The Daily COVID-19 Literature Surveillance Summary

July 30, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

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

Epidemiology

- Researchers from Thailand reviewed epidemiological data on universal Bacillus Calmette-Guérin (BCG) vaccination and found that countries without universal BCG vaccination have the highest number of COVID-19 deaths. They attribute this to the theory that the BCG vaccine enhances both adaptive and innate immune response for viral clearance though acknowledge that the supporting evidence is limited.
- A retrospective study including 442 patients with COVID-19 found that male sex was the factor most associated with greater illness severity. Additionally, older age, African American race, obesity, and pre-existing conditions such as hypertension and diabetes mellitus were associated with higher illness severity while individuals chronically using ACE inhibitors had less severe illness.

Understanding the Pathology

- A case series from the Netherlands describes 4 young, previously healthy, male patients in their 20s (2 pairs of brothers from unrelated families) with severe COVID-19 who required mechanical ventilation in the ICU. Genetic sequencing of these patients found two different loss of function variants of TLR-7, resulting in diminished type I and II interferon activity when compared to healthy controls. These findings point to potential genetic predispositions that increase the risk of developing severe COVID-19.

Transmission and Prevention

- A study conducted at the National Biodefense Analysis and Countermeasures Center in Maryland, United States found that SARS-CoV-2 decays rapidly in simulated sunlight though the rate was dependent on the aerosol suspension matrix as well as the intensity of simulated sunlight, whereas the relative humidity did not significantly affect the decay rate.

Management

- A systematic review and meta-analysis of 14 studies, including 10,127 patients, explored the relationship between angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), and the morbidity and mortality of COVID-19. Results revealed no increase in morbidity or mortality in COVID-19 patients taking ACEIs/ARBs and provides continued support for their safety amid the pandemic.

Adjusting Practice During COVID-19

- Surgical oncologists from Massachusetts General Hospital created a risk stratification scoring system for breast cancer patients whose surgeries were delayed due to COVID-19. The score considers patient and tumor characteristics, length of delay, and tumor response to neoadjuvant chemotherapy and was found to agree with experienced surgeons' judgement when validated. The authors offer this score as a tool to prioritize higher risk patients as surgeries resume.

R&D: Diagnosis and Treatments

- A group of researchers validated 3 different SARS-CoV-2 antibody assays, including one chemiluminescent test (Abbott COVID-2 IgG) and two lateral flow tests (STANDARD Q IgM/IgG Duo and Wondfo Total Antibody Test). Each assay detected antibodies in 100% of all COVID-19 positive samples by 2 weeks after symptom onset, with only SQ IgM showing suboptimal results (85.7% positive rate). The authors support the use of serological testing in COVID-19 as part of diagnostic testing, particularly 14 days after symptom onset.
- Researchers conducted a systematic review and meta-analysis of 29 studies (including randomized control studies, prospective and retrospective studies involving a total of 5,207 total patients) which examined outcomes of COVID-19 patients treated with hydroxychloroquine, remdesivir, ritonavir/lopinavir, convalescent plasma therapy, and tocilizumab. Results revealed that hydroxychloroquine was associated with increased morbidity and mortality and none of the other interventions significantly changed the course of COVID-19 infection outcomes, though further study is indicated.

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EPIDEMIOLOGY

POTENTIAL ROLE OF BACILLUS CALMETTE-GUÉRIN (BCG) VACCINATION IN COVID-19 PANDEMIC MORTALITY: EPIDEMIOLOGICAL AND IMMUNOLOGICAL ASPECTS

Charoenlap S, Piromsopa K, Charoenlap C.. Asian Pac J Allergy Immunol. 2020 Jul 20. doi: 10.12932/AP-310520-0863. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Researchers from Thailand reviewed epidemiological data on universal Bacillus Calmette-Guérin (BCG) vaccination and found countries without universal BCG vaccination have the highest number of COVID-19 deaths (per million people) compared to countries with prior or current universal BCG vaccination policy (Figure 1). They believed the lower mortality rates in countries with universal BCG vaccines are associated with lower transmission rates because the BCG vaccine enhances both adaptive and innate immune response for viral clearance (Figure 3). The researchers acknowledged the supporting evidence is limited due to variable changes from the pandemic and additional data is warranted for further recommendations.

ABSTRACT

SARS-CoV-2 had already killed more than 400,000 patients around the world according to data on 7 June 2020. Bacillus Calmette-Guerin (BCG) vaccine is developed from live-attenuated Mycobacterium bovis, which is a microorganism found in a cow. Discovered by Dr. Albert Calmette and Camille Guerin since 1921, the BCG has served as a protection against tuberculosis and its complications. It is noticeable that countries which use mandatory BCG vaccination approach had lower COVID-19 infection and death rate. Current review aims to clarify this issue through epidemiological illustration of correlation between national BCG immunization and COVID-19 mortality, in addition to biological background of BCG-induced immunity Epidemiological data shows that universal BCG policy countries have lower median mortality rate compare to countries with past universal BCG policy and non-mass immunization BCG. (18 May 2020). Still, the links between BCG vaccination and better COVID-19 situation in certain countries are unclear, and more data on actual infection rate using SAR-CoV-2 antibody testing in large population sample is crucial for disease spreading comparison. Two immunological mechanisms, heterologous effects of adaptive immunity and trained innate immunity which induced by BCG vaccination, may explain host tolerance against COVID-19 infection, however, there is no direct evidence to support this biological background. Clinical trials related to BCG vaccination against COVID-19 are under investigation. Without a strong evidence, BCG must not be recommended for COVID-19 prevention, although, this should not be absolute contraindication. Risk of local and systemic complications from the vaccine should be informed to individual, who request BCG immunization.

FIGURES

Figure 1. Median per capita death rate of country group according to national BCG immunization policies.
The median deaths per million population of the country groups in accordance with vaccination policies were illustrated by ignoring the number with zero respect to date (15 Feb 2020 to 20 May 2020). A. Daily median per capita mortality rate B. Accumulative median per capita mortality rate. Python programming language with Pandas library was used as data processor. The plots are generated with the Pyplot library from Matplotlib. Abbreviations: BCG, Bacillus Calmette-Guérin; NBV, Non-mass BCG Vaccination; PBV, Past universal BCG Vaccination; UBV, Universal BCG Vaccination.

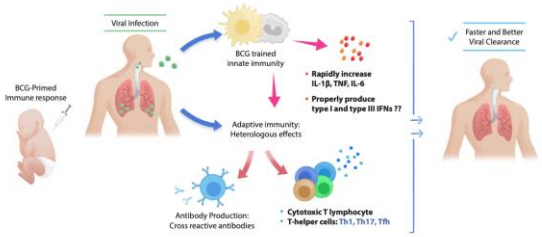


Figure 3. Proposed BCG-primed host immune responses during SARS-CoV-2 infection.
The initial phase of viral infection, BCG trained innate immunity at the site of infection orchestrate effective immune function with adaptive immunity eliminate virus from the target cells before the virus spreads. The trained macrophages recognize neutralized viruses and apoptotic cells and clear them by phagocytosis. The rapidly increasing of pro-inflammatory cytokine production from trained innate immune cells consisting of Il-1b, TNF, IL-6 and properly produce type I and type III IFNs could reduce viremia. Moreover, BCG vaccination could induce heterologous effect against virus via adaptive immune response.

SYMPTOMS AND CLINICAL PRESENTATION

HYPOXIA AND THROMBOSIS IN COVID-19: NEW CONSIDERATIONS FOR AIR PASSENGERS

Parker S, Mahomed O.. J Travel Med. 2020 Jul 25:taaa122. doi: 10.1093/jtm/taaa122. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Authors affiliated with University of Cape Town and University of KwaZulu Natal in South Africa explore the relationship between hypoxia and thrombosis in COVID-19 patients traveling on aircrafts. They found that "silent" hypoxia experienced by COVID-19 patients may be worsened by the lower cabin air pressure which may contribute to venous thromboembolism (VTE) in this population. The authors suggest that pre-board symptom and inflight pulse-oximetry screening may assist in identifying these patients and avoid an inflight medical emergencies.

ADULTS

PRE-EXISTING TRAITS ASSOCIATED WITH COVID-19 ILLNESS SEVERITY

Ebinger JE, Achamallah N, Ji H, Claggett BL, Sun N, Botting P, Nguyen TT, Luong E, Kim EH, Park E, Liu Y, Rosenberry R, Matusov Y, Zhao S, Pedraza I, Zaman T, Thompson M, Raedschelders K, Berg AH, Grein JD, Noble PW, Chugh SS, Bairey Merz CN, Marbán E, Van Eyk JE, Solomon SD, Albert CM, Chen P, Cheng S.. PLoS One. 2020 Jul 23;15(7):e0236240. doi: 10.1371/journal.pone.0236240. eCollection 2020.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A retrospective study including 442 patients with COVID-19 confirmed by RT-PCR who received care in the Cedars-Sinai Health System in Los Angeles, California found that the male sex was the factor most associated with greater illness severity and the need for a higher level of care in hospitalized patients. Additionally, older age (Figure 1), African American race (Figure 2), obesity, and pre-existing conditions such as hypertension and diabetes mellitus were associated with higher illness severity (notably the effect of diabetes and obesity on COVID-19 severity was stronger in younger patients than older patients) while individuals chronically using ACE inhibitors had less severe illness (Table 2). These findings contribute to a growing knowledge base on how demographics and pre-existing factors influence illness severity.

