The Daily COVID-19 Literature Surveillance Summary

September 17, 2020

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

Epidemiology

- A multicenter study of 286 patients with lab-confirmed COVID-19 infections, 94.3% of whom were on antiretroviral therapy (88.7% with HIV viral suppression and 80.8% with comorbidities) found that the presence of comorbidities and lower CD4 counts (200 cells/mm-cubed) were significantly correlated with poorer outcomes including higher hospitalization rates, higher ICU admission rates, and reduced overall survival, whereas there was no correlation of outcomes to antiretroviral regimen or lack of viral suppression.

Adjusting Practice During COVID-19

- A retrospective cross-sectional study of emergency physicians (EPs; n=32) at Monash Medical Center in Australia found physician productivity (defined as number of patients examined per hour) decreased by 48.5% during the COVID-19 pandemic compared to historical performances, which authors attribute to increased workload from COVID-19 preparation. Researchers suggest new technical and adaptive challenges during the pandemic calls for strong role modeling and leadership to address complexities encountered by EPs and other healthcare providers.

R&D: Diagnosis & Treatments

- A retrospective propensity score-matched case-control study at Mount Sinai Hospital, New York investigated the effects of convalescent plasma therapy (CPT) in 39 patients with severe or life-threatening COVID-19 infection and found that by day 14 post-transplant, O2 requirements worsened in only 17.9% of CPT recipients when compared to 28.2% of propensity score-matched controls (potentially confounded by therapeutic anticoagulant use in the transplant cohort), in addition to statistically significant improved survival in plasma recipients when compared to controls.

TABLE OF CONTENTS

EPIDEMIOLOGY

SYMPTOMS AND CLINICAL PRESENTATION

CHARACTERISTICS, COMORBIDITIES, AND OUTCOMES IN A MULTICENTER REGISTRY OF PATIENTS WITH HIV AND CORONAVIRUS DISEASE-19

Dandachi D, Geiger G, Montgomery MW, Karmen-Tuohy S, Golzy M, Antar AAR, Llibre JM, Camazine M, Díaz-De Santiago A, Carlucci PM, Zacharioudakis IM, Rahimian J, Wanjalla CN, Slim J, Arinze F, Kratz AMP, Jones JL, Patel SM, Kitchell E, Francis A, Ray M, Koren DE, Baddley JW, Hill B, Sax PE, Chow J; HIV-COVID-19 consortium.. Clin Infect Dis. 2020 Sep 9:ciaa1339. doi: 10.1093/cid/ciaa1339. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A multicenter study conducted by multiple medical schools from April 1 - July 1, 2020 included 286 patients with lab-confirmed COVID-19 infections, 94.3% of whom were on antiretroviral therapy, 88.7% had HIV viral suppression, and 80.8% with comorbidities. Presence of comorbidities and lower CD4 counts (200 cells/mm-cubed) were significantly correlated with poorer outcomes including higher hospitalization rates, higher ICU admission rates, and reduced overall survival (Figure 1), whereas there was no correlation of outcomes to antiretroviral regimen or lack of viral suppression.

ABSTRACT

BACKGROUND: People with HIV (PWH) may have numerous risk factors for acquiring Coronavirus disease-19 (COVID-19) and developing severe outcomes, but current data are conflicting. METHODS: Healthcare providers enrolled consecutively by non-random sampling PWH with lab-confirmed COVID-19, diagnosed at their facilities between April 1st and July 1st, 2020. De-identified data were entered into an electronic Research Electronic Data Capture (REDCap). The primary endpoint was severe outcome, defined as a composite endpoint of intensive care unit (ICU) admission, mechanical ventilation, or death. The secondary outcome was the need for hospitalization. RESULTS: 286 patients were included; the mean age was 51.4 years (SD, 14.4), 25.9% were female, and 75.4% were African-American or Hispanic. Most patients (94.3%) were on antiretroviral therapy (ART), 88.7% had HIV virologic suppression, and 80.8% had comorbidities. Within 30 days of positive SARS-CoV-2 testing, 164 (57.3%) patients were hospitalized, and 47 (16.5%) required ICU admission. Mortality rates were 9.4% (27/286) overall, 16.5% (27/164) among those hospitalized, and 51.5% (24/47) among those admitted to an ICU. The primary composite endpoint occurred in 17.5% (50/286) of all patients and 30.5% (50/164) of hospitalized patients. Older age, chronic lung disease, and hypertension were associated with severe outcomes. A lower CD4 count (<200 cells/mm3) was associated with the primary and secondary endpoints. There was no association between the antiretroviral regimen or lack of viral suppression and predefined outcomes. CONCLUSION: Severe clinical outcomes occurred commonly in PWH and COVID-19. The risk for poor outcomes was higher in those with comorbidities and lower CD4 cell counts, despite HIV viral suppression.

