The Daily COVID-19 Literature Surveillance Summary

July 21, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

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

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

EXECUTIVE SUMMARY

Epidemiology:

- A retrospective cohort study from New York found that all 16 patients with confirmed SARS-CoV-2 that received a lower extremity computed tomography angiogram (CTA) over a 3-month time period had at least one blood clot on lower extremity CTA compared to just 69% (n=22/36) in propensity-matched patient control data. Limb amputation was also more frequent in COVID-19 patients versus patient controls with peripheral vascular disease, and those presenting with limb ischemia and respiratory symptoms had higher rates of amputation and mortality (p=0.001). Authors use this study to further highlight the morbidity and mortality associated with COVID-19 coagulopathy.

Transmission and Prevention:

- An analysis of contact tracing data from South Korea describes how age and proximity affect SARS-CoV-2 transmission within people living in the same household. They found:
    - Household contacts had a higher risk of transmission, with 11.8% of household contacts positive for COVID-19 compared to 1.9% of non-household contacts.
      - The highest rate of transmission was from the 10-19 year old age group (18.6%)
      - The lowest rate of transmission was from the 0-9 year old age group (5.3%), which was likely a result of stringent social distancing due to the typically high rate of infection transmission in preschool and daycare settings.
- A retrospective study from the Mayo Clinic explored the efficacy of screening for COVID-19 with reverse transcription polymerase chain reaction (RT-PCR) alone versus RT-PCR plus chest CT in adults undergoing operative procedures. They found that among 625 asymptomatic participants who underwent CT scans, 520 (83.2%) had normal scans, 1 (0.16%) had features typical of COVID-19, and 86 (13.76%) had atypical features (Table 1). Only one participant - who had an atypical CT scan - tested positive by RT-PCR. The authors argue that the addition of CT scan to RT-PCR is not an effective method for screening in a population with low prevalence, though they acknowledge this conclusion may not be generalizable to symptomatic populations or those with high prevalence
- A study evaluating aerosol and surface transmission of SARS-CoV-2 at a designated COVID-19 hospital found that all 135 aerosolized samples, and 88 out of 90 surfaces, were negative for SARS-CoV-2 RNA suggesting that proper disinfection procedures and room ventilation are important and effective means for prevention of nosocomial infection.

Management

- A case report conducted at Changi General Hospital discusses a 45-year-old patient who was diagnosed with Hashimoto's thyroiditis following a COVID-19 infection, indicating a potential link between the hyper-inflammatory state caused by the SARS-CoV-2 virus and the development of autoimmune diseases.

R&D: Diagnosis and Treatments

- An analysis of laboratory tests, imaging results, and vaginal swabs of 13 pregnant persons with suspected COVID-19 found that 12 tested positive for SARS-CoV-2 via RT-PCR from respiratory tract samples, but all vaginal swab samples tested negative. These findings add to the growing evidence that sexual or vertical transmission of SARS-CoV-2 is unlikely and may assist in decision-making regarding obstetrical management.
- A study utilized 109 patient samples to compare the point-of-care variplex test system to RT-PCR systems and found that variplex had a false-negative rate of 83% when compared with PCR. The authors suggest that variplex testing detection of SARS-CoV-2 was low due to lack of RNA extraction, and propose it could be remedied by utilizing loop-mediated isothermal amplification method for RNA extraction prior to variplex testing.

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A STOCHASTIC AGENT-BASED MODEL OF THE SARS-COV-2 EPIDEMIC IN FRANCE

Hoertel N, Blachier M, Blanco C, Olfson M, Massetti M, Rico MS, Limosin F, Leleu H.. Nat Med. 2020 Jul 14. doi: 10.1038/s41591-020-1001-6. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

In this Nature article, epidemiologists describe a stochastic agent-based model analyzing the impact of non-pharmaceutical interventions on SARS-CoV-2 transmission in France (Figure 1). Their model indicates that post-lockdown physical distancing and universal masking slow transmission and decrease mortality (Figure 2), but maintaining adequate ICU capacity also requires shielding of vulnerable populations (Figure 4). The authors imply that adoption of all three measures could prevent a second lockdown in France.

ABSTRACT

Many European countries have responded to the COVID-19 pandemic by implementing nationwide protection measures and lockdowns1. However, the epidemic could rebound when such measures are relaxed, possibly leading to a requirement for a second or more, repeated lockdowns2. Here, we present results of a stochastic agent-based microsimulation model of the COVID-19 epidemic in France. We examined the potential impact of post-lockdown measures, including physical distancing, mask-wearing and shielding individuals who are the most vulnerable to severe COVID-19 infection, on cumulative disease incidence and mortality, and on intensive care unit (ICU)-bed occupancy. While lockdown is effective in containing the viral spread, once lifted, regardless of duration, it would be unlikely to prevent a rebound. Both physical distancing and mask-wearing, although effective in slowing the epidemic and in reducing mortality, would also be ineffective in ultimately preventing ICUs from becoming overwhelmed and a subsequent second lockdown. However, these measures coupled with the shielding of vulnerable people would be associated with better outcomes, including lower mortality and maintaining an adequate ICU capacity to prevent a second lockdown. Benefits would nonetheless be markedly reduced if most people do not adhere to these measures, or if they are not maintained for a sufficiently long period.

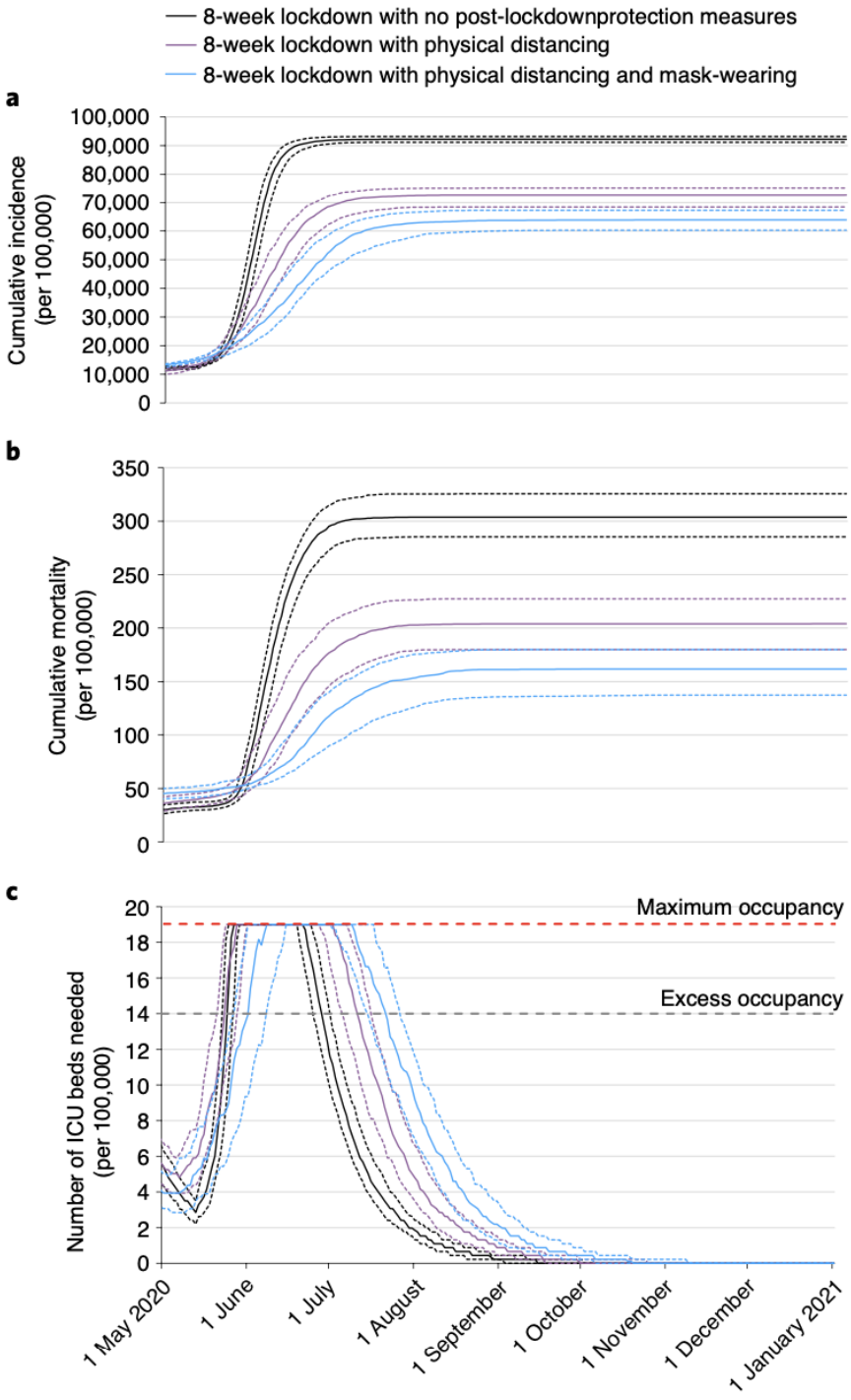


Fig. 2 | Model-predicted cumulative incidence, mortality, and number of ICU beds needed associated with post-lockdown physical distancing and mask-wearing for the general population. a–c, Model-predicted cumulative incidence (**a**), cumulative mortality (**b**) and number of ICU beds needed (**c**) associated with post-lockdown physical distancing and mask-wearing for the general population. The dotted lines represent the uncertainty range (first to last quartile) stemming from the uncertainty in the parameter values.

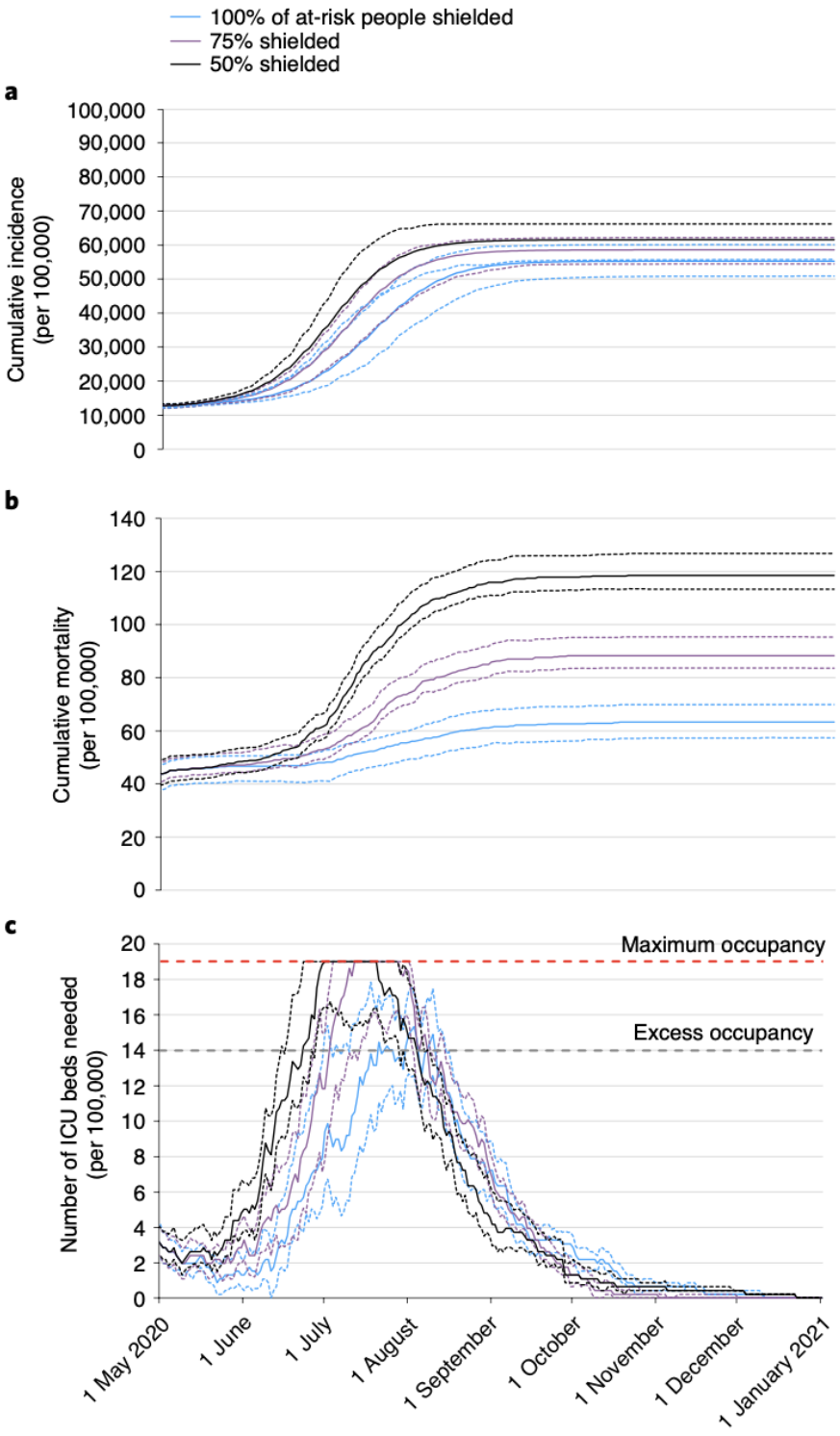


Fig. 4 | Model-predicted cumulative incidence, mortality, and number of ICU beds needed according to the proportion of at-risk people shielded. **a**–**c**, Model-predicted cumulative incidence (**a**), cumulative mortality (**b**) and number of ICU beds needed (**c**) according to the proportion of at-risk people shielded. The dotted lines represent the uncertainty range (first to last quartile) stemming from the uncertainty in the parameter values.

