct contact with the ocular surface:

1. Close your eyes when squirting the sanitizer
2. Rub the sanitizer below the level of your eyes
3. Keep the room well ventilated by opening the window
4. Avoid using the sanitizer with an A/C on
5. Use sodium hyaluronate-based lubricants in the case of having pre-existing ocular surface disease
6. Use soap and water if you are susceptible to ocular surface disease

ABSTRACT

Since the onset of the COVID-19 pandemic, there has been an advisory for regular and thorough cleaning of hands besides other measures such as social distancing and self-isolation. The rationale for the same is to prevent the transfer of the virus from hands that have come in contact with fomites. While both alcohol-based hand rubs (ABHR) or washing with soap and water are claimed to have been effective, hand sanitizers have gained more popularity due to the ease of use. The increased frequency of ABHR use and the aerosols generated pose a potential threat to the skin and exposed mucosal surfaces, especially that of the eye due to the proximity of use. The adverse effects of alcohol in these sanitizers can be manifold. An allergic or inflammatory response can occur depending on the predisposing or preexisting conditions. This article describes the risks, underlying mechanisms, and preventive measures for sanitizer aerosol-driven ocular surface disease.

FIGURES

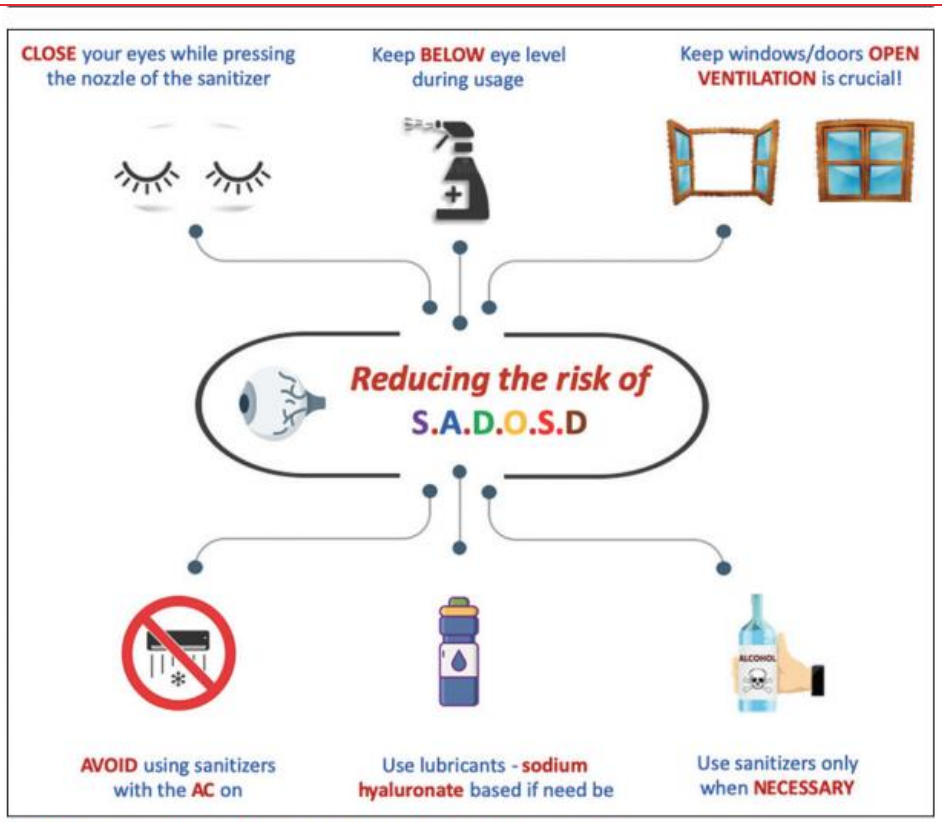

Figure 1. Precautionary measures to prevent sanitizer aerosol-driven ocular surface disease

AMPLIFICATION OF HUMAN B-GLUCORONIDASE GENE FOR APPRAISING THE ACCURACY OF NEGATIVE SARS-COV-2 RT-PCR RESULTS IN UPPER RESPIRATORY TRACT SPECIMENS

