The Daily COVID-19 Literature Surveillance Summary

July 29, 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

Climate

- The Immunization Action Coalition and the Vanderbilt School of Medicine discuss the progress of developing a COVID-19 vaccine, detailing the 11 vaccines in phase 1/2 clinical trials and the inclusion of multiple countries in the development of a Target Product Profile, a tool for quantifying critical vaccine characteristics. The authors emphasize the need for well-established infrastructure and logistical planning in order to distribute a potential COVID-19 vaccine safely and effectively to the world in a timely manner.

Epidemiology

- Researchers in the United States and United Kingdom used Twitter data to predict human mobility in and out of China and estimate global spread of COVID-19 and found a high correlation between country-level Twitter user visits and reported COVID-19 cases. These findings highlight the utility of geolocated platforms for public health authorities to develop response protocols and assess impending risks of COVID-19.

Understanding the Pathology

- A systematic review and meta-analysis of 13 studies, including 1341 cases, investigated abnormal coagulation function markers to predict severity of COVID-19 infection. They found that decreased platelet counts, elevated d-dimer, and increased fibrinogen are correlated with disease severity, whereas prothrombin time and activated partial thromboplastin time have no significant correlation with disease severity.
- Based on literature of prostaglandins in SARS-CoV-1 and MERS-CoV, a group from the University of Edinburgh cite the potential roles of multiple prostaglandins (including PGD2, PGE2, PGI2) in the pathogenesis of COVID-19 and consider the possible benefits of NSAID usage in COVID-19 patients.

Management

- A study found that among 59 patients with symptoms consistent with COVID-19, fibrinogen levels were markedly higher in patients who ultimately tested positive on RT-PCR compared to those who tested negative. Additionally, the neutrophil-to-lymphocyte ratio was increased in critically ill COVID-19 patients. These results suggest that fibrinogen may have value as a diagnostic marker in patients with suspected COVID-19 and that neutrophil to lymphocyte ratio may be useful as a prognostic marker indicative of COVID-19 disease severity.

Adjusting Practice During COVID-19

- A cross sectional study of 26 heart failure patients found a 16.2% decrease in daily step count on wearable accelerometers during the first 3 weeks of quarantine compared to regular activity suggesting that widespread COVID-19 quarantine mandates were detrimental to physical activity habits in these patients. These findings highlight the importance of physical activity during the pandemic in reducing deterioration in cardiovascular health.

R&D: Diagnosis and Treatments

- Investigators in China measured SARS-CoV-2-specific antibodies among moderate and severe COVID-19 patients as well as non-COVID-19 patients and found that IgA and IgG were higher among severe patients compared to moderate patients whereas no difference was observed between the groups in IgM. Based on their findings, the authors suggest that IgA-IgG serological diagnosis of COVID-19 may be more effective than the traditional detection of IgM-IgG combined antibodies.
- A group from Stanford University School of Medicine conducted a case-control study to assess for differences in inflammatory cytokine levels by comparing 15 hospitalized patients with severe COVID-19 to critically ill patients with ARDS or sepsis due to another cause. The authors found no differences in IL-1b, IL-1RA, IL-6, IL-8, IL-18, and TNFα levels between patients with COVID-19 and controls with ARDS or sepsis. The authors discuss how numerous phase 3 trials testing the broad use of immunosuppressants in ARDS and sepsis have failed previously and state that these therapies may be unnecessary in COVID-19 as well.

TABLE OF CONTENTS

CLIMATE

GLOBAL

LOGISTICAL CHALLENGES FOR POTENTIAL SARS-COV-2 VACCINE AND A CALL TO RESEARCH INSTITUTIONS, DEVELOPERS AND MANUFACTURERS

Kartoglu UH, Moore KL, Lloyd JS.. Vaccine. 2020 Jul 22;38(34):5393-5395. doi: 10.1016/j.vaccine.2020.06.056. Epub 2020 Jun 23.

Level of Evidence: Other - Opinion

BLUF

This opinion piece by the Immunization Action Coalition and the Vanderbilt School of Medicine discusses the progress of developing a COVID-19 vaccine, which currently includes 11 vaccines in phase 1/2 clinical trials and the inclusion of multiple countries in the development of a Target Product Profile, a tool for quantifying critical vaccine characteristics. Furthermore, the paper highlights the use of Vaccine Vial Monitors (Figure 1) to monitor temperature during storage and the need for countries to have robust storage, established transport, and modes of effective vaccine management (e.g. trained medical professionals) in order to ensure effective global immunization. This paper emphasizes the need for well-established infrastructure and logistical planning in order to safely and effectively distribute a potential COVID-19 vaccine to the world in a timely manner.

FIGURES

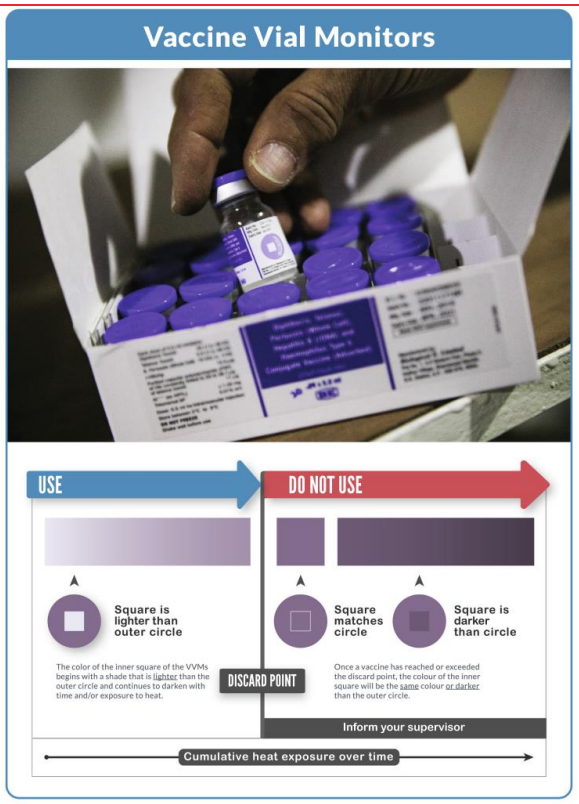

Fig. 1. How VVM works.

EPIDEMIOLOGY

MODELING

GEOLOCATED TWITTER SOCIAL MEDIA DATA TO DESCRIBE THE GEOGRAPHIC SPREAD OF SARS-COV-2

Bisanzio D, Kraemer MUG, Brewer T, Brownstein JS, Reithinger R.. J Travel Med. 2020 Jul 23:taaa120. doi: 10.1093/jtm/taaa120. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

Researchers in the United States and United Kingdom used Twitter data to predict human mobility in and out of China and estimate global spread of COVID-19, which has implications for public health authorities in development of response protocols and assessing COVID-19 risks (see summary).

SUMMARY

Review of study findings as follows:
A modeling study by authors in the United States and United Kingdom assessed geolocated Twitter data (including 9,678 users and 1,063,908 tweets) from 2013-2015 to estimate human mobility in and out of China in 2019-2020 and predict global spread of COVID-19. They found 48.1% (n=4,669) of users posted tweets outside China but 68.8% (n=3,215) of this group also posted more than 2 tweets in China (from 1 December to 15 February of 2014 or 2015), and within 30 days after leaving China following their second tweet users posted tweets from 2,381 cities in 140 countries (IQR=3–13 cities visited; most visited countries included USA [46.5%], Japan [15.1%], and UK [13.9%]). Authors suggest a high correlation between country-level Twitter user visits and reported COVID-19 cases (Spearman's rank correlation coefficient (ρ)=0.71, p<0.01), highlighting the utility of geolocated platforms for public health authorities to develop response protocols and assess impending risks of COVID-19.