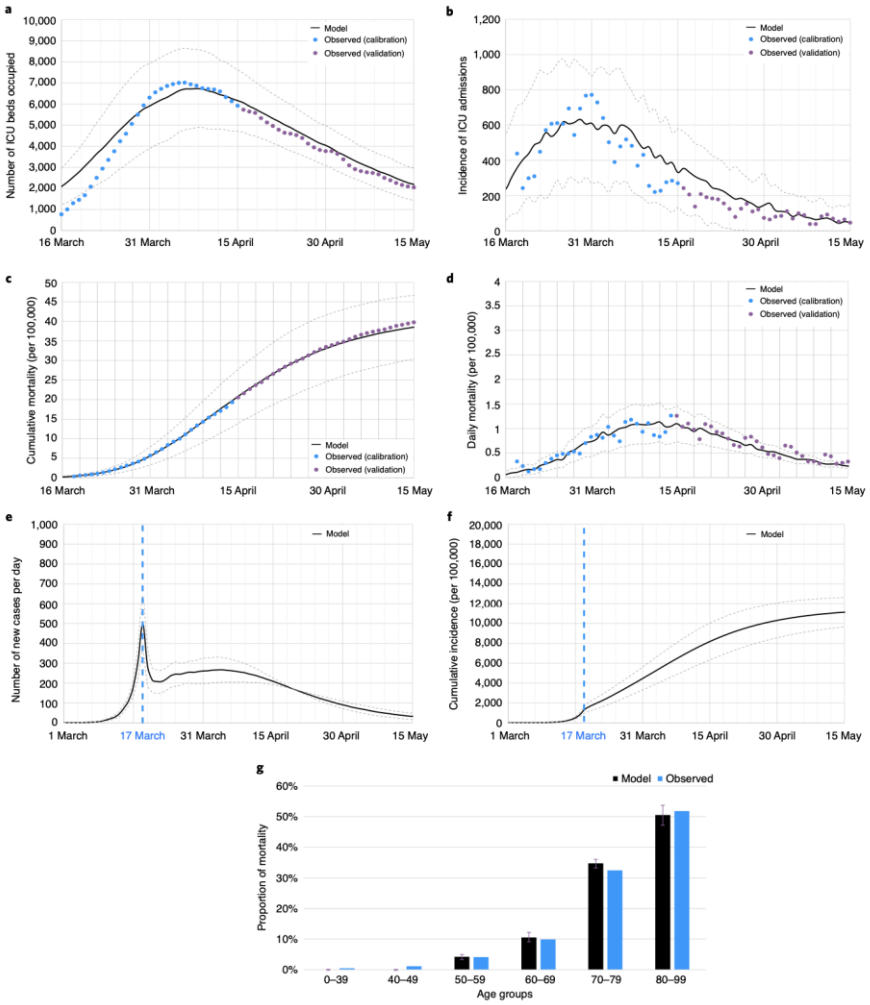


Fig. 1 | Model-predicted and observed ICU-bed occupancy, daily ICU admissions, cumulative mortality, daily mortality and age distribution of deceased people, and model-predicted daily number of new cases and cumulative incidence. a–g, Model-predicted and observed ICU-bed occupancy (**a**), daily ICU admissions (**b**), cumulative mortality (**c**), daily mortality (**d**) and age distribution of deceased people (**g**), and model-predicted daily number of new cases (**e**) and cumulative incidence (**f**). The dotted lines in panels **a**–**f** and error bars in panel **g** represent the uncertainty range (first to last quartile) stemming from the uncertainty in the parameter values. On 17 March, France ordered a general lockdown.

SYMPTOMS AND CLINICAL PRESENTATION

LOWER EXTREMITY ARTERIAL THROMBOSIS ASSOCIATED WITH COVID-19 IS CHARACTERIZED BY GREATER THROMBUS BURDEN AND INCREASED RATE OF AMPUTATION AND DEATH

Goldman IA, Ye K, Scheinfeld MH.. Radiology. 2020 Jul 16:202348. doi: 10.1148/radiol.2020202348. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective cohort study conducted at Montefiore Medical Center in Bronx, New York from January to April 2020 found all SARS-CoV-2 positive patients (n=16) had at least one blood clot on lower extremity computed tomography angiogram (CTA) compared to just 69% (n=22/36) in propensity-matched patient control data from January to April 2018 and 2019 (Table 4), limb amputation was more frequent in COVID-19 patients versus patient controls with peripheral vascular disease (Table 5), and those presenting with limb ischemia and respiratory symptoms had higher rates of amputation and mortality (p=0.001; Table 3). Authors suggest an association exists between SARS-CoV-2 infection and lower extremity arterial thromboses, as well as significant increases in leg amputation and death.

ABSTRACT

Background During the peak of COVID-19 pandemic, we have noted an increase in positive lower extremity CT angiogram (CTA) exams in patients presenting with leg ischemia. The goal of this study was to determine whether lower extremity arterial thrombosis was associated with COVID-19 and whether it was characterized by greater severity in these patients. Methods In this IRB approved retrospective propensity score-matched study, 16 SARS-CoV-2 positive patients who underwent CTA of the lower extremities and 32 SARS-CoV-2 negative patients observed from January to April in 2018-2020 were compared using three scoring system: two systems including all vessels with weighting given in one system to more proximal vessel and in the other to more distal vessels, and a third system where only the common iliac through popliteal arteries were considered. Correlation with presenting symptoms and outcomes was computed. Fisher exact tests were used to compare COVID-19 positive to negative patients regarding presence of clots and presenting symptoms. A Mantel-Haenszel test was used to associate outcome of death/amputation with COVID-19 adjusted by the history of peripheral vascular disease (PVD). Results Sixteen patients with confirmed COVID-19 (70 +/- 14 years, 7 women) underwent CTA and 32 propensity-score matched control patients (71 +/- 15 years, 16 women) were included. All COVID-19 patients (100%, 95%CI: 79-100%) had at least one thrombus while only 69% (95%CI: 50-84%) of controls had thrombi (p=0.02). 94% (95%CI: 70-99.8%) of COVID-19 patients had proximal thrombi compared to 47% (95%CI: 29-65%) of controls (p<0.001). Mean thrombus score using any of the three scoring systems yielded greater scores in the COVID-19 patients (p<0.001). Adjusted for history of PVD, death or limb amputation was more common in COVID-19 patients (OR 25, 95%CI 4.3-147, p<0.001). COVID-19 patients presenting with symptoms of leg ischemia only were more likely to avoid amputation or death than patients presenting also with pulmonary or systemic symptoms (p=0.001). Conclusion COVID-19 is associated with lower extremity arterial thrombosis characterized by greater clot burden and a more dire prognosis.

FIGURES

Table 3: Association between presenting symptoms and limb amputation or death in COVID-19 patients.

(AMS, altered mental status)

	Leg symptoms only (n=5)	Leg and other symptoms (n=11)	Notes on other symptoms (n=11)
No death, No amputation	5	1	1. Dyspnea, Fever
Death or Amputation	0	10	1. AMS, Dyspnea 2. AMS, Dyspnea 3. Cough 4. Cough, Hypoxia 5. Cough, Dyspnea 6. Cough, Dyspnea, Fever 7. Cough, Dyspnea, Fever 8. Dyspnea 9. Dyspnea, Hypoxia 10. Hypoxia

Table 3. Association between presenting symptoms and limb amputation or death in COVID-19 patients. (AMS, altered mental status)

	COVID-19 Cases	Matched controls	P values
Proximal weighted	10, 7.6, (range 2-10)	3.5, 5.0 (range 0-16)	p<0.001
Distal weighted	14.5, 11.4 (range 6-29)	4.0, 9.3 (range 0-28)	p<0.001
Unweighted proximal only	4, 4.3 (range 0-14),	0, 3.3 (range 0-10)	p<0.001

Table 4. Clot scores using the three scoring systems. P values are calculated after controlling for PVD in the linear regression model. Significance of scores in COVID-19 patients persisted even when considering just clot positive patients and excluding patients without clots (p = 0.001 by Welch two sample T-tests). Note that clot scores are greater in the COVID-19 patients regardless of the scoring system. Data is presented as Median, IQR Interquartile range (range).

		COVID-19 (n=16)	Non- COVID-19 (n=32)
No PVD (n=21)	Amputation	3	0
	Death	3	1
	No Amputation or Death	2	12
PVD (n=27)	Amputation	1	1
	Death	3	0
	No Amputation or Death	4	18

Table 4. Clot scores using the three scoring systems. P values are calculated after controlling for PVD in the linear regression model. Significance of scores in COVID-19 patients persisted even when considering just clot positive patients and excluding patients without clots (p = 0.001 by Welch two sample T-tests). Note that clot scores are greater in the COVID-19 patients regardless of the scoring system. Data is presented as Median, IQR Interquartile range (range).

COMPARISON OF VENOUS THROMBOEMBOLISM RISKS BETWEEN COVID-19 PNEUMONIA AND COMMUNITY-ACQUIRED PNEUMONIA PATIENTS

Mei F, Fan J, Yuan J, Liang Z, Wang K, Sun J, Guan W, Huang M, Li Y, Zhang WW.. Arterioscler Thromb Vasc Biol. 2020 Jul 6:ATVBAHA120314779. doi: 10.1161/ATVBAHA.120.314779. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective review of 616 patients admitted to Yichang Central People's Hospital in Hubei, China between January 1st and March 23rd 2020 compared the rates of venous thromboembolism (VTE) in patients with COVID-19 pneumonia (n=256) versus patients with CAP (n=360). Both cohorts had similar rates of VTE despite receiving either mechanical and/or pharmaceutical VTE prophylaxis (2% and 3.6% respectively, p=0.229; Table 2) calling into question previous reports regarding increased VTE events in COVID-19 patients.

SUMMARY

Additional findings:
- 15.6% of COVID-19 pneumonia patients and 10% of CAP patients (p=0.036) met criteria for on the Padua score for being at high risk for VTE.
- Within this group, the incidence of VTE was non-significantly lower in COVID-19 pneumonia compared to CAP (12.5% vs 16.7%, p=0.606; Table 4); but in-hospital mortality of COVID-19 pneumonia was non-significantly higher (6.3% vs 3.9%, P=0.180).

ABSTRACT

OBJECTIVE: The objectives were to investigate and compare the risks and incidences of venous thromboembolism (VTE) between the 2 groups of patients with coronavirus disease 2019 (COVID-19) pneumonia and community-acquired pneumonia (CAP). Approach and Results: Medical records of 616 pneumonia patients who were admitted to the Yichang Central People's Hospital in Hubei, China, from January 1 to March 23, 2020, were retrospectively reviewed. The patients with COVID-19 pneumonia were treated in the dedicated COVID-19 units, and the patients with CAP were admitted to regular hospital campus. Risks of VTE were assessed using the Padua prediction score. All the patients received pharmaceutical or mechanical VTE prophylaxis. VTE was diagnosed using Duplex ultrasound or computed tomography pulmonary angiogram. Differences between COVID-19 and CAP groups were compared statistically. All statistical tests were 2 sided, and P<0.05 was considered as statistically significant. All data managements and analyses were performed by IBM SPSS, version 24, software (SPSS, Inc, Chicago, IL). Of the 616 patients, 256 had COVID-19 pneumonia and 360 patients had CAP. The overall rate of VTE was 2% in COVID-19 pneumonia group and 3.6% in CAP group, respectively (P=0.229). 15.6% of the COVID-19 pneumonia patients and 10% of the CAP patients were categorized as high risk for VTE (Padua score, >4), which were significantly different (P=0.036).