ABSTRACT

IMPORTANCE: Certain individuals, when infected by SARS-CoV-2, tend to develop the more severe forms of Covid-19 illness for reasons that remain unclear. OBJECTIVE: To determine the demographic and clinical characteristics associated with increased severity of Covid-19 infection. DESIGN: Retrospective observational study. We curated data from the electronic health record, and used multivariable logistic regression to examine the association of pre-existing traits with a Covid-19 illness severity defined by level of required care: need for hospital admission, need for intensive care, and need for intubation. SETTING: A large, multihospital healthcare system in Southern California. PARTICIPANTS: All patients with confirmed Covid-19 infection (N = 442). RESULTS: Of all patients studied, 48% required hospitalization, 17% required intensive care, and 12% required intubation. In multivariable-adjusted analyses, patients requiring a higher levels of care were more likely to be older (OR 1.5 per 10 years, P<0.001), male (OR 2.0, P = 0.001), African American (OR 2.1, P = 0.011), obese (OR 2.0, P = 0.021), with diabetes mellitus (OR 1.8, P = 0.037), and with a higher comorbidity index (OR 1.8 per SD, P<0.001). Several clinical associations were more pronounced in younger compared to older patients (Pinteraction<0.05). Of all hospitalized patients, males required higher levels of care (OR 2.5, P = 0.003) irrespective of age, race, or morbidity profile. CONCLUSIONS AND RELEVANCE: In our healthcare system, greater Covid-19 illness severity is seen in patients who are older, male, African American, obese, with diabetes, and with greater overall comorbidity burden. Certain comorbidities paradoxically augment risk to a greater extent in younger patients. In hospitalized patients, male sex is the main determinant of needing more intensive care. Further investigation is needed to understand the mechanisms underlying these findings.

FIGURES

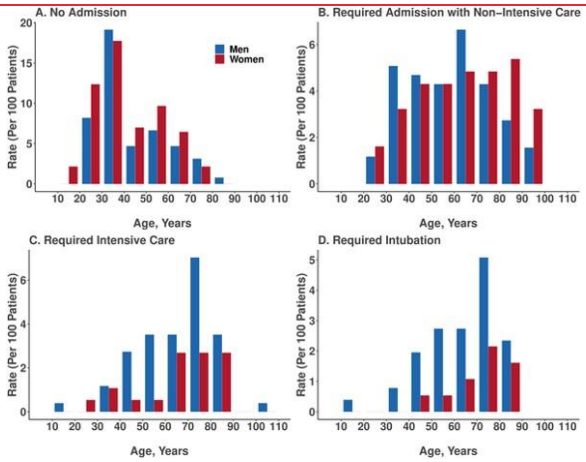


Figure 1. Age and sex distribution of patients with COVID-19, stratified by admission status. The frequency of laboratory confirmed COVID-19 was higher in males compared to females particularly among individuals requiring hospital admission, individuals with critical illness (requiring intensive care), individuals with respiratory failure (requiring intubation).

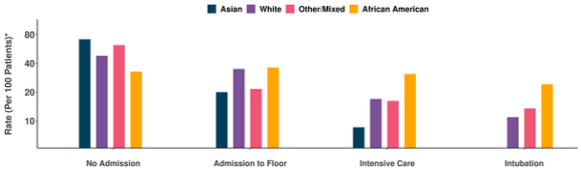


Figure 2. Rates of clinical outcomes of all patients with COVID-19, stratified by race. The frequency of African Americans manifesting more severe forms of COVID-19 illness, requiring higher levels of clinical care, was greater than that for other racial groups. *Rate was calculated as proportion of cases within each racial group.

	Age- and Sex-Adjusted Models		Multivariable-Adjusted Model†	
	OR (95% CI)	*P value*	OR (95% CI)	*P value*
Age, per 10 years	1.68 (1.52,1.87)	<0.001	**1.49 (1.30,1.70)**	**<0.001**
Male sex	1.87 (1.26,2.77)	0.002	**2.01 (1.34,3.04)**	**0.001**
African American race /	2.46 (1.45,4.18)	<0.001	**2.13 (1.19,3.83)**	**0.011**
Hispanic ethnicity	1.54 (0.91,2.60)	0.11	1.39 (0.79,2.45)	0.26
Obesity	1.96 (1.19,3.24)	0.009	**1.95 (1.11,3.42)**	**0.021**
Hypertension	1.97 (1.27,3.05)	0.003	1.19 (0.71,1.99)	0.52
Diabetes mellitus	2.25 (1.41,3.57)	0.001	**1.77 (1.03,3.03)**	**0.037**
Elixhauser comorbidity score, per SD	1.63 (1.33,2.01)	<0.001	**1.77 (1.37,2.28)**	**<0.001**
Prior myocardial infarction or heart failure	1.72 (0.96,3.09)	0.07	0.56 (0.27,1.18)	0.13
Prior COPD or asthma	1.23 (0.75,2.03)	0.41	0.76 (0.44,1.31)	0.34
ACE inhibitor use	0.69 (0.35,1.38)	0.29	0.48 (0.22,1.04)	0.06
Angiotensin receptor blocker use	1.18 (0.63,2.19)	0.61	1.05 (0.54,2.06)	0.89

*The primary outcome of Covid-19 illness severity score in the total sample was defined as an ordinal variable wherein: 0 = referent, 1 = required admission but never ICU level care, 2 = required ICU level care but never intubated, 3 = required intubation.
† All listed covariates shown were included in the full multivariable-adjusted model.
/The referent is non-African American race.

https://doi.org/10.1371/journal.pone.0238240.t002

Figure 2. Rates of clinical outcomes of all patients with COVID-19, stratified by race. The frequency of African Americans manifesting more severe forms of COVID-19 illness, requiring higher levels of clinical care, was greater than that for other racial groups. *Rate was calculated as proportion of cases within each racial group.

CONJUNCTIVITIS AS SOLE SYMPTOM OF COVID-19: A CASE REPORT AND REVIEW OF LITERATURE

Ozturker ZK.. Eur J Ophthalmol. 2020 Jul 24:1120672120946287. doi: 10.1177/1120672120946287. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

This case report describes a 55-year-old male nurse from Turkey who presented with right eyelid edema and serous secretions as his only symptom of COVID-19 on May 8, 2020 (Figure 1); he tested positive for SARS-CoV-2 on repeat nasopharyngeal swab two days after exposure to a COVID-19 family member. Imaging of the chest was negative for pneumonia and the patient was started on hydroxychloroquine and azithromycin. Bilateral conjunctival swabs were negative for SARS-CoV-2 and his conjunctivitis improved with topical antibiotics. The authors suggest RT-PCR testing for patients with conjunctivitis to rule out SARS-CoV-2 infection.

ABSTRACT

INTRODUCTION: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus causing an ongoing pandemic in 2020. Although the symptomatic patients infected by SARS-CoV-2 generally show respiratory distress, atypical manifestations such as conjunctivitis are also observed. A series of cases is reported in which reverse transcriptase polymerase chain reaction (RT-PCR) testing on tears had demonstrated the presence of the virus. However, the transmission of the virus through ocular fluids remains unknown. CASE DESCRIPTION: In this case report, the development of conjunctivitis is presented as the sole symptom of a new coronavirus disease 2019 (COVID-19) in an emergency health care worker. The patient's first application was to the ophthalmology clinic due to redness, stinging, tearing, and photophobia for one day in the right eye. The patient had no symptoms of fever, cough, shortness of breath, or fatigue. Two days later, the RT-PCR test, blood analysis, and chest computed tomography (CT) were applied to the patient for being in contact with a COVID positive patient. Conjunctival swabs did not identify SARS-CoV-2 by RT-PCR. However, nasopharyngeal swab and blood test confirmed the diagnosis of COVID-19. Chest CT did not show pneumonia. CONCLUSION: This phenomenon shows that conjunctivitis may occur as a sole manifestation of COVID-19 which needs to be carefully evaluated by health care workers and eye care professionals during the pandemic.

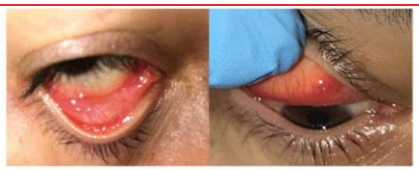


Figure 1. Follicular conjunctival reaction in the upper and lower fornices, serous secretion, and mild chemosis in the right eye of the patient 2 days before the diagnosis of COVID-19.