FIGURES

Figure 1

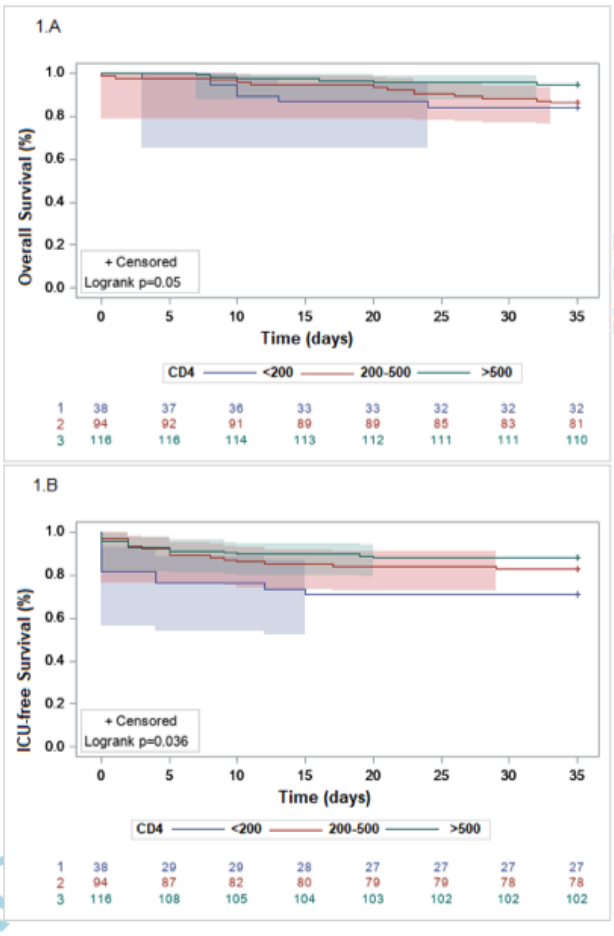


Figure 1A. Overall survival curves by CD4 groups (< 200, 200 - 500, > 500 cells/mm3) (p=0.05). 1B. ICU-free survival curves by CD4 groups (p=0.04).

ADULTS

CLINICAL CHARACTERISTICS OF PATIENTS WITH SEVERE PNEUMONIA CAUSED BY THE SARS-COV-2 IN WUHAN, CHINA

Wang Y, Zhou Y, Yang Z, Xia D, Hu Y, Geng S.. Respiration. 2020 Aug 25:1-9. doi: 10.1159/000507940. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Chinese pulmonologists describe cross-sectional characteristics of 110 COVID-19 patients with either severe (n=38) or non-severe pneumonia (n=72) admitted to The Central Hospital of Wuhan between January 1 and February 10, 2020. While authors identified a number of risk factors for severe disease (low lymphocyte count, male sex) (Table 1), binomial logistics regression analysis revealed only age > 60 and elevated D-dimer as independent risk factors (age > 60 in 71% of severe vs. 12.5% of non-severe [p<0.001], mean D-dimer 1.11 vs. 0.37 [p<0.001])(Table 2). Based on this, they suggest clinicians could use these characteristics to identify high risk patients at an earlier stage.

ABSTRACT

BACKGROUND: A new virus broke out in Wuhan, Hubei, China, that was later named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The clinical characteristics of severe pneumonia caused by SARS-CoV-2 are still not clear. OBJECTIVES: The aim of this study was to explore the clinical characteristics and risk factors of severe pneumonia caused by the SARS-CoV-2 in Wuhan, China. METHODS: The study included patients hospitalized at the Central Hospital of Wuhan who were diagnosed with COVID-19. Clinical features, chronic comorbidities, demographic data, laboratory examinations, and chest computed tomography (CT) scans were reviewed through electronic medical records. SPSS was used for data analysis to explore the clinical characteristics and risk factors of patients with severe pneumonia caused by SARS-CoV-2. RESULTS: A total of 110 patients diagnosed with COVID-19 were included in the study, including 38 with severe pneumonia and 72 with nonsevere pneumonia. Statistical analysis showed that advanced age, increased D-Dimer, and decreased lymphocytes were characteristics of the patients with severe pneumonia. Moreover, in the early stage of the disease, chest CT scans of patients with severe pneumonia showed that the illness can progress rapidly. CONCLUSIONS: Advanced age, decreased lymphocytes, and D-Dimer elevation are important characteristics of patients with severe COVID-19. Clinicians should focus on these characteristics to identify high-risk patients at an early stage.

FIGURES

Table 2. The risk factors of 2019 Novel Coronavirus Severe Pneumonia

	OR	95% CI	P
Age (years)			0.004
≤40			
>40, ≤60	12.28	[1.628,92.664]	0.015
≥60	25.314	[3.687,173.783]	0.001
Ly/SD	0.322	[0.137,0.756]	0.009
D-dimer/SD	17.054	[2.547,114.171]	0.003

- Sex, age, COPD, hypertension, lymphocyte count, platelet count, serum creatinine, blood urea nitrogen, aspartate aminotransferase, serum albumin, C-reactive protein, serum procalcitonin, D-dimer, and B-type natriuretic peptide were used in the logistic regression equation.
- Ly: lymphocyte; SD: standard deviation;
- The SD of the absolute value of the lymphocytes is 0.55;
- The SD of the D-dimer is 3.25.