Albert E, Ferrer B, Torres I, Serrano A, Alcaraz MJ, Buesa J, Solano C, Colomina J, Bueno F, Huntley D, Olea B, Valdivia A, Navarro D.. J Med Virol. 2020 Jun 2. doi: 10.1002/jmv.26112. Online ahead of print.
Level of Evidence: 4

BLUF

Scientists in Spain report the use of the human beta-glucuronidase gene to distinguish between positive and negative SARS-CoV-2 RT-PCR results from nasopharyngeal swabs (21/47 patients were known positives). They detail an increase in cycle threshold for beta-glucoronidase in SARS-CoV-2 negative samples relative to positive (p=0.07), yielding "a true negative ratio of 89% and accuracy of 70%" (Table 1). Despite the low power of the study, they hope this gene may be used to gauge the accuracy of negative SARS-CoV-2 RT-PCR results.

ABSTRACT

Real-time reverse transcription polymerase-chain reaction (RT-PCR) is the mainstay of Covid-19 diagnosis.1 Up to 30% of patients clinically suspected of Covid-19 may have initial or repeat RT-PCR negative results prior to positive test conversion, most notably when upper respiratory tract (URT) specimens are processed.2-7 This article is protected by copyright. All rights reserved.

FIGURES

β-glucoronidase gene C_T	SARS-CoV-2 RT-PCR	
	Positive[a]	Negative[b]
≤31.2	18	18
>31.2	3	8

C_T, RT-PCR cycle threshold.

[a]The REALQUALITY RQ-2019-nCoV was used in 7 specimens. The LightMix® Modular SARS-CoV-2 (COVID-19) E-gene/LightMix® Modular SARS-CoV-2 (COVID-19) RdRP gene was used in 6 specimens. The SARS-COV-2 REALTIME PCR KIT was used in 4 specimens. The SARS-CoV-2 (S gene) – BD MAX™ System (VIASURE Real Time PCR Detection Kits) was used in 4 specimens.

[b]The LightMix® Modular SARS-CoV-2 (COVID-19) was used in 17 specimens. The REALQUALITY RQ-2019-nCoV was used in 6 specimens. The SARS-COV-2 REALTIME PCR KIT was used in 3 specimens.

Table 1. Accuracy of negative SARS-CoV-2 RT-PCR results in upper respiratory tract specimens from patients with microbiological diagnosis of COVID-19 upon β-Glucuronidase gene RT-PCR Ct value.

HYDROXYCHLOROQUINE OR CHLOROQUINE FOR TREATMENT OR PROPHYLAXIS OF COVID-19: A LIVING SYSTEMATIC REVIEW

Hernandez AV, Roman YM, Pasupuleti V, Barboza JJ, White CM.. Ann Intern Med. 2020 May 27. doi: 10.7326/M20-2496. Online ahead of print.
Level of Evidence: 1

BLUF

A systematic review including 4 randomized controlled trials, 10 cohort studies and 9 case series found that evidence was conflicting and insufficient regarding the use of hydoxychloroquine and chloroquine in decreasing mortality, disease progression, clinical symptoms, and viral clearance in patients with COVID-19.

SUMMARY

In this systematic review, several studies demonstrated an increase in prolonged QTc interval in those taking hydroxychloroquine or chloroquine, and one study comparing dosages of chloroquine was stopped early due to increased lethality and QTc prolongation in the high dose arm. There were no studies evaluating the use of these medications as COVID-19 prophylaxis. The authors acknowledge that many of the studies included suffered from small sample size, lack of controls, and lack of blinding of either patients or clinicians to the treatment. The authors conclude that there is no conclusive evidence in favor of or against the usage of hydroxychloroquine or chloroquine in the treatment of COVID-19 (see Tables 1, 2, and 3).