FIGURES

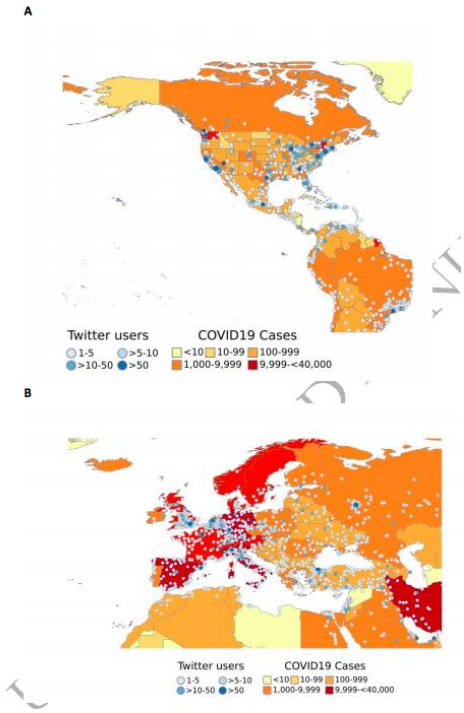

Figure 1. Location visited by visited by the study cohort of Twitter users who were followed-up for 30 days after having tweeted at least two times on consecutive days from Wuhan between December 1, 2013, and February 15, 2014 and December 1, 2014, and February 15, 2015. North and Central America (A), Europe (B), Asia (C), South America (D), Africa and Middle East (E), Oceania (F).

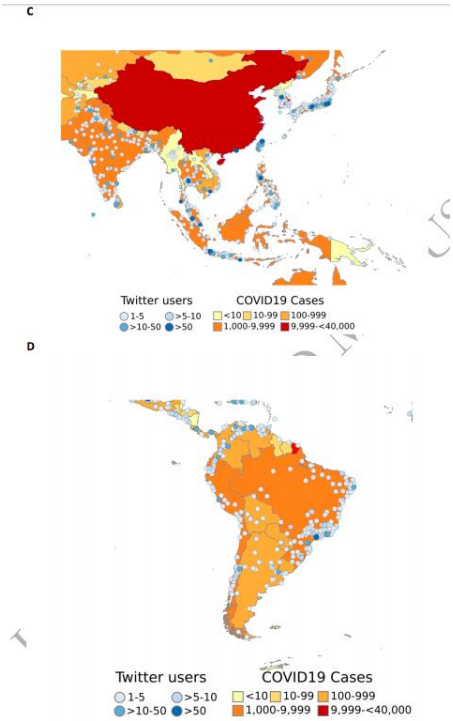

Figure 2. Location visited by visited by the study cohort of Twitter users who were followed-up for 30 days after having tweeted at least two times on consecutive days from Wuhan between December 1, 2013, and February 15, 2014 and December 1, 2014, and February 15, 2015. North and Central America (A), Europe (B), Asia (C), South America (D), Africa and Middle East (E), Oceania (F).

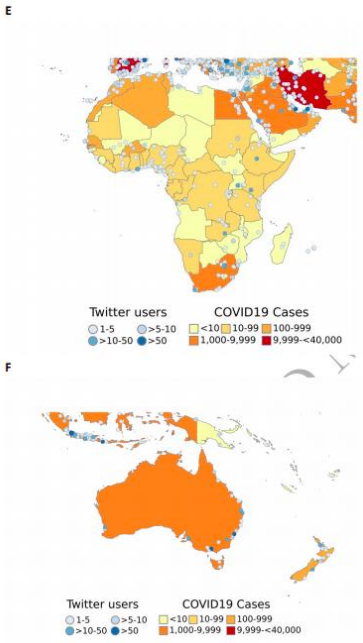

Figure 3. Location visited by visited by the study cohort of Twitter users who were followed-up for 30 days after having tweeted at least two times on consecutive days from Wuhan between December 1, 2013, and February 15, 2014 and December 1, 2014, and February 15, 2015. North and Central America (A), Europe (B), Asia (C), South America (D), Africa and Middle East (E), Oceania (F).

COVID-19 AND COAGULATION DYSFUNCTION IN ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Lin J, Yan H, Chen H, He C, Lin C, He H, Zhang S, Shi S, Lin K.. J Med Virol. 2020 Jul 24. doi: 10.1002/jmv.26346. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

A systematic review and meta-analysis of 13 qualifying studies with 1341 cases published in China in 2020 (Figure 1) investigating the use of abnormal coagulation function markers to predict severity of COVID-19 infection found the following: decreased platelet counts, elevated d-dimer, and increased fibrinogen are correlated with disease severity, whereas prothrombin time (PT) and activated partial thromboplastin time (APTT) have no significant correlation with disease severity. These markers are suggested as reliable risk factors for greater severity of COVID-19 infection and predicting factors for COVID-19 complications, including thrombogenesis, consumptive coagulopathy, coagulation factor deficiency, and fibrinolysis.

SUMMARY

Severe COVID-19 infection was associated with:
- Reduced platelet counts [6.1% heterogeneity; Weighted Mean Difference (WMD)=-24.83, 95% CI (-34.12, -15.54), p<0.001]
- Elevated D-dimer [52.1% heterogeneity; WMD=0.19, 95% CI (0.09, 0.29), p<0.001]
- Increased fibrinogen [66.8% heterogeneity; WMD=1.02, 95% CI (0.50, 1.54), p<0.001].

No significant correlation with COVID-19 severity:
- Prothrombin Time (PT) [65.2% heterogeneity; WMD=0.19, 95% CI (-0.13, 0.51), p=0.243, I2 = 65.2%]
- Activated Partial Thromboplastin Time (APTT) [91.5% heterogeneity; WMD was -1.56 (95% CI: -5.77, 2.64; p=0.465)] were not found to have any correlation with disease severity.

ABSTRACT

BACKGROUND: The outbreak of 2019 novel coronavirus disease (COVID-19) has posed a grave threat to the global public health. The COVID-19-induced infection is closely related to coagulation dysfunction in the affected patients. This paper attempts to conduct a meta-analysis and systematically review the blood coagulation indicators in severe COVID-19 patients. METHODS: A meta-analysis of eligible studies was performed to compare the blood coagulation indicators in severe and non-severe COVID-19 patients. PubMed, Embase, Web of Science, and the Cochrane Library were searched for studies published between December 1, 2019 and May 7, 2020. RESULTS: A total of 13 studies with 1,341 adult patients were enrolled in this analysis. Platelet [WMD=-24.83, 95% CI (-34.12, -15.54), p<0.001], d-dimer [WMD=0.19, 95% CI (0.09, 0.29), p<0.001] and fibrinogen [WMD=1.02, 95% CI (0.50, 1.54), p<0.001] were significantly associated with the severity in COVID-19 patients. The meta-analysis revealed that no correlation was evident between an increased severity risk of COVID-19 and activated partial thromboplastin time (APTT) [WMD=-1.56, 95% CI (-5.77, 2.64), p=0.468] or prothrombin time (PT) [WMD=0.19, 95% CI (-0.13, 0.51), p=0.243]. The single arm meta-analysis showed that, compared with the non-severe group, the severe group had a lower pooled platelet [165.12 (95% CI: 157.38-172.85) vs. 190.09 (95% CI: 179.45-200.74)], higher d-dimer [0.49 (95% CI: 0.33-0.64) vs. 0.27 (95% CI: 0.20-0.34)] and higher fibrinogen [4.34 (95% CI: 1.98-6.70) vs. 3.19 (95% CI: 1.13-5.24)]. CONCLUSIONS: Coagulation dysfunction is closely related to the severity of COVID-19 patients, in which low platelet, high d-dimer and fibrinogen upon admission may serve as risk indicators for increased aggression of the disease. These findings are of great clinical value for timely and effective treatment of the COVID-19 cases.

