The Daily COVID-19 Literature Surveillance Summary

January 06, 2021

DISCLAIMER

This free and open source document represents a good faith effort to provide real time, distilled information for guiding best practices during the COVID-19 pandemic. This document is not intended to and cannot replace the original source documents and clinical decision making. These sources are explicitly cited for purposes of reference but do not imply endorsement, approval or validation.

This is not an official product or endorsement from the institutions affiliated with the authors, nor do the ideas and opinions described within this document represent the authors' or their affiliated institutions' values, opinions, ideas or beliefs. This is a good faith effort to share and disseminate accurate summaries of the current literature.

NOW LIVE!

Daily audio summaries of the literature in 10 minutes or less.
https://www.covid19lst.org/podcast/

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

- American physicians from Yale and the University of Maryland argue that the US government should mandate vaccination of migrant detainees against COVID-19. They assert the crowded and inadequate sanitary conditions in these facilities create epicenters for disease proliferation and that without federal mandates, states will fail to vaccinate this vulnerable population. Authors suggest such policy is both sound medical practice and a moral imperative.

Epidemiology

- A team of Spanish physicians conducted a retrospective cohort-study using the SEMI-COVID-19 Registry of 12,170 COVID-19 patients from 150 hospitals in Spain to investigate impact of arterial stiffness on mortality. They found arterial stiffness (pulse pressure greater than or equal to 60 mmHg) and systolic blood pressure (SBP) less than 120 mmHg on admission significantly and independently predicted all-cause in-hospital mortality (ORadj: 1.27, p=.0001; ORadj: 1.48, p=.0001, respectively). Authors concluded SBP and pulse pressure values on admission are independent predictors of mortality in COVID-19 patients.

Management

- A single-center retrospective cohort study of 157 hospitalized COVID-19 patients in Wuhan, China analyzed 43 demographic, clinical, and laboratory parameters and found an association between higher systolic blood pressure (SBP) on admission and increased mortality. They also utilized regression models to predict mortality and survivability based of available data and they suggest utilizing these models for risk stratification and appropriate triaging of patients to improve outcomes.

TABLE OF CONTENTS

DISCLAIMER **2**

NOW LIVE! 2

LEVEL OF EVIDENCE **3**

EXECUTIVE SUMMARY **4**

TABLE OF CONTENTS **5**

CLIMATE **6**

DISPARITIES 6

Vaccinating Detained Migrants against SARS-CoV-2 - Preventing Another Tragedy 6

EPIDEMIOLOGY **7**

SYMPTOMS AND CLINICAL PRESENTATION 7

Impact of arterial stiffness on all-cause mortality in patients hospitalized with COVID-19 in Spain 7

UNDERSTANDING THE PATHOLOGY **8**

SARS-CoV-2-Induced ARDS Associates with MDSC Expansion, Lymphocyte Dysfunction, and Arginine Shortage 8

Differential serological and neutralizing antibody dynamics after an infection by a single SARS-CoV-2 strain 10

MANAGEMENT **12**

ACUTE CARE 12

High systolic blood pressure at hospital admission is an important risk factor in models predicting outcome of COVID-19 patients. 12

ACKNOWLEDGEMENTS **14**

CLIMATE

DISPARITIES

VACCINATING DETAINED MIGRANTS AGAINST SARS-COV-2 - PREVENTING ANOTHER TRAGEDY

Foppiano Palacios C, Travassos MA.. N Engl J Med. 2020 Dec 30. doi: 10.1056/NEJMpv2035416. Online ahead of print.
Level of Evidence: 5 - Opinion

BLUF

American physicians from Yale and the University of Maryland argue that the US government should mandate vaccination of migrant detainees against COVID-19. They assert the crowded and inadequate sanitary conditions in these facilities create epicenters for disease proliferation and that without federal mandates, states will fail to vaccinate this vulnerable population. Authors suggest such policy is both sound medical practice and a moral imperative.