ABSTRACT

BACKGROUND: Hydroxychloroquine and chloroquine have antiviral effects in vitro against severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2).
PURPOSE: To summarize evidence about the benefits and harms of hydroxychloroquine or chloroquine for the treatment or prophylaxis of coronavirus disease 2019 (COVID-19).
DATA SOURCES: PubMed (via MEDLINE), EMBASE (via Ovid), Scopus, Web of Science, Cochrane Library, bioRxiv, Preprints, ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform, and the Chinese Clinical Trials Registry from 1 December 2019 until 8 May 2020.
STUDY SELECTION: Studies in any language reporting efficacy or safety outcomes from hydroxychloroquine or chloroquine use in any setting in adults or children with suspected COVID-19 or at risk for SARS-CoV-2 infection.
DATA EXTRACTION: Independent, dually performed data extraction and quality assessments.
DATA SYNTHESIS: Four randomized controlled trials, 10 cohort studies, and 9 case series assessed treatment effects of the medications, but no studies evaluated prophylaxis. Evidence was conflicting and insufficient regarding the effect of hydroxychloroquine on such outcomes as all-cause mortality, progression to severe disease, clinical symptoms, and upper respiratory virologic clearance with antigen testing. Several studies found that patients receiving hydroxychloroquine developed a QTc interval of 500 ms or greater, but the proportion of patients with this finding varied among the studies. Two studies assessed the efficacy of chloroquine; 1 trial, which compared higher-dose (600 mg twice daily for 10 days) with lower-dose (450 mg twice daily on day 1 and once daily for 4 days) therapy, was stopped owing to concern that the higher dose therapy increased lethality and QTc interval prolongation. An observational study that compared adults with COVID-19 receiving chloroquine phosphate 500 mg once or twice daily with patients not receiving chloroquine found minor fever resolution and virologic clearance benefits with chloroquine.
LIMITATION: There were few controlled studies, and control for confounding was inadequate in observational studies.
CONCLUSION: Evidence on the benefits and harms of using hydroxychloroquine or chloroquine to treat COVID-19 is very weak and conflicting.
PRIMARY FUNDING SOURCE: Agency for Healthcare Research and Quality.