UNDERSTANDING THE PATHOLOGY

PRESENCE OF GENETIC VARIANTS AMONG YOUNG MEN WITH SEVERE COVID-19

van der Made CI, Simons A, Schuurs-Hoeijmakers J, van den Heuvel G, Mantere T, Kersten S, van Deuren RC, Steehouwer M, van Reijmersdal SV, Jaeger M, Hofste T, Astuti G, Corominas Galbany J, van der Schoot V, van der Hoeven H, Hagmolen Of Ten Have W, Klijn E, van den Meer C, Fiddelaers J, de Mast Q, Bleeker-Rovers CP, Joosten LAB, Yntema HG, Gilissen C, Nelen M, van der Meer JWM, Brunner HG, Netea MG, van de Veerdonk FL, Hoischen A.. JAMA. 2020 Jul 24. doi: 10.1001/jama.2020.13719. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

A case series from the Netherlands describes 4 young, previously healthy, male patients in their 20s (2 pairs of brothers from unrelated families) admitted to Radboud University Medical Center with severe COVID-19 who required mechanical ventilation in the ICU. Rapid whole-exome genetic sequencing of these patients and their families found two different loss of function variants of X-chromosomal TLR-7 (Figure 1), resulting in diminished type I and II interferon activity in peripheral blood mononuclear cells on TLR-7 stimulation with agonist imiquimod when compared to healthy controls (Figure 2). These findings point to potential genetic predispositions that increase the risk of developing severe COVID-19.

ABSTRACT

Importance: Severe coronavirus disease 2019 (COVID-19) can occur in younger, predominantly male, patients without preexisting medical conditions. Some individuals may have primary immunodeficiencies that predispose to severe infections caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Objective: To explore the presence of genetic variants associated with primary immunodeficiencies among young patients with COVID-19. Design, Setting, and Participants: Case series of pairs of brothers without medical history meeting the selection criteria of young (age <35 years) brother pairs admitted to the intensive care unit (ICU) due to severe COVID-19. Four men from 2 unrelated families were admitted to the ICUs of 4 hospitals in the Netherlands between March 23 and April 12, 2020. The final date of follow-up was May 16, 2020. Available family members were included for genetic variant segregation analysis and as controls for functional experiments. Exposure: Severe COVID-19. Main Outcome and Measures: Results of rapid clinical whole-exome sequencing, performed to identify a potential monogenic cause. Subsequently, basic genetic and immunological tests were performed in primary immune cells isolated from the patients and family members to characterize any immune defects. Results: The 4 male patients had a mean age of 26 years (range, 21-32), with no history of major chronic disease. They were previously well before developing respiratory insufficiency due to severe COVID-19, requiring mechanical ventilation in the ICU. The mean duration of ventilatory support was 10 days (range, 9-11); the mean duration of ICU stay was 13 days (range, 10-16). One patient died. Rapid clinical whole-exome sequencing of the patients and segregation in available family members identified loss-of-function variants of the X-chromosomal TLR7. In members of family 1, a maternally inherited 4-nucleotide deletion was identified (c.2129_2132del; p.[Gln710Argfs*18]); the affected members of family 2 carried a missense variant (c.2383G>T; p.[Val795Phe]). In primary peripheral blood mononuclear cells from the patients, downstream type I interferon (IFN) signaling was transcriptionally downregulated, as measured by significantly decreased mRNA expression of IRF7, IFNB1, and ISG15 on stimulation with the TLR7 agonist imiquimod as compared with family members and controls. The production of IFN-gamma, a type II IFN, was decreased in patients in response to stimulation with imiquimod. Conclusions and Relevance: In this case series of 4 young male patients with severe COVID-19, rare putative loss-of-function variants of X-chromosomal TLR7 were identified that were associated with impaired type I and II IFN responses. These preliminary findings provide insights into the pathogenesis of COVID-19.

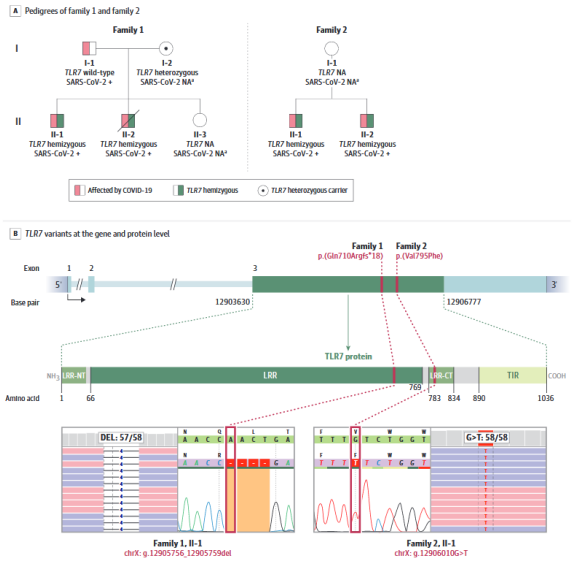


Figure 1. Identification ofTLR7Variants in 4 Patients From 2 Families With Severe Coronavirus Disease 2019 (COVID-19).

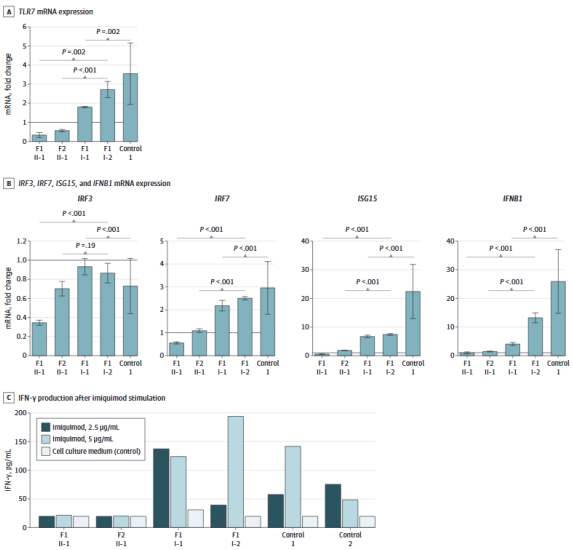


Figure 2. Assessment of Type I and II Interferon (IFN) Responses in Peripheral Blood Mononuclear Cells Derived From Patients and Controls.

AIRBORNE SARS-COV-2 IS RAPIDLY INACTIVATED BY SIMULATED SUNLIGHT

Schuit M, Ratnesar-Shumate S, Yolitz J, Williams G, Weaver W, Green B, Miller D, Krause M, Beck K, Wood S, Holland B, Bohannon J, Freeburger D, Hooper I, Biryukov J, Altamura LA, Wahl V, Hevey M, Dabisch P.. J Infect Dis. 2020 Jul 23;222(4):564-571. doi: 10.1093/infdis/jiaa334.
Level of Evidence: Other - Modeling

BLUF

A modeling study conducted at National Biodefense Analysis and Countermeasures Center in Maryland, United States found SARS-CoV-2 decays rapidly in simulated sunlight but decay constant for infectivity was dependent on intensity of simulated sunlight ($p<0.0001$) and suspension matrix ($p=0.0004$), while relative humidity did not significantly affect decay (Figures 2,3). Authors suggest UVA and UVB levels similar to natural sunlight can inactivate airborne SARS-CoV-2, thus aerosol transmission may be influenced by environmental conditions.

ABSTRACT

Aerosols represent a potential route of transmission of COVID-19. This study examined the effect of simulated sunlight, relative humidity, and suspension matrix on the stability of SARS-CoV-2 in aerosols. Both simulated sunlight and matrix significantly affected the decay rate of the virus. Relative humidity alone did not affect the decay rate; however, minor interactions between relative humidity and the other factors were observed. Decay rates in simulated saliva, under simulated sunlight levels representative of late winter/early fall and summer were 0.121+-0.017 min-1 (90% loss: 19 minutes) and 0.379+-0.072 min-1 (90% loss: 6 minutes), respectively. The mean decay rate without simulated sunlight across all relative humidity levels was 0.008+-0.011 min-1 (90% loss: 125 minutes). These results suggest that the potential for aerosol transmission of SARS-CoV-2 may be dependent on environmental conditions, particularly sunlight. These data may be useful to inform mitigation strategies to minimize the potential for aerosol transmission.