IMPACT OF ARTERIAL STIFFNESS ON ALL-CAUSE MORTALITY IN PATIENTS HOSPITALIZED WITH COVID-19 IN SPAIN

Rodilla E, Lopez-Carmona MD, Cortes X, Cobos-Palacios L, Canales S, Saez MC, Campos-Escudero S, Rubio-Rivas M, Diez-Manglano J, Freire-Castro SJ, Vazquez-Piqueras N, Mateo-Sanchis E, Pesqueira-Fontan PM, Magallanes-Gamboa JO, Gonzalez-Garcia A, Madrid-Romero V, Tamargo-Chamorro L, Gonzalez Moraleja J, Villanueva-Martinez J, Gonzalez-Noya A, Suárez-Lombraña A, Gracia-Gutierrez A, Lopez Reboiro ML, Ramos-Rincon JM, Gomez-Huelgas R.. Hypertension. 2020 Dec 30. doi: 10.1161/HYPERTENSIONAHA.120.16563. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

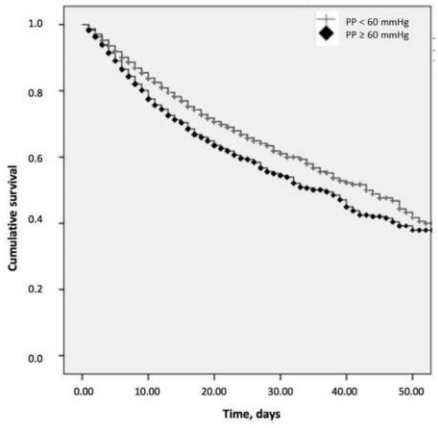
A team of Spanish physicians conducted a retrospective cohort-study using the SEMI-COVID-19 Registry of 12,170 COVID-19 patients from 150 hospitals in Spain to investigate impact of arterial stiffness on mortality. They found arterial stiffness (pulse pressure greater than or equal to 60 mmHg) (Figure 2) and systolic blood pressure (SBP) less than 120 mmHg on admission significantly and independently predicted all-cause in-hospital mortality (ORadj: 1.27, p=.0001; ORadj: 1.48, p=.0001, respectively). Authors concluded SBP and pulse pressure values on admission are independent predictors of mortality in COVID-19 patients.

ABSTRACT

Older age and cardiovascular comorbidities are well-known risk factors for all-cause mortality in COVID-19 patients. Hypertension (HT) and age are the two principal determinants of arterial stiffness (AS). This study aimed to estimate AS in COVID-19 patients requiring hospitalization and analyze its association with all-cause in-hospital mortality. This observational, retrospective, multicenter cohort-study analyzed 12,170 patients admitted to 150 Spanish centers included in the SEMI-COVID-19 Network. We compared AS, defined as pulse pressure {greater than or equal to} 60 mmHg, and clinical characteristics between survivors and nonsurvivors. Mean age was 67.5 {plus minus} 16.1 years and 42.5% were women. Overall, 2,606 (21.4%) subjects died. Admission systolic blood pressure (SBP) < 120 and {greater than or equal to} 140 mmHg was a predictor of higher all-cause mortality (23.5% and 22.8%, respectively, p < .001), compared to BP =120-140 mmHg (18.6%). The 4,379 patients with AS (36.0%) were older and had higher systolic and lower diastolic BP. Multivariate analysis showed that AS and SBP < 120 mmHg significantly and independently predicted all-cause in-hospital mortality (ORadj: 1.27, p=.0001; ORadj: 1.48, p=.0001, respectively) after adjusting for sex (males, ORadj: 1.6, p=.0001), age tertiles (second and third tertiles, ORadj: 2.0 and 4.7, p=.0001), Charlson Comorbidity Index (second and third tertiles, ORadj: 4.8 and 8.6, p=.0001), heart failure, and previous and in-hospital antihypertensive treatment. Our data show that AS and admission SBP < 120 mmHg had independent prognostic value for all-cause mortality in COVID-19 patients requiring hospitalization.