In those high-risk patients, the incidence of VTE was 12.5% in COVID-19 pneumonia group and 16.7% in CAP group (P=0.606). Subgroup analysis of the critically ill patients showed that VTE rate was 6.7% in COVID-19 group versus 13% in CAP group (P=0.484). In-hospital mortality of COVID-19 and CAP was 6.3% and 3.9%, respectively (P=0.180). CONCLUSIONS: Our study suggested that COVID-19 pneumonia was associated with hypercoagulable state. However, the rate of VTE in COVID-19 pneumonia patients was not significantly higher than that in CAP patients.

FIGURES

	All, n (Range/%)	2019-NcoV, n (Range/%)	CAP, n (Range/%)	*P* Value
Total number	616	256	360	
Age, y	58.5 (0.5–95)	55.5 (0.5–87)	61 (15–95)	0.005
Men	342 (55.5)	131 (51.2)	211 (58.6)	0.067
>65 y old, y	215 (34.9)	77 (30.1)	138 (38.3)	0.034
Hospital stay, d	14 (4–60)	28 (5–58)	9 (4–60)	<0.001
CAD	140 (22.7)	29 (11.3)	111 (30.8)	<0.001
CVD	89 (14.4)	15 (5.9)	74 (20.6)	<0.001
Hypertension	161 (26.1)	60 (23.4)	101 (28.1)	0.199
Diabetes mellitus	89 (14.4)	46 (18.0)	43 (11.9)	0.036
History of VTE	5 (0.8)	0 (0)	5 (1.4)	0.079*
History of malignancy	110 (17.9)	4 (1.6)	106 (29.4)	<0.001
Acute liver dysfunction	13 (2.1)	12 (4.7)	1 (0.3)	<0.001
Acute renal failure	20 (3.2)	15 (5.9)	5 (1.4)	0.002
CTPA	6(0.974)	0 (0)	6 (1.7)	0.044*
Treatment				
Mask oxygen inhalation	68 (11.0)	51 (19.9)	17 (4.7)	<0.001
Corticosteroid use	237 (38.5)	151 (59.0)	86 (23.9)	<0.001
CRRT	20 (3.2)	15 (5.9)	5 (1.4)	0.002
ECOM	1 (0.2)	1 (0.4)	0 (0)	0.416*
Ventilator support	99 (16.1)	45 (17.6)	54 (15.0)	0.391
Death	30 (4.9)	16 (6.3)	14 (3.9)	0.180

χ^2 test. CAD indicates coronary artery disease; CAP, community-acquired pneumonia; CRRT, continuous renal replacement therapy; CTPA, computed tomography pulmonary angiogram; CVD, cerebrovascular disease; ECOM, extracorporeal membrane oxygenation; and VTE, venous thromboembolism.
*Fisher exact test.

Table 1: Demographics and Characteristics of COVID-19 Pneumonia and CAP Patients.

	COVID-19 Pneumonia	CAP	*P* Value
Patients with Padua score >4	n=40	n=36	0.606
VTE	5 (12.5%)	6 (16.7%)	
Non-VTE	35 (87.5%)	30 (83.3%)	
Patients requiring ventilator support	n=45	n=54	0.484
VTE	3 (6.7%)	7 (13%)	
Non-VTE	42 (93.3%)	47 (87%)	

Table 4: Incidences of VTE in High-Risk Patients and Critically Ill Patients.

	All, %	COVID-19, %	CAP, %	*P* Value
PE	4 (0.6)	1 (0.4)	3 (0.8)	0.869*
DVT	15 (2.4)	4 (1.6)	11 (3.1)	0.236
VTE	18† (2.9)	5 (2.0)	13† (3.6)	0.229

χ^2 test. CAP indicates community-acquired pneumonia; COVID-19, coronavirus disease 2019; DVT, deep venous thrombosis; PE, pulmonary embolism; and VTE, venous thromboembolism.
*χ^2 test with continuity correction.
†One patient had both PE and DVT in CAP group.

Table 4: Incidences of VTE in High-Risk Patients and Critically Ill Patients.

ADULTS

CLINICAL CHARACTERISTICS AND PREDICTORS OF MORTALITY IN AFRICAN-AMERICANS WITH COVID-19 FROM AN INNER-CITY COMMUNITY TEACHING HOSPITAL IN NEW YORK

Gayam V, Chobufo MD, Merghani MA, Lamichanne S, Garlapati PR, Adler MK.. J Med Virol. 2020 Jul 16. doi: 10.1002/jmv.26306. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

A retrospective cohort study of 408 Black patients with COVID-19 at Interfaith Medical Center, a teaching hospital in Brooklyn, New York, from March 1st to April 9th 2020 found that the most common clinical presentations included cough (62.50%), myalgia (43.87%), fever/chills (53.68%), shortness of breath (66.91%), and gastrointestinal symptoms (27.21%). Comparing the survivors (n=276) to the non-survivors (n=132), the main predictors of mortality were age (odd ratio [OR] 1.06), high BMI (OR 1.07), elevated serum ferritin (OR 1.99), C-reactive protein (OR 2.42), and D-dimer levels (OR 3.79; Figure 1). These findings reveal that Black Americans have similar clinical manifestations of COVID-19 compared to other races and suggest using generalized predictors of mortality to assist in inpatient care and management for this population until more research becomes available.

ABSTRACT

BACKGROUND: There is limited data on the clinical presentation and predictors of mortality in the African-American(AA) patients hospitalized with COVID-19 despite the disproportionately higher burden and mortality. The aim of this study is to report on the clinical characteristics and the predictors of mortality in hospitalized AA patients with COVID-19 infection. METHODS: In this retrospective cohort review, we included all AA patients with confirmed COVID-19 infection admitted to an inner-city teaching community hospital in New York City. Demographics, clinical presentation, baseline co-morbidities, and laboratory data were compared between survivors and non-survivors. The predictors of mortality were assessed using multivariate logistic regression analysis. RESULTS: Of the 408 (median age, 67years) patients included, 276(66.65%, median age 63years) survived while 132(33.35%, median age 71years) died. The most common presenting symptoms were cough, myalgia, fever/chills, shortness of breath, and gastrointestinal symptoms (nausea, vomiting, diarrhea, and abdominal pain), with a prevalence of 62.50%, 43.87%, 53.68%, and 27.21%, respectively. Age (OR 1.06, CI 1.04-1.08, P-<0.001), body mass index (OR 1.07, CI 1.04-1.11, P-<0.001), elevated serum ferritin(OR 1.99, CI 1.08-3.66, P-0.02), C-reactive protein (OR 2.42, CI 1.36-4.33, P-0.01), and D-dimers(OR 3.79, CI 2.21-6.50, P-<0.001) at the time of presentation were identified as the independent predictors of mortality. CONCLUSIONS: Cough, shortness of breath, fever/chills, gastrointestinal symptoms, and myalgia were the predominant presentation among African-Americans hospitalized with COVID-19 infection. Advanced age, higher BMI, elevated serum ferritin, C-reactive protein, and D-dimers are independent predictors of mortality among hospitalized African-Americans with COVID-19 infection.

FIGURES

Variable	Categories	All(N=408)	Non-survivors(N=132)	Survivors(N=276)	p-value[+]
Vitals on Presentation (Continuous*)					
Oxygen Saturation (%)		95(92-98)	94(89-97)	96(93-98)	<0.001
Temperature(°F)		99.7(98.2-101.1)	100(98.2-100.8)	99.5(98.2-101.4)	0.29
Respiratory rate(cycles/min)		20(19-22)	20(20-22)	20(19-21)	0.006
Pulse(beats/min)		99(87-111)	100(99-114)	98(86-110)	0.259
Systolic blood pressure (mm Hg)		128(112-142)	131(115-144)	126(111-142)	0.048
Diastolic blood pressure (mm Hg)		75(66-82)	75(65-82)	76(67-83)	0.732
Symptoms on arrival (Categorical[**])					
Cough	Yes	255(62.50)	81(31.76)	174(68.24)	0.743
	No	153(37.50)	51(33.33)	102(66.67)	

Myalgia	Yes	179(43.87)	46(25.70)	133(74.30)	0.011
	No	229(56.13)	86(37.55)	143(62.45)	
Fever/chills	Yes	219(53.68)	153(69.86)	66(30.14)	0.303
	No	189(46.32)	66(34.92)	123(65.08)	
Shortness of breath	Yes	273(66.91)	99(36.26)	174(63.74)	0.016
	No	135(33.09)	33(24.44)	102(75.56)	
Fatigue	Yes	143(35.22)	50(34.97)	93(65.03)	0.391
	No	263(64.78)	81(30.80)	182(69.20)	
GI symptoms[***]	Yes	111(27.21)	36(32.43)	75(67.75)	0.983
	No	297(72.79)	96(32.32)	201(67.68)	

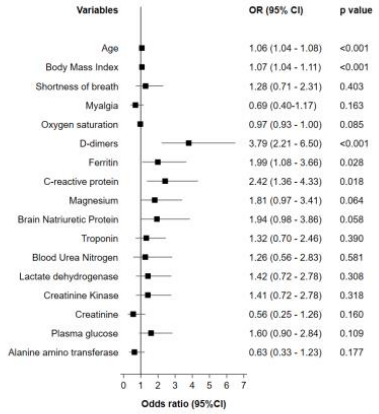
*Continuous variables, presented as median (interquartile range)

**Categorical variables displayed as frequency(percentage)

***Gastrointestinal symptoms (GI) (nausea, vomiting, diarrhea and abdominal pain)

+Compares differences in a respective variable between survivors and non-survivors, values less than 0.05 are considered statistically significant.

Table: 2 Clinical presentation on admission and triage vitals



Age, Body mass index and Oxygen saturations are modelled as continuous variables and OR (odds ratio) represent the odds of dying for every unit increase in respective parameter

Shortness of Breath and Myalgia are modelled as continuous variables. OR represent the odds of dying in those who had the respective symptom compared to those who did not.

All other variables were transformed from continuous to categorical and modelled as categorical variables. OR represents odds of dying in those with values in the 4^{th} quartile compared to those in lower quartiles(1^{st}, $2^{nd.}$ and 3^{rd} quartiles).

Figure 1: Forest plot showing predictors of mortality

ENCEPHALITIC SYNDROME AND ANOSMIA IN COVID-19: DO THESE CLINICAL PRESENTATIONS REALLY REFLECT SARS-COV-2 NEUROTROPISM? A THEORY BASED ON THE REVIEW OF 25 COVID-19 CASES

Pouga L.. J Med Virol. 2020 Jul 16. doi: 10.1002/jmv.26309. Online ahead of print.
Level of Evidence: 4 - Review / Literature Review

BLUF

An author at the Hôpital Necker in France reviews 25 cases involving COVID-19-related brain damage and examines the potential mechanisms of SARS-CoV-2 central nervous system (CNS) invasion for various neurologic symptoms (i.e. encephalitis, meningitis, anosmia). Based on the findings of the 25 cases (illustrated below) and literature review, the author presents different possible mechanisms of SARS-CoV-2 invasion of the CNS in light of different neurological manifestations (Figure 1) and suggests that most reported neurological symptoms are due to indirect impact of SARS-CoV-2 infection rather than direct SARS-COV-2 invasion of brain tissue.

SUMMARY

Among the 25 cases, findings included:
- 4/10 were positive for SARS-CoV-2 in the CNS via reverse transcription polymerase chain reaction (RT-PCR)
- 2/8 were positive for SARS-CoV-2 with CSF samples via RT-PCR
- cerebral MRI was abnormal in 6/12 cases (revealing inflammatory lesions missed by CT)
- 7/14 lumbar punctures were abnormal (5/14 had lymphocytic pleocytosis and 2/14 had elevated CSF proteins)
- almost half of all cases had severe respiratory infections.

ABSTRACT

Since the discovery of COVID-19, a disease caused by the new coronavirus SARS-CoV-2, the pathology showed different faces. There is an increasing number of cases described as (meningo)encephalitis although evidence often lacks. Anosmia, another atypical form of COVID-19, has been considered as testimony of the potential of neuroinvasiveness of SARS-CoV-2, though this hypothesis remains highly speculative. We did a review of the cases reported as brain injury caused by SARS-CoV-2. Over 98 papers found, 21 were analyzed. Only four publications provided evidence of the presence of SARS-CoV-2 within the CNS. When facing acute neurological abnormalities during an infectious episode it is often difficult to disentangle neurological symptoms induced by the brain infection and those due to the impact of host immune response on the CNS. Cytokines release can disturb neural cells functioning and can have in the most severe cases vascular and cytotoxic effects. An inappropriate immune response can lead to the production of auto-antibodies directed toward CNS components. In the case of proven SARS-CoV-2 brain invasion, the main hypothesis found in the literature focus on a neural pathway, especially the direct route via the nasal cavity, although the virus is likely to reach the CNS using other routes. Our ability to come up with hypotheses about the mechanisms by which the virus might interact with the CNS may help to keep in mind that all neurological symptoms observed during COVID-19 do not always rely on CNS viral invasion. This article is protected by copyright. All rights reserved.