FIGURES

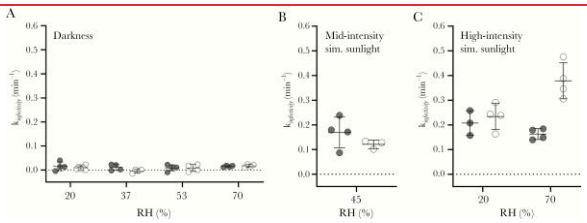


Figure 2. Aerosol decay data for SARS-CoV-2 at 20°C. Tests were conducted in darkness (A), at midintensity simulated (Sim.) sunlight (B), and at high-intensity simulated sunlight (C). Data from tests with the virus suspended in simulated saliva and culture medium are shown in white and grey, respectively, with bars indicating the arithmetic mean ± standard deviation of the kInfectivity values for each data set. kInfectivity was dependent on the simulated sunlight intensity and the suspension matrix ($P < .0001$ and $P = .0004$, respectively), but not relative humidity (RH).

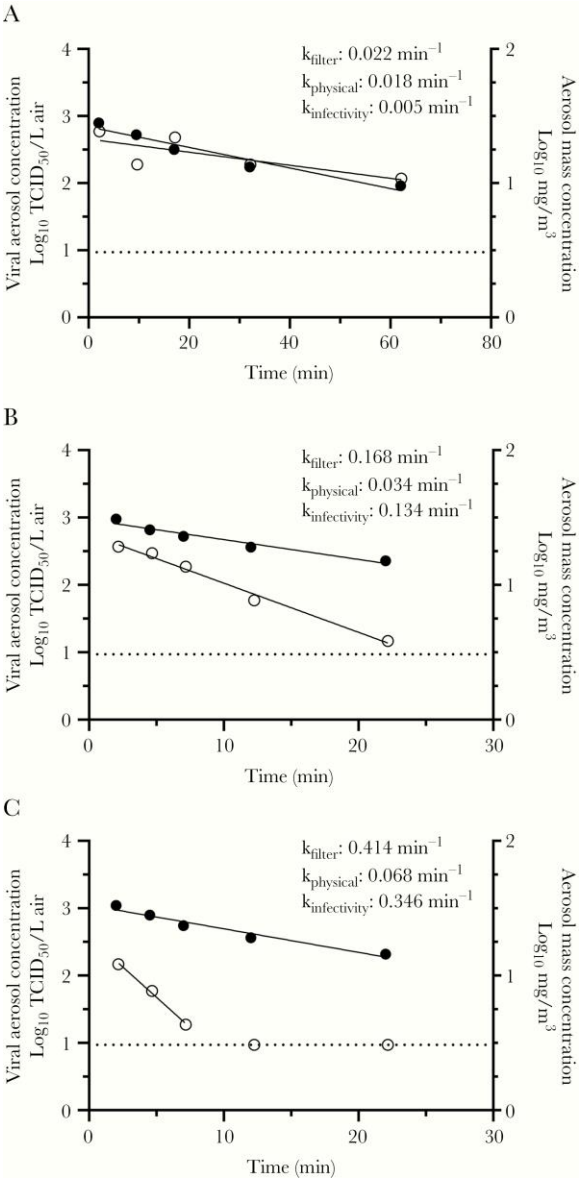


Figure 3. Representative viral and mass aerosol concentration profiles for SARS-CoV-2 in simulated saliva. Representative decay profiles and associated decay constants for both viral infectivity and aerosol mass from individual tests are shown for (A) no simulated sunlight at 20% relative humidity and 20°C, (B) midintensity simulated sunlight at 45% relative humidity and 20°C, and (C) high-intensity simulated sunlight at 70% relative humidity and 20°C. The decay of the aerosol mass concentration, in log10 mg/m3 (black circles), was similar across the 3 tests, while the decay rate of infectious viral aerosols, in log10 median tissue culture infectious dose/L (TCID50/L) air (white circles), increased as the intensity of simulated sunlight was increased. The dashed line at 0.97 log TCID50/Lair indicates the limit of detection for infectious virus; points on this line were not included in curve fits.

MANAGEMENT

ACUTE CARE

OUTCOMES OF RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKERS IN PATIENTS WITH COVID-19: A SYSTEMATIC REVIEW AND META-ANALYSIS

Greco A, Buccheri S, D'Arrigo P, Calderone D, Agnello F, Monte M, Milluzzo RP, Franchina AG, Ingala S, Capodanno D.. Eur Heart J Cardiovasc Pharmacother. 2020 Jul 16:pvaa074. doi: 10.1093/ehjcvp/pvaa074. Online ahead of print.
Level of Evidence: 1 - Review / Literature Review

BLUF

The authors reviewed the literature regarding the relationship between angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) and the morbidity and mortality of COVID-19. 175 studies were evaluated and 14 were included in the final design which included 10,127 patients. The review revealed no increase in morbidity or mortality in COVID-19 patients taking ACEIs/ARBs and supports evidence for their safety amid the pandemic (Figure 1). The authors recommend continued therapeutic use of the medications as they provide definite value to patients with cardiovascular disease.

FIGURES

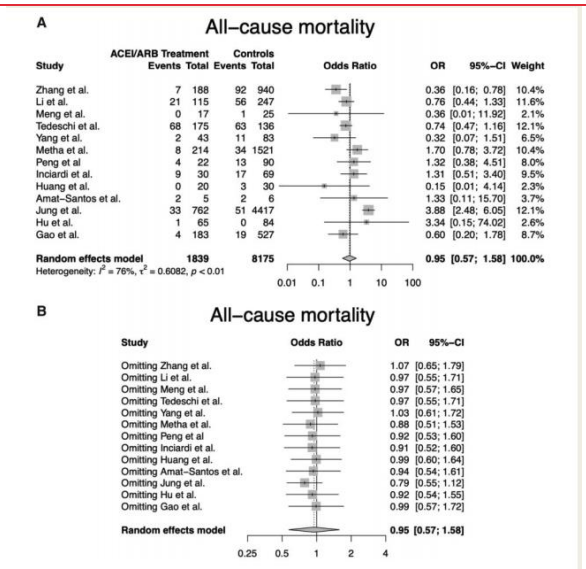


Figure 1 Forest plot (A) and leave-one-out sensitivity analysis (B) for all-cause mortality according to the use of ACEIs/ARBs. Abbreviations: ACEI,
angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CI, confidence interval; OR, odds ratio.

MEDICAL SUBSPECIALTIES

HEMATOLOGY AND ONCOLOGY

CLINICAL COURSE AND RISK FACTORS FOR MORTALITY FROM COVID-19 IN PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES

Sanchez-Pina JM, RodrÃguez Rodriguez M, Castro Quismondo N, Gil Manso R, Colmenares R, Gil Alos D, Paciello ML, Zafra D, Garcia-Sanchez C, Villegas C, Cuellar C, CarreÃ±o G, Zamanillo I, Poza M, IÃ±iguez R, Gutierrez X, Alonso R, RodrÃguez A, Folgueira MD, Delgado R, Ferrari JM, Lizasoain M, Aguado JM, Ayala R, Martinez-Lopez J, Calbacho M.. Eur J Haematol. 2020 Jul 24. doi: 10.1111/ejh.13493. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

Researchers from Madrid followed 39 hematological cancer patients (HP) that tested positive for COVID-19 between March 7, 2020 and April 7, 2020 (Table 1) and compared their outcomes against 53 COVID-19 patients without hematological comorbidities. They sought to determine how the clinical course of COVID-19 differs between these populations and what factors might contribute to poorer outcomes among the hematologic cancer group, with findings including the following:
- The overall mortality was higher (34%) in the HP group compared to the non-HP group (13.2%) and to the estimated mortality in the general population in Spain (8.5%) at the time of this study
- Increased age (greater than 70 years old; p=0.003), a diagnosis of chronic lymphoblastic leukemia (CLL, p=0.008), and treatment with angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs; p=0.003) correlated with increased COVID-19 mortality (Table 2)
- Univariate and multivariate logistic regression analysis showed that hypertension (p=0.039), a need for oxygen therapy (p=0.008), and a C-reactive protein (CRP) greater than 10 (p=0.010) were all associated with increased COVID-19 mortality among the HP group (Table 3)

ABSTRACT

BACKGROUND: The impact of coronavirus disease 2019 (COVID-19) in haematological patients (HP) has not been reported to date. METHODS: We analyzed 39 patients with SARS-CoV-2 infection and haematological malignancies. Clinical characteristics and outcomes were compared to a matched control group of 53 non-cancer patients with COVID-19. Univariate and multivariate analyses were carried out to assess the risk factors associated with poor outcome. RESULTS: The most frequent haematological diseases were lymphoma (30%) and multiple myeloma (30%). Eighty-seven % HP developed moderate or severe disease. Patients with haematological malignancies had a significantly higher mortality rate compared to non-cancer patients (35.9% vs 13.2%; P=0.003 (odds ratio 6.652). The worst outcome was observed in chronic lymphocytic leukemia patients. Only age >70 years and C reactive protein >10 mg/dl at admission were associated with higher risk of death (odds ratio 34.86, p= 0.003 and 13.56, p=0.03). Persistant viral sheddind was detected in 5 HP. Active chemotherapy, viral load at diagnosis and COVID-19 therapy were not predictors of outcome. CONCLUSION: Mortality of COVID-19 is significantly higher in patients with haematological malignancies compared to non-cancer patients. The impact of persistant viral shedding must be considered in order to re-start therapies and maintain infectious control measures.
‘

Table 1. Clinical Characteristics at baseline of haematological malignancies patients with COVID-19. Non-survivor and survivors are compared. Descriptive statistics were used to summarize the data. Categorical variables were summarized as counts and percentages. Percentages refer to the total number of patients in its column. The χ^2 and Fisher's exact two-sided tests were used for comparisons between categorical variables.