FIGURES

Figure 2: Kaplan-Meier curves in patients with/without AS. Log rank p < .001.



SARS-COV-2-INDUCED ARDS ASSOCIATES WITH MDSC EXPANSION, LYMPHOCYTE DYSFUNCTION, AND ARGININE SHORTAGE

Reizine F, Lesouhaitier M, Gregoire M, Pinceaux K, Gacouin A, Maamar A, Painvin B, Camus C, Le Tulzo Y, Tattevin P, Revest M, Le Bot A, Ballerie A, Cador-Rousseau B, Lederlin M, Lebouvier T, Launey Y, Latour M, Verdy C, Rossille D, Le Gallou S, Dulong J, Moreau C, Bendavid C, Roussel M, Cogne M, Tarte K, Tadié JM.. J Clin Immunol. 2021 Jan 2. doi: 10.1007/s10875-020-00920-5. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A multidisciplinary team of physicians from Pontchaillou University Hospital in France conducted a prospective observational study of 26 COVID-19 patients admitted to the intensive care unit from March to May 2020. They found the 13 patients with acute respiratory distress syndrome (ARDS) had increased myeloid-derived suppressor cells and a decreased number of CD8 positive effector memory cells (Figure 2) compared to the 13 patients with moderate pneumonia. Increased myeloid-derived suppressor cells were associated with enhanced arginase activity (Figure 4a). The authors suggest that COVID-19 related ARDS is associated with myeloid-derived suppressor cell expansion and T cell dysfunction via arginine depletion, and recommend further research to investigate potential benefits of arginine repletion.

ABSTRACT

PURPOSE: The SARS-CoV-2 infection can lead to a severe acute respiratory distress syndrome (ARDS) with prolonged mechanical ventilation and high mortality rate. Interestingly, COVID-19-associated ARDS share biological and clinical features with sepsis-associated immunosuppression since lymphopenia and acquired infections associated with late mortality are frequently encountered. Mechanisms responsible for COVID-19-associated lymphopenia need to be explored since they could be responsible for delayed virus clearance and increased mortality rate among intensive care unit (ICU) patients. METHODS: A series of 26 clinically annotated COVID-19 patients were analyzed by thorough phenotypic and functional investigations at days 0, 4, and 7 after ICU admission. RESULTS: We revealed that, in the absence of any difference in demographic parameters nor medical history between the two groups, ARDS patients presented with an increased number of myeloid-derived suppressor cells (MDSC) and a decreased number of CD8pos effector memory cell compared to patients hospitalized for COVID-19 moderate pneumonia. Interestingly, COVID-19-related MDSC expansion was directly correlated to lymphopenia and enhanced arginase activity. Lastly, T cell proliferative capacity in vitro was significantly reduced among COVID-19 patients and could be restored through arginine supplementation. CONCLUSIONS: The present study reports a critical role for MDSC in COVID-19-associated ARDS. Our findings open the possibility of arginine supplementation as an adjuvant therapy for these ICU patients, aiming to reduce immunosuppression and help virus clearance, thereby decreasing the duration of mechanical ventilation, nosocomial infection acquisition, and mortality.

Fig. 2

From: SARS-CoV-2-Induced ARDS Associates with MDSC Expansion, Lymphocyte Dysfunction, and Arginine Shortage