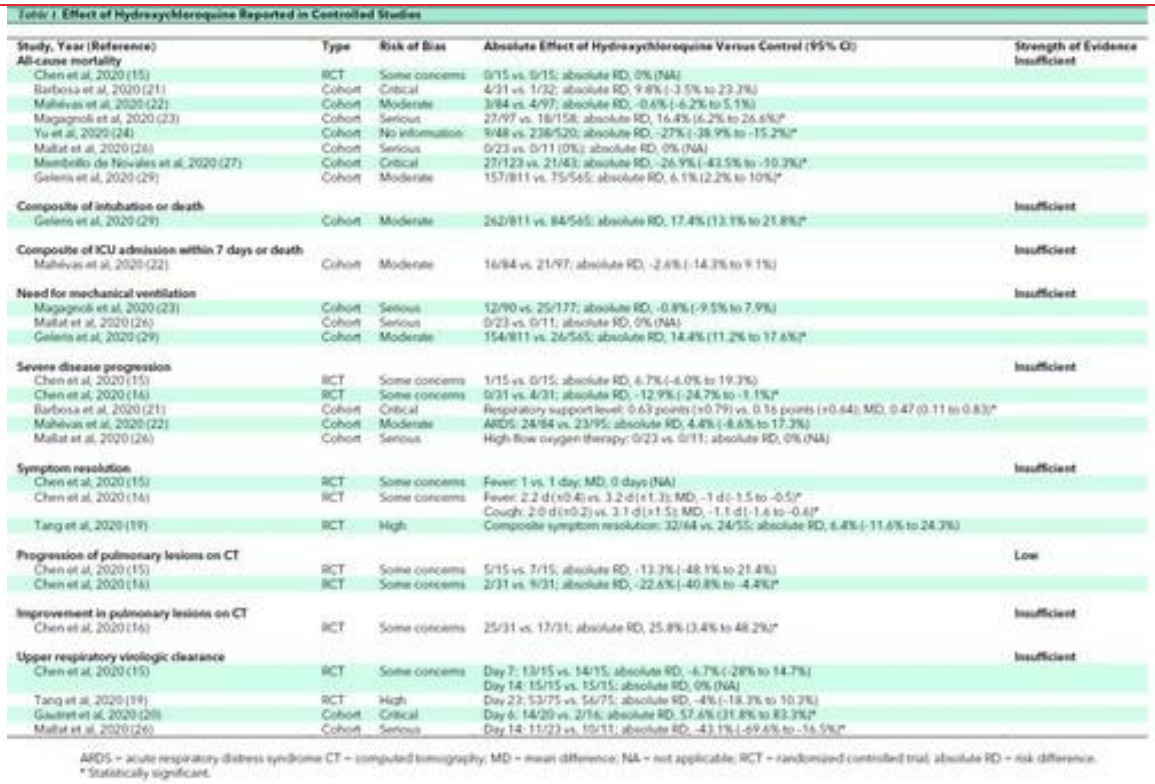

Table 1. Effect of Hydroxychloroquine Reported in Controlled Studies

Table 2. **Effect of Chloroquine Reported in Controlled Studies***

Study, Year (Reference)	Type	Risk of Bias	Absolute Effect of Chloroquine Versus Control (95% CI)	Strength of Evidence
All-cause mortality				Insufficient
Borba et al, 2020 (17, 18)	RCT	High	16/41 vs. 6/40; absolute RD, 24% (5.4% to 42.6%)†	
Huang et al, 2020 (28)	Cohort	Critical	0/197 vs. 0/176; absolute RD, 0% (NA)	
ICU admission				Insufficient
Borba et al, 2020 (17, 18)	RCT	High	1/2 vs. 1/11; absolute RD, 40.9% (–30.4% to 112.3%)	
Huang et al, 2020 (28)	Cohort	Critical	0/197 vs. 0/176; absolute RD, 0% (NA)	
Need for mechanical ventilation				Insufficient
Borba et al, 2020 (17, 18)	RCT	High	4/20 vs. 2/19; absolute RD, 9.5% (–12.8% to 31.8%)	
Need for oxygen support				Insufficient
Borba et al, 2020 (17, 18)	RCT	High	3/15 vs. 1/13; absolute RD, 12.3% (–12.6% to 37.2%)	
Symptom resolution				Insufficient
Huang et al, 2020 (28)	Cohort	Critical	Time to normal body temperature (GM): 1.2 vs. 1.9 d; MD, –0.7 d (95% CI NR)	
Upper respiratory virologic clearance				Insufficient
Borba et al, 2020 (17, 18)	RCT	High	Day 4: 0/14 vs. 1/12; absolute RD, –8.3% (–24% to 7.3%)	
Huang et al, 2020 (28)	Cohort	Critical	Day 10: 180/197 vs. 101/176; absolute RD, 34% (25.7% to 42.3%)† Day 14: 189/197 vs. 140/176; absolute RD, 16.4% (9.8% to 23%)†	

GM = geometric mean; ICU = intensive care unit; MD = mean difference; NA = not applicable; NR = not reported; RCT = randomized controlled trial; RD: risk difference.
* Borba et al compared high-dose versus low-dose chloroquine; Huang et al compared chloroquine versus non-chloroquine control.
† Statistically significant.

Table 2. Effect of Chloroquine Reported in Controlled Studies*

Table 3. **Reported Harms and Adverse Events for Hydroxychloroquine and Chloroquine in Controlled Studies**