	Total n=39	Non-survivor n=14	Survivor n=25	p value
Characteristic				
Age (mean, range)	64.7 (36-88)	74 (39-88)	59.5 (36-80)	0.003
Sex (M, male; F; female) (%)	M 23 (59) F 16 (41)	M 8 (57) F 6 (43)	M 15 (60) F 10 (40)	0.531
Body Mass (mean)	26.22	25.11	26.85	0.163
Coexisting disorder (%)				
Any	22 (56.4)	11 (78.6)	11 (44)	0.037
Diabetes	7 (20)	4 (28.6)	3 (12)	0.196
Hypertension	19 (48.7)	10 (71)	9 (36)	0.034
Cardiac disease	6 (15.4)	2 (14.4)	4 (16)	0.887
COPD	2 (5,1)	1 (7,1)	1 (4)	0.669
Thrombosis	4 (10,3)	2 (14.3)	2 (8)	0.535
Concomitant treatment (%)				
ACEi/ARBs	11 (28.2)	8 (57.1)	3 (12)	0.003
OAC/DOACs	6 (15.4)	4 (28,6)	2 (8)	0.088
Hematological malignancies (%)				
Multiple Myeloma	12 (30.8)	2 (14.4)	10 (40)	0.095
Lymphoma	12 (30.8)	2 (14.4)	10 (40)	0.059
Chronic Lymphocytic Leukemia	6 (15,4)	5 (35.5)	1 (4)	0.008
Acute leukemia and MDS	5 (12.8)	3 (21.3)	2 (8)	0.229
cMPN	2 (5.1)	0	2 (8)	0.277
Histiocytosis	2 (5.1)	2 (14.4)	0	0.052
Previous transplantation or CAR-T in the last year, active treatment and Type (%)				
Transplantation/CAR-T	5 (12.8)	0	5 (20)	0.073
Auto	3 (7.7)	0	3 (12)	0.177
Allo	1 (2.27)	0	1 (4)	0.448
CD19 CAR_T	1 (2.27)	0	1 (4)	0.448
Active treatment (Yes/No)	Yes 24 (61.5) No 15 (38.5)	Yes 8 (57.1) No 6 (42.9)	Yes 16 (64) No 9 (36)	0.673
1- Chemotherapy	4 (10.3)	4 (26.8)	0	0.005
2- Targeted	5 (12.8)	2 (14.3)	3 (12)	0.838
3- ITK	2 (5.1)	0	2 (8)	0.277
4- Proteasome inhibitor	7 (17.9)	1 (14.3)	6 (24)	0.188
5- Monoclonal antibody	5 (12.8)	1 (7.1)	4 (16)	0.427
6- IMIDs	3 (7.7)	0 (14.3)	3 (12)	0.177
7- Steroids	12 (30.8)	4 (28.6)	8 (32)	0.824
Symptoms				
Mean duration of symptoms before diagnosis (range)	5.6 (1-17)	4.7 (1-17)	6.2 (1-14)	0.304
Respiratory symptoms (%)	32 (82.1)	13 (92.9)	19 (76)	0.188
Cough (%)	31 (79.5)	12 (85.7)	19 (76)	0.471
Dyspnea (%)	15 (38.5)	7 (50)	8 (32)	0.268
Odynophagia (%)	6 (15.4)	2 (14.3)	4 (16)	0.887
Sputum production (%)	0	0	0	
Headache (%)	7 (17.9)	1 (7.1)	6 (24)	0.188
Rhinorrhea (%)	7 (17.9)	4 (28.6)	3 (12)	0.196
Diarrhea (%)	7 (17.9)	2 (14.3)	2 (20)	0.656
Anosmia/Ageusia (%)	3 (7.7)	0 (0)	3 (12)	0.177
Conjunctivitis (%)	0	0	0	
Temperature >38ºC (%)	35 (89.7%)	13 (92.9%)	22 (88%)	0.632
Oxygen therapy (to obtain > 94% SaO2) (%)				0.033
1- None	20 (51.3)	3 (21.4)	17 (68)	
2- Low-flow Oxygen	12 (30.7)	7 (50)	5 (20)	
3- High flow oxygen (reservoir mask)	6 (15.4)	3 (21.4)	3 (12)	
4- Positive pressure	1 (2.6)	1 (7.2)	0	
WHO severity scale (%)				0.004
1- MILD	5 (12.8)	2 (14.3)	3 (12)	
2- MODERATE	16 (41)	1 (7.1)	15 (60)	
3- SEVERE	18 (46.2)	11 (78.6)	7 (28)	

Table 1. Clinical Characteristics at baseline of hematological malignancies patients with COVID-19. Non-survivor and survivors are compared. Descriptive statistics were used to summarize the data. Categorical variables were summarized as counts and percentages. Percentages refer to the total number of patients in its column. The chi-squared and Fisher's exact two-sided tests were used for comparisons between categorical variables.

	Total (n=39)	Non-survivor (n=14)	Survivor (n=25)	p value
Laboratory data				
Lymphocytes x 10^9 cells/L [mean ± SD]	0.8 (±0.8)	5.5 (±0.4)	1. (±0.7)	0.96
Neutrophils x 10^9 cells/L [mean ± SD]	3.6 (±2.8)	4.4 (±3.4)	3.2 (±2.3)	0.21
Platelets x 10^9 /L [mean ± SD]	163.7 (±96.8)	129.4 (±75.9)	182.9 (±103)	0.098
D-Dimer ng/ml [mean ± SD]	1286 (±1467)	1698 (±1782)	984 (±1157)	0.228
LDH U/L [mean ± SD]	308 (±129.6)	356 (±156.4)	272.5 (±95.1)	0.066
ALT/GPT U/L [mean ± SD]	24 (±17.3)	19.8 (±8.3)	26.6 (±20.8)	0.250
AST/GOT U/L [mean ± SD]	29 (±19.9)	31.3 (±14.8)	27.7 (±16.7)	0.509
Ferritin pg/mL [mean ± SD]	1061.2 (±950.7)	431 (±217.4) 17.8 (±15.3)	1206 (±999.9)	0.214
CRP mg/dL [mean ± SD]	10.9 (±11.2)	4.203 (±1.731)		0.008
Viral load Log_{10} [mean ± SD]	3.94 (±1.78)		7.1 (±7) 3.764 (±1.84)	0.518
Chest Radiography (%)				0.495
- Normal	9 (23.1)	4 (28.6)	5 (20)	
- Lobar pneumonia	2 (5.2)	0	2 (8)	
- Bilateral pneumonia	28 (71,7)	10 (71,4)	18 (72)	

Table 2. Laboratory and radiologic data at COVID-19 diagnosis of haematological malignancies patients with COVID-19. Non-survivor and survivor are compared. Descriptive statistics were used to summarize the data. Results are reported as medians and ranges or means and standard deviations, as appropriate. Categorical variables were summarized as counts and percentages. Percentages refers to the total number of patients in its column. The chi-squared and Fischer's exact two-sided tests were used for comparisons between categorical variables, and the Wilcoxon, Rank sum, or t-test was used for continuous variables.

Table 3. Univariate and multivariate logistic regression analysis determining risk factors of death in haematological malignancies patients with COVID-19.

	Univariate			Multivariate		
Variable	OR	95% CI	p value	OR	95% CI	p value
Age>70	19.25	3.641-101.773	0.000	34.86	3.407-356.8	0.003
Hypertension	4.444	1.076-18.355	0.039			
ACEi/ARBs	9.778	1.965-48.665	0.005			
Need of Oxygen therapy	7.792	1.690-35924	0.008			
Severity > moderate	9.429	2.008-44.271	0.004			
CRP>10	7.6	1.609-35.906	0.010	13.56	1.28-143.45	0.03

Table 2. Laboratory and radiologic data at COVID-19 diagnosis of haematological malignancies patients with COVID-19. Non-survivor and survivor are compared. Descriptive statistics were used to summarize the data. Results are reported as medians and ranges or means and standard deviations, as appropriate. Categorical variables were summarized as counts and percentages. Percentages refers to the total number of patients in its column. The chi-squared and Fischer's exact two-sided tests were used for comparisons between categorical variables, and the Wilcoxon, Rank sum, or t-test was used for continuous variables.