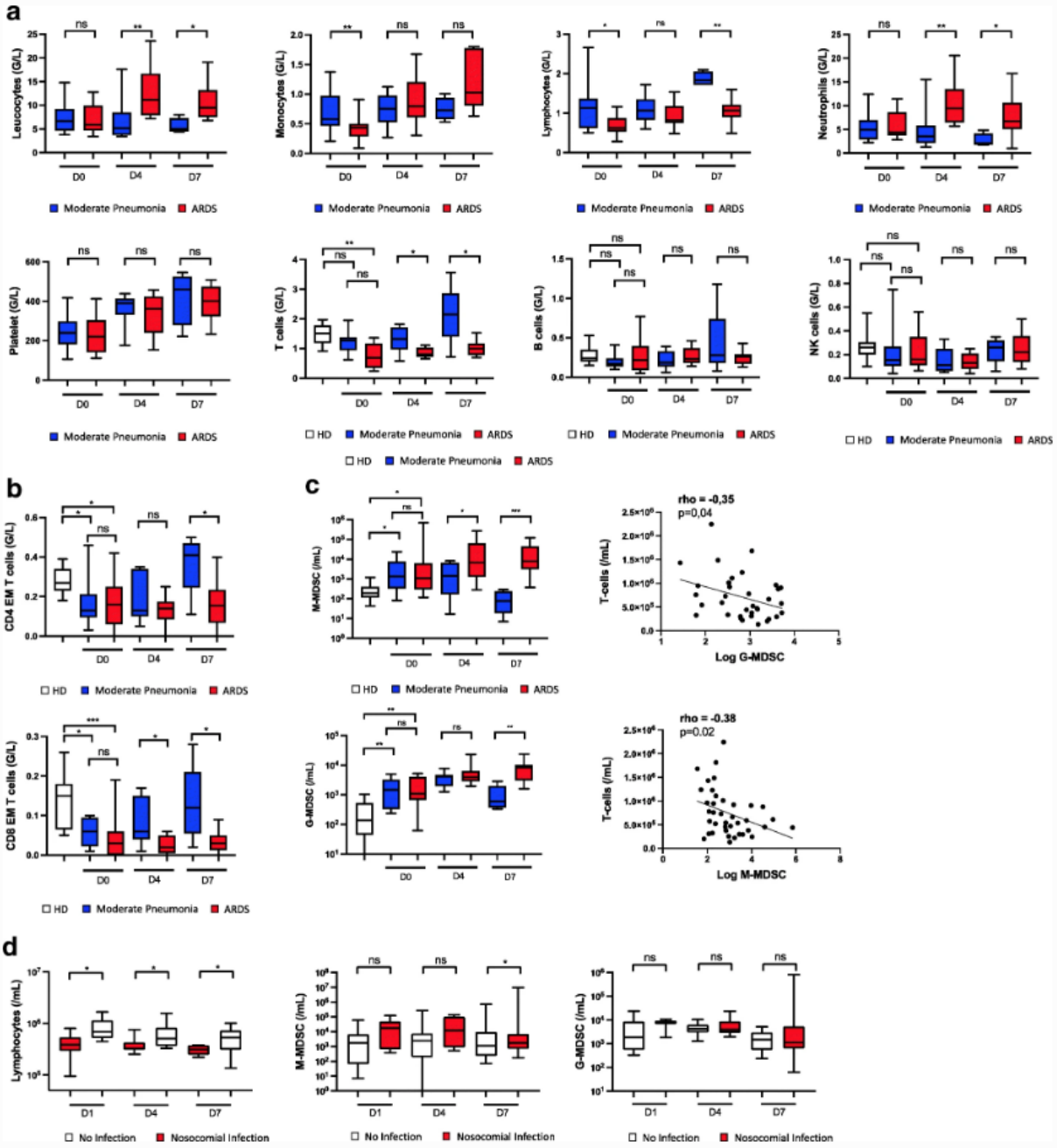


Figure 2a. SARS-CoV-2-induced acute respiratory distress syndrome (ARDS) is associated with lymphopenia and an accumulation of circulating myeloid-derived suppressor cells (MDSC) leading to a higher susceptibility to nosocomial infections. A Blood count from 13 patients hospitalized for SARS-CoV-2 moderate pneumoniae (MP) and 13 patients hospitalized for SARS-CoV-2 ARDS (ARDS) 24 h after their admission (D0), 4 days after (D4), and 7 days after (D7) and lymphocytes subsets defined by flow cytometry from 13 healthy donors (HD), 13 patients hospitalized for SARS-CoV-2 MP, and 13 patients hospitalized for SARS-CoV-2 ARDS. B CD4 and CD8 effector memory (EM) T cell numeration by flow cytometry. C Peripheral monocytic-MDSC (M-MDSC) and granulocytic-MDSC (G-MDSC) recruitment among ARDS patients, moderate COVID cases, and HD. D Two groups were defined according to the presence or absence of a nosocomial infection. Lymphocyte count, M-MDSC, and G-MDSC recruitment according to the acquisition of nosocomial infection. Nosocomial infections as defined by the Centers for Disease Control and Prevention were screened among patients hospitalized for a SARS-CoV-2 infection over 28 days after their admission. Box and whiskers plot features are as follows: central line in the box is the median, bottom line of the box is first quartile (25%), and top line of box is third quartile (75%). Bottom of whiskers is