FIGURES

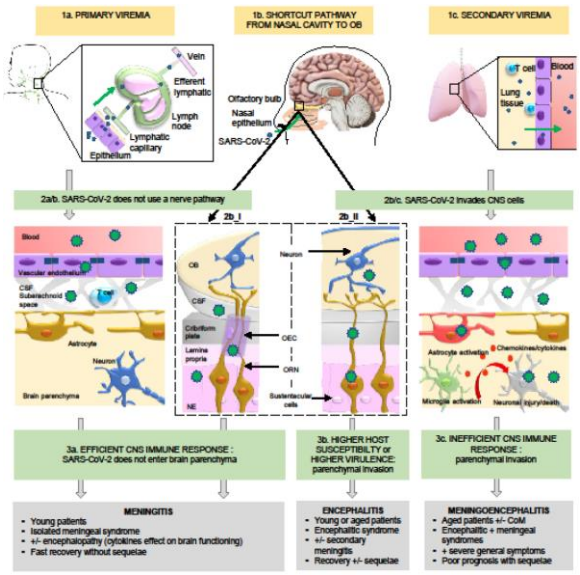


Figure 1: Possible mechanisms of SARS-CoV-2 brain invasion CNS: Central nervous system; CoM: comorbidities; CSF: Cerebrospinal fluid; NE: Nasal epithelium; OB: Olfactory bulb; OEC: Olfactory ensheathing cell; ORN: Olfactory receptor neuron. 1a. The primary viremia: during a viral infection a small amount of virus can reach the bloodstream. As lymphatic vessels drain into the circulatory system, virus particles can freely reach the bloodstream via this way. Taking advantage from the disruption of the BBB caused by the inflammation or using ACE-2 receptors present at the surface of BBB endothelial cells, SARS-COV-2 could then enter the CSF (2a), without any proliferation within the brain parenchyma (3a). In this case symptoms would be limited to a meningeal syndrome. 1.b. The shortcut pathway from nasal cavity: When SARS-CoV-2 enters the nasal cavity it could reach the CNS via two routes. 2b_i: It could "passively" reach the CSF via the OECs that have an open connection with the CSF; the CNS immune response should prevent spread of SARS-CoV-2 into the brain parenchyma (3a). 2b_ii: SARS-CoV-2 could also invade ORNs with the assumption that ACE-2 is present in those cells; in this case the virus would use a nerve pathway by being transported retrogradely from ORNs to the OB and could continue to spread through chains of connected neurons to reach the brain (3b), which might result in possible irreversible damage to the CNS. 1c. The secondary viremia: during a sustained viral replication due to the host inability to clear the viral proliferation a large amount of virus is produced and the respiratory epithelium can be disrupted, allowing the virus to reach the bloodstream. The virus could then cross the endothelial barrier by taking advantage from the disruption of the BBB caused by the inflammation or using ACE-2 receptors present at the surface of BBB endothelial cells (2c). The ineffective immune response leads to a viral proliferation within the brain parenchyma leading to neural cells damages and severe neurological symptoms (3c).

TRANSMISSION & PREVENTION

ARE SALIVARY GLANDS THE KEY PLAYERS IN SPREADING COVID-19 ASYMPTOMATIC INFECTION?

da Silva Pedrosa M.. J Med Virol. 2020 Jul 18. doi: 10.1002/jmv.26316. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

This letter to the editor written by an author from University of Sao Paulo, School of Dentistry in Brazil discussed expression of angiotensin converting enzyme 2 (ACE2) and transmembrane serine proteases 2 (TMPRSS2) in salivary glands as evidence for salivary glands being COVID-19 infection reservoirs (Song et al, 2020), whereas high viral loads during late stage of disease may be responsible for SARS-CoV-2 expression in salivary glands (Chen et al, 2020). Authors suggest preventive measures (i.e. mouthwash) could decrease the risk of SARS-CoV-2 transmission via limiting viral load in saliva droplets, but further research is needed to examine the role of salivary glands in COVID-19 infection/transmission to adopt appropriate safety measures in oral healthcare.

ABSTRACT

We read with great interest the article by Song et al.1 on the assessment of the expression of angiotensin-converting enzyme 2 (ACE2) and transmembrane serine proteases 2 (TMPRSS2) in salivary glands using publicly available databases.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

CONTACT TRACING DURING CORONAVIRUS DISEASE OUTBREAK, SOUTH KOREA, 2020

Park YJ, Choe YJ, Park O, Park SY, Kim YM, Kim J, Kweon S, Woo Y, Gwack J, Kim SS, Lee J, Hyun J, Ryu B, Jang YS, Kim H, Shin SH, Yi S, Lee S, Kim HK, Lee H, Jin Y, Park E, Choi SW, Kim M, Song J, Choi SW, Kim D, Jeon BH, Yoo H, Jeong EK; COVID-19 National Emergency Response Center, Epidemiology and Case Management Team.. Emerg Infect Dis. 2020 Jul 16;26(10). doi: 10.3201/eid2610.201315. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

This report from South Korea examined contact tracing data to determine how age and proximity (household versus non-household) affected the rate of COVID-19 transmission from 5,706 index cases of COVID-19 to 59,073 contacts from January 20 - March 27, 2020 (Table 1). The study revealed the following:
- Household contacts had a higher risk of transmission, with 11.8% of household contacts positive for COVID-19 compared to 1.9% of non-household contacts (Table 2)
- The highest rate of transmission was from the 10-19 year old age group (18.6% [95% CI 14.0%-19.0%], Table 2)
- The lowest rate of transmission was from the 0-9 year old age group (5.3% [95% CI 1.3%-13.7%], Table 2), which was likely a result of stringent social distancing due to the typically high rate of infection transmission in preschool and daycare settings
The authors note that the data highlights the need for continued study of the transmission of SARS-CoV-2 as societies begin to reopen, especially because confounding factors like social distancing and school closures have an effect on the variables underlying transmission.

ABSTRACT

We analyzed reports for 59,073 contacts of 5,706 coronavirus disease (COVID-19) index patients reported in South Korea during January 20-March 27, 2020. Of 10,592 household contacts, 11.8% had COVID-19. Of 48,481 nonhousehold contacts, 1.9% had COVID-19. Use of personal protective measures and social distancing reduces the likelihood of transmission.

FIGURES

Table 1

Contacts traced by age group of index coronavirus disease patients, South Korea, January 20–March 27, 2020

Index patient age, y	No. (%) index patients	No. (%) contacts traced	No. contacts traced/index patient	Average time contacts monitored, d
0–9	29 (0.5)	237 (0.4)	8.2	12.5
10–19	124 (2.2)	457 (0.8)	3.7	9.0
20–29	1,695 (29.7)	15,810 (26.8)	9.3	9.8
30–39	668 (11.7)	8,636 (14.6)	12.9	11.1
40–49	807 (14.1)	9,709 (16.4)	12.0	11.0
50–59	1,107 (19.4)	11,353 (19.2)	10.3	9.6
60–69	736 (12.9)	8,490 (14.4)	11.5	8.2
70–79	338 (5.9)	2,389 (4.0)	7.1	8.5
≥80	202 (3.5)	1,992 (3.4)	9.9	9.4
Total	5,706	59,073	10.4	9.9

Table 1. Contacts traced by age group of index coronavirus disease patients, South Korea, January 20–March 27, 2020

Table 2

Rates of coronavirus disease among household and nonhousehold contacts, South Korea, January 20–March 27, 2020

	Household		Nonhousehold	
Index patient age, y	No. contacts positive/no. contacts traced	% Positive (95% CI)	No. contact positive/no. contacts traced	% Positive (95% CI)
0–9	3/57	5.3 (1.3–13.7)	2/180	1.1 (0.2–3.6)
10–19	43/231	18.6 (14.0–24.0)	2/226	0.9 (0.1–2.9)
20–29	240/3,417	7.0 (6.2–7.9)	138/12,393	1.1 (0.9–1.3)
30–39	143/1,229	11.6 (9.9–13.5)	70/7,407	0.9 (0.7–1.2)
40–49	206/1,749	11.8 (10.3–13.4)	161/7,960	2.0 (1.7–2.3)
50–59	300/2,045	14.7 (13.2–16.3)	166/9,308	1.8 (1.5–2.1)
60–69	177/1,039	17.0 (14.8–19.4)	215/7,451	2.9 (2.5–3.3)
70–79	86/477	18.0 (14.8–21.7)	92/1,912	4.8 (3.9–5.8)
≥80	50/348	14.4 (11.0–18.4)	75/1,644	4.6 (3.6–5.7)
Total	1,248/10,592	11.8 (11.2–12.4)	921/48,481	1.9 (1.8–2.0)

Table 2. Rates of coronavirus disease among household and nonhousehold contacts, South Korea, January 20–March 27, 2020.

SERUM PREALBUMIN DESERVES MORE SIGNIFICANCE IN THE EARLY TRIAGE OF COVID-19 PATIENTS

Guo XL, Zhang Y, Zeng YH, Zhao FY, Liu WP, Xiao L, Yin MG, Zhang CL.. Clin Chem Lab Med. 2020 Jul 20:/j/cclm.ahead-of-print/cclm-2020-0663/cclm-2020-0663.xml. doi: 10.1515/cclm-2020-0663. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

A clinical trial conducted by Zigong First People's Hospital and Neijiang Second People's Hospital measured the levels of serum prealbumin and C-reactive protein (CRP) in 31 individuals with COVID-19 and 51 individuals without COVID-19 to determine which biomarker is a better indicator of predicting a patient's COVID-19 status. The study found that serum prealbumin was decreased in patients with COVID-19 compared to individuals in the control group (p less than 0.001) whereas serum CRP did not have a statistical difference between the two groups. (Table 1, Figure 1). Although further clinical data needs to be gathered, serum prealbumin may be a strong candidate for a new, worthwhile COVID-19 biomarker.

FIGURES

	COVID-19 group (n=31)	Non-COVID-19 group (n=51)	p-Value*
Age, years			
Mean (SD)	40.45 (12.8)	29.3 (14.9)	0.001
≤39	14 (45%)	42 (82%)	
40–59	15 (48%)	6 (12%)	
≥60	2 (7%)	3 (6%)	
Sex			
Female	16 (52%)	26 (51%)	0.956
Male	15 (48%)	25 (49%)	
Common symptoms			
Fever	21/31	40/51	0.282
Cough	20/31	13/51	<0.001
Laboratory findings			
CRP, median (IQR) (0–5 mg/L)	4.1 (1.31–14.69)	15.2 (1.08–34.4)	0.1
>5 mg/L	15/31 (48.39%)	36/51 (70.59%)	
Prealbumin, median (IQR) (180–400 mg/L)	141.4 (123.5–153.67)	228 (193–263.5)	<0.001
<180 mg/L	28/31 (90.32%)	7/51 (13.73%)	

*p-Values indicate differences between COVID-19 group and non-COVID-19 group. p<0.05 was considered statistically significant.

Table 1. Baseline characteristics of patients in COVID-19 group and control group.

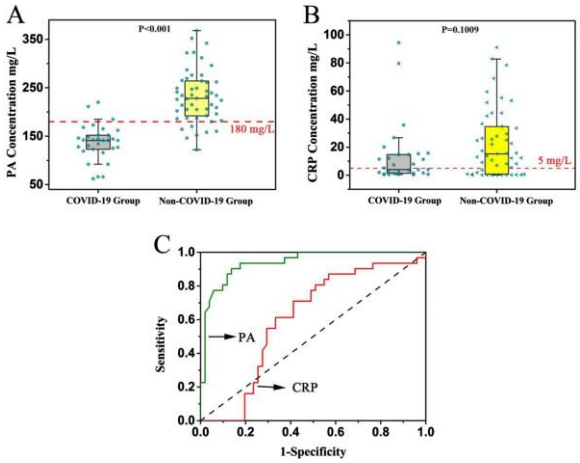


Figure 1. Prealbumin and CRP in COVID-19 patients. (A, B) Distribution of results of prealbumin and CRP in the two groups.