COVID-19 INFECTION IN PATIENTS WITH SÉZARY SYNDROME: REPORT OF TWO CASES

Gonzaga Y, Batista Fontes Santos M, Silva MM, Nucci M.. Dermatol Ther. 2020 Jul 23:e14042. doi: 10.1111/dth.14042. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

This letter discusses 2 case reports of Sezary Syndrome (SS) patients from Brazil who passed away shortly after testing positive for COVID-19 due to rapid disease progression. The authors discuss how immunosuppressive treatment of cancers such as SS leaves patients vulnerable to infection and suggest that patients with stable SS should postpone chemotherapy to reduce mortality risk during the pandemic.

SUMMARY

-Case 1: 56 year old woman with history of relapsing Sezary Syndrome (SS; erythroderma pictured in Figure 1) diagnosed in 6/2018 presented with "fever, chills and progressive cutaneous and nodal disease," subsequently testing positive for SARS-CoV-2 infection. She was treated with broad spectrum antibiotics and initial chest x-ray was normal. Of note, CT was not performed due to logistical reasons. She passed away 5 days after admission due to progression of her SS.

-Case 2: "78-year old woman with well-controlled arterial hypertension and asthma" was diagnosed with Sezary Syndrome (SS) in 2/2020 and was started on gemcitabine after 6 weeks due to worsening progression of her SS. Following two cycles of chemotherapy, the patient presented with fever and hypotension. Fluid resuscitation was successful and she became afebrile. Ten days later, she developed dry cough and respiratory distress. CT revealed bilateral ground glass opacities occupying more than 50% of the lungs (Figure 2). She tested positive for COVID-19 and her disease progressed over the next 8 days, leading to death.

FIGURES

Figure 1 - Patient with erythroderma at diagnosis of SS.

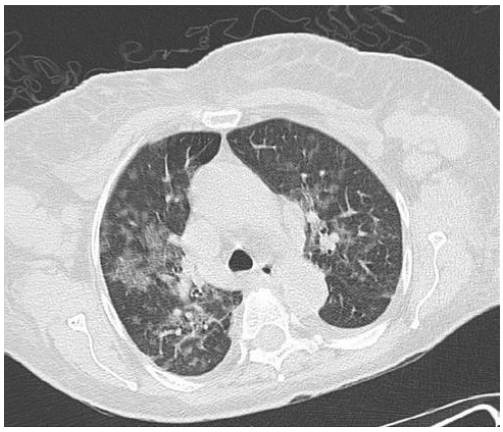


Figure 2 - Chest CT scan showing bilateral ground glass opacities.

CARDIOLOGY

EXPECTING THE UNEXPECTED: ECHO LABORATORY PREPAREDNESS IN THE TIME OF COVID-19

Goldberg AB, Kyung S, Swearingen S, Rao A.. Echocardiography. 2020 Jul 13. doi: 10.1111/echo.14763. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

Since the first cases of COVID-19 in Chicago were confirmed in March 2020, the cardiology department at Rush University Medical Center has taken precautions such as suspending non-urgent, elective, and outpatient echocardiogram testing indefinitely, assuring proper PPE for teams performing essential echocardiograms, providing preassembled "COVID-Kits" for all equipment used, and utilizing limited studies comprised of only the essential 7 cardiac windows (Figure 5) in order to reduce exposure time. They suggest their methods will limit exposure of essential sonographers while continuing to provide high-quality, timely, and clinically relevant cardiac images regardless of circumstances.

ABSTRACT

COVID-19 poses a unique set of challenges to the healthcare system due to its rapid spread, intensive resource utilization, and relatively high morbidity and mortality. Healthcare workers are at especially high risk of exposure given the viruses spread through close contact. Reported cardiac complications of COVID-19 include myocarditis, acute coronary syndrome, cardiomyopathy, pericardial effusion, arrhythmia, and shock. Thus, echocardiography is integral in the timely diagnosis and clinical management of COVID-19 patients. Rush University Medical Center has been at the forefront of the COVID-19 response in Illinois with high numbers of cases reported in Chicago and surrounding areas. The echocardiography laboratory at Rush University Medical Center (RUMC) proactively took numerous steps to balance the imaging needs of a busy, nearly 700-bed academic medical center while maintaining safety.

FIGURES

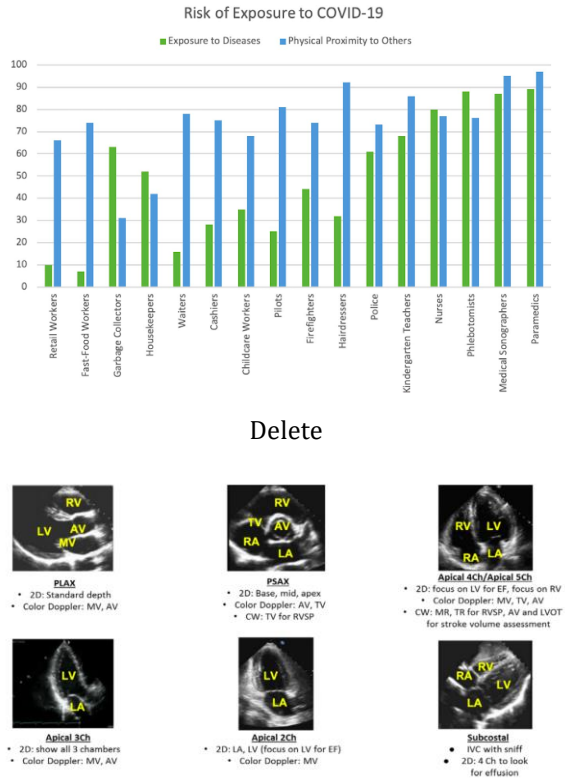


Figure 5. Standard views obtained for a limited COVID TTE at RUMC.

GENERAL SURGERY

A SYSTEM FOR RISK STRATIFICATION AND PRIORITIZATION OF BREAST CANCER SURGERIES DELAYED BY THE COVID-19 PANDEMIC: PREPARING FOR RE-ENTRY

Smith BL, Nguyen A, Korotkin JE, Kelly BN, Specht MC, Spring LM, Moy B, Isakoff SJ, Gadd MA.. Breast Cancer Res Treat. 2020 Jul 25. doi: 10.1007/s10549-020-05792-2. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Surgical oncologists from Massachusetts General Hospital created a risk stratification scoring system of breast cancer patients whose surgeries were delayed due to COVID-19. The score considers patient and tumor characteristics, length of delay, and tumor response to neoadjuvant chemotherapy; a higher score indicates higher risk of a poor outcome if surgery is delayed (Table 2). Risk scores agree closely with experienced surgeons' judgement (Table 3), suggesting this score can be used to prioritize higher risk patients as surgeries resume.

ABSTRACT

PURPOSE: During the COVID-19 pandemic, most breast surgery for benign and malignant conditions has been postponed, creating a backlog of patients who will need surgery. A fair and transparent system for assessing the risk of further delaying surgery for individual patients to prioritize surgical scheduling is needed. METHODS: Factors related to risk of delaying surgery for breast patients were identified. Scores were assigned to each factor, with higher scores indicating a greater risk from delaying surgery. REDCap and Microsoft Excel tools were designed to track and score delayed patients. RESULTS: Published data and multidisciplinary clinical judgement were used to assign risk scores based on patient and tumor factors, length of delay, and tumor response to preoperative therapy. Patients completing neoadjuvant chemotherapy were assigned the highest scores as their options for delaying surgery are most limited. Among patients receiving neoadjuvant endocrine therapy or no medical therapy, higher scores were assigned for low-estrogen receptor or high-genomic risk scores, higher grade, larger tumors, younger age and longer delay. High priority scores were assigned for progression during preoperative therapy. Low scores were assigned for re-excisions, atypical lesions and other benign indications. There was good agreement of the tool's ranking of sample patients with rankings by experienced clinicians. The tool generates risk-stratified patient lists by surgeon or institution to facilitate assignment of surgery dates. CONCLUSIONS: This tool generates a clinically consistent, risk-stratified priority list of breast surgical procedures delayed by the COVID-19 pandemic. This systematic approach may facilitate surgical scheduling as conditions normalize.
‘

