

The Daily COVID-19 Literature Surveillance Summary

December 23, 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 case-control study by a multidisciplinary team of Italian researchers examined autoimmune and inflammatory markers in 40 hospitalized COVID-19 patients compared to 40 healthy control patients and found that in addition to having elevated inflammatory markers such as IL-6, LDH and ferritin, blood samples of these COVID-19 patients also showed the [presence of IgG autoantibodies such as ANA, ANCA, and ASCA IgG](#). Authors argue that patients with COVID-19 may be more susceptible to developing a new autoimmune response which can correlate to more severe disease and worse prognosis.

Understanding the Pathology

- A physician from the University of Oxford, UK explains the [biology of the infectious cycle of SARS-CoV-2 and the immunopathology behind the clinical symptoms of the virus](#): cells that express the ACE2 receptor and TMPRSS2 serine protease are more susceptible to SARS-CoV-2 infection, disease progression is related to both an abnormal immune response and viral spread, and the lymphopenia and cytokine storms seen in COVID-19 are due to down-regulation of major histocompatibility complex 1 restricted antigen presentation and increased secretion of pro-inflammatory cytokines.

Management

- Investigators from [Regeneron Pharmaceuticals report results from their ongoing, randomized, double-blind, phase 1-3 trial](#) of their neutralizing antibody cocktail (REGN-COV2) in non-hospitalized patients with COVID-19 between June 16 and August 13, 2020. They found the least-squares mean difference in SARS-CoV-2 viral load at seven days between the REGN-COV2 dose group ($n=182$) and the placebo group ($n=93$) was $-0.41 \log_{10}$ copies/mL (95% CI: -0.71 to -0.10), with a more significant reduction in subjects who had not mounted an antibody response at the time of randomization. No significant adverse effects were reported. The authors concluded the REGN-COV2 antibody cocktail reduced viral load without significant adverse effects but, because there was no formal hypothesis testing, recommend further analysis of this ongoing trial to confirm these results.

Adjusting Practice During COVID-19

- A team of American cardiologists and emergency medicine physicians used a US registry (CARES) of out-of-hospital cardiac arrest (OHCA) to compare outcomes between March 16 and April 30, 2020 to the same period in 2019 and found [lower rates of sustained return of spontaneous circulation \(ROSC\) during the COVID-19 pandemic](#) compared to 2019 (23.0% vs 29.8%; $p<0.001$), with higher incidence of OHCA in communities with high (adjusted mean difference [AMD], 38.6 [95% CI, 37.1-40.1] per million residents) and very high (AMD, 28.7 [95% CI, 26.7-30.6] per million residents) COVID-19 mortality. Survival to discharge after OHCA was also lower during the pandemic than in 2019 (6.6% vs 9.8%, $p=0.048$). Authors suggest the lower rates of sustained ROSC indicates a need to better understand potential underlying causes, such as the impact of infection prevention protocols implemented early in the pandemic, and care-seeking behaviors in the community.

R&D: Diagnosis & Treatments

- A systematic review and meta-analysis of 26 articles conducted by gastrointestinal specialists in Spain found [liver injury and elevated liver function tests \(LFTs\) upon admission were significantly associated with higher risk of severe COVID-19](#). They identified markers including elevations of AST, ALT and bilirubin, which were associated with worse outcomes (specificities of 78%, 77%, and 94% respectively), suggesting the usefulness of incorporating these laboratory markers into existing tools for COVID-19 monitoring and prognosis determination.

Mental Health & Resilience Needs

- A multidisciplinary team of researchers associated with the Centers for Disease Control and Prevention (CDC) discuss evidence of [increased emergency room visits and hospitalizations for child abuse/neglect](#) during the COVID-19 pandemic when compared to 2019. Authors attribute this trend to increases in stress, substance use, mental health issues, and financial hardships as a result of the pandemic and advocate for increased awareness of child abuse/neglect and outline specific prevention strategies recommended by the CDC.