minimum value; top of whiskers is maximum value. Groups were compared using Kruskal Wallis test with Dunn's multiple comparison test (A, B, and C) or Mann-Whitney U test (A and D) as appropriate. Pearson correlation coefficients (rho) and P values are indicated for each correlation (C). *P < 0.05; **P < 0.01; ***P < 0.001

Fig. 4

From: SARS-CoV-2-Induced ARDS Associates with MDSC Expansion, Lymphocyte Dysfunction, and Arginine Shortage

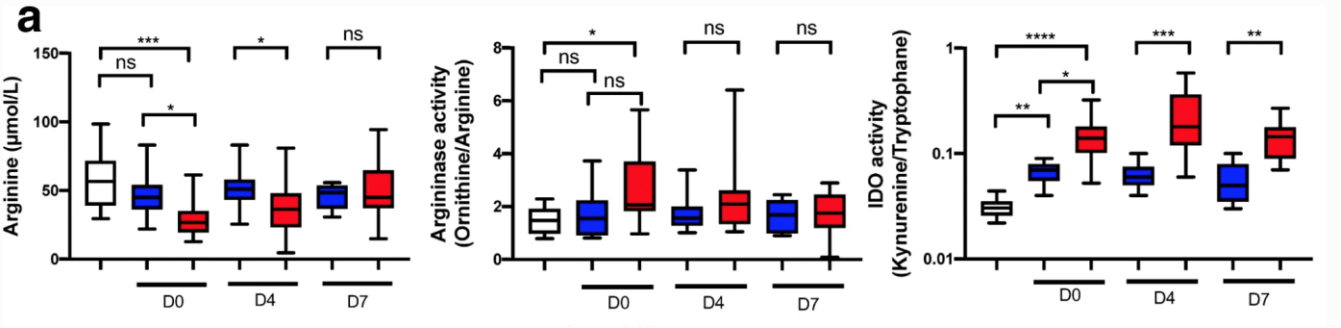


Figure 4a.SARS-CoV-2 ARDS induces a significant decrease in plasma arginine concentration; its supplementation restores the ability of T-cells to proliferate in-vitro. A Plasma arginine, ornithine, kynurenine, and tryptophan concentrations were measured by liquid chromatography coupled with tandem mass spectrometry among 13 healthy donors (HD), 13 patients hospitalized for SARS-CoV-2 moderate pneumonia (MP), and 13 patients hospitalized for SARS-CoV-2 ARDS (ARDS) 24 h after their admission (D0), 4 days after (D4), and 7 days after (D7). Arginase activity was calculated using the ornithine/arginine ratio and IDO activity was calculated using the kynurenine/tryptophan ratio. Pearson correlation coefficients (rho) and P values are indicated for each correlation (a). *P < 0.05; **P < 0.01; ***P < 0.001