Table 2 Score assignments for factors related to risk of delaying breast surgery

Risk factor	Risk score
Indication priority score—all patients	
Indication score	
Cancer—neoadjuvant chemotherapy	30
Cancer—neoadjuvant endocrine therapy or ER- DCIS or ER-, no chemotherapy	10
Re-excision, positive lumpectomy margin	4
ADH	3
Other atypia/probably benign	2
High-risk gene mutation	1
Symmetry/cosmetic	0
Scored only for cancer patients receiving neoadjuvant endocrine therapy	
Endocrine sensitivity score	
If genomic risk testing done	
Genomic risk test score—Oncotype DX	
< 18	0
≥ 18, < 31	1
≥ 31	5
Genomic risk test score—MammaPrint, EndoPredict, or other	
Low risk	0
High risk	5
If no genomic risk testing done	
ER strength score	
≥ 50% strong/moderate	0
11–49% strong/moderate	1
Any % faint or 1–10% strong/moderate or ER-	4
PR strength score	
Strong/moderate	0
Weak/negative	1
Tumor grade score	
1	1
2	2
3	3
Tumor size (cm) score	
DCIS	0
Microinvasion (≤ 0.1)	1
> 0.1, ≤ 1.0	1
> 1.0, ≤ 2.0	2
> 2.0, ≤ 3.0	3
> 3.0	4
Patient age score	
≥ 70	0
≥ 50, < 70	1
≥ 35, < 50	3
< 35	4
Delay score	
Time since biopsy	
≥ 0, < 3 months	0
≥ 3, < 4 months	1
≥ 4, < 6 months	2
≥ 6 months	3
Imaging response score	
Responding	0
Stable	1
Progressing any site	4
Physical exam response score	
Not palpable and not palpable at diagnosis	0
Responding	0
Stable	1
Progressing any site	5
Scored only for cancer patients receiving neoadjuvant chemotherapy	
ER score—neoadjuvant chemotherapy patients	
ER strong/moderate or low genomic risk	0
ER weak/negative or high genomic risk	10
Total risk score	
Total score	

ER estrogen receptor, *PR* progesterone receptor

Table 3 Priority ranks generated by the scoring system compared with priority ranks generated by experienced breast surgeons

Priority rank	Patient (system score)			Scoring system		Test patient and tumor characteristics
	Surgeon 1	Surgeon 2	Surgeon 3	Patient	Score	
1	F (18)	H (20)	H (20)	H	20	H: 45 yo, 2.5 cm grade 2 IDC, moderate ER+, PR-, N0
2	H (20)	F (18)	F (18)	F	18	F: 49 yo, 1.8 cm grade 2 IDC, ER, Oncotype = 25, N0
3	G (16)	A (17)	G (16)	A	17	A: 49 yo, 1.2 cm grade 2 IDC, strongly ER/PR+, N0
4	I (14)	G (16)	A (17)	G	16	G: 68 yo, 1.3 cm grade 3 IDC, strongly ER/PR+, N0
5	A (17)	I (14)	D (13)	I	14	I: 55 yo, 0.9 cm grade 2 IDC, ER+ Oncotype = 16, N0
6	C (14)	C (14)	I (14)	C	14	C: 63 yo, 0.9 cm grade 2 ILC, ER+ Oncotype = 11, N0
7	B (12)	D (13)	C (14)	D	13	D: 60 yo, 1.4 cm grade 1 DCIS+mi, strongly ER/PR+, N0
8	D (13)	E (13)	E (13)	E	13	E: 62 yo, 1.0 cm grade 2 DCIS, strongly ER+, N0
9	E (13)	B (12)	B (12)	B	12	B: 90 yo, 1.0 cm grade 1 IDC, strongly ER/PR+, N0
10	J (11)	J (11)	J (11)	J	11	J: 79 yo, grade 1 DCIS, strongly ER/PR+, N0

Scores of 18 or higher were considered highest risk, 15–17 considered medium risk, and 14 or lower considered lowest risk

yo years old, *ER* estrogen receptor, *PR* progesterone receptor, *IDC* invasive ductal cancer, *DCIS* ductal carcinoma in situ; mi: microinvasion, *ILC* invasive lobular cancer

COVID-19 DOES NOT STOP OBSTETRICS: WHAT WE NEED TO CHANGE TO GO ON SAFELY BIRTHING. THE EXPERIENCE OF A UNIVERSITY OBSTETRICS AND GYNECOLOGY DEPARTMENT IN MILAN

Alfieri N, Manodoro S, Marconi AM.. J Perinat Med. 2020 Jul 7:/j/jpme.ahead-of-print/jpm-2020-0218/jpm-2020-0218.xml. doi: 10.1515/jpm-2020-0218. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

Physicians describe the change in management of the Obstetrics and Gynecology Unit at University Hospital in Milan, Italy during the COVID-19 pandemic. During this time the hospital was converted to a COVID-19 hospital and to minimize patient exposure many functions were converted to a remote modality. In addition, clinical visits were reduced and all non-preventative and non-cancer services in gynecology were suspended. The authors state while it is important to protect the health of the patient population from risk of infection, it is also essential to continue to provide quality support and care for patients.

SUMMARY

The authors report the following changes made to adapt to the COVID-19 pandemic in their Obstetrics and Gynecology Department:
-Conversion of the antepartum care/day surgery area to a COVID-19 ward
-A 13 item triage questionnaire for all patients entering the clinic
-Creation and implementation of brochures and tele-health modalities culturally receptive to migrant patients
-Use of zoom platforms for prenatal and other educational classes
-Video or telephone call service for new mothers
-Reduction in frequency of onsite visits and spacing of inpatient visits, so as to avoid multiple people in the waiting room
-Requiring all patients to wear masks and gloves
-Nasopharyngeal swab of patients if they showed symptoms of acute respiratory infections
-Creation of isolation rooms for patients while they waited for the outcome of tests
-Having patients wear sterile gloves and surgical masks during procedures
-Allowing no visitors in the maternity ward during this time
-Clinical education services utilized online learning

ABSTRACT

Since SARS-COV-2 appeared in Wuhan City, China and rapidly spread throughout Europe, a real revolution occurred in the daily routine and in the organization of the entire health system. While non-urgent clinical services have been reduced as far as possible, all kind of specialists turned into COVID-19 specialists. Obstetric assistance cannot be suspended and, at the same time, safety must be guaranteed. In addition, as COVID-19 positive pregnant patients require additional care, some of the clinical habits need to be changed to face emerging needs for a vulnerable but unstoppable kind of patients. We report the management set up in an Obstetrics and Gynecology Unit during the COVID-19 era in a University Hospital in Milan, Italy.

PERSISTENT COVID-19 IN AN IMMUNOCOMPROMISED PATIENT TEMPORARILY RESPONSIVE TO TWO COURSES OF REMDESIVIR THERAPY

Helleberg M, Niemann CU, Moestrup K, Kirk O, Lebech AM, Lane C, Lundgren J.. J Infect Dis. 2020 Jul 23:jiaa446. doi: 10.1093/infdis/jiaa446. Online ahead of print.
Level of Evidence: 4 - Case Report

BLUF

This case report from Copenhagen University Hospital describes the suppressive effect of remdesivir in a 50-year-old immunocompromised patient with a 9-week course of COVID-19. Following a 10-day inpatient course of remdesivir, he was rehospitalized after lymphocytosis and increased inflammatory markers suggested a relapse 3 days post-discharge, which was managed with another 10-day course of remdesivir (Figure 1). While the authors suggest remdesivir can suppress SARS-CoV-2, it may not eradicate the virus, and further study is needed to determine optimal dosing protocols.

ABSTRACT

The antiviral drug remdesivir has been shown clinically effective for treatment of COVID-19. We here demonstrate suppressive but not curative effect of remdesivir in an immunocompromised patient. A man in his fifties treated with chemoimmunotherapy for chronic lymphocytic leukemia experienced a 9-week course of COVID-19 with high fever, and severe viral pneumonia. During two 10-day courses of remdesivir starting days 24 and 45 after fever onset, the pneumonia and spiking fevers remitted, but relapsed after discontinuation. Kinetics of temperature, C-reactive protein, and lymphocyte counts mirrored the remitting/relapsing SARS-CoV-2 infection. Combination therapy or longer treatment duration may be needed in immunocompromised patients.

FIGURES

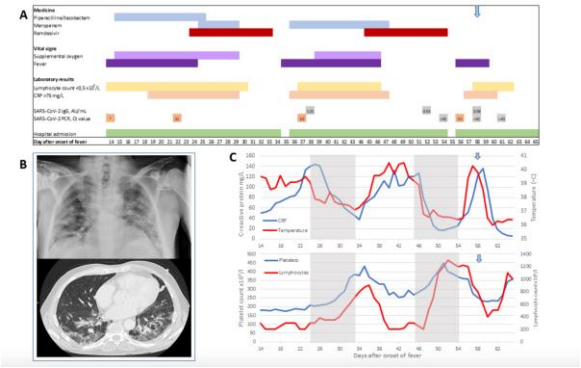


Figure 1: Timeline of hospital admissions, treatments, tests for SARS-CoV-2 (A), radiology (B) and kinetics of temperature, C-reactive protein, platelet and lymphocyte counts before, during and after treatment with remdesivir (C).