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EPIDEMIOLOGY

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

SARS-COV-2 INFECTION AS A TRIGGER OF AUTOIMMUNE RESPONSE

Sacchi MC, Tamiazzo S, Stobbiione P, Agatea L, De Gaspari P, Stecca A, Lauritano EC, Roveta A, Tozzoli R, Guaschino R, Bonometti R.. Clin Transl Sci. 2020 Dec 11. doi: 10.1111/cts.12953. Online ahead of print.

Level of Evidence: 4 - Case-series or case-control studies, or poor quality prognostic cohort study

BLUF

A case-control study by a multidisciplinary team of Italian researchers examined autoimmune and inflammatory markers in 40 hospitalized COVID-19 patients compared to 40 healthy control patients. In addition to having elevated inflammatory markers such as IL-6, LDH and ferritin, blood samples of these COVID-19 patients also showed the presence of IgG autoantibodies such as ANA, ANCA, and ASCA IgG (Table 5). Authors argue that patients with COVID-19 may be more susceptible to developing a new autoimmune response which can correlate to more severe disease and worse prognosis.

ABSTRACT

Nowadays, few evidences have shown the possible involvement of autoimmunity in patients affected by Coronavirus disease 2019 (COVID-19). In this study, we elucidate whether severe acute respiratory syndrome (SARS-CoV-2) stimulates autoantibody production and contributes to autoimmunity activation. We enrolled 40 adult patients (66.8 years mean age) admitted to Alessandria hospital between March and April 2020. All the patients had a confirmed COVID-19 diagnosis and no previously clinical record of autoimmune disease. 40 blood donors were analyzed for the same markers and considered as healthy controls. Our patients had high levels of common inflammatory markers, such as C Reactive Protein, Lactate Dehydrogenase, ferritin and creatinine. Interleukin-6 concentrations were also increased, supporting the major role of this interleukin during COVID-19 infection. Lymphocytes number were generally lower compared to healthy individuals. All the patients were also screened for the most common autoantibodies. We found a significant prevalence of ANA, ANCA and ASCA IgA antibodies. We observed that patients having a de novo autoimmune response had the worst acute viral disease prognosis and outcome. Our results sustain the hypothesis that COVID-19 infection correlates with the autoimmunity markers. Our study might help clinicians to: a) better understand the heterogeneity of this pathology and b) correctly evaluate COVID-19 clinical manifestations. Our data explained why drugs used to treat autoimmune diseases may also be useful for SARS-CoV-2 infection. In addition, we highly recommend checking COVID-19 patients for autoimmunity markers, mainly when deciding on whether to treat them with plasma transfer therapy.

FIGURES

| Autoantibodies | All Patients (40) | | Healthy Subjects (40) | | Chi Square (with Yates Correction) | p value |
|----------------------|-------------------|-------------|-----------------------|-------------|---------------------------------------|---------|
| | pos | neg | pos | neg | | |
| ANA | 23 (57.50%) | 17 (42.50%) | 05 (12.50%) | 35 (87.50%) | 0.0001* | |
| Anti-Cardiolipin | 05 (12.50%) | 35 (87.50%) | 05 (12.50%) | 35 (87.50%) | 0.7353 | |
| Anti β2-Glycoprotein | 02 (5%) | 38 (95%) | 01 (2.50%) | 39 (97.50%) | 1.0000 | |
| ENA | 01 (2.5%) | 39 (97.50%) | 00 (0%) | 40 (100%) | nv | |
| Anti-R3 | 01 (2.5%) | 39 (97.50%) | 00 (0%) | 40 (100%) | nv | |
| Anti-MPO | 00 (0%) | 40 (100%) | 00 (0%) | 40 (100%) | nv | |
| ANCA | 10 (25%) | 30 (75%) | 01 (2.50%) | 39 (97.50%) | 0.0094* | |
| ASCA IgA | 10 (25%) | 30 (75%) | 01 (2.50%) | 39 (97.50%) | 0.0094* | |
| ASCA IgG | 07 (17.5%) | 33 (82.50%) | 01 (2.50%) | 39 (97.40%) | 0.0624 | |