PATIENTS WITH PROLONGED POSITIVITY OF SARS-COV-2 RNA BENEFIT FROM CONVALESCENT PLASMA THERAPY: A RETROSPECTIVE STUDY

Wu Y, Hong K, Ruan L, Yang X, Zhang J, Xu J, Pan S, Ren L, Chen L, Huang C, Shang Y.. Virol Sin. 2020 Aug 31. doi: 10.1007/s12250-020-00281-8. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

Intensivists affiliated with academic hospitals in Wuhan conducted a retrospective case review of 27 RT-PCR confirmed COVID-19 patients with prolonged positivity of SARS-CoV-2 RNA (median 44 days [30-47]) who received convalescent plasma (CP) therapy (n=27) between January 1 and April 20, 2020. Patients whose SARS-CoV-2 RT-PCR became negative 7 days or sooner after CP initiation (early negative group, n=15) had lower viral loads at days 3, 5, 7 (Figure 2), improved imaging findings (Figure 1) and shorter hospital stays (37 vs 52 days, no p-value)(Table 3) compared to those in the late negative group (>7 days). Based on this the authors suggest rapid reduction in viral load may benefit COVID-19 patients with prolonged positivity but the implications for CP efficacy were unclear given study design.

ABSTRACT

Convalescent plasma therapy has been implemented in a few cases of severe coronavirus disease 2019. No report about convalescent plasma therapy in treating patients with prolonged positivity of SARS-CoV-2 RNA has been published. In this study, we conducted a retrospective observational study in 27 patients with prolonged positivity of SARS-CoV-2 RNA, the clinical benefit of convalescent plasma therapy were analyzed. qRT-PCR test of SARS-CoV-2 RNA turned negative (<= 7 days) in a part of patients (early negative group, n = 15) after therapy, others (late negative group, n = 12) turned negative in more than 7 days. Pulmonary imaging improvement was confirmed in 7 patients in early negative group and 8 in late negative group after CP therapy. Viral load decreased in early negative group compared with late negative group at day 3, 5, 7 after implementing convalescent plasma therapy. Patients in early negative group had a shorter median length of hospital stay. In conclusion, convalescent plasma therapy might help eliminate virus and shorten length of hospital stay in patients with prolonged positivity of SARS-CoV-2 RNA.

FIGURES

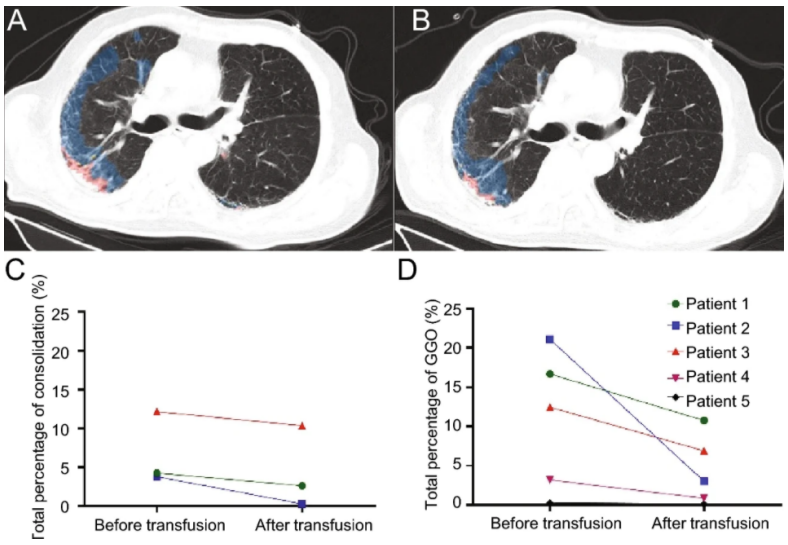


Figure 1.
CT images before and after CP therapy. A Results of AI-assisted diagnostic system in patient 2 before CPT, blue areas represent GGO in CT images, red areas represent consolidation in CT images. B Results of AI-assisted diagnostic system in patient 2 after CPT. C Consolidation of CT in patients 1, 2, and 3 decreased after the transfusion. D GGO of CT in patients 1, 2, 3, 4, and 5 decreased after CP therapy.