FIGURES

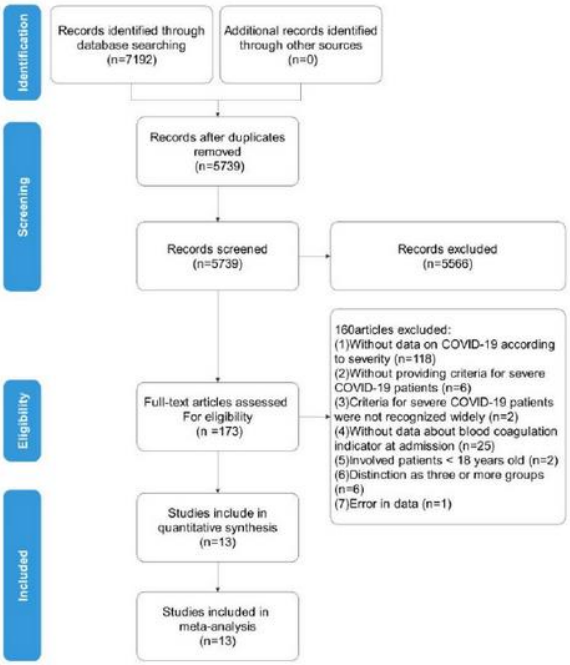

Figure 1. Flow-chart of study selection.

SYSTEMIC ENDOTHELIAL DYSFUNCTION: A COMMON PATHWAY FOR COVID-19, CARDIOVASCULAR AND METABOLIC DISEASES

De Lorenzo A, Escobar S, TibiriÃ§Ã¡ E.. Nutr Metab Cardiovasc Dis. 2020 Jul 24;30(8):1401-1402. doi: 10.1016/j.numecd.2020.05.007. Epub 2020 May 18.
Level of Evidence: Other - Expert Opinion

BLUF

In this letter to the editor, the authors indicate a need for further examination of endothelial dysfunction in patients with cardiometabolic disease and coinciding COVID-19 in order to help minimize the severity of disease in this patient population. Endothelial dysfunction is known to cause an inflammatory state, increased oxidative stress, altered nitric oxide, and insulin resistance (Figure 1), and is observed in comorbidities that have been associated with greater severity of COVID-19 infection - including diabetes, hypertension, and hyperlipidemia. The authors suggest developing therapeutic strategies targeting this pathology to help mitigate the severity of COVID-19 in patients with these comorbidities.

ABSTRACT

Some of the mechanisms and conditions underlying endothelial dysfunction.A-human skin capillaries, visualized with high-resolution intravital color microscopy in the finger of a patient with obesity, metabolic syndrome and coronary artery disease.B- healthy control. The reduced number of capillaries can be noticed in A compared to B.Image 1.

FIGURES

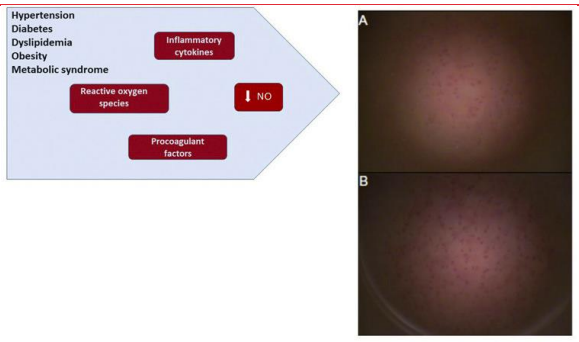

Figure 1. Some of the mechanisms and conditions underlying endothelial dysfunction. A) Human skin capillaries, visualized with high-resolution intravital color microscopy in the finger of a patient with obesity, metabolic syndrome, and coronary artery disease. B) In a healthy control: the reduced number of capillaries can be noticed in A compared to B.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS, PROSTAGLANDINS AND COVID-19

Robb CT, Goepp M, Rossi AG, Yao C.. Br J Pharmacol. 2020 Jul 23. doi: 10.1111/bph.15206. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Authors from the University of Edinburgh review the relationship between non-steroidal anti-inflammatory drugs (NSAIDs) and prostaglandins in the setting of SARS-CoV-2 infection. Based on literature of prostaglandins in SARS-CoV-1 and MERS-CoV, the authors cite the potential roles of multiple prostaglandins (PGD2, PGE2, PGI2) in the pathogenesis of COVID-19 and consider the possible benefits and side effects of NSAID usage in COVID-19 patients (Figure 3, Figure 4). The authors suggest further investigation into prostaglandins' impact on anti- and pro-inflammatory processes in COVID-19 in order to better understand the role of NSAIDs in COVID-19 management.

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of the novel coronavirus disease 2019 (COVID-19), a highly pathogenic and sometimes fatal respiratory disease responsible for the current 2020 global pandemic. Presently, there remains no effective vaccine nor efficient treatment strategies against COVID-19. Non-steroidal anti-inflammatory drugs (NSAIDs) are medicines very widely used to alleviate fever, pain and inflammation (common symptoms of COVID-19 patients) through effectively blocking production of prostaglandins (PGs) via inhibition of cyclooxygenase enzymes. PGs can exert either pro- or anti-inflammatory effects depending on the inflammatory scenario. In this review, we implicate the potential roles that NSAIDs and PGs may play during SARS-CoV-2 infection and the development and progression of COVID-19.

FIGURES

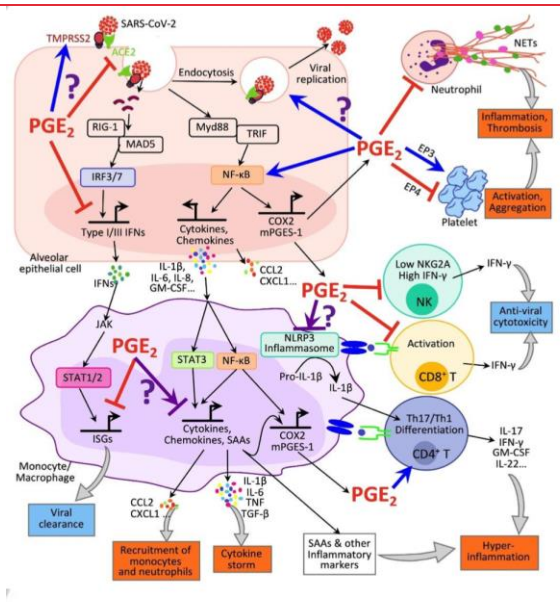

Figure 3. Possible mechanisms for PGE2 modulation of immune cell functions in COVID-19.