Table 5. List of the autoantibodies detected in COVID-19 patients and healthy individual.

| Inflammatory markers | Nomal range | All paents | <60ys | ≥ 60ys | p value |
|----------------------|-------------------|----------------|---------------|-----------------|-----------------------|
| LDH | 230-500 U/L | 690.03±259.18 | 645.36±202.72 | 715.58±284.31 | 0.31 (T-test) |
| Ferriti | 10-291ng/ml | 1005.29±892.40 | 889.90±591.65 | 1099.61±1011.24 | 0.26 (T-test) |
| Lymphocytes number | 0.9-5.2 x1000/mcl | 3.80±13.80 | 1.00±0.43 | 5.31±17.17 | 0.67 (M-W) |
| Creatin | 0.4-1 mg/dl | 1.13±0.76 | 0.77±0.15 | 1.32±0.89 | 0.69 (M-W) |
| PCR | 0-0.8 mg/dl | 10.33±12.78 | 7.59±10.87 | 9.21±6.52 | 0.21 (T-test) |
| C 3 | 82-160 mg/dl | 145.38±36.45 | 158.07±31.86 | 138.23±37.75 | 0.02 (T-test)* |
| C4 | 12-36 mg/dl | 37.35±13.37 | 37.35±13.79 | 37.42±13.22 | 0.40 (T-test) |
| IL-6 | 0-5.9 mg/dl | 58.59±102.92 | 11.99±11.01 | 85.23±123.29 | 0.02 (M-W)* |

Table 4. List of the inflammatory markers analyzed in the 40 COVID-19 patients.

UNDERSTANDING THE PATHOLOGY

LOSS OF SMELL IN PATIENTS WITH COVID-19: MRI DATA REVEAL A TRANSIENT EDEMA OF THE OLFACTORY CLEFTS

Eliezer M, Hamel AL, Houdart E, Herman P, Housset J, Jourdaine C, Eloit C, Verillaud B, Hautefort C.. Neurology. 2020 Dec 8;95(23):e3145-e3152. doi: 10.1212/WNL.0000000000010806. Epub 2020 Sep 11.

Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

This prospective case-controlled study conducted by a physicians at AP-HP Lariboisiere Hospital in Paris, France used MRI of the olfactory clefts (OC, Figures 4 and 5) and visual olfactory scores (VOS) to evaluate cases (n=27) of SARS-CoV-2 infected patients with olfactory function loss (OFL) at initial infection and again one month later, compared with 20 age-matched healthy controls (normal VOS and no obstruction shown on MRI). At early stages of infection the VOS scores were 2.8 +/- 2.7 (range 0-8) and total obstruction, likely from inflammation and edema, was shown in 19 of 20 cases. After 1 month, the VOS improved (8.3 +/- 1.9 with a range of 4-10) and only 7 of 20 patients showed any obstruction on MRI ($p=0.004$), suggesting that olfactory function loss in SARS-CoV-2 patients is associated with reversible olfactory cleft obstruction over time (Table).

ABSTRACT

OBJECTIVE: To assess the physiopathology of olfactory function loss (OFL) in COVID-19 patients, we evaluated the olfactory clefts on MRI during the early stage of the disease and one month later. **METHODS:** This was a prospective monocentric case-controlled study. Twenty SARS-CoV2-infected patients with OFL were included and compared to 20 age-matched control healthy subjects. All infected patients underwent olfactory function assessment and 3T MRI, performed both at the early stage of the disease and at one-month follow-up. **RESULTS:** At the early stage, SARS-CoV2-infected patients had a mean olfactory score of 2.8 +/- 2.7 (range 0-8), and MRI displayed a complete obstruction of the OC in 19 out of 20 patients. Controls had normal olfactory scores and no obstruction of the OC on MRI. At one month follow-up, the olfactory score had improved to 8.3 +/- 1.9 (range 4-10) in patients, and only 7 out of 20 patients still had an obstruction of the OC. There was a correlation between olfactory score and obstruction of the OC ($p=0.004$). **CONCLUSION:** OFL in SARS-CoV2-infected patients is associated with a reversible obstruction of the OC.