DIFFERENTIAL SEROLOGICAL AND NEUTRALIZING ANTIBODY DYNAMICS AFTER AN INFECTION BY A SINGLE SARS-COV-2 STRAIN

Billon-Denis E, Ferrier-Rembert A, Garnier A, Cheutin L, Vigne C, Tessier E, Denis J, Badaut C, Rougeaux C, Depeille Wuille A, Timera H, Boutin LI, Drouet I, Verguet N, Nolent F, Gorgé O, Ferraris O, Tournier JN.. Infection. 2021 Jan 2. doi: 10.1007/s15010-020-01556-8. Online ahead of print.
Level of Evidence: 4 - Case-series

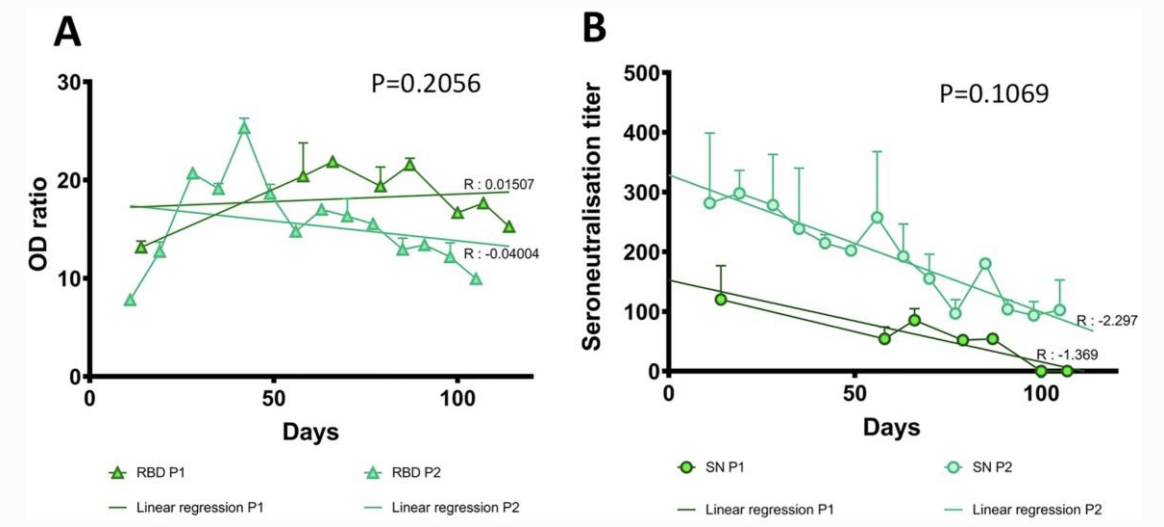
BLUF

Microbiologists from the Institut de Recherche Biomédicale des Armées and Institut Pasteur in France analyzed the antibody responses of two coworkers infected with the same SARS-CoV-2 strain and differing clinical presentations: a 26-year-old female with only anosmia, asthenia, and agueusia (patient 1) and a 51-year-old male with mild respiratory symptoms (patient 2). While both patients had strong IgG anti-receptor-binding domain (RBD) responses, patient 2 had a stronger neutralizing antibody response compared to patient 1 (Figure 1). Authors suggest the neutralizing antibody response may not correlate with the IgG immune response against RBD and individual host factors cause variety in the immune responses that are independent of the virus genotype.

ABSTRACT

BACKGROUND: We report here the case of two coworkers infected by the same SARS-CoV-2 strain, presenting two different immunological outcomes. CASE: One patient presented a strong IgG anti-receptor-binding domain immune response correlated with a low and rapidly decreasing titer of neutralizing antibodies. The other patient had a similar strong IgG anti-receptor-binding domain immune response but high neutralizing antibody titers. DISCUSSION AND CONCLUSION: Thus, host individual factors may be the main drivers of the immune response varying with age and clinical severity.