PREVENTION IN THE COMMUNITY

FACTORS ASSOCIATED WITH CLOTH FACE COVERING USE AMONG ADULTS DURING THE COVID-19 PANDEMIC - UNITED STATES, APRIL AND MAY 2020

Fisher KA, Barile JP, Guerin RJ, Vanden Esschert KL, Jeffers A, Tian LH, Garcia-Williams A, Gurbaxani B, Thompson WW, Prue CE.. MMWR Morb Mortal Wkly Rep. 2020 Jul 17;69(28):933-937. doi: 10.15585/mmwr.mm6928e3.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

To evaluate the use of cloth face coverings during the pandemic as well as behavioral and sociodemographic components that may influence the decision to wear a cloth mask, researchers from the United States Centers for Disease Control administered a Porter Novelli internet survey to one group of 503 adults between April 7th and April 9th, 2020 and to another group of 502 adults between May 11th and 13th, 2020. Survey results showed that an understanding of the importance of wearing a cloth face covering and a positive attitude toward wearing a cloth mask increased the likelihood of mask use (Table 2). They also

found an overall increase in the use of cloth masks over the span of one month, with the most drastic increases among non-Hispanic white individuals (54.3% to 75.1%), individuals 65 years and older (36.6% to 79.2%), and individuals located in the Midwest (43.7% to 73.8%) (Table 1). The authors indicate more research is needed in this this area, including study of the types of masks worn and why individuals may choose not to wear masks.

ABSTRACT

On April 3, 2020, the White House Coronavirus Task Force and CDC announced a new behavioral recommendation to help slow the spread of coronavirus disease 2019 (COVID-19) by encouraging the use of a cloth face covering when out in public (1). Widespread use of cloth face coverings has not been studied among the U.S. population, and therefore, little is known about encouraging the public to adopt this behavior. Immediately following the recommendation, an Internet survey sampled 503 adults during April 7-9 to assess their use of cloth face coverings and the behavioral and sociodemographic factors that might influence adherence to this recommendation. The same survey was administered 1 month later, during May 11-13, to another sample of 502 adults to assess changes in the prevalence estimates of use of cloth face coverings from April to May. Within days of the release of the first national recommendation for use of cloth face coverings, a majority of persons who reported leaving their home in the previous week reported using a cloth face covering (61.9%). Prevalence of use increased to 76.4% 1 month later, primarily associated with increases in use among non-Hispanic white persons (54.3% to 75.1%), persons aged >=65 years (36.6% to 79.2%), and persons residing in the Midwest (43.7% to 73.8%). High rates were observed in April and by May, increased further among non-Hispanic black persons (74.4% to 82.3%), Hispanic or Latino persons (77.3% to 76.2%), non-Hispanic persons of other race (70.8% to 77.3%), persons aged 18-29 years (70.1% to 74.9%) and 30-39 years (73.9% to 84.4%), and persons residing in the Northeast (76.9% to 87.0%). The use of a cloth face covering was associated with theory-derived constructs that indicate a favorable attitude toward them, intention to use them, ability to use them, social support for using them, and beliefs that they offered protection for self, others, and the community. Research is needed to understand possible barriers to using cloth face coverings and ways to promote their consistent and correct use among those who have yet to adopt this behavior.

FIGURES

	Adults who left house in past week and used cloth face covering					
	Total (N = 593)		April 2020 (n = 255)		May 2020 (n = 338)	
Construct and information source*	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)
Attitude toward behavior						
It is important for me to wear a cloth face covering when I am out in public	487	81.8 (78.36–85.22)	213	75.3 (69.87–80.77)	274	87.8 (83.65–91.97)
It is important for everyone to wear a cloth face covering when they are out in public	493	79.5 (76.07–82.98)	213	71.3 (65.83–76.83)	280	87.3 (83.25–91.39)
I think it is a good idea for me to wear a cloth face covering while out in public	500	78.1 (74.61–81.66)	217	70.7 (65.26–76.13)	283	85.2 (80.81–89.68)
I think it is a good idea for everyone to wear a cloth face covering while out in public	487	77.9 (74.31–81.42)	217	70.7 (65.24–76.10)	270	85.1 (80.70–89.61)
Behavioral intention						
I intend to wear a cloth face covering when I go to public spaces	500	84.2 (81.01–87.44)	213	78.7 (73.38–84.02)	287	89.0 (85.23–92.73)
I plan to wear a cloth face covering every time I go out in a public space	482	85.3 (82.13–88.50)	212	79.7 (74.50–84.95)	270	90.5 (86.78–94.16)
Personal agency						
Wearing a cloth face covering while I am out in public is easy for me	434	83.4 (79.86–86.96)	191	78.6 (73.04–84.26)	243	87.7 (83.26–92.19)
I am able to wear a cloth face covering when I am out in public	510	78.0 (74.53–81.40)	216	70.0 (64.57–75.52)	294	85.2 (81.11–89.32)
Perceived susceptibility						
I think it is likely that I will become infected with COVID-19	179	81.8 (76.04–87.51)	74	74.4 (65.32–83.58)	105	88.1 (80.97–95.19)
Perceived norms						
People who are important to me want me to wear a cloth face covering when I am out in public	468	81.9 (78.41–85.45)	201	76.5 (70.95–82.06)	267	86.7 (82.26–91.09)
People who are important to me believe that I should wear a cloth face covering when I am out in public	474	81.5 (78.03–84.90)	196	74.2 (68.48–79.83)	278	87.6 (83.62–91.65)
Outcome expectations						
I would protect others from coronavirus if I wear a cloth face covering when out in public	481	76.8 (73.19–80.48)	212	69.5 (63.95–75.13)	269	83.9 (79.33–88.51)
I would protect myself from coronavirus if I wear a cloth face covering when out in public	433	77.4 (73.57–81.22)	185	69.2 (63.34–75.16)	248	85.1 (80.32–89.89)
Everyone wearing cloth face coverings while out in public would prevent the spread of coronavirus in our community	439	76.3 (72.48–80.11)	184	68.1 (62.16–74.05)	255	83.8 (79.05–88.54)
Wearing a cloth face covering while out in public would lessen the chance that I could unknowingly spread coronavirus to others	495	74.4 (71.82–78.02)	213	66.3 (60.81–71.74)	282	82.4 (77.81–86.96)
I can help stop the coronavirus outbreak in my community if I wear a cloth face covering while out in public	469	76.1 (72.40–79.82)	201	68.7 (63.03–74.40)	268	83.0 (78.28–87.76)
Sources of information about cloth face coverings						
TV	395	72.1 (68.05–76.08)	173	64.3 (58.27–70.31)	222	79.7 (74.48–84.91)
Internet	278	70.7 (65.84–75.54)	126	66.1 (59.08–73.15)	152	75.3 (68.69–82.01)
Social media	263	69.5 (64.35–74.64)	124	66.9 (59.58–74.13)	139	72.2 (64.90–79.52)
E-mail message	134	78.8 (71.81–85.78)	71	77.8 (68.21–87.40)	63	80.0 (69.80–90.22)
Newspapers	159	83.1 (77.32–88.82)	65	77.3 (67.89–86.71)	94	88.2 (81.45–95.03)
Grocery store	188	77.7 (71.90–83.47)	71	76.1 (66.80–85.45)	117	78.7 (71.26–86.05)
Radio	146	80.2 (73.79–86.62)	71	77.1 (67.75–86.45)	75	83.3 (74.48–92.09)
Health care provider	187	80.8 (75.05–86.54)	65	80.2 (70.79–89.56)	122	81.1 (73.86–88.43)

Abbreviations: CI = confidence interval; COVID-19 = coronavirus disease 2019.
* Likert-type response items were dichotomized to assess agreement (strongly agree and agree versus neutral, disagree, and strongly disagree).
† Adjusted for age, sex, race/ethnicity, and region.

Table 2. Attitude, behavioral intention, personal agency, perceived susceptibility, perceived norms, outcome expectation, and information sources associated with cloth face covering use among adults who left the house in the past week, by construct and information source - Porter Novelli Internet Survey, United States, April-May 2020.

	Adults who left the house in past week and used cloth face covering			
	Survey wave			
	April 7–9, 2020 (n = 408)		May 11–13, 2020 (n = 431)	
Characteristic	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)
Total	**255**	**61.9 (56.99–66.89)**	**338**	**76.4 (71.98–80.81)**
Sex				
Men	129	61.0 (54.03–68.09)	170	77.6 (71.19–84.00)
Women	126	62.8 (55.83–69.78)	168	75.3 (69.20–81.38)
Race/Ethnicity				
White, non-Hispanic	154	54.3 (48.11–60.41)	235	75.1 (69.86–80.44)
Black, non-Hispanic	35	74.4 (61.25–87.55)	40	82.3 (70.68–94.01)
Hispanic or Latino	40	77.3 (65.52–89.18)	43	76.2 (63.84–88.65)
Other race,* non-Hispanic	26	70.8 (53.63–87.92)	20	77.3 (59.12–95.54)
Age group (yrs)				
18–29	66	70.1 (60.53–79.75)	69	74.9 (64.71–85.17)
30–39	55	73.9 (63.42–84.49)	83	84.4 (76.37–92.47)
40–49	47	61.4 (49.47–73.31)	53	68.0 (56.02–79.99)
50–64	63	65.9 (56.34–75.55)	78	75.3 (66.60–84.06)
≥65	24	36.6 (24.48–48.64)	55	79.2 (69.17–89.15)
Census region				
Northeast	56	76.9 (66.99–86.92)	66	87.0 (78.28–95.81)
Midwest	34	43.7 (32.25–55.16)	68	73.8 (64.18–83.35)
South	99	62.4 (54.38–70.40)	118	71.0 (63.22–78.72)
West	66	65.2 (55.37–75.01)	86	80.1 (71.76–88.52)
Employment status				
Employed†	184	67.3 (61.35–73.17)	216	79.5 (74.16–84.80)
Not employed§	71	52.7 (44.06–61.38)	122	71.9 (64.46–79.42)
Income				
<$25,000	43	62.1 (50.36–73.76)	55	73.1 (62.71–83.42)
$25,000–$49,999	69	60.3 (50.96–69.65)	82	76.9 (68.07–85.71)
$50,000–$99,999	70	56.3 (46.96–65.75)	101	72.2 (64.08–80.29)
≥$100,000	73	71.3 (62.24–80.27)	100	84.8 (76.82–92.82)
Home ownership				
Own	174	66.0 (59.88–72.08)	202	79.2 (73.69–84.80)
Rent	67	59.0 (49.74–68.29)	110	78.1 (70.64–85.50)
Living with others at no cost	14	39.6 (22.33–56.91)	26	56.6 (40.42–72.75)
Education				
High school or less	78	62.1 (53.53–70.62)	98	71.5 (63.37–79.62)
Some college to bachelor's degree	123	58.8 (51.82–65.86)	180	79.5 (73.76–85.23)
Any postgraduate education	54	72.5 (61.71–83.32)	60	79.1 (68.84–89.33)

Abbreviation: CI = confidence interval.
* Other race includes responses of Native American/Alaska Native, Asian, and other; these were combined because of small sample size.
† Working fulltime, part time, or self-employed.
§ Student, homemaker, retired, or not currently employed.

Table 1. Cloth face covering use among adults aged >= 18 years who left the house in the past week (N=839), by sex, race/ethnicity, age, region, employment status, income, home ownership, and education, by survey wave - Porter Novelli Internet Survey, United States, April-May 2020.

PREVENTION IN THE HOSPITAL

THE UTILITY OF CHEST CT AND RT-PCR SCREENING OF ASYMPTOMATIC PATIENTS FOR SARS-COV-2 (COVID-19) PRIOR TO SEMI-URGENT OR URGENT HOSPITAL PROCEDURES

Shah A, Walkoff LA, Kuzo RS, Callstrom MR, Brown MJ, Kendrick ML, Narr BJ, Berbari E.. Infect Control Hosp Epidemiol. 2020 Jul 16:1-11. doi: 10.1017/ice.2020.331. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

In this retrospective study, researchers from the Mayo Clinic explore the efficacy of screening for COVID-19 with reverse transcription polymerase chain reaction (RT-PCR) alone versus RT-PCR plus chest CT in adults undergoing operative procedures. They found that among 625 asymptomatic participants who underwent CT scans, 520 (83.2%) had normal scans, 1 (0.16%) had features typical of COVID-19, and 86 (13.76%) had atypical features (Table 1). Only one participant - who had an atypical CT scan - tested positive by RT-PCR. The authors argue that the addition of CT scan to RT-PCR is not an effective method for screening in a population with low prevalence, though they acknowledge this conclusion may not be generalizable to symptomatic populations or those with high prevalence.