Study, Year (Reference)	Type	Risk of Bias	Absolute Effect of Hydroxychloroquine/Chloroquine Versus Control, or High- Versus Low-Dose Chloroquine (95% CI)	Strength of Evidence
Severe adverse events				Insufficient
Chen et al, 2020 (16)	RCT	Some concerns	0/31 vs. 0/31; absolute RD, 0% (NA)	
Huang et al, 2020 (28)*	Cohort	Critical	0/197 vs. 0/176; absolute RD, 0% (NA)	
Adverse events				Insufficient
Chen et al, 2020 (15)	RCT	Some concerns	4/15 vs. 3/15; absolute RD, 6.7% (-23.5% to 36.8%)	
Chen et al, 2020 (16)	RCT	Some concerns	2/31 vs. 0/31; absolute RD, 6.5% (-2.2% to 15.1%)	
Tang et al, 2020 (19)	RCT	High	21/70 vs. 7/80; absolute RD, 21.3% (8.9% to 33.6%)†	
Huang et al, 2020 (28)*	Cohort	Critical	53/197 vs. 57/176; absolute RD, -5.5% (-14.8% to 3.8%)	
Diarrhea				Insufficient
Chen et al, 2020 (15)	RCT	Some concerns	2/15 vs. 0/15[0%]; absolute RD, 13.3% (-3.9% to 30.5%)	
Tang et al, 2020 (19)	RCT	High	7/70 vs. 0/80; absolute RD, 10% (3% to 17%)†	
Huang et al, 2020 (28)*	Cohort	Critical	6/197 vs. 11/176; absolute RD, -3.2% (-7.5% to 1.1%)	
Abnormal liver function				Insufficient
Chen et al, 2020 (15)	RCT	Some concerns	1/15 vs. 1/15; absolute RD, 0% (-1.7.9% to 17.9%)	
Rash				Insufficient
Chen et al, 2020 (16)	RCT	Some concerns	1/31 vs. 0/31; absolute RD, 3.1% (-2.9% to 9.2%)	
Huang et al, 2020 (28)*	Cohort	Critical	1/197 vs. 0/176; absolute RD, 0.5% (-0.5% to 1.5%)	
Headache				Insufficient
Chen et al, 2020 (16)	RCT	Some concerns	1/31 vs. 0/31; absolute RD, 3.1% (-2.9% to 9.2%)	
Huang et al, 2020 (28)*	Cohort	Critical	3/197 vs. 3/176; absolute RD, 0.2% (-2.7% to 2.4%)	
QTc prolongation				Insufficient
Mahévas et al, 2020 (22)	Cohort	Moderate	7/84 vs. 0/97; absolute RD, 8.3% (2.4% to 14.2%)†	
Severe QTc prolongation (>500 ms)				Insufficient
Borba et al, 2020 (17, 18)‡	RCT	High	7/37 vs. 4/36; absolute RD, 7.8% (-8.5% to 24.1%)	
Mahévas et al, 2020 (22)	Cohort	Moderate	1/84 vs. 0/97; absolute RD, 1.2% (-1.1% to 3.5%)	
Ventricular tachycardia				Insufficient
Borba et al, 2020 (17, 18)‡	RCT	High	2/37 vs. 0/36; absolute RD, 5.4% (-1.9% to 12.7%)	
Anemia				Insufficient
Chen et al, 2020 (15)	RCT	Some concerns	0/15 vs. 1/15; absolute RD, -6.7% (-19.3% to 6%)	
Borba et al, 2020 (17, 18)‡	RCT	High	Decrease in hemoglobin level >3 g/dL or ≥30% from baseline: 7/24 vs. 4/18; absolute RD, 6.9% (-19.5% to 33.4%)	
Elevated serum creatinine level				Insufficient
Chen et al, 2020 (15)	RCT	Some concerns	0/15 vs. 1/15; absolute RD, -6.7% (-19.3% to 6%)	
Borba et al, 2020 (17, 18)‡	RCT	High	Serum creatinine level ≥30% from baseline: 7/14 vs. 6/19; absolute RD, 18.4% (-15.1% to 51.9%)	

RCT = randomized controlled trial; RD: risk difference.
* Huang et al compared chloroquine versus nonchloroquine control.
† Statistically significant.
‡ Borba et al compared high-dose versus low-dose chloroquine.

Table 2. Effect of Chloroquine Reported in Controlled Studies

COLCHICINE'S EFFECTS ON METABOLIC AND INFLAMMATORY MOLECULES IN ADULTS WITH OBESITY AND METABOLIC SYNDROME: RESULTS FROM A PILOT RANDOMIZED CONTROLLED TRIAL

Demidowich AP, Levine JA, Apps R, Cheung FK, Chen J, Fantoni G; CHI Consortium, Patel TP, Yanovski JA.. Int J Obes (Lond). 2020 May 27. doi: 10.1038/s41366-020-0598-3. Online ahead of print.
Level of Evidence: 2