FIGURES



Patients 1 and 2 IgG ELISA OD ratio against SARS-CoV-2 and seroneutralizing titers. a Green triangle, OD ratio RBD signal patient 1 (RBD P1); blue triangle, OD ratio RBD signal patient 2 (RBD P2). b Green sphere, seroneutralizing titers patient 1 (SN P1); blue sphere, seroneutralizing titers patient 2 (SN P2)

HIGH SYSTOLIC BLOOD PRESSURE AT HOSPITAL ADMISSION IS AN IMPORTANT RISK FACTOR IN MODELS PREDICTING OUTCOME OF COVID-19 PATIENTS

Caillon A, Zhao K, Klein KO, Greenwood C, Lu Z, Paradis P, Schiffrin EL.. Am J Hypertens. 2021 Jan 2:hpaa225. doi: 10.1093/ajh/hpaa225. Online ahead of print.
Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

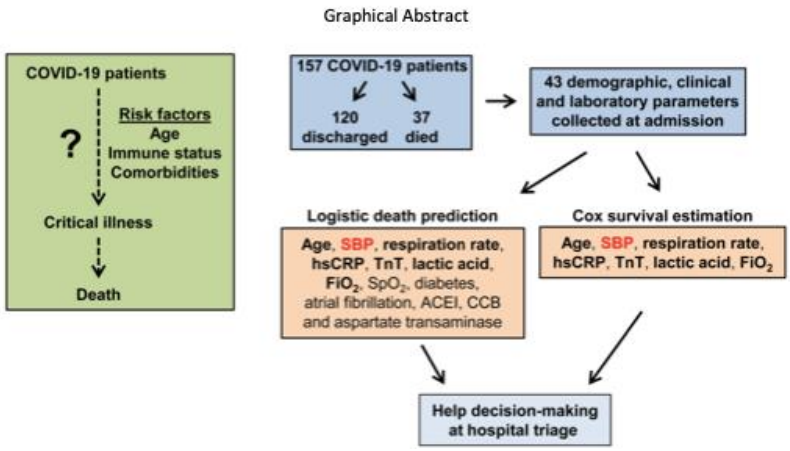
BLUF

A single-center retrospective cohort study of 157 hospitalized COVID-19 patients in Wuhan, China analyzed 43 demographic, clinical, and laboratory parameters (Figure 1) and found an association between higher systolic blood pressure (SBP) on admission and increased mortality. They also utilized regression models to predict mortality and survivability based of available data (Figure 3), and they suggest utilizing these models for risk stratification and appropriate triaging of patients to improve outcomes.

ABSTRACT

BACKGROUND: The risk that COVID-19 patients develop critical illness that can be fatal depends on their age and immune status and may also be affected by comorbidities like hypertension. The goal of this study was to develop models that predict outcome using parameters collected at admission to the hospital. METHODS AND RESULTS: This is a retrospective single-center cohort study of COVID-19 patients at the Seventh Hospital of Wuhan City, China. Forty-three demographic, clinical and laboratory parameters collected at admission plus discharge/death status, days from COVID-19 symptoms onset and days of hospitalization were analyzed. From 157 patients, 120 were discharged and 37 died. Pearson correlations showed that hypertension and systolic blood pressure (SBP) were associated with death and respiratory distress parameters. A penalized logistic regression model efficiently predicts the probability of death with 13 of 43 variables. A regularized Cox regression model predicts the probability of survival with 7 of above 13 variables. SBP but not hypertension was a covariate in both mortality and survival prediction models. SBP was elevated in deceased compared to discharged COVID-19 patients. CONCLUSIONS: Using an unbiased approach, we developed models predicting outcome of COVID-19 patients based on data available at hospital admission. This can contribute to evidence-based risk prediction and appropriate decision-making at hospital triage to provide the most appropriate care and ensure the best patient outcome. High SBP, a cause of end-organ damage and an important comorbid factor, was identified as a covariate in both mortality and survival prediction models.