ABSTRACT

OBJECTIVE: At present, there is a paucity of evidence guiding clinicians on the optimal approach to safely screen patients for SARS-CoV-2 (COVID-19) infection prior to a non-emergent hospital procedure. In this report we describe our experience in screening for SARS-CoV-2 (COVID-19) prior to semi-urgent and urgent hospital procedures. DESIGN: Retrospective case series. SETTING: Single tertiary medical center. PARTICIPANTS: Patients >= 18 years of age who had semi-urgent or urgent hospital procedures or surgeries. METHODS: 625 patients were screened for SARS-CoV-2 (COVID-19) using a combination of phone questionnaire (7 days prior to the anticipated procedure), RT-PCR and chest CT, between 3/1/2020 and 4/30/2020. RESULTS: Of the 625 patients, 520 scans (83.2%) were interpreted as normal, 1 (0.16%) as having typical features, 18 scans (2.88%) as having indeterminate features, and 86 (13.76%) as having atypical features of SARS-CoV-2 (COVID-19). A total of 640 RT-PCRs were performed, with 1 positive result (0.15%) in a patient with CT scan read as atypical. Out of 18 patients with

chest CTs categorized as indeterminate, 5 underwent repeat negative RT-PCR nasopharyngeal swab one week after their initial swab. 1 patient with chest CT categorized as typical had a follow up repeat negative RT-PCR, indicating that the chest CT was likely a false positive. None of the patients, after surgery, developed signs or symptoms suspicious of COVID-19, needing repeat RT-PCR or CT scan. CONCLUSION: In our experience, chest CT scanning did not prove provide valuable information in detecting asymptomatic cases of SARS-CoV-2 (COVID-19) in our low prevalence population.

FIGURES

Imaging (625)	Age (mean, range)	Sex (Female %)	RT-PCR (positive)
Typical (1)	41	1 (100)	0
Indeterminate (18)	60 (31-81)	8 (44)	0
Atypical (86)	63 (30-95)	37 (43)	1
Normal (520)	58 (18-90)	220 (42)	0

Table 1. Summary of results.

AEROSOL AND ENVIRONMENTAL SURFACE MONITORING FOR SARS-COV-2 RNA IN A DESIGNATED HOSPITAL FOR SEVERE COVID-19 PATIENTS

Li YH, Fan YZ, Jiang L, Wang HB.. Epidemiol Infect. 2020 Jul 14:1-14. doi: 10.1017/S0950268820001570. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A study evaluating aerosol and surface transmission of SARS-CoV-2 at Union Hospital (a hospital designated for treating patients with severe COVID-19) in Wuhan during 20 February to 5 March 2020 found that all 135 aerosolized samples, and 88 out of 90 surfaces, were negative for SARS-CoV-2 RNA suggesting that proper disinfection procedures and room ventilation are important and effective means for prevention of nosocomial infection.

FIGURES

Table 1. SARS-CoV-2 RNA test results from environmental surfaces in a COVID-19 designated hospital

	Sampling locations	No. of samples*	No. of positive samples#
High-risk area	**Bed rails and nightstands** in the ICU ward for COVID-19 patients	9	-
	Patients' personal belongings (mobile phone, clothes, pillowcase, towel)	12	-
	Surfaces of medical supplies (infusion pump, operating table in nurse station, temperature gun, etc.)	12	-
	Hands of doctor/nurse in the ICU	6	-
	Toilet and sink in isolation ward	6	-
	Door handle in isolation ward	6	-
	Inside of the patient's mask	3	2 (1st and 2nd)
	Goggles after use	6	-
Medium-risk area	**Door handle in buffer zone**	6	-
	Inner wall of waste container	6	-
Low-risk area	Hands of doctor/nurse in clean zone	6	-
	Computer keyboard in nurse station	6	-
	Computer mouse in nurse station	6	
Total		90	2

*All samples were collected 1 hour after routine cleaning. # All samples were tested by qualitative reverse-transcription polymerase chain reaction (RT-PCR). Sampling and testing were repeated three times at each location.

Table 2. SARS-CoV-2 RNA test results for aerosol samples from a COVID-19 designated hospital

	Sampling locations	Number of samples*	No. of positive samples#
High-risk area	Corridor of ICU Ward	9	-
	ICU Ward	9	-
	Isolation ward	18	-
	Fever clinic	9	-
	Storage locations for infectious waste	9	-
Medium-risk area	Buffer room in the ICU ward	9	-
	Buffer room in the isolation ward	9	-
Low-risk area	Clean zone in the ICU	9	-
	Clean zone in the isolation ward	18	-
	Public area of the hospital	9	-
	Conference room	18	-
Total		135	-

*All samples were collected after routine cleaning. # All samples were analysed by qualitative reverse-transcription polymerase chain reaction (RT-PCR). Sampling and testing were repeated three times at each location.

MANAGEMENT

ACUTE CARE

SUBCLINICAL CORONARY ARTERY DISEASE IN COVID-19 PATIENTS

Nai Fovino L, Cademartiri F, Tarantini G.. Eur Heart J Cardiovasc Imaging. 2020 Jul 16:jeaa202. doi: 10.1093/ehjci/jeaa202. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A retrospective cohort study of 53 hospitalized COVID-19 positive patients by researchers at the University of Padua Medical School in Italy argues that because a coronary calcium score (GCS) can be used to predict worse in-hospital outcomes in patients without COVID-19, it stands to reason that it would be highly applicable in patients with COVID-19 because of the known vulnerability conferred to this cohort of patients of clinical or subclinical cardiac disease.

SUMMARY

The authors found that a coronary calcium score (CCS) - which can be used to assess coronary artery disease (CAD) status and is obtainable at time of high-resolution CT (HRCT) - of greater than or equal to 400 was associated with a significantly higher odds of their composite endpoint (CE), a measure of risk of in-hospital mortality and ICU admission (OR 7.86, 95% CI 1.16-53.01), compared to patients with a CCS less than 400 (Table 1). They also found that half of the patients with a high CCS died - compared to 8.9% with a low CCS - and that myocardial infarction occurred more often in patients with a high CCS. These results suggest that evaluation of subclinical CAD at the time of performance of HRCT in COVID-19 patients could provide a prognostic indicator for patients at risk of worse hospital outcome.

FIGURES

Table 1 Characteristics of patients with COVID-19 according to coronary calcium score

Clinical characteristics	Total (53)	Calcium score <400 (45)	Calcium score ≥400 (8)	*P*-value
Age, years	65.3 ± 14.6	62.9 ± 14.5	78.6 ± 4.9	**0.004**
Female	18 (34%)	16 (36%)	2 (25%)	0.561
Hypertension	28 (53%)	20 (46.5%)	8 (100%)	**0.005**
Diabetes mellitus	13 (24.5%)	11 (25%)	2 (25%)	1.00
Smoking	10 (19%)	3 (7%)	7 (87.5%)	**0.001**
ACEi/ARB use history	14 (26%)	10 (22%)	4 (50%)	0.120
White blood cells, /μL	7.64 ± 5.12	7.31 ± 5.18	9.44 ± 4.55	0.282
Neutrophils, /μL	5.19 ± 3.29	5.02 ± 3.15	6.19 ± 4.17	0.393
Lymphocytes, /μL	1.76 ± 3.09	1.81 ± 3.32	1.49 ± 1.00	0.821
Creatinine, mg/dL	1.15 ± 1.20	1.15 ± 1.31	1.16 ± 0.34	0.993
D-dimer, μg/L	566.48 ± 1124.16	618.12 ± 1210.47	264.00 ± 78.24	0.447
CRP, mg/L	126.76 ± 96.91	115.53 ± 98.10	182.87 ± 71.55	0.072
Procalcitonin, μg/L	1.41 ± 3.29	1.02 ± 2.10	3.15 ± 6.36	0.099
SpO_2, %	90 ± 10.35	91 ± 8.75	88 ± 11.65	0.704
Lactic acid, mmol/L	1.79 ± 0.97	1.79 ± 1.03	1.82 ± 0.82	0.956
Hs-Troponin I on admission, ng/L	175 ± 450	23 ± 48	754 ± 642	0.057
Hs-Troponin I peak, ng/L	660 ± 1396	419 ± 1092	1424 ± 2139	0.084
Imaging features				
Consolidation, %	16 (30%)	13 (29%)	3 (37.5%)	0.685
Ground-glass opacity, %	24 (45%)	19 (42%)	5 (62.5%)	0.444
Bilateral infiltration, %	40 (75.5%)	33 (73%)	7 (87.5%)	0.662
Medical treatment				
Antibiotic therapy	53 (100%)	45 (100%)	8 (100%)	1.00
Antiviral therapy	5 (9%)	4 (9%)	1 (12.5%)	0.911
Hydroxychloroquine	37 (70%)	30 (67%)	7 (87.5%)	0.579
Corticosteroid	35 (66%)	29 (64%)	6 (75%)	0.937
Tocilizumab	9 (17%)	6 (13%)	3 (37.5%)	0.186
Outcomes				
Composite endpoint	15 (28%)	9 (20%)	6 (75%)	**0.004**
Intensive care unit admission	13 (24.5%)	8 (18%)	5 (62.5%)	**0.028**
Invasive mechanical ventilation	10 (19%)	7 (15.5%)	3 (37.5%)	0.218
Death	8 (15%)	4 (9%)	4 (50%)	**0.003**

Values are mean ± SD or *n* (%). The values in bold represent statistical significant differences between groups.
ACEi, angiotensin converting-enzyme inhibitor; ARB, angiotensin receptor blocker; CRP, C-reactive protein Hs-Troponin, high-sensitivity troponin.

Table 1. Characteristics of patients with COVID-19 according to coronary calcium score. Values are mean ± SD or n (%). The values in bold represent statistical significant differences between groups. ACEi, angiotensin converting-enzyme inhibitor; ARB, angiotensin receptor blocker; CRP, C-reactive protein Hs-Troponin, high-sensitivity troponin.

MEDICAL SUBSPECIALTIES

ENDOCRINOLOGY

COVID-19 COMPLICATED BY HASHIMOTO'S THYROIDITIS

Tee LY, Hajanto S, Rosario BH.. Singapore Med J. 2020 Jul 16. doi: 10.11622/smedj.2020106. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

A case report conducted at Changi General Hospital discusses a 45-year-old patient who was diagnosed with Hashimoto's thyroiditis following a COVID-19 infection, indicating a potential link between the hyper-inflammatory state caused by the SARS-CoV-2 virus and the development of autoimmune diseases. This finding suggests that clinicians should stay wary about the development of autoimmune diseases in patients with COVID-19.

SUMMARY

A 45-year old Chinese man presented with one day of rhinorrhea and non-productive cough, followed by a positive RT-PCR test for SARS-CoV-2. One week following the diagnosis, the patient admitted to resolution of his upper respiratory symptoms, but also complained of new-onset muscle weakness and fatigue. He was otherwise healthy and in good shape. His physical exam was unremarkable, however his labs revealed an elevated TSH and low fT4. Inflammatory markers and imaging were normal. The patient was started on levothyroxine 25 mcg daily. 5 weeks after starting the medication, the patient reported improvement in his muscle weakness and fatigue.

OBGYN

SARS-COV-2 IS NOT PRESENT IN THE VAGINAL FLUID OF PREGNANT WOMEN WITH COVID-19

Aslan MM, Uslu Yuvacı H, Köse O, Toptan H, Akdemir N, Köroğlu M, Cevrioğlu AS, Özden S.. J Matern Fetal Neonatal Med. 2020 Jul 16:1-3. doi: 10.1080/14767058.2020.1793318. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Authors at Sakarya Training and Research Hospital and Sakarya University in Turkey performed an analysis of laboratory tests, imaging results, and vaginal swabs of 13 pregnant persons with suspected COVID-19 from 19 April to 19 May 2020 in a single tertiary university hospital and found that 12 tested positive for SARS-CoV-2 via reverse transcriptase polymerase chain reaction (RT-PCR) from respiratory tract samples, but all vaginal swab samples tested negative. These findings add to the growing evidence that sexual or vertical transmission of SARS-CoV-2 is unlikely and may assist in decision-making regarding obstetrical management.

ABSTRACT

BACKGROUND: Data concerning the presence of SARS-CoV-2 in the female genital system is scarce; however, this information is important for understanding whether the virus can transmit sexually or from mother to child. The aim of this study was to investigate whether pregnant women with COVID-19 have virus in their lower genital tract. METHODS: In this cross-sectional study, we present an analysis of prospectively gathered data collected at a single tertiary university hospital from 19 April to 19 May 2020. We included 13 pregnant women hospitalized with suspected COVID-19. Results of laboratory tests, imaging tests, and nucleic acid tests on vaginal swabs for SARS-CoV-2 were also analyzed for pregnant women with a clinical diagnosis of COVID-19. RESULTS: Twelve pregnant women with confirmed COVID-19 were included in this study. Mean age was 32 +- 7.9 years. All patients had mild symptoms and were followed in the maternity ward, with none of them needing critical care unit follow-up. All lower genital tract samples were negative for SARS-CoV-2. CONCLUSION: We demonstrated that SARS-CoV-2 was not present in the vaginal fluid of pregnant women. This finding may indicate that the female genital tract is not a route of SARS-CoV-2 transmission.