FIGURES

Table Clinical and radiologic characteristics of patients with SARS-CoV2 infection and OFL

| Patients | Early-stage MRI and olfactory functional assessment | | | | | | | | Follow-up MRI and olfactory functional assessment at 1 mo | | | | | | | |
|----------|---|-----|----------------------------|-----|-----------------|------|----------------|--|---|-----|-----------------|------|----|--|---|---|
| | | | MRI | | | | | | | | MRI | | | | | |
| | OC obstruction | | OB volume, mm ³ | | Olfactory score | | OC obstruction | | OB volume, mm ³ | | Olfactory score | | | | | |
| No. | Age, y | Sex | R | L | R | L | | | R | L | R | L | | | R | L |
| 1 | 27 | M | Yes | Yes | 33.9 | 51.3 | 0 | | No | Yes | 49 | 43 | 8 | | | |
| 2 | 27 | M | Yes | Yes | 43.1 | 41.4 | 2 | | No | No | 30 | 26.6 | 8 | | | |
| 3 | 31 | M | Yes | Yes | 32.7 | 34.8 | 0 | | No | No | 25.5 | 17 | 10 | | | |
| 4 | 27 | F | Yes | Yes | 36.8 | 32 | 0 | | No | No | 20.6 | 19.5 | 10 | | | |
| 5 | 26 | M | Yes | Yes | 60.2 | 61 | 7 | | No | No | 57.7 | 54.5 | 10 | | | |
| 6 | 50 | M | Yes | No | 36.7 | 40.4 | 0 | | No | No | 44.8 | 38.3 | 10 | | | |
| 7 | 32 | F | Yes | Yes | 33.2 | 43.4 | 1 | | Yes | No | 39.8 | 30 | 8 | | | |
| 8 | 53 | M | Yes | Yes | 33.2 | 39.1 | 0 | | Yes | Yes | 38.2 | 41.9 | 5 | | | |
| 9 | 47 | F | Yes | Yes | 56.2 | 43.2 | 1 | | Yes | No | 49.7 | 51.2 | 9 | | | |
| 10 | 34 | F | Yes | Yes | 31 | 32.5 | 5 | | No | Yes | 33.8 | 27.3 | 9 | | | |
| 11 | 38 | F | Yes | Yes | 32.8 | 42.1 | 3 | | No | No | 29.2 | 39.3 | 10 | | | |
| 12 | 40 | F | Yes | Yes | 38.1 | 36.3 | 1 | | No | No | 36.9 | 41.9 | 7 | | | |
| 13 | 29 | F | No | Yes | 48.3 | 40.9 | 7 | | No | No | 39.8 | 41.9 | 9 | | | |
| 14 | 41 | F | Yes | Yes | 24.1 | 32.1 | 8 | | No | No | 28 | 33.8 | 10 | | | |
| 15 | 27 | F | Yes | Yes | 32.2 | 31.6 | 5 | | No | No | 33.3 | 32.4 | 9 | | | |
| 16 | 21 | F | Yes | Yes | 46.8 | 45 | 7 | | No | No | 49.5 | 51.4 | 10 | | | |
| 17 | 27 | M | Yes | Yes | 42.3 | 46.2 | 4 | | No | Yes | 42.8 | 55 | 4 | | | |
| 18 | 35 | M | Yes | No | 44.2 | 48.4 | 3 | | Yes | No | 43.8 | 56.6 | 10 | | | |
| 19 | 47 | M | No | No | 27.5 | 22.3 | 0 | | No | No | 28.8 | 23.7 | 5 | | | |
| 20 | 42 | M | No | No | 30.8 | 40.7 | 1 | | No | No | 41.5 | 38.6 | 6 | | | |

Abbreviations: OB = olfactory bulbs; OC = olfactory clefts; OFL = olfactory function loss; SARS-CoV2 = severe acute respiratory syndrome coronavirus 2.