BLUF

This is a single-center, double-blind, randomized, placebo-controlled trial that secondarily analyzed the effect of colchicine on 1305 circulating factors in 35 adults with characteristics of high BMIs (over 30 kg/m^2), metabolic syndrome, and no significant chronic medical conditions. After participants took colchicine for 3 months, the authors found a significant decrease in concentration of 26 molecules associated with neutrophil function and the innate immune system (including IL-6) and an increase in 8 molecules associated with metabolism and tissue repair (see Figure 1). The authors posit that further research to investigate colchicine's therapeutic potential in COVID-19 infection may be merited, especially given the negative correlation found between colchicine and IL-6.

ABSTRACT

OBJECTIVE: Recent clinical trials have demonstrated that colchicine may have metabolic and cardiovascular and benefits in at-risk patients; however, the mechanisms through which colchicine may improve outcomes are still unclear. We sought to examine colchicine's effects on circulating inflammatory and metabolic molecules in adults with obesity and metabolic syndrome (MetS).
METHODS: Blood samples were collected pre- and post-intervention during a double-blind randomized controlled trial in which 40 adults with obesity and MetS were randomized to colchicine 0.6 mg or placebo twice-daily for 3 months. Serum samples were analyzed for 1305 circulating factors using the SomaScan Platform. The Benjamini-Hochberg procedure was used to adjust the false discovery rate (FDR) for multiple testing.
RESULTS: At baseline, age (48.0 +- 13.8 vs. 44.7 +- 10.3 years) and BMI (39.8 +- 6.4 vs. 41.8 +- 8.2 kg/m2) were not different between groups. After controlling for the FDR, 34 molecules were significantly changed by colchicine. Colchicine decreased concentrations of multiple inflammatory molecules, including C-reactive protein, interleukin 6, and resistin, in addition to vascular-related proteins (e.g., oxidized low-density lipoprotein receptor, phosphodiesterase 5A). Conversely, relative to placebo, colchicine significantly increased concentrations of eight molecules including secreted factors associated with metabolism and anti-thrombosis.

CONCLUSIONS: In adults with obesity, colchicine significantly affected concentrations of proteins involved in the innate immune system, endothelial function and atherosclerosis, uncovering new mechanisms behind its cardiometabolic effects. Further research is warranted to investigate whether colchicine's IL-6 suppressive effects may be beneficial in COVID-19.