PGE2 likely modulates immune responses in various cell types during SARS-CoV-2 infection, influencing COVID-19 pathogenesis. In epithelial cells, attachment of SARS-CoV-2 with ACE2 and TMPRSS2 leads to endocytosis, viral replication, and cell damage, activating RLR (RIG-1 and MAD5)-dependent production of type I and III interferons (IFNs) and the TLR-dependent NF-kB pathway. The NF-kB pathway induces expression of proinflammatory cytokines (eg. IL-1b, IL-6, IL-8, GM-CSF), chemokines (eg. CCL2, CXCL1) and other inflammatory mediators such as COX-2 and mPGES-1, resulting in PGE2 secretion. Here, while it suppresses the production of type I (and possible type III) IFNs, PGE2, further amplifies NF-kB signaling and production of cytokines and chemokines in a positive feedback loop. PGE2 may also directly modulate ACE2 and

TMPRSS2 gene expression, endocytosis, and viral replication. In monocytes/macrophages, activation of NF-kB and STAT3 mediates production of large amounts of inflammatory cytokines which contributes to the development of cytokine secretion syndrome (ie. cytokine storm), chemokines that recruit monocytes and neutrophils, inflammatory biomarkers (eg. SAAs, CPR, D-dimer) as well as PGE2. Here, PGE2 again represses IFN-induced expression of ISGs, contributing to delay of viral clearance. Importantly, PGE2 context-dependently affects (either positively or negatively) not only NLRP3 inflammasome activation and related IL-1b maturation but also NF-kB-dependent monocyte/macrophage cytokine production. PGE2 differentially regulates platelet aggregation via different receptors and likely inhibits NETosis associated with inflammation and thrombosis. PGE2 also down-regulates IFN-gamma production and cytotoxicity of NK and CD8 T cells that kill cells infected with SARS-CoV-2 but promotes differentiation of pro-inflammatory Th17 and Th1 cells, the chief cellular sources of the cytokine storm at late stages of COVID-19.

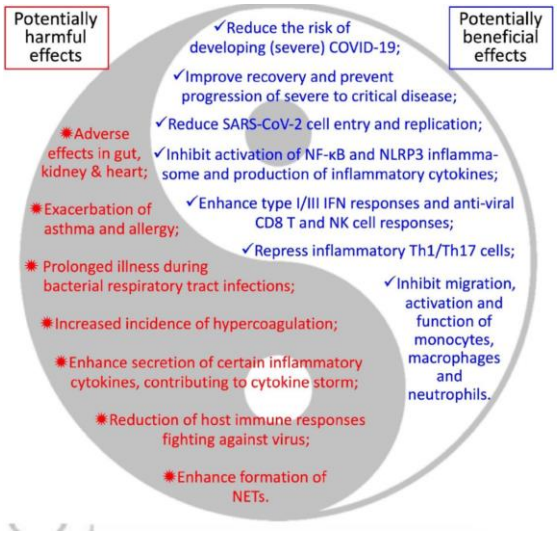

Figure 4. Yin and Yang of NSAIDs in COVID-19: potential effects.
A diagram showing potentially positive and negative effects of NSAID use in COVID-19 patients.

ANALYSIS OF PREDICTION AND EARLY WARNING INDEXES OF PATIENTS WITH COVID-19

Song L, Dong Y, Xu M, Shi D, Guo W, Li Y, Zhang X, Ma X.. Expert Rev Respir Med. 2020 Jul 23:1-4. doi: 10.1080/17476348.2020.1793674. Online ahead of print.
Level of Evidence: 4 - Cohort study or control arm of randomized trial

BLUF

A retrospective cohort study conducted at the Fourth People's Hospital of Taiyuan, China from January 21 to February 24, 2020 looked at 59 patients - 19 critically ill patients with confirmed COVID-19, 17 general patients with confirmed COVID-19 but less severe illness, and 23 patient with suspected COVID-19 but ultimately negative RT-PCR tests - and found that fibrinogen levels differed significantly between suspected and confirmed COVID-19 patients (odds ratio (OR) = 2.52, 95% confidence interval (CI) = 1.18-5.36, p value less than 0.05, Table 2). Additionally, the neutrophil-to-lymphocyte ratio (NLR) was increased in the critically ill group of COVID-19 confirmed patients compared to the less sick general group of COVID-19 confirmed patients (OR = 2.91, 95% CI = 1.36-6.21, p = 0.006). These results suggest that fibrinogen may have value as a diagnostic marker in patients with suspected COVID-19 and that NLR may be useful as a prognostic marker indicative of COVID-19 disease severity.

ABSTRACT

BACKGROUND: The aim was to compare the laboratory data of patients with suspected and confirmed new coronavirus pneumonia (COVID-19) and look for diagnostic predictive and early warning indicators, which will help to better manage the disease. METHODS: A total of 36 confirmed COVID-19 patients were divided into the general (n = 17) and critical group (n = 19). The suspected group enrolled 23 suspected COVID-19 patients with the negative nucleic acid test result. We collected all patients' clinical characteristics and some laboratory indicators at the time of admission and conducted Logistic regression analysis after comparing the differences between groups. RESULTS: There were no significant differences in age, gender, disease duration, fever history, and comorbidities between the suspected and general group (P > 0.05); however, fibrinogen was statistically different (P < 0.05). Compared with the general group, the oxygenation index and lymphocytes were significantly reduced and the Neutrophil-to-lymphocyte Ratio (NLR) and total bilirubin were increased in the critical group (P < 0.05). The fibrinogen OR value was 2.52 (95% CI 1.18-5.36, P = 0.017) and the NLR OR value was 2.91 (95% CI 1.36-6.21, P = 0.006). CONCLUSIONS: Fibrinogen is a valuable diagnostic predictor for patients with suspected COVID-19. For confirmed COVID-19 patients, the NLR is a valuable early warning indicator.

FIGURES

Table 2. Laboratory indicators of study subjects.

	Suspected group (n = 23)	General group (n = 17)	Critical group (n = 19)	P Value
PO_2/FIO_2	352.2 ± 31.6	342.5 ± 61.8	269.5 ± 85.0*#	0.003
CRP(0–4 mg/L)	16.8(1.4–36.0)	25.5(4.4–61.5)	59.3(12.9–97.0)	0.060
PCT(<0.5ng/L)	0.07(0.05–0.13)	0.10(0.05–0.12)	0.08(0.05–0.20)	0.790
WBC(3.5–9.5 × 10^9/L)	6.0(4.7–7.7)	4.7(3.5–5.9)	4.7(3.6–7.5)	0.124
Neut (1.8–6.3 × 10^9/L)	3.57(2.6–5.4)	2.8(2.0–4.2)	3.4(2.9–6.6)	0.209
Lymph (1.1–3.2 × 10^9/L)	1.7 ± 0.5	1.4 ± 0.4	0.6(0.5–1.1)*#	0.000
NLR	2.2(1.6–3.4)	2.4 ± 1.0	7.2 ± 4.5*#	0.000
PLT(125–350 × 10^9/L)	230.4 ± 56.1	160.5(130.8–221.8)	203.6 ± 64.7	0.067
ALT(9–50 U/L)	22.1(12.9–53.9)	20.7(16.8–29.5)	28.6(24.8–56.4)	0.220
TBIL(0–23 μmol/L)	13.4 ± 6.6	10.1(9.0–10.9)	16.0(11.8–20.5)#	0.005
SCr(57–97 μmol/L)	66.7 ± 15.1	70.0(52.5–73.7)	56.1(51.1–61.9)	0.128
LDH(120–250 U/L)	189.9 ± 46.3	250.9 ± 89.8	308.60 ± 92.2*	0.000
CK(50–310 U/L)	72.2(54.2–117.7)	126.2(73.5–255.2)	97.1(59.8–144.6)	0.183
cTnI(<1.68 μg/L)	0.08(0.05–0.24)	0.17 ± 0.12	0.12(0.11–0.24)	0.357
FIB(2–4 g/L)	3.7 ± 1.0	4.5 ± 0.8*	4.5 ± 1.0*	0.009
D-Dimer (0–300 ng/mL)	8(0.3–26)	8(35.5–128.3)	44(8–546)*	0.018