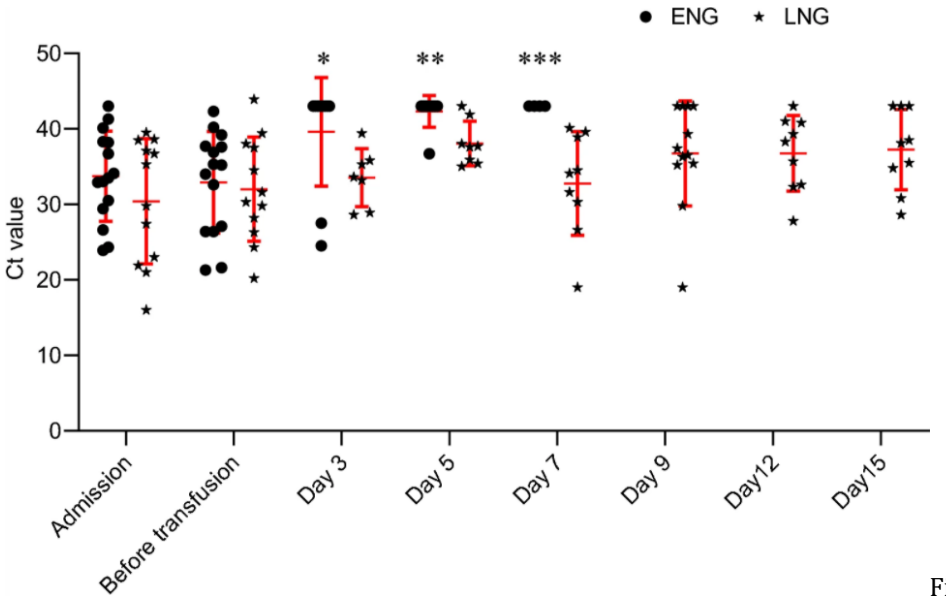


Figure 2.
Variation trend of viral load of patients before and after CP therapy: Ct value of < 43 is defined to be positive, and Ct value of > 47 would be undetectable. *The median Ct value in early negative group (ENG) was significantly greater than late negative group (LNG) on day 3 after the transfusion, P = 0.043. **: The median Ct value in early negative group was significantly greater than late negative group on day 5, P = 0.008. ***: The median Ct value in early negative group was significantly greater than late negative group on day 7, P = 0.003.

Characteristic	Total n = 27	EN group n = 15	LN group n = 12	*P* value
Total volume dose of CP, median (IQR)—mL	400 (200–600)	400 (200–400)	400 (400–800)	0.861
Transfusion-related adverse reactions—no. (%)	0 (0)	0 (0)	0 (0)	
Interval between first transfusion and discharge, median (IQR)—d	11.0 (6.0–25.0)	7.0 (4.0–11.0)	24.0 (14.7–28.7)	
Pulmonary imaging improvement	15/20	7/8	8/12	0.603
Length of hospital stay, median (IQR)—d	43.0 (24.0–54.0)	37.0 (19.0–50.0)	52.0 (35.0–63.7)	
Mortality of 60 days—no. (%)	3 (11.1)	0 (0)	3 (25)	

Table 3. Patients' status after transfusion and outcome after CP therapy.

CARDIOLOGY

ERRORS IN STATISTICAL NUMBERS AND DATA IN STUDY OF CARDIOVASCULAR MAGNETIC RESONANCE IMAGING IN PATIENTS RECENTLY RECOVERED FROM COVID-19

Nagel E, Puntmann VO.. JAMA Cardiol. 2020 Aug 25. doi: 10.1001/jamacardio.2020.4661. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

In this letter to the editor, authors of Puntmann et al, 2020 -- a recent study detailing cardiovascular magnetic resonance imaging (MRI) findings in recovered COVID-19 patients -- aim to correct inconsistencies and errors in their original article by delineating steps to correct these errors including using appropriate statistical tests, adding missing data sets, and amending other calculation errors. Authors claim these adjustments did not change the basic conclusion of their original article, which indicated 78% of patients in their cohort who recovered from COVID-19 also experienced cardiac involvement, highlighting the need for ongoing investigation of cardiovascular consequences in post-COVID-19 patients.

COVID-19 MODELS FOR HOSPITAL SURGE CAPACITY PLANNING: A SYSTEMATIC REVIEW

Klein MG, Cheng CJ, Lii E, Mao K, Mesbahi H, Zhu T, Muckstadt JA, Hupert N.. Disaster Med Public Health Prep. 2020 Sep 10:1-17. doi: 10.1017/dmp.2020.332. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

A systematic review conducted between May 15, 2020 and July 15, 2020 found 6 studies that highlight available planning models to estimate hospital capacity requirements during COVID-19 surges (Figure 1). This review suggests several capacity planning models (see summary) for COVID-19 resource management and provides resources to prepare for scenario-based plans for responding to the outbreak.