FIGURES

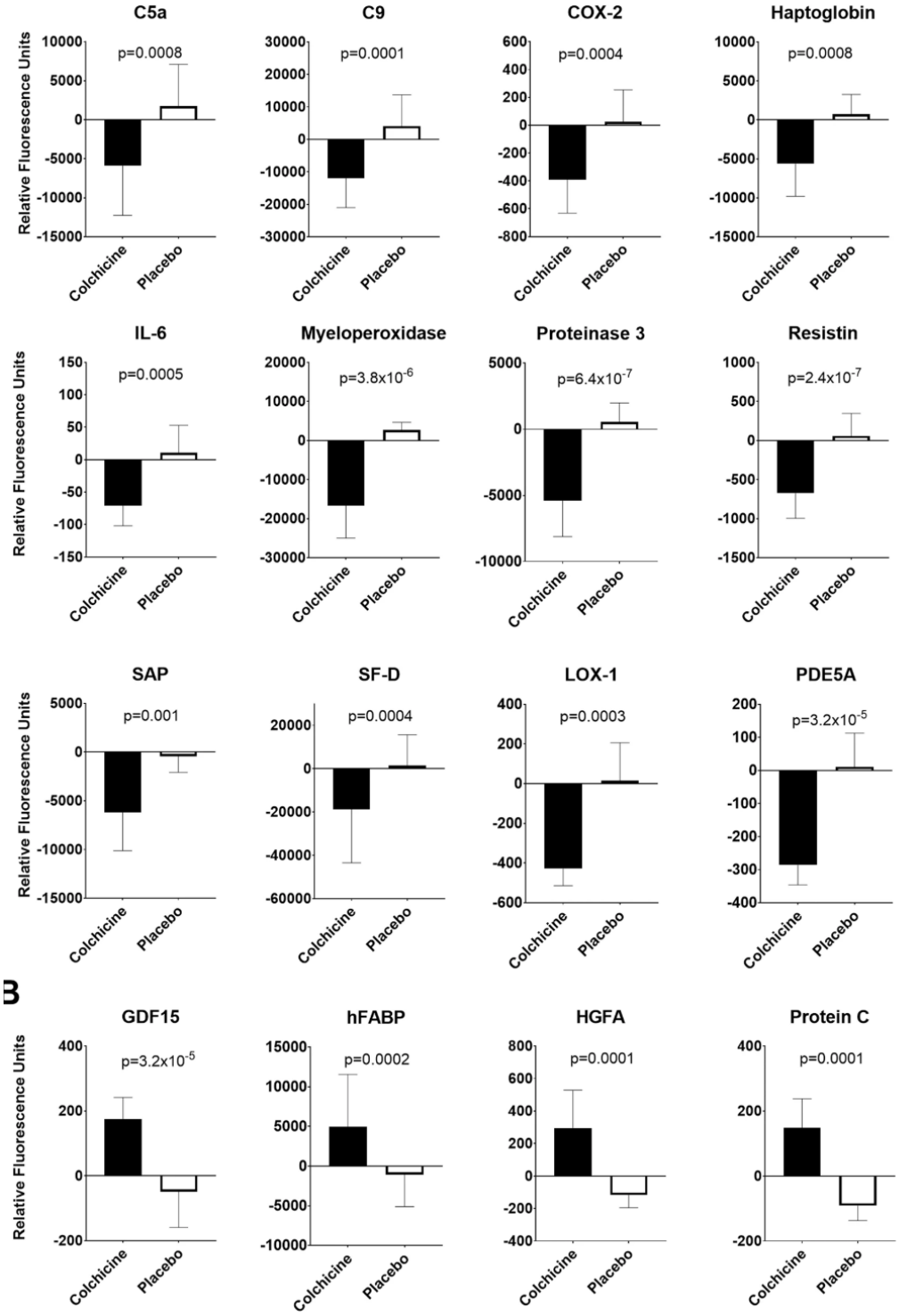

Figure 1: Changes in Selected Circulating Biomakers. Selected circulating biomarkers that were significantly a decreased or b increased in the colchicine arm as compared with placebo after adjustment for the false discovery rate. Bars represent median values, whiskers represent the 95% confidence interval. All values are expressed as relative fluorescence units.

A CASE REPORT OF SERIOUS HAEMOLYSIS IN A GLUCOSE-6-PHOSPHATE DEHYDROGENASE-DEFICIENT COVID-19 PATIENT RECEIVING HYDROXYCHLOROQUINE

Maillart E, Leemans S, Van Noten H, Vandergraesen T, Mahadeb B, Salaouatchi MT, De Bels D, Clevenbergh P.. Infect Dis (Lond). 2020 Jun 4:1-3. doi: 10.1080/23744235.2020.1774644. Online ahead of print.
Level of Evidence: 5

BLUF

Belgian physicians warn against blind use of hydroxychloroquine (HCQ) as standard of care in a case report of acute hemolysis in a 65-year-old patient with undiagnosed G6PD deficiency who was positive for SARS-CoV-2 by PCR. Patient history revealed only hypertension and type 2 diabetes, and the patient was prescribed HCQ and azithromycin without G6PD testing. Subsequently, the patient developed hemolytic anemia, a known side effect of HCQ. The authors urge caution in off-label uses of therapies without proper clinical validation.

ABSTRACT

While the COVID-19 epidemic occurred since December 2019, as of end April 2020, no treatment has been validated or invalidated by accurate clinical trials. Use of hydroxychloroquine has been popularised on mass media and put forward as a valid treatment option without strong evidence of efficacy. Hydroxychloroquine (HCQ) has its own side effects, some of which are very serious like acute haemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficient patients. Side effects may be worse than the disease itself. Belgian national treatment guidelines recommend the use of HCQ in mild to severe COVID-19 disease. As opinions, politics, media and beliefs are governing COVID-19 therapy, performance of randomised controlled blinded clinical trials became difficult. Results of sound clinical trials are eagerly awaited. We report a case of acute haemolysis leading to admission in intensive care unit and renal failure in a patient with uncovered G6PD deficiency.