PO_2/FIO_2 = Oxygenation Index; CRP = C reactive protein; PCT = Procalcitonin; WBC = white blood cells; Neut = neutrophil; Lymph = lymphocyte; NLR = neutrophil-to-lymphocyte ratio; PLT = Platelet; ALT = alanine aminotransferase; TBIL = Total Bilirubin; SCr = blood creatinine; LDH = lactate dehydrogenase; CK = creatine kinase; cTnI = Troponin; FIB = fibrinogen; D-Dimer = D dimer.
*Compared with the suspect group, $P < 0.05$ #compared with the general group, $P < 0.05$.

Table 2. Laboratory indicators of study subjects. PO2/FIO2 = Oxygenation Index; CRP = C reactive protein; PCT = Procalcitonin; WBC = white blood cells; Neut = neutrophil; Lymph = lymphocyte; NLR = neutrophil-to-lymphocyte ratio; PLT = Platelet; ALT = alanine aminotransferase; TBIL = Total Bilirubin; SCr = blood creatinine; LDH = lactate dehydrogenase; CK = creatine kinase; cTnI = Troponin; FIB = fibrinogen; D-Dimer = D dimer.

ADJUSTING PRACTICE DURING COVID-19

FOR HEALTHCARE PROFESSIONALS

HEART FAILURE CLINICAL TRIAL OPERATIONS DURING THE COVID-19 PANDEMIC: RESULTS FROM A MULTICENTER SURVEY

Samsky MD, DeVore AD, McIlvennan CK, Granger CB, Granger BB, Hernandez AF, Felker GM, Fonarow GC, Albert NM, Piña IL, Lanfear D, Allen LA.. Circ Heart Fail. 2020 Jul 23. doi: 10.1161/CIRCHEARTFAILURE.120.007456. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A self-reported survey (conducted between May 11 to 18, 2020) of 87 clinical research coordinators (CRC) from various centers involved with the heart failure (HF) clinical trial CONNECT-HF revealed that 75/87 CRCs reported some level of limitation to their CONNECT-HF operations with 18/87 having to completely shutdown their HF research due to COVID-19 (Figure). "As of May 2020, 32% of sites had resumed clinical research activities, 27% planned to loosen restrictions in the next 2-3 months, and 41% had no plans to resume." These findings suggest that COVID-19 has had a significant impact on HF clinical research in the United States with many sites not yet having plans to resume operations.

FIGURES

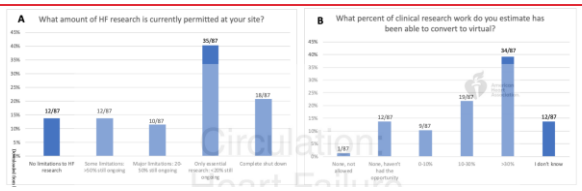

Figure. Bar graphs representing answers to survey questions. HF=Heart failure.

MEDICAL SUBSPECIALTIES

CARDIOLOGY

THE DETRIMENTAL EFFECT OF COVID-19 NATIONWIDE QUARANTINE ON ACCELEROMETER-ASSESSED PHYSICAL ACTIVITY OF HEART FAILURE PATIENTS

Vetrovsky T, Frybova T, Gant I, Semerad M, Cimler R, Bunc V, Siranec M, Miklikova M, Vesely J, Griva M, Precek J, Pelouch R, Parenica J, Belohlavek J.. ESC Heart Fail. 2020 Jul 22. doi: 10.1002/ehf2.12916. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

A cross sectional study of 26 heart failure (HF) patients (Table 1) conducted in the Czech Republic from 24 February to 5 April 2020 found a 16.2% decrease in daily step count on accelerometer during the first 3 weeks of quarantine compared to regular activity ($p<0.05$; Figure 1), suggesting nationwide COVID-19 quarantine mandates were detrimental to physical activity habits of HF patients. Authors highlight the importance of maintaining sufficient physical activity during the COVID-19 pandemic to reduce deterioration in cardiovascular health and limit further adverse health effects.

ABSTRACT

AIMS: A reduction of habitual physical activity due to prolonged COVID-19 quarantine can have serious consequences for patients with cardiovascular diseases, such as heart failure. This study aimed to explore the effect of COVID-19 nationwide quarantine on accelerometer-assessed physical activity of heart failure patients. METHODS AND RESULTS: We analysed the daily number of steps in 26 heart failure patients during a 6-week period that included 3 weeks immediately preceding the onset of the quarantine and the first 3 weeks of the quarantine. The daily number of steps was assessed using a wrist-worn accelerometer worn by the patients as part of an ongoing randomized controlled trial. Multilevel modelling was used to

explore the effect of the quarantine on the daily step count adjusted for weather conditions. As compared with the 3 weeks before the onset of the quarantine, the step count was significantly lower during each of the first 3 weeks of the quarantine ($P < 0.05$). When the daily step count was averaged across the 3 weeks before and during the quarantine, the decrease amounted to 1134 (SE 189) steps per day ($P < 0.001$), which translated to a 16.2% decrease. CONCLUSIONS: The introduction of the nationwide quarantine due to COVID-19 had a detrimental effect on the level of habitual physical activity in heart failure patients, leading to an abrupt decrease of daily step count that lasted for at least the 3-week study period. Staying active and maintaining sufficient levels of physical activity during the COVID-19 pandemic are essential despite the unfavourable circumstances of quarantine.

FIGURES

	n = 26
Age (years)	58.8 (9.8)
Female/male (*n*)	8/18
HFpEF/HFrEF (*n*)	7/19
NYHA II/NYHA III (*n*)	23/3
Body mass index (kg/m^2)	31.5 (5.4)
Left ventricular ejection fraction (%)	37.2 (12.1)
6-min walk test (m)	391 (70)
NT-proBNP (pg/mL)	778 (726)
Beck Depression Inventory-II score (points)	6.1 (3.7)
General Self-Efficacy Scale (points)	31.6 (5.7)
Days elapsed since randomization into the trial	219 (137)
Intervention/follow-up phase of the trial (*n*)	12/14

HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; NYHA, New York Heart Association; NT-proBNP, N-terminal pro-brain natriuretic peptide.
Data are presented as mean (standard deviation) or *n* (number of patients).

Table 1. Patient characteristics.

Circumstance A vs. B	A	B
Living in a city with more vs. less than 10 000 inhabitants	8	18
Living in a flat vs. house with garden	8	18
Walking distance to countryside: less vs. more than 10 min	15	11
Number of adults living with the patient in one household: none or one vs. two or more	17	9
Living with kids up to 15 years in one household: yes vs. no	5	21
Having a dog that requires walking outside: yes vs. no	11	15
Employed vs. not employed	9	17

Data are presented as number of patients living under Circumstance A vs. B.