ADJUSTING PRACTICE DURING COVID-19

FACE-TO-FACE COMPARED WITH ONLINE COLLECTED ACCOUNTS OF HEALTH AND ILLNESS EXPERIENCES: A SCOPING REVIEW

Davies L, LeClair KL, Bagley P, Blunt H, Hinton L, Ryan S, Ziebland S.. Qual Health Res. 2020 Jul 15:1049732320935835. doi: 10.1177/1049732320935835. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A scoping review of 11 articles (565 participants, 43% online) by authors in the fields of medicine and research compared online and face-to-face approaches for gathering health and illness experiences for qualitative research and found that compared to in-person responses, online responses were shorter, more straightforward, and involved less contextual information. Additionally, online alternatives reached a larger range of respondents but were not necessarily cost-effective and had lower levels in relational satisfaction and relationship development. Although the COVID-19 pandemic has created new opportunities for online alternatives, the authors suggest that online approaches can be useful in reaching specific populations but require knowledge on a given population's technological accessibility and skills.

ABSTRACT

Advocates of online alternatives to face-to-face interviewing suggest online approaches save money and time, whereas others have raised concerns about the quality and content of the resulting data. These issues affect researchers designing and costing their studies and application reviewers and research funders. We conducted a scoping review of English language articles describing the range of online alternative approaches. Furthermore, we systematically identified studies directly comparing online alternatives with face-to-face approaches. Synthesis of these 11 articles (565 participants) suggests that online alternatives should not be viewed as a straightforward replacement for face-to-face, a particularly important finding given the rapid communication changes occurring in the COVID-19 pandemic. When applied with consideration of the evolving evidence on their strengths and weaknesses, online methods may increase the likelihood of obtaining the desired sample, but responses are shorter, less contextual information is obtained, and relational satisfaction and consensus development are lower.

SURGICAL SUBSPECIALTIES

INTERPRETATION OF COVID-19 PCR TESTING- WHAT SURGEONS NEED TO KNOW

Johnston C, Healy B.. Br J Surg. 2020 Jul 20. doi: 10.1002/bjs.11804. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

A letter to the editor written by the Department of Microbiology and Infectious Diseases at Morriston Hospital in the United Kingdom discusses the processes behind RT-PCR and chest CT screening for SARS-CoV-2 in pre-surgical patients. They suggest reviewing the screening processes for pre-surgical patients, as there is a chance for false negatives and/or false positives from RT-PCR screening, with a sensitivity of 95%, in addition to chest CT having a low specificity (37%) in asymptomatic individuals.

SAFETY PERSPECTIVES ON PRESENTLY CONSIDERED DRUGS FOR THE TREATMENT OF COVID-19

Penman SL, Kiy RT, Jensen RL, Beoku-Betts C, Alfirevic A, Back D, Khoo SH, Owen A, Pirmohamed M, Park BK, Meng X, Goldring CE, Chadwick AE.. Br J Pharmacol. 2020 Jul 17. doi: 10.1111/bph.15204. Online ahead of print.
Level of Evidence: 1 - Review / Literature Review

BLUF

This review from the University of Liverpool highlights the mechanisms, side effects, and applicability of the most popular repurposed pharmaceuticals used to treat SARS-CoV-2 infection (Figure 1). The authors suggest that due to the rapid expansion of therapies for COVID-19, safety and potential risks must be at the forefront of every decision and that drug choice should be made "in the context of the individual and specific phase of disease in order to formulate a comprehensive harm-benefit balance."

ABSTRACT

Intense effort is underway to evaluate potential therapeutic agents for the treatment of COVID-19. In order to respond quickly to the crisis, the repurposing of existing drugs is the primary pharmacological strategy. Despite the urgent clinical need for these therapies, it is imperative to consider potential safety issues. This is important due to the harm-benefit ratios that may be encountered when treating COVID-19, which can depend on the stage of the disease, when therapy is administered and underlying clinical factors in individual patients. Treatments are currently being trialled for a range of scenarios from prophylaxis (where benefit must greatly exceed risk) to severe life-threatening disease (where a degree of potential risk may be tolerated if it is exceeded by the potential benefit). In this perspective, we have reviewed some of the most widely-researched repurposed agents in order to identify potential safety considerations using existing information in the context of COVID-19.

FIGURES

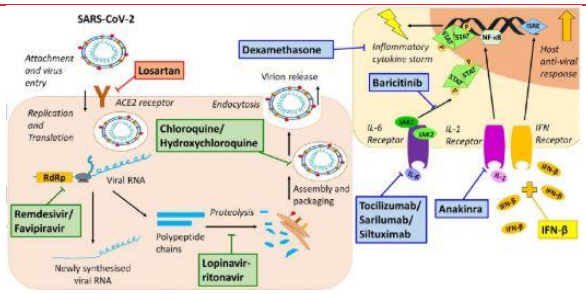


Figure 1. Overview of the mechanisms of action of the repurposed drugs undergoing clinical trials for the treatment of COVID-19 that will be reviewed in this perspective. Compounds in red represent those that are viral entry inhibitors, compounds in green represent disruptors of cellular viral processing, compounds in blue are modulators of the hyperinflammatory phase of infection and compounds in yellow stimulate host immunomodulatory and anti-viral activity. Abbreviations: ACE2, angiotensin converting enzyme 2; IL-6, interleukin‐6; IL-1, interleukin- 1; JAK, janus kinase; RdRp, RNA-dependent RNA polymerases; STAT, signal transducer and activator of transcription proteins; P, phosphate; NF-KB, nuclear factor kappa-light-chain-enhancer of activated B cells; IFN-beta, interferon-beta; ISRE, interferon stimulated response element

COVID-19 AS PART OF THE HYPERFERRITINEMIC SYNDROMES: THE ROLE OF IRON DEPLETION THERAPY

Perricone C, Bartoloni E, Bursi R, Cafaro G, Guidelli GM, Shoenfeld Y, Gerli R.. Immunol Res. 2020 Jul 17. doi: 10.1007/s12026-020-09145-5. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

In this review, researchers from Italy, Israel, and Russia evaluate the potential role of iron/ferritin in the pathophysiology of COVID-19 and draw comparisons with other hyperferritinemia syndromes (Table 1). They review literature indicating iron:
1. Has a critical role in SARS-CoV replication - and thus perhaps also in SARS-CoV-2 replication,

2. Regulates T cell activation and inflammation pathways, and
3. Contributes to reactive oxygen species formation and resultant damage (Figure 1).
Given these relationships, the authors argue that iron chelator therapy warrants consideration and cite evidence that chelators have anti-viral effects on other pathogens.

ABSTRACT

SARS-CoV-2 infection is characterized by a protean clinical picture that can range from asymptomatic patients to life-threatening conditions. Severe COVID-19 patients often display a severe pulmonary involvement and develop neutrophilia, lymphopenia, and strikingly elevated levels of IL-6. There is an over-exuberant cytokine release with hyperferritinemia leading to the idea that COVID-19 is part of the hyperferritinemic syndrome spectrum. Indeed, very high levels of ferritin can occur in other diseases including hemophagocytic lymphohistiocytosis, macrophage activation syndrome, adult-onset Still's disease, catastrophic antiphospholipid syndrome and septic shock. Numerous studies have demonstrated the immunomodulatory effects of ferritin and its association with mortality and sustained inflammatory process. High levels of free iron are harmful in tissues, especially through the redox damage that can lead to fibrosis. Iron chelation represents a pillar in the treatment of iron overload. In addition, it was proven to have an anti-viral and anti-fibrotic activity. Herein, we analyse the pathogenic role of ferritin and iron during SARS-CoV-2 infection and propose iron depletion therapy as a novel therapeutic approach in the COVID-19 pandemic.

FIGURES

Hyperferritinemic syndromes

Name	Aetiology	Clinical features	Therapeutic strategy
Secondary haemophagocytic lymphohistiocytosis	Infections • Viruses • Bacteria • Parasites • Fungi Malignancies • Mainly malignant lymphoma Autoinflammatory or autoimmune disorders Other causes • Transplantation • Metabolic • Traumatic • Iatrogenic (immunosuppression, vaccination, surgery, haemodialysis) • Pregnancy	Fever, rash, hepatosplenomegaly, lymph node enlargement, bleeding diathesis, sepsis-like syndrome, variable degrees of neurologic symptoms, possibly rapidly unexpected progress to multiple organ failure	HLH-94 protocol: • Glucocorticoids • Cyclosporine A • Intrathecal therapy • Etoposide Treatment of the specific trigger/underlying disease: • Glucocorticoids • Anti-viral drugs • Anti-CD20 (rituximab) • Intravenous immunoglobulins • Chemotherapy • IL-1 inhibitors (anakinra, canakinumab) • IL6 inhibitors (tocilizumab) Currently being tested: • JAK1/2 inhibitors (ruxolitinib) • anti-IFN-γ (alemtuzumab, emapalumab)
Catastrophic antiphospholipid syndrome	Trigger supposed to be infections in the presence of antiphospholipid antibodies	Microvascular thrombosis: renal insufficiency, acute respiratory distress syndrome/pulmonary embolism, encephalopathy, stroke, seizures, headache and coma, heart failure, myocardial infarction, valvular defects, livedo reticularis, skin necrosis and digital ischemia; spleen, adrenal glands, pancreas, retina and bone marrow infarction	Intravenous heparin Glucocorticoids Intravenous immunoglobulins Cyclophosphamide Anti-CD20 (rituximab) Plasmapheresis Eculizumab
Adult onset Still's disease	Not clearly defined • Viruses • Bacteria • Solid cancers • Haematological malignancies	Fever, arthritis, skin rash, myalgias, splenomegaly, lymphadenopathy, sore throat, liver involvement, pleurisy or pericarditis, abdominal pain, aseptic meningitis, disseminated intravascular coagulation, haemolysis	Glucocorticoids Hydroxychloroquine Intravenous immunoglobulins Methotrexate Cyclosporine IL-1 inhibitors (anakinra, canakinumab, rilonacept) IL-6 inhibitors (tocilizumab) TNF-inhibitors (infliximab, etanercept and adalimumab)
Septic shock	Infections • Viruses • Bacteria • Parasites • Fungi	Fever, rash, disseminated intravascular coagulation, variable degrees of neurologic symptoms, possibly rapidly unexpected progress to multiple organ failure	Broad spectrum antibiotic therapy Fluid resuscitation Vasopressors

Table 1. The spectrum of hyperferritinemic syndromes: suspected etiologies, clinical features, and therapeutic strategies.

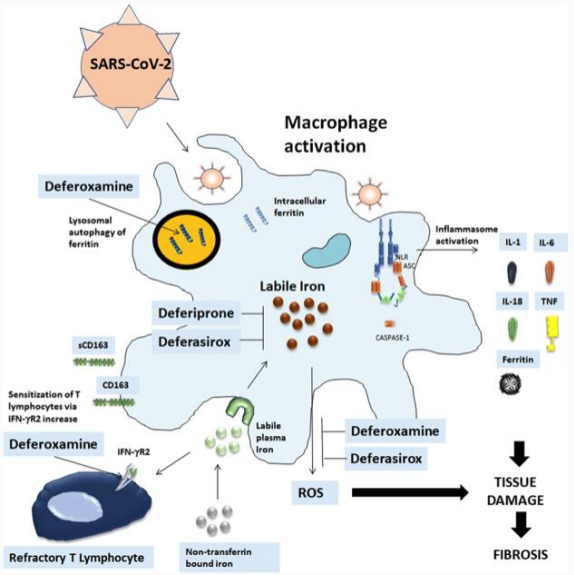


Figure 1. Iron chelation therapy in SARS-CoV-2 infection. SARS-CoV-2, likely through inflammasome activation, leads to stimulation of infiltrating macrophages that can promote hyperinflammation, characterized by increased levels of IL-6, TNF-α, IL-1β, ferritin and subsequent possible lung fibrotic complications. The increased ferritin production allows adequate storage of iron and deprives the pathogen of iron. Labile iron in the cell contributes to the formation of reactive oxygen species that further promote tissue damage and fibrosis. Iron accumulates in the reticuloendothelial macrophages and the shedding of CD163 is the marker of macrophage activation. Iron chelation therapy can interrupt these steps. (a) Deferoxamine (DFO) has a direct effect on ferritin since promotes ferritin degradation in lysosomes by inducing autophagy. Both deferiprone and deferasirox are likely to chelate cytosolic iron and iron which is extracted from ferritin prior to ferritin degradation by proteasomes. (b) DFO can induce an up-regulation of IFN-γR2 expression on the cell surface on activated T cells thus restoring T cell response to SARS-CoV-2 infection. (c) Deferasirox and DFO reduce fibrosis-inhibiting the production of free radicals, macrophage tissue infiltration and cause a remarkable decrease of IL-6 levels

DEVELOPMENTS IN DIAGNOSTICS

DIAGNOSTIC VALUE OF PERIPHERAL HEMATOLOGIC MARKERS FOR CORONAVIRUS DISEASE 2019 (COVID-19): A MULTICENTER, CROSS-SECTIONAL STUDY

Peng J, Qi D, Yuan G, Deng X, Mei Y, Feng L, Wang D.. J Clin Lab Anal. 2020 Jul 17:e23475. doi: 10.1002/jcla.23475. Online ahead of print.
Level of Evidence: 3 - Non-consecutive studies, or studies without consistently applied reference standards

BLUF

A cross-sectional study from the Chongqing Province in China analyzed the relationship between hematological markers and ARDS incidence in COVID-19 patients as compared to influenza pneumonia (IP) patients. Authors found that low white blood cell count is an early predictor of ARDS in COVID-19 patients and describe the use of monocyte-to-lymphocyte ratio (MLR) as a potential diagnostic marker for COVID-19 ($P<0.05$). While they were unable to use MLR to differentiate between COVID-19 and IP patients, the authors did find MLR diagnostically valuable in differentiating COVID-19 patients from healthy ones (Figure 1), and they propose MLR should be used clinically to assist in diagnosis of COVID-19.