SUMMARY

The models are the following:

- Cornell COVID caseload calculator with capacity and ventilators (C5V): provides option to model one wave, two waves, or an empirical distribution supplied by the user and creates projections broken into medical-surgical and ICU beds and ventilators
- COVID-19 acute and intensive care resource tool (CAIC-RT): estimates maximum manageable daily number of incident cases based on case distribution and severity and beds available
- COVID-19 Hospital Impact Model for Epidemics (CHIME): projects forecasts for outcomes of the outbreak that can be used to predict epidemic curves and adjust resources accordingly
- COVID-19 ICU and floor projection: estimates daily number of medical resources to facilitate hospital planning
- COVID-19 Surge: created by the CDC, estimates number of patients with different needs to facilitate reasonable allocations
- Surge capacity bed management tools: project up to 30 days in advance for hospital bed demand and occupancy to address concerns relating to capacity, supply consumption, operational decisions.

ABSTRACT

OBJECTIVE: Health system preparedness for COVID-19 includes projecting the number and timing of cases requiring various types of treatment. Several tools were developed to assist in this planning process. This review highlights models that project both caseload and hospital capacity requirements over time. METHODS: We systematically reviewed the medical and engineering literature according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We completed searches using PubMed, EMBASE, ISI Web of Science, Google Scholar and the Google search engine. RESULTS: The search strategy identified 690 articles. For detailed review, we selected six models that met our pre-defined criteria. Half of the models did not include age-stratified parameters, and only one included the option to represent a second wave. Hospital patient flow was simplified in all models; however, some considered more complex patient pathways. One model included fatality ratios with Length of Stay (LOS) adjustments for survivors versus those who die, and accommodated different LOS for critical care patients with or without a ventilator. CONCLUSION: The results of our study provide information to physicians, hospital administrators, emergency response personnel and governmental agencies on available models for preparing scenario-based plans for responding to the COVID-19 or similar type of outbreak.

FIGURES

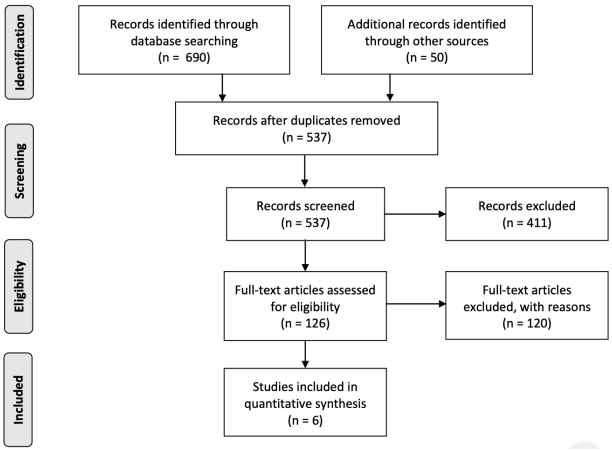


Figure 1 – PRISMA Flow Diagram for Systematic Review

ACUTE CARE

EMERGENCY MEDICINE

DESCRIPTION OF THE EFFECT OF PATIENT FLOW, JUNIOR DOCTOR SUPERVISION AND PANDEMIC PREPARATION ON THE ABILITY OF EMERGENCY PHYSICIANS TO PROVIDE DIRECT PATIENT CARE

Lim A, Gupta N, Lim A, Hong W, Walker K.. Aust Health Rev. 2020 Aug 31. doi: 10.1071/AH20180. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This retrospective cross-sectional study of emergency physicians (EPs; n=32) at Monash Medical Center in Australia from February 1 to February 29, 2020 found physician productivity (defined as number of patients examined per hour) decreased by 48.5% during the COVID-19 pandemic compared to historical performances, which authors attribute to increased workload from COVID-19 preparation (Box 1; Figures 1,2). Researchers acknowledge the unidimensional variable only captures one measure of productivity but suggest new technical and adaptive challenges during the pandemic calls for strong role modeling and leadership to address complexities encountered by EPs and other healthcare providers.

ABSTRACT

ObjectiveA pilot study to: (1) describe the ability of emergency physicians to provide primary consults at an Australian, major metropolitan, adult emergency department (ED) during the COVID-19 pandemic when compared with historical performance; and (2) to identify the effect of system and process factors on productivity.MethodsA retrospective cross-sectional description of shifts worked between 1 and 29 February 2020, while physicians were carrying out their usual supervision, flow and problem-solving duties, as well as undertaking additional COVID-19 preparation, was documented. Effect of supervisory load, years of Australian registration and departmental flow factors were evaluated. Descriptive statistical methods were used and regression analyses were performed.ResultsA total of 188 shifts were analysed. Productivity was 4.07 patients per 9.5-h shift (95% CI 3.56-4.58) or 0.43 patients per h, representing a 48.5% reduction from previously published data (P<0.0001). Working in a shift outside of the resuscitation area or working a day shift was associated with a reduction in individual patient load. There was a 2.2% (95% CI: 1.1-3.4, P<0.001) decrease in productivity with each year after obtaining Australian medical registration. There was a 10.6% (95% CI: 5.4-15.6, P<0.001) decrease in productivity for each junior physician supervised. Bed access had no statistically significant effect on productivity.ConclusionsEmergency physicians undertake multiple duties. Their ability to manage their own patients varies depending on multiple ED operational factors, particularly their supervisory load. COVID-19 preparations reduced their ability to see their own patients by half.What is known about the topic?An understanding of emergency physician productivity is essential in planning clinical operations. Medical productivity, however, is challenging to define, and is controversial to measure. Although baseline data exist, few studies examine the effect of patient flow and supervision requirements on the emergency physician's ability to perform primary consults. No studies describe