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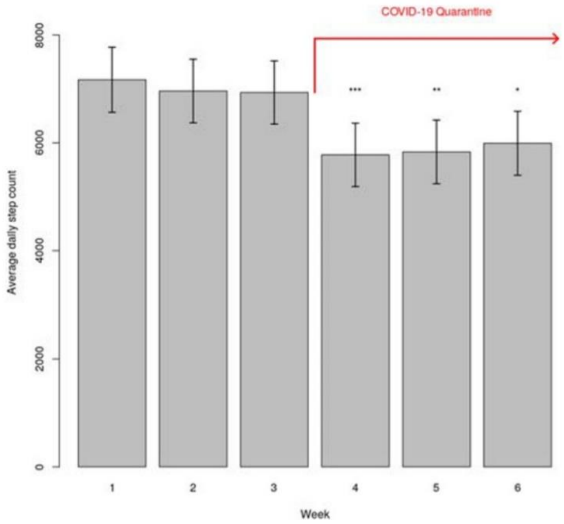

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HEMATOLOGY AND ONCOLOGY

DISTANCING WITHOUT ISOLATING-CONNECTION IN THE ERA OF COVID-19

Cook KA, Kahn JM.. JAMA Oncol. 2020 Jul 23. doi: 10.1001/jamaoncol.2020.2725. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Radiation oncologists at Oregon Health & Science University discuss challenges in the field of oncology presented by the COVID-19 pandemic, especially associated with limited in-person visits, and emphasize the psychological stress placed on patients. With factors affecting cancer patients that range from social isolation to optimization of risk and benefits of treatment, the authors urge physicians to ease this burden by identifying signs of emotional and medical distress in vulnerable patients in order to intervene appropriately (Table 1).

FIGURES

Table. Common Distress Themes and Recommendations in Patients With Cancer During the Coronavirus Disease 2019 (COVID-19) Pandemic

Distress	Patient reactions	Recommendations
Isolation	"I don't have anyone to talk to about this." "It feels strange to be on my own during this."	• Check in more frequently. • Recommend virtual support groups. Include family in telephone/virtual visits if possible.
Abandonment	"I haven't met my doctor; we only spoke on the phone." "I don't know if my treatment will continue given what's going on."	• Opt for virtual visits over telephone visits to allow visual connection. • Allow extra time during visits to listen and provide reassurance.
Risk of COVID-19	"I am nervous about coming to a medical facility so many times." "Am I at greater risk because I have cancer?"	• Share disinfection/social distancing measures the facility has taken. • Validate concerns; provide active listening.
Changes to treatment plan	"How do we know the shorter treatment will work as well?" "Will this delay negatively affect my cancer care?"	• Reiterate constant communication among treatment team, both intramurally and extramurally. • Share data when appropriate. • Discuss risks and benefits of changes.

Table 1: Common Distress Themes and Recommendations

CHARACTERISTICS AND ROLES OF SARS-COV-2 SPECIFIC ANTIBODIES IN PATIENTS WITH DIFFERENT SEVERITIES OF COVID-19

Huang Z, Chen H, Xue M, Huang H, Zheng P, Luo W, Liang X, Sun B, Zhong N.. Clin Exp Immunol. 2020 Jul 24. doi: 10.1111/cei.13500. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

This prospective, observational study by authors from the First Affiliated Hospital of Guangzhou Medical University measured SARS-CoV-2-specific antibodies (IgM, IgA, IgG) using a chemiluminescence method among moderate (n=24) and severe/critical (n=19) COVID-19 patients and non-COVID-19 patients (n=61) from February to April 2020 in Guangdong, China (Table 1). Based on their findings, the authors suggest that IgA-IgG serological diagnosis of COVID-19 may be more effective than the traditional detection of IgM-IgG combined antibodies (Table 2).

SUMMARY

Some of the results of the study are summarized below:
•IgA and IgG levels were higher among severe/critical COVID-19 patients compared to moderate COVID-19 patients, while no difference was found in IgM levels among the two groups (Figure 3).
•In the early stages of COVID-19, IgA detection was found to be more suitable than IgM detection (Figure 2).

ABSTRACT

BACKGROUND: The diagnosis of COVID-19 relies mainly on viral nucleic acid detection, but false negatives can lead to missed diagnosis and misdiagnosis. SARS-CoV-2-specific antibody detection is convenient, safe, and highly sensitive. IgM and IgG are commonly used to serologically diagnose COVID-19; however, the role of IgA is not well known. We aimed to quantify the levels of SARS-CoV-2-specific IgM, IgA, and IgG antibodies, identify changes in them based on COVID-19 severity, and establish the significance of combined antibody detection. METHODS: COVID-19 patients, divided into a severe & critical group and a moderate group, and non-COVID-19 patients with respiratory disease were included in this study. A chemiluminescence method was used to detect the levels of SARS-CoV-2-specific IgM, IgA, and IgG in the blood samples from the three groups. Epidemiological characteristics, symptoms, blood test results, and other data were recorded for all patients. RESULTS: Compared to the traditional IgM-IgG combined antibodies, IgA-IgG combined antibodies are better for diagnosing COVID-19. During the disease process, IgA appeared first and disappeared last. All three antibodies had significantly higher levels in COVID-19 patients than in non-COVID-19 patients. IgA and IgG were also higher for severe & critical disease than for moderate disease. All antibodies were at or near low levels at the time of tracheal extubation in critical patients. CONCLUSIONS: Detection of SARS-CoV-2-specific combined IgA-IgG antibodies is advantageous in diagnosing COVID-19. IgA detection is suitable during early and late stages of the disease. IgA and IgG levels correspond to disease severity.

Table 1. Comparison of patient characteristics between groups.

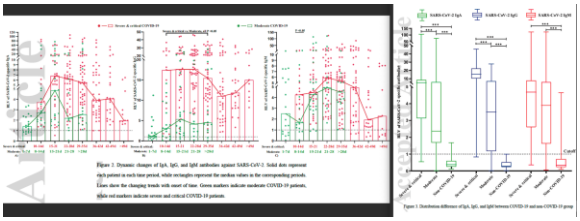
	Severe and critical COVID-19	Moderate COVID-19	Non-COVID-19	P value
Number of patients	19(severe:9, critical:10)	24	61	-
Demographic information				
Male/Female	15/4	13/11	42/19	P=0.210#
Age, median (IQR)	50 (27, 58)	60 (50, 67)	47 (32, 64)	p=0.069#
Epidemiology				
Wuhan exposure history	13/19	9/24	0/61	**P <0.05***
History of confirmed case exposure	7/19	10/24	5/61	P=0.748*
Symptoms at the onset, n/total				
Fever	17/19a	17/24a	24/61b	**P <0.01***
Cough	14/19	13/24	32/61	P=0.254*
Wheezing	13/19a	13/24a	16/61b	**P <0.01***
Fatigue	12/19a	7/24a	5/61b	**P <0.01***
Blood cell analysis, median (IQR)				
Leukocyte	8.71 (7.42, 9.70) a	4.73 (3.87, 5.28) b	7.75 (6.41, 10.24) a	**P <0.01#**
Lymphocyte	1.01 (0.77, 1.23) a	1.40 (1.14, 1.53) ab	1.52 (1.16, 2.11) b	**P <0.01#**
Hemoglobin	0.18 (0.07, 0.26)	0.09 (0.08, 0.10)	0.10 (0.05, 0.20)	p=0.355#
Eosinophil	0.02 (0.01, 0.04)	0 (0, 0.01)	0.02 (0, 0.05)	p=0.261#
Basophil	91.80 (87.41, 111.82) a	117.43 (101.60, 120.89) ab	132.08 (113.20, 149.25) b	**P <0.01#**
Other laboratory tests, n/total				
Suspected viral pneumonia by CT	19/19	24/24	10/61	-
Antibody positive rate at peak time, n/total				
IgM antibody against SARS-CoV-2	19/19	24/24	10/61	-
IgG antibody against SARS-CoV-2	19/19	22/24	0/61	-
IgA antibody against SARS-CoV-2	19/19	24/24	2/61	-