FIGURES



Graphical Abstract

Figure 1

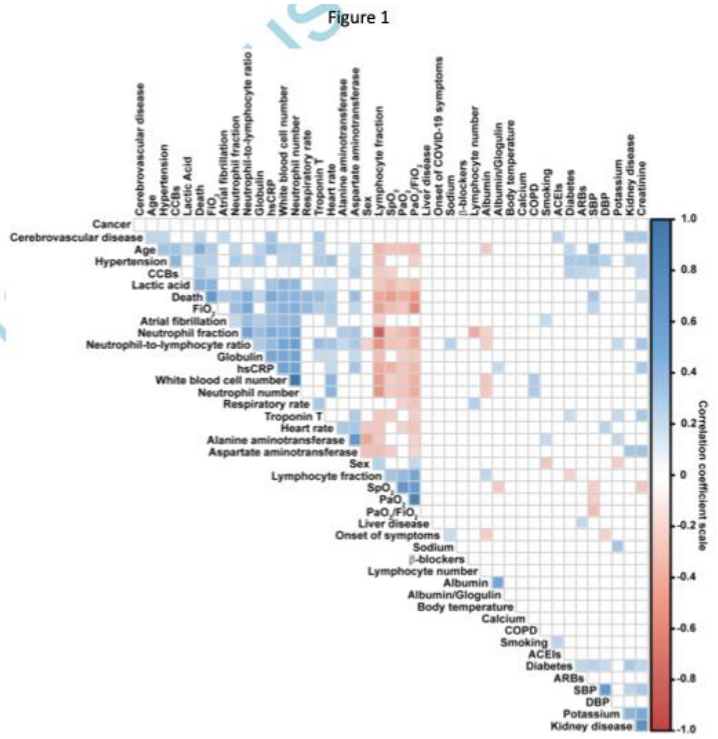


Figure 1. Correlogram of the correlation coefficients of the 43 parameters collected at admission and death status. Correlations were determined using a Pearson Product Moment correlation. Correlations with P value <0.01 were considered significant. The insignificant correlation coefficient values are left blank. Correlation coefficient scale is represented on the right of the figure with the blue square showing positive correlation and red square negative correlation. Abbreviations: ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; FiO2, fraction of inspired oxygen; hsCRP, high-sensitivity C-reactive protein; PaO2, partial pressure of oxygen; SBP, systolic blood pressure; SpO2, peripheral oxygen saturation.

Figure 3

Variable	N	Events	Hazard ratio	Hazard ratio (95% confidence interval)	P values	Penalized Coefficient	Standard Deviation
Age	157	38		2.359 (1.215, 4.580)	0.0112	0.3001	14.57
SBP	157	38		1.433 (1.002, 2.050)	0.0485	0.1027	17.42
Respiration Rate	157	38		1.649 (1.276, 2.132)	0.0001	0.2348	2.34
hsCRP	157	38		2.247 (1.626, 3.106)	<0.0001	0.5219	68.47
Troponin T	157	38		1.138 (0.950, 1.364)	0.1607	0.0959	0.09
Lactic acid	157	38		1.158 (0.927, 1.446)	0.1958	0.0417	1.07
FiO_2	157	38		1.368 (1.071, 1.748)	0.0121	0.3211	0.13

Figure 3. The estimated hazard ratios for each predictor of the counting process Cox proportional hazard regression model predicting survival of COVID-19 patients. Hazard ratios in the Figure are for a one-standard deviation change in the covariate. Abbreviations: FiO2, fraction of inspired oxygen; hsCRP, high-sensitivity C-reactive protein; PaO2, partial pressure of oxygen; SBP, systolic blood pressure.

ACKNOWLEDGEMENTS

CONTRIBUTORS

Brad Mott
Jonathan Baker
Leah Merker
Renate Meckl

EDITORS

Maresa Woodfield
Stephen Ferraro

SENIOR EDITORS

Avery Forrow
Kyle Ellingsen

SENIOR EXECUTIVE EDITOR

Sangeetha Thevuthasan

CHIEF EDITOR

Charlotte Archuleta

ADVISOR

Will Smith