these metrics during COVID-19.What does this paper add?This pilot study provides a novel cross-sectional description of the effect of COVID-19 preparations on the ability of emergency physicians to provide direct patient care. It also examines the effect of selected system and process factors in a physician's ability to complete primary consults.What are the implications for practitioners?When managing an emergency medical workforce, the contribution of emergency physicians to the number of patients requiring consults should take into account the high volume of alternative duties required. Increasing alternative duties can decrease primary provider tasks that can be completed. COVID-19 pandemic preparation has significantly reduced the ability of emergency physicians to manage their own patients.

FIGURES

COVID-19 preparations:

- Personal protective equipment (PPE) and scenario simulation training
- Undertaking hand hygiene training and certification
- Donning, doffing, and spotting PPE
- Infection control precautions for almost all patients
- Training junior and non-Emergency Department (ED) healthcare workers
- Notifying Department of Health of all suspected or confirmed COVID-19 patients (this was required during the early pandemic phase)

Communication

- Disseminating daily Department of Health protocol changes to ED staff (testing eligibility, contact definitions, PPE guidelines)
- Advice on COVID-19 recommendations and screening processes
  - In-hospital staff and hospital administrators
  - Community healthcare workers (GPs, paramedics, aged-care facility enquiries)
  - Patients, families and community members (e.g. for testing, isolation, test results)
  - Managing community enquiries about hospital safety and visiting rules

Clinical care

- Supervision of redeployed junior doctors with minimal emergency medicine experience
- Managing and assisting with ambulance safe entry into the ED for suspected COVID-19 patients
- Assisting with ED flow decisions to improve social distancing in EDs
- Supervision of nursing, orderly and cleaning staff regarding infection control requirements (including supervising room cleaning)

Box 1. Increased duties of emergency physicians during the COVID-19 pandemic

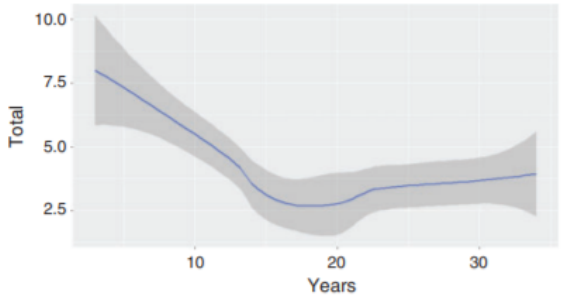


Figure 1. Relationship between years of Australian registration and the number of primary consults per 9.5-h shift.

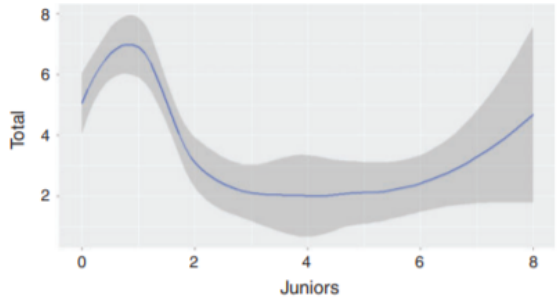


Figure 2. Relationship between number of junior doctors supervised and the number of primary consults per 9.5-h shift.

R&D: DIAGNOSIS & TREATMENTS

DEVELOPMENTS IN DIAGNOSTICS

DISCOVERY OF SANDWICH TYPE COVID-19 NUCLEOCAPSID PROTEIN DNA APTAMERS

Zhang L , Fang X , Liu X , Ou H , Zhang H , Wang J , Li Q , Cheng H , Zhang W , Luo Z .. Chem Commun (Camb). 2020 Sep 11;56(70):10235-10238. doi: 10.1039/d0cc03993d. Epub 2020 Aug 5.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

In an in vitro study conducted by Nankai University in China, researchers developed four distinct DNA molecules that bind COVID-19 nucleocapsid protein (Np), a highly abundant capsid protein that is currently in use for COVID-19 detection tests, with an affinity below 5 nM in length. The authors demonstrated sandwich like binding of the aptamers and detection at the tens of picomolar level which enables their use in ELISA assays for detection of COVID-19, indicating that these molecular tools could be used for point-of-care-testing and biosensors for personal or home use to improve diagnostic capability through the remainder of the pandemic.