Note: Note: #P-value was significant between the three groups. *P-value was significant between severe & critical COVID-19 and moderate COVID-19 groups. If the same letter (a vs. a or ab) is included between two groups, no significant difference was found.

Table 2. Positive / negative rates and consistency in pair-wise combinations of IgA, IgG, and IgM.

	IgA vs. IgM			IgA vs. IgG			IgM vs. IgG		
	Severe & critical	Moderate	Non-COVID-19	Severe & critical	Moderate	Non-COVID-19	Severe & critical	Moderate	Non-COVID-19
A (Po-Po)	207	66	2	216	62	0	207	62	0
B (Po-Ne)	10	7	0	1	11	2	10	5	0
C (Ne-Po)	1	4	8	1	5	0	1	8	10
D (Ne-Ne)	0	4	51	0	3	59	0	6	51
Consistency	94.95%	86.42%	86.89%	99.08%	80.25%	96.72%	94.95%	83.95%	83.61%
Positive Rate#	100.00%	93.06%	-	100.00%	96.30%	-	100.00%	92.59%	-
Negative Rate*		-	83.61%	-	-	96.72%	-	-	83.61%

Note: # The numbers of both or any one antibodies positive / total numbers. * The numbers of both of the two antibodies negative / total numbers. Po, positive, Ne, negative.



CYTOKINE PROFILE IN PLASMA OF SEVERE COVID-19 DOES NOT DIFFER FROM ARDS AND SEPSIS

Wilson JG, Simpson LJ, Ferreira AM, Rustagi A, Roque JA, Asuni A, Ranganath T, Grant PM, Subramanian AK, Rosenberg-Hasson Y, Maecker H, Holmes S, Levitt JE, Blish C, Rogers AJ.. JCI Insight. 2020 Jul 24:140289. doi: 10.1172/jci.insight.140289. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

Authors from Stanford University School of Medicine conducted a case-control study to assess for differences in inflammatory cytokine levels by comparing 15 hospitalized patients with severe COVID-19 to critically ill patients with ARDS (n=12) or sepsis (n=16). The authors found no differences in IL-1b, IL-1RA, IL-6, IL-8, IL-18, and TNFα levels between patients with COVID-19 and controls with ARDS or sepsis, which indicates that use of broad immunosuppressive therapies may be unnecessary due to the questionable role of the "cytokine storm" in COVID-19 associated mortality and morbidity (Figure 1).

SUMMARY

The authors analyzed differences in the levels of 70 additional cytokines and found statistically significant lower levels of IL-16 and TSLP and higher levels of PDGF-BB in the moderate COVID-19 group. The study's findings are limited by the study's small sample size and lack of power.

ABSTRACT

BACKGROUND: Elevated levels of inflammatory cytokines have been associated with poor outcomes among COVID-19 patients. It is unknown, however, how these levels compare to those observed in critically ill patients with ARDS or sepsis due to other causes. METHODS: We used a luminex assay to determine expression of 76 cytokines from plasma of hospitalized COVID-19 patients and banked plasma samples from ARDS and sepsis patients. Our analysis focused on detecting statistical differences in levels of 6 cytokines associated with cytokine storm (IL-1b, IL-1RA, IL-6, IL-8, IL-18, and TNFalpha) between patients with moderate COVID-19, severe COVID-19, and ARDS or sepsis. RESULTS: 15 hospitalized COVID-19 patients, 9 of whom were critically ill, were compared to critically ill patients with ARDS (n = 12) or sepsis (n = 16). There were no statistically significant differences in baseline levels of IL-1b, IL-1RA, IL-6, IL-8, IL-18, and TNFalpha between patients with COVID-19 and critically ill controls with ARDS or sepsis. CONCLUSIONS: Levels of inflammatory cytokines were not higher in severe COVID-19 patients than in moderate COVID-19 or critically ill patients with ARDS or sepsis in this small cohort. Broad use of immunosuppressive therapies in ARDS has failed in numerous Phase 3 studies; use of these therapies in unselected patients with COVID-19 may be unwarranted. FUNDING: A.J.R.: Stanford ICU Biobank NHLBI K23 HL125663. C.A.B.: Burroughs Wellcome Fund Investigators in the Pathogenesis of Infectious Diseases #1016687; NIH/NIAID U19AI057229-16 (PI MM Davis); Stanford Maternal Child Health Research Institute; Chan Zuckerberg Biohub.

FIGURES

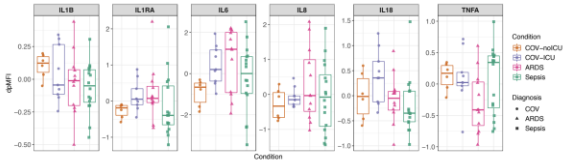


Figure 1. Expression of inflammatory cytokines does not differ between COVID-19 and non-COVID sepsis and ARDS.

CROSSTALK BETWEEN COVID-19 AND PROSTATE CANCER

Bahmad HF, Abou-Kheir W.. Prostate Cancer Prostatic Dis. 2020 Jul 24. doi: 10.1038/s41391-020-0262-y. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

Authors from the American University of Beirut and Mount Sinai Medical Center discuss the potential for re-purposing prostate cancer drugs for patients infected with SARS-CoV-2. SARS-CoV-2 entry into a host cell is dependent on its spike glycoprotein binding to angiotensin-converting enzyme 2 (ACE2) receptors and this process is regulated by transmembrane protease, serine 2 (TMPRSS2). TMPRSS2 is also involved in driving prostate cancer progression and is a target of androgen-deprivation therapy (ADT) (Figure 1), so ADT, along with other anti-androgen drugs and TMPRSS2 inhibitors, could reduce viral entry into host cells and therefore provide a potential treatment option for COVID-19.

ABSTRACT

A new coronavirus, named SARS-CoV-2, emerged in Wuhan city, China, in December 2019 causing atypical pneumonia and affecting multiple body organs. The rapidly increasing numbers of infected patients and deaths due to COVID-19 disease necessitated declaring it as a global pandemic. Efforts were combined since then to rapidly develop a treatment and/or a vaccine to combat the deadly virus. Drug repurposing approach has been pursued as a temporary management tactic to treat COVID-19 patients. However, reports about the efficacy of many of the used drugs had been controversial with a dire need to keep the ongoing efforts for rapid development of new treatments. Promising data came out pointing to a possible hidden liaison between prostate cancer (PCa) and COVID-19, where androgen-deprivation therapies (ADT) used in PCa had been shown to instigate a protective role against COVID-19. Delving into the possible mechanisms underlying the crosstalk between COVID-19 and PCa alludes a potential association between SARS-CoV-2 targets on host epithelial cells and PCa genetic aberrations and molecular signatures, including AR and TMPRSS2. The question remains: Can PCa treatments serve as potential therapeutic options for COVID-19 patients?