ABSTRACT

BACKGROUND: To determine the diagnostic value of hematologic markers for coronavirus disease 2019 (COVID-19) and explore their relationship with disease severity. METHODS: Subjects included 190 COVID-19 patients, 190 healthy subjects, and 105 influenza pneumonia (IP) patients. COVID-19 patients were divided into the ARDS and non-ARDS groups. Routine blood examination, biochemistry indicator, days in hospital, body temperature, pneumonia severity index (PSI), CURB-65, and MuLBSTA were recorded. Correlations between variables were assessed using Spearman's correlation analysis. Receiver operating characteristic (ROC) curves were used to study the accuracy of the various diagnostic tests. RESULTS: Compared with healthy subjects, COVID-19 patients had lower white blood cell (WBC), lymphocyte, platelet, and hemoglobin levels; higher percentages of neutrophils and monocytes; lower percentages of lymphocytes and higher neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) values ($P < .05$). COVID-19 patients had higher WBC and neutrophil levels and lower percentages of lymphocytes compared to IP ($P < .05$). ROC curve analysis revealed that MLR had a high diagnostic value in differentiating COVID-19 patients from healthy subjects, but not from IP patients. NLR showed significant positive correlations with PSI, CURB-65, and MuLBSTA. Lymphocyte count was lower in the ARDS group and yielded a higher diagnostic value than the other variables. CONCLUSIONS: Monocyte-to-lymphocyte ratio showed an acceptable efficiency to separate COVID-19 patients from healthy subjects, but failed to rule out IP patients. NLR may be a reliable marker to evaluate the disease severity of COVID-19. Lymphocyte count may be useful to establish the early diagnosis of ARDS in the COVID-19 patients.

FIGURES

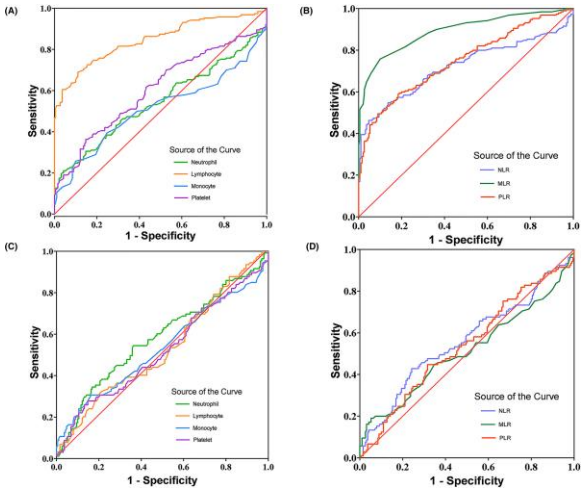


Figure 1: Receiver operating characteristic (ROC) curve was carried out to evaluate the diagnostic value of hematologic markers for COVID-19. A, Diagnostic value of neutrophil, lymphocyte, monocyte, and platelet in differentiating COVID-19 patients from healthy subjects; B, diagnostic value of NLR, MLR, and PLR in differentiating COVID-19 patients from healthy subjects; C, diagnostic value of neutrophil, lymphocyte, monocyte, and platelet in differentiating COVID-19 patients from influenza pneumonia patients; D, diagnostic value of NLR, MLR, and PLR in differentiating COVID-19 patients from influenza pneumonia patients

VARIPLEX™ TEST SYSTEM FAILS TO RELIABLY DETECT SARS-COV-2 DIRECTLY FROM RESPIRATORY SAMPLES WITHOUT RNA EXTRACTION

Eckel F, Küsters F, Drossel B, Konert M, Mattes H, Schopf S.. Eur J Clin Microbiol Infect Dis. 2020 Jul 17. doi: 10.1007/s10096-020-03983-9. Online ahead of print.

Level of Evidence: 3 - Non-consecutive studies, or studies without consistently applied reference standards

BLUF

A retrospective chart study (n = 109) at RoMed Klinik Bad Aibling hospital in Germany compared concurrent testing of samples with the point-of-care variplex test system and real time polymerase chain reaction (RT-PCR) systems in an attempt to validate variplex testing as a fast and reliable system. The authors reported a prevalence of PCR-confirmed COVID-19 of 43.1%, while variplex testing was positive in only 13.8% of cases and had a false-negative rate of 83% when compared with PCR (Table 3). The author suggest that variplex testing detection of SARS-CoV-2 was low due to lack of RNA extraction, which could be remedied by utilizing the loop-mediated isothermal amplification (LAMP) method for RNA extraction prior to variplex testing.

ABSTRACT

Diagnosis of COVID is performed by PCR methods, but their capacity is limited by the requirement of high-level facilities and instruments. The loop-mediated isothermal amplification (LAMP) method has been utilized for the detection of isolated virus-specific RNA. Preliminary data suggest the possibility of isothermal amplification directly from respiratory samples without RNA extraction. All patients admitted to our hospital were screened for SARS-CoV-2 by routine. Respiratory samples were tested by variplex system based on LAMP method directly without RNA extraction and by PCR. Primary endpoint was the false-negative rate of variplex test compared with PCR as gold standard. In 109 patients variplex test and PCR assay were performed simultaneously. Median age was 80 years and male/female ratio was 40/60%. The prevalence of PCR-confirmed COVID diagnosis was 43.1%. Variplex test was positive in 13.8%. False-negative rate of variplex test compared with PCR was 83.0%. The potential of LAMP technology using isolated RNA has been demonstrated impressively by others, and excellent sensitivity and specificity of detecting SARS-CoV-2 has been reported. However, without RNA extraction, the variplex test system failed to reliably detect SARS-CoV-2 directly in respiratory samples.

FIGURES

Sensitivity	17.0% (7.6%–30.8%)
Specificity	88.7% (78.1–95.3%)
PPV	53.3% (26.6–78.7%)
NPV	58.5% (47.9–68.6%)
Accuracy	57.8% (48.0–67.2%)

Table 3: Results of Variplex test and RT-PCR assay performed simultaneously in 109 patients (95% CI)

EVALUATIONS OF THE SEROLOGICAL TEST IN THE DIAGNOSIS OF 2019 NOVEL CORONAVIRUS (SARS-COV-2) INFECTIONS DURING THE COVID-19 OUTBREAK

Lin D, Liu L, Zhang M, Hu Y, Yang Q, Guo J, Dai Y, Xu Y, Cai Y, Chen X, Huang K, Zhang Z.. Eur J Clin Microbiol Infect Dis. 2020 Jul 17. doi: 10.1007/s10096-020-03978-6. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A group of researchers in Shenzhen, China, created a chemiluminescence immunoassay (CLIA) method to detect IgM and IgG antibodies through their recombinant nucleocapsids. Through evaluation using plasma from 29 healthy controls, 51 tuberculosis patients, and 79 COVID-19 patients, in addition to parallel comparison with a commercial ELISA kit, they found that their CLIA method demonstrated higher sensitivity and specificity than ELISA for both IgM and IgG tests** (Table 3), with greater relative light units seen for COVID-19 patients than tuberculosis or healthy patients (Figure 1). These results indicate that this newly-developed CLIA method can potentially be used to screen and diagnose COVID-19 (in combination with RT-PCR) with higher accuracy.

SUMMARY

** The sensitivity and specificity for IgG were 82.28% and 97.5% respectively, and the sensitivity and specificity for IgM were 60.76% and 92.25% respectively; there was a higher detection rate for symptom onset after 7 days in addition to fewer false positives (for IgM) and higher sensitivity (for IgM and IgG) compared to the conventional ELISA method of detecting antibodies.

ABSTRACT

We developed a chemiluminescence immunoassay method based on the recombinant nucleocapsid antigen and assessed its performance for the clinical diagnosis of severe acute respiratory syndrome coronavirus (SARS-CoV)-2 infections by detecting SARS-CoV-2-specific IgM and IgG antibodies in patients. Full-length recombinant nucleocapsid antigen and tosyl magnetic beads were used to develop the chemiluminescence immunoassay approach. Plasmas from 29 healthy cohorts, 51 tuberculosis patients, and 79 confirmed SARS-CoV-2 patients were employed to evaluate the chemiluminescence immunoassay method performance for the clinical diagnosis of SARS-CoV-2 infections. A commercial ELISA kit (Darui Biotech, China) using the same nucleocapsid antigen was used for the in-parallel comparison with our chemiluminescence immunoassay method. The IgM and IgG manner of testing in the chemiluminescence immunoassay method showed a sensitivity and specificity of 60.76% (95% CI 49.1 to 71.6) and 92.25% (95% CI 83.4 to 97.2) and 82.28% (95% CI 72.1 to 90.0) and 97.5% (95% CI 91.3 to 99.7), respectively. Higher sensitivity and specificity were observed in the chemiluminescence immunoassay method compared with the Darui Biotech ELISA kit. The developed high sensitivity and specificity chemiluminescence immunoassay IgG testing method combined with the RT-PCR approach can improve the clinical diagnosis for SARS-CoV-2 infections and thus contribute to the control of COVID-19 expansion.

FIGURES

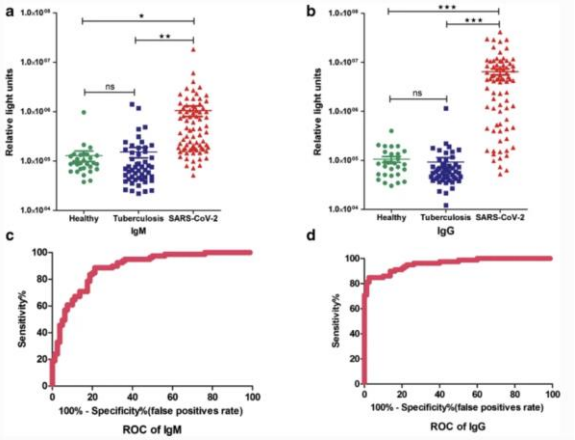


Figure 1. (a) and (b) show the relative light units (RLU) of healthy, tuberculosis, and COVID-19 patients for the IgM and IgG chemiluminescence immunoassay detection methods. For IgM testing, there is a six-fold increase in RLU from healthy patients and an eight-fold increase from tuberculosis patients for SARS-CoV-2. For IgG testing, there is a sixty-fold increase in RLU from healthy patients and an seventy-fold increase from tuberculosis patients for SARS-CoV-2. Based on these results, receiver operating characteristic curves were calculated for the IgM (c) and IgG (d) tests.

Methods	Control group (total 64 cases)		SARS-CoV-2 confirmed patients (total 65 cases)	
	IgM false-positive /%	IgG false-positive /%	IgM-positive /%	IgG-positive /%
ELISA	14/21.8%	0/0%	30/46.1%	15/23%
Chemiluminescence	6/9.38%	2/3.1%	40/61.54%	53/81.5%
Identified in both	1/1.56%	0/0%	25/38.46%	15/23%

Table 3. Comparison of the chemiluminescence immunoassay IgM and IgG method and detection of IgM and IgG from the ELISA method

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CONTRIBUTORS

Alisa Malyavko
Ben Showalter
Carter Butuk
Colin Bartz-Overman
Dax Cvancara
Jacqueline Fezza
Krithika Kumarasan
Maresa Woodfield
Priscilla Natcher
Ryan Wertz
Simran Mand
Sindhu Thevuthasan
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Tasha Ramparas
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