ABSTRACT

Here, we report for the first time DNA aptamers targeted toward the COVID-19 nucleocapsid protein (Np). Np is one of the most abundant structural proteins and it serves as a diagnostic marker for the accurate and sensitive detection of COVID-19. After five rounds of selection, we obtained four DNA sequences with an affinity below 5 nM. The best one displayed a superb binding performance toward Np with a Kd value of 0.49 nM. Interestingly, we found that the four pairs of aptamers could bind to Np successively, suggesting a sandwich-type interaction. Using these sandwiched aptamers in ELISA and colloidal gold immunochromatographic strips, we were able to detect Np at the tens of pM level. The results demonstrate that aptamers are powerful molecular tools for virus detection, diagnosis, and antiviral therapy.

DEVELOPMENTS IN TREATMENTS

CONVALESCENT PLASMA TREATMENT OF SEVERE COVID-19: A PROPENSITY SCORE-MATCHED CONTROL STUDY

Liu STH, Lin HM, Baine I, Wajnberg A, Gumprecht JP, Rahman F, Rodriguez D, Tandon P, Bassily-Marcus A, Bander J, Sanky C, Dupper A, Zheng A, Nguyen FT, Amanat F, Stadlbauer D, Altman DR, Chen BK, Krammer F, Mendu DR, Firpo-Betancourt A, Levin MA, Bagiella E, Casadevall A, Cordon-Cardo C, Jhang JS, Arinsburg SA, Reich DL, Aberg JA, Bouvier NM.. Nat Med. 2020 Sep 15. doi: 10.1038/s41591-020-1088-9. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A retrospective propensity score-matched case-control study performed from March 24 - April 8, 2020 at Mount Sinai Hospital in NYC investigated the effects of convalescent plasma therapy (CPT) in 39 patients with severe or life-threatening COVID-19 infection (Figure 3). By day 14 post-transplant, O2 requirements worsened in only 17.9% of CPT recipients when compared to 28.2% of propensity score-matched controls (potentially confounded by therapeutic anticoagulant use in the transplant cohort), in addition to statistically significant improved survival in plasma recipients when compared to controls (Figures 1 & 2). Further randomized control trials with adequately powered sample size will be needed to truly confirm the beneficial effects of convalescent plasma therapy.

ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a new human disease with few effective treatments1. Convalescent plasma, donated by persons who have recovered from COVID-19, is the acellular component of blood that contains antibodies, including those that specifically recognize SARS-CoV-2. These antibodies, when transfused into patients infected with SARS-CoV-2, are thought to exert an antiviral effect, suppressing virus replication before patients have mounted their own humoral immune responses2,3. Virus-specific antibodies from recovered

persons are often the first available therapy for an emerging infectious disease, a stopgap treatment while new antivirals and vaccines are being developed1,2. This retrospective, propensity score-matched case-control study assessed the effectiveness of convalescent plasma therapy in 39 patients with severe or life-threatening COVID-19 at The Mount Sinai Hospital in New York City. Oxygen requirements on day 14 after transfusion worsened in 17.9% of plasma recipients versus 28.2% of propensity score-matched controls who were hospitalized with COVID-19 (adjusted odds ratio (OR), 0.86; 95% confidence interval (CI), 0.75-0.98; chi-square test P value = 0.025). Survival also improved in plasma recipients (adjusted hazard ratio (HR), 0.34; 95% CI, 0.13-0.89; chi-square test P = 0.027). Convalescent plasma is potentially effective against COVID-19, but adequately powered, randomized controlled trials are needed.

FIGURES

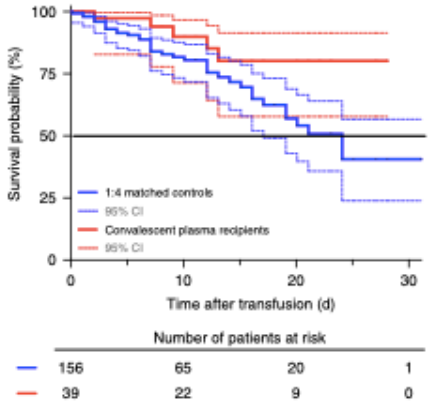
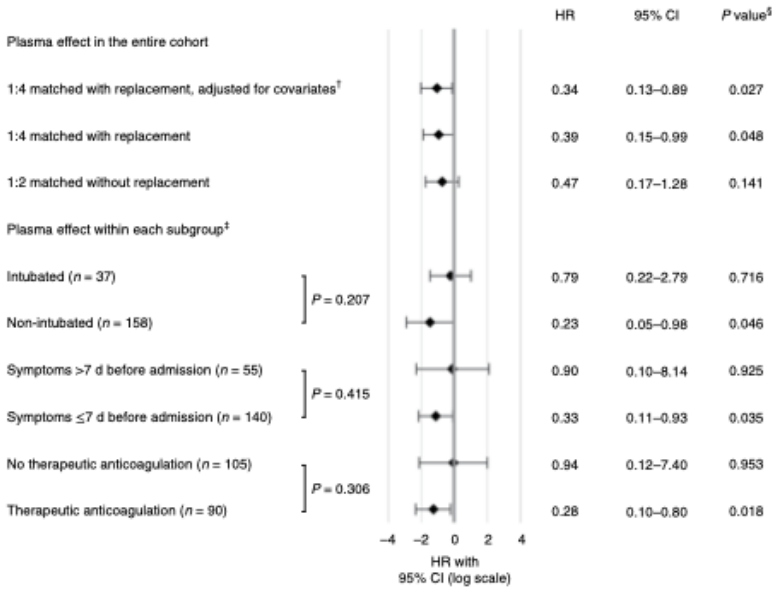