FIGURES

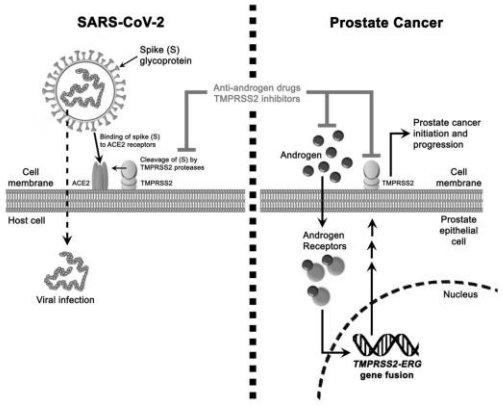


Figure 1. Schematic representation of the crosstalk between COVID-19 and prostate cancer. Potential association is present between SARS-CoV-2 targets on host epithelial cells on one hand, and prostate cancer genetic aberrations and molecular signatures, such as AR and TMPRSS2, on the other hand. Antiandrogen drugs and TMPRSS2 inhibitors used in prostate cancer might hence serve as common therapeutic options for COVID-19 patients.

THE POTENTIAL BENEFIT OF TELMISARTAN TO PROTECT OVERWEIGHT COPD PATIENTS FROM THE ACQUISITION OF COVID-19

Kow CS, Hasan SS.. Obesity (Silver Spring). 2020 Jul 21. doi: 10.1002/oby.22976. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Authors affiliated with the International Medical University and the University of Huddersfield discuss the benefits of telmisartan, an angiotensin receptor blocker, as an intervention for overweight patients with COVID-19 and chronic obstructive pulmonary disease (COPD). Specifically, telmisartan may have protective effects in this population since overweight COPD patients have been shown to have elevated ACE2 expression, increasing their risk of severe COVID-19. The authors urge for trials with telmisartan in overweight COPD patients due to its possible advantages in preventing/mitigating COVID-19 and reducing adipogenesis.

ABSTRACT

Individuals with chronic obstructive pulmonary disease (COPD) have long been identified to have an elevated serum level of angiotensin-converting enzyme 2 (ACE2), the cellular entry receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The newest discoveries by Higham et al. (1) were the increased ACE2 expression in the bronchial epithelium of overweight COPD patients compared to their non-overweight counterparts.

THE RELATIONSHIP BETWEEN RESILIENCE, ANXIETY, AND DEPRESSION AMONG PATIENTS WITH MILD SYMPTOMS OF COVID-19 IN CHINA: A CROSS-SECTIONAL STUDY

Zhang J, Yang Z, Wang X, Li J, Dong L, Wang F, Li Y, Wei R, Zhang J.. J Clin Nurs. 2020 Jul 23. doi: 10.1111/jocn.15425. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Authors from China administered the Connor-Davidson Resilience Scale (CD-RISC) and the Hospital Anxiety and Depression Scale (HADS) to 296 patients with mild COVID-19 symptoms between March 3 and March 5, 2020 at FangCang hospital in Wuhan. The results revealed that:
- Sociodemographic factors affecting anxiety included gender (p less than 0.003) and having a colleague infected with COVID-19 (p less than 0.003; Table 3)
- Having a family member diagnosed with COVID-19 contributed significantly to depression symptoms (p less than 0.023; Table 4)
- Patients with a lower resilience score were more likely to experience symptoms of anxiety (p less than 0.001) and depression (p less than 0.001; Table 2)
These findings provide insight into how the current pandemic is affecting mental health as well as how pre-existing psychiatric conditions affect an individual's outlook after a positive COVID-19 test.

ABSTRACT

AIMS AND OBJECTIVES: To explore the role of resilience in anxiety and depression and to clarify their relationships among patients with mild symptoms of coronavirus disease 2019 (COVID-19) in Wuhan, China. BACKGROUND: The outbreak of COVID-19 has negatively affected some individuals but resilience plays a decisive role in the response of individuals under pressure and can help them deal with pressure more effectively. DESIGN: The cross-sectional descriptive correlational survey was reported in line with the STROBE guidelines. SUBJECT AND SETTING: In total, 296 patients from FangCang Hospital in Wuhan, Hubei, China with mild symptoms of COVID-19 were recruited. METHODS: Participants were recruited through convenience sampling. The data collected included their demographic information, the Connor-Davidson Resilience Scale, and Hospital Anxiety and Depression Scale. RESULTS: A small number of the patients in this study had above threshold anxiety (subthreshold anxiety and major anxiety) and depression (subthreshold depression and major depression). The mean total resilience score of the participants was slightly below the normal level of ordinary Chinese adults. Resilience was inversely associated with and was a protective factor for both anxiety and depression in our samples. Risk factors for anxiety include being female and having colleagues with COVID-19, while a risk factor for depression was having family members with COVID-19. CONCLUSIONS: This study shows that after taking the general demographics into consideration, higher levels of resilience was associated with lower anxiety and depression among mild COVID-19 patients in Wuhan, China. RELEVANCE TO CLINICAL PRACTICE: Health professionals, especially clinical nurses, need to be aware of the psychological status of COVID-19 patients and promote resilience in order to improve their mental health.

FIGURES

Variables	N	Resilience (Rank mean)	Resilience (Rank sum)
Normal group	234	162.18	37949.00
Anxiety group	62	96.89	6007.00
Z/p		-5.342/<0.001*	
Normal group	241	162.51	39165.50
Depression group	55	87.10	4790.50
Z/p		-5.898/<0.001*	

Table 2. The difference of resilience among patients between normal groups and anxiety or depression group. Note: *, p less than 0.05. Because the data are not normally distributed, Mann Whitney tests were used in the analysis of the difference of resilience among patients between normal groups and anxiety or depression group.

Model	Assignment description	B	SE	Wald	p	OR	95%CI
Constant		-0.845	0.614	1.893	0.169	0.430	
Gender	Male=0, female=1	0.801	0.308	6.744	0.009*	2.227	1.217-4.075
Colleagues confirmed	No=0, yes=1	1.047	0.369	8.066	0.005*	2.849	1.383-5.866
Resilience	Low level of resilience =1, Moderate level of resilience =2, High level of resilience =3.	-1.016	0.222	20.978	<0.001*	0.362	0.235-0.559

Note: *, p< 0.05.

Table 3. Logistic Regression analysis examining covariates of anxiety. Note: *, p less than 0.05.

Model	Assignment description	B	SE	Wald	p	OR	95%CI
Constant		0.228	0.480	0.225	0.635	1.256	
Family members confirmed	No=0, yes=1	0.712	0.345	4.263	0.039*	2.039	1.037-4.010
Resilience	Low level of resilience =1, Moderate level of resilience =2, High level of resilience =3.	-1.201	0.238	25.416	<0.001*	0.301	0.189-0.480

Note: *, p< 0.05.

Table 3. Logistic Regression analysis examining covariates of anxiety. Note: *, p less than 0.05.

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