MENTAL HEALTH & RESILIENCE NEEDS

FEASIBILITY AND PRELIMINARY RESULTS OF EFFECTIVENESS OF SOCIAL MEDIA-BASED INTERVENTION ON THE PSYCHOLOGICAL WELL-BEING OF SUSPECTED COVID-19 CASES DURING QUARANTINE

Zhou L, Xie RH, Yang X, Zhang S, Li D, Zhang Y, Liu J, Pakhale S, Krewski D, Wen SW.. Can J Psychiatry. 2020 Jun 2:706743720932041. doi: 10.1177/0706743720932041. Online ahead of print.
Level of Evidence: 3

BLUF

A cohort study from Guangdong, China evaluated the efficacy of social media-based counseling for 63 patients hospitalized with suspected COVID-19 during hospital quarantine from 2/2/2020 - 4/7/2020. The patients were counseled individually via two daily face-to-face sessions on WeChat. During these sessions they were given emotional support and provided with accurate updates about COVID-19. The authors found a significant reduction, p <0.01, in both anxiety and depression among the 15 qualified patients (initial score of 8 or higher on the Hospital Anxiety and Depression Scale [HADS]) two weeks after the first intervention (Table 1). They suggest this approach will help establish a cost-effective intervention to reduce stress and anxiety in suspected COVID-19 patients or other patients during quarantine.

FIGURES

Scale	Before Intervention ($n = 15$)	After Intervention ($n = 15$)	t Value[a]	P Value
HADS-A	12.6 ± 3.6	6.1 ± 2.1	6.5	<0.01
HADS-D	10.1 ± 2.8	4.4 ± 2.2	6.1	<0.01
HADS	22.7 ± 6.2	10.6 ± 4.2	6.4	<0.01

Note. HADS = Hospital Anxiety and Depression Scale.
[a]Paired t statistic.

Table 1. Comparison of Suspected COVID19 Patients' HADS Scores before and after Psychological Intervention.

COVID-19'S IMPACT ON HEALTHCARE WORKFORCE

COVID-19 AND THE NEED FOR PERINATAL MENTAL HEALTH PROFESSIONALS: NOW MORE THAN EVER BEFORE

Hynan MT.. J Perinatol. 2020 May 27. doi: 10.1038/s41372-020-0696-z. Online ahead of print.
Level of Evidence: Other

BLUF

A letter written by an American psychologist stresses the need for more perinatal mental health professionals to support distressed parents and neonatal intensive care unit (NICU) staff due to the anticipated increase in mental health issues during and after the COVID-19 pandemic.

SUMMARY

The author reports perinatal mental health professionals such as psychologists and social workers have been deemed non essential during the COVID-19 pandemic and have been forced to transition to keeping up with patients via telehealth visits. While the author acknowledges the great efforts made to maintain the physical health of patients and providers, they believe psychological health should also be equally important. They report 20-30% of newborn parents in the NICU experienced psychological trauma and 26.7% of surveyed Californian NICU staff qualified for burnout and emotional exhaustion.To

mitigate worsening prevalence of mental health issues during the COVID-19 pandemic, the author suggests additional hiring of mental health staff in the perinatal setting and NICU.

RESOURCES

SPECIAL EDITION: COVID-19 GUEST EDITORIAL

Rose P, Levine WN.. J Am Acad Orthop Surg. 2020 Jun 1;28(11):435. doi: 10.5435/JAAOS-D-20-00337.
Level of Evidence: Other

BLUF

In this article, the Deputy Editor and Editor-in-Chief of the Journal of the American Academy of Orthopaedic Surgeons (JAAOS) introduce the June 2020 special edition of JAAOS, which discusses the effects that COVID-19 has had on the public, and includes clinical guidelines for adjusting clinical practice, medical education, and finances during the COVID-19 pandemic.

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