The blue arrow indicates the day of infusion of convalescent plasma. In panel A red boxes for SARS-CoV-2 PCR represents positive test. Grey boxes for SARS-CoV-2 antibody and PCR represents negative tests. *Ct value not available for that test. In panel C the grey shade marks the time period of remdesivir treatment.

VALIDATION AND PERFORMANCE COMPARISON OF THREE SARS-COV-2 ANTIBODY ASSAYS

Paiva KJ, Grisson RD, Chan PA, Huard RC, Caliendo AM, Lonks JR, King E, Tang EW, Pytel-Parenteau DL, Nam GH, Yakirevich E, Lu S.. J Med Virol. 2020 Jul 25. doi: 10.1002/jmv.26341. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

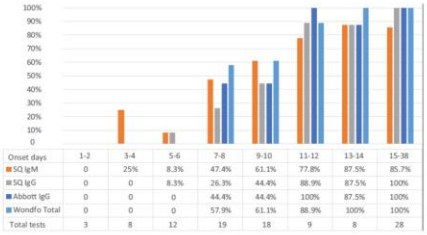
A study by authors affiliated with Brown University and the Rhode Island Department of Health validates 3 different SARS-CoV-2 antibody assays, including one chemiluminescent test (Abbott COVID-2 IgG) and two lateral flow tests (STANDARD Q [SQ] IgM/IgG Duo and Wondfo Total Antibody Test). Each assay detected antibodies in 100% of all COVID-19 positive samples by 2 weeks after symptom onset (Figure 1), with only SQ IgM showing suboptimal results (85.7% positive rate). The authors support the use of serological testing in COVID-19 as part of diagnostic testing, particularly 14 days after symptom onset.

ABSTRACT

Serology testing of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is increasingly being used during the current pandemic of Coronavirus Disease 2019 (COVID-19), although its clinical and epidemiologic utilities are still debatable. Characterizing these assays provides scientific basis to best use them. The current study assessed one chemiluminescent assay (Abbott COVID-2 IgG) and two lateral flow assays (STANDARD Q [SQ] IgM/IgG Duo and Wondfo Total Antibody Test) using 113 blood samples from 71 PCR-confirmed COVID-19 hospitalized patients, 119 samples with potential cross-reactions, and 1068 negative controls including 942 pre-pandemic samples. SARS-CoV-2 IgM antibodies became detectable 3-4 days post-symptom onset using SQ IgM test and IgG antibodies were first detected 5-6 days post-onset using SQ IgG. Abbott IgG and Wondfo Total were able to detect antibodies 7-8 days post-onset. After 14 days post-symptom onset, the SQ IgG, Abbott IgG and Wondfo Total tests were able to detect antibodies from 100% of the PCR-confirmed patients in this series; 87.5% sensitivity for SQ IgM. Overall agreement was 88.5% between SQ IgM/IgG and Wondfo Total and 94.6% between SQ IgG and Abbott IgG. No cross-reaction due to recent sera with three of the endemic coronaviruses was observed. Viral hepatitis and autoimmune samples were the main source of limited cross-reactions. The specificities were 100% for SQ IgG and Wondfo Total, 99.62% for Abbott IgG, and 98.87% for SQ IgM. These findings demonstrated high sensitivity and specificity of appropriately validated SARS-CoV-2 serologic assays with implications for clinical use and epidemiological seroprevalence studies.

FIGURES

SQ IgM: STANDARD Q COVID-19 IgM (SD BIOSENSOR); SQ IgG: STANDARD Q COVID-19 IgG (SD BIOSENSOR); Wondfo Total: SARS-CoV-2 Total Antibody Test (Wondfo).



Onset days	1-2	3-4	5-6	7-8	9-10	11-12	13-14	15-38
SQ IgM	0	25%	8.3%	47.4%	61.1%	77.8%	87.5%	85.7%
SQ IgG	0	0	8.3%	26.3%	44.4%	88.9%	87.5%	100%
Abbott IgG	0	0	0	44.4%	44.4%	100%	87.5%	100%
Wondfo Total	0	0	0	57.9%	61.1%	88.9%	100%	100%
Total tests	3	8	12	19	18	9	8	28

Figure 1. Positive rates of four tests based on symptom onset days

SYSTEMATIC REVIEW AND META-ANALYSIS OF EFFECTIVENESS OF TREATMENT OPTIONS AGAINST SARS-COV-2 INFECTION

Chandrasekar VT, Venkatesalu B, Patel HK, Spadaccini M, Manteuffel J, Ramesh M.. J Med Virol. 2020 Jul 15. doi: 10.1002/jmv.26302. Online ahead of print.
Level of Evidence: 1 - Systematic review of randomized trials or n-of-1 trials

BLUF

Researchers conducted a systematic review and meta-analysis of 29 articles (including randomized control studies, prospective and retrospective studies involving a total of 5,207 total patients) published between December 1, 2019 and May 11, 2020 related to the various treatments of SARS-CoV-2 infection. The review examined outcomes of COVID-19 patients treated with hydroxychloroquine, remdesivir, ritonavir/lopinavir, convalescent plasma therapy, and tocilizumab and results revealed that hydroxychloroquine was associated with increased morbidity and mortality (Figure 2B) and none of the other interventions significantly changed the course of COVID-19 infection or the disease outcomes (Figure 2A). The authors recommend more randomized clinical trials to further study the safety and efficiency of different therapeutic measures.

ABSTRACT

Treatment options for Severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) are limited with no clarity on efficacy and safety profiles. We performed a systematic review and meta-analysis of studies on patients >= 18 years reporting data on therapeutic interventions in SARS-CoV-2. Primary outcome was all-cause mortality and secondary outcomes were rates of mechanical ventilation, viral clearance, adverse events, discharge and progression to severe disease. Pooled rates and odds ratios (OR) were calculated. Twenty-nine studies with 5207 patients were included. Pooled all-cause mortality in intervention arm was 12.8% (95%CI: 8.1%-17.4%). Mortality was significantly higher for studies using hydroxychloroquine (HCQ) for intervention (OR: 1.36, 95% CI: 0.97-1.89). Adverse events were also higher in HCQ sub-group (OR: 3.88, 95% CI: 1.60 - 9.45). There was no difference in other secondary outcomes. There is a need for well-designed randomized clinical trials for further investigation of every therapeutic intervention for further insight into different therapeutic options.

FIGURES

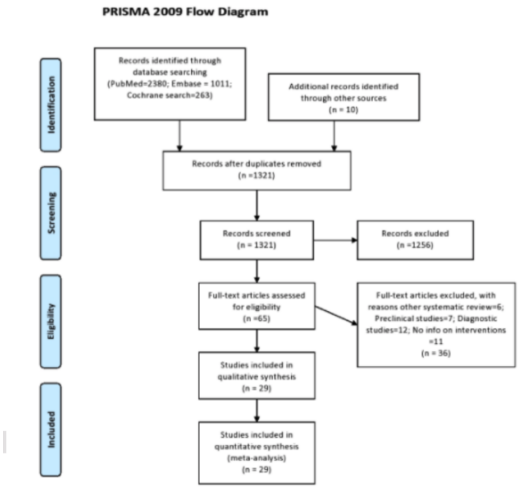


Figure 1 – PRISMA Flow diagram

Figure 2A - Odds ratio comparing all-cause in hospital mortality in intervention and control arms

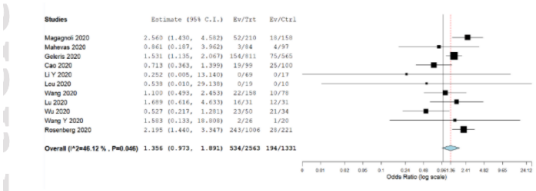


Figure 2B – Odds ratio comparing all-cause in hospital mortality in intervention and control arms in hydroxychloroquine based studies

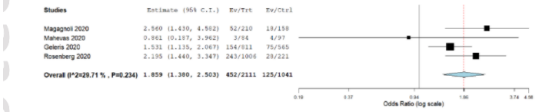


Figure 2A - Odds ratio comparing all-cause in hospital mortality in intervention and control arms
Figure 2B – Odds ratio comparing all-cause in hospital mortality in intervention and control arms in hydroxychloroquine based studies

Figure 3A – Odds ratio comparing rates of mechanical ventilation

control arms

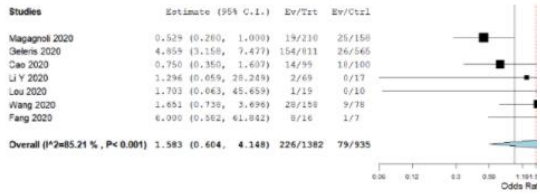


Figure 3B – Odds ratio comparing clinical recovery rates in interv

arms

Figure 2A - Odds ratio comparing all-cause in hospital mortality in intervention and control arms
Figure 2B – Odds ratio comparing all-cause in hospital mortality in intervention and control arms in hydroxychloroquine based studies

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