Fig. 1 | Survival probability. As of 1 May 2020, 5 (12.8%) of 39 convalescent plasma recipients and 38 (24.4%) of 156 1:4 matched control patients had died. The median follow-up time was 11 d (range 1–28 d) for the plasma group and 9 d (0–31 d) for the control group. Overall, improved survival was observed for the plasma versus the control group.



§P value by chi-square test
†Covariates: duration of symptoms before admission, therapeutic anticoagulation and broad-spectrum antibiotics
‡P value by chi-square test for homogeneity

Fig. 2 | HRs for in-hospital mortality. In a covariates-adjusted Cox model, convalescent plasma transfusion was significantly associated with improved survival (HR, 0.34; 95% CI, 0.13–0.89; chi-square test, P = 0.027). Subgroup analyses showed significant survival benefits of convalescent plasma in patients who were not intubated, had a shorter duration of symptoms and received therapeutic anticoagulation. However, these subgroups were not significantly different from their complementary subgroups (chi-square test for homogeneity P = 0.207, P = 0.415 and P = 0.306, respectively). All statistical tests are two-sided.

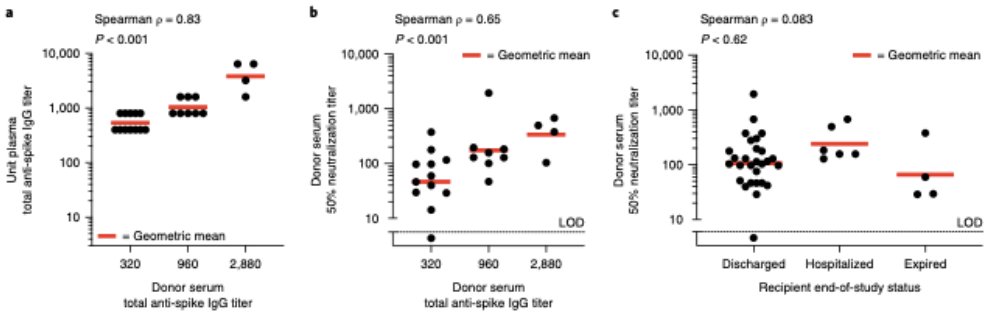


Fig. 3 | Donor antibody levels and convalescent plasma-recipient outcomes. a, Total anti-SARS-CoV-2 spike protein IgG titers in serum, obtained from plasma donors by clinical MSH-ELISA assay, positively correlate with the total anti-spike IgG titers in plasma units, measured by a lab-based ELISA (Spearman ρ, 0.83; P < 0.001). b, Total anti-spike IgG titers from donors also correlate with the reciprocal serum dilution required to neutralize virus infectivity by 50%, as measured by microneutralization assay (Spearman ρ, 0.65; P < 0.001). c, No correlation was observed between donor neutralization titers and convalescent plasma-recipient outcomes at the end of the study period (Spearman ρ, 0.083; P = 0.62). Plasma ELISAs (a) were performed once (n = 1 replicate per plasma sample), and microneutralization assays (b and c) were performed in duplicate (n = 2 replicates per serum sample). Data from n = 24 donors (a and b) and n = 38 recipients (c) were used to calculate Spearman correlation coefficients and P values. One serum sample showed no measurable neutralization activity in vitro; this point is shown below the dotted line indicating the limit of detection (LOD) (b and c). Donor serum neutralization titer was unavailable for one convalescent plasma recipient who expired; donor titers for the remaining four deceased recipients are shown (c). All statistical tests are two-sided.

ACKNOWLEDGEMENTS

CONTRIBUTORS

Eva Shelton
Jonathan Baker
Kersti Bellardi
Renate Meckl
Zainab Awan

EDITORS

Alvin Rafou
Julie Tran
Maresa Woodfield
Michelle Arnold

SENIOR EDITORS

Avery Forrow
Cameron Richards
Charlotte Archuleta
Sangeetha Thevuthasan

SENIOR EXECUTIVE EDITOR

Ann Staudinger Knoll

CHIEF EDITOR

Brennan Enright

ADVISOR

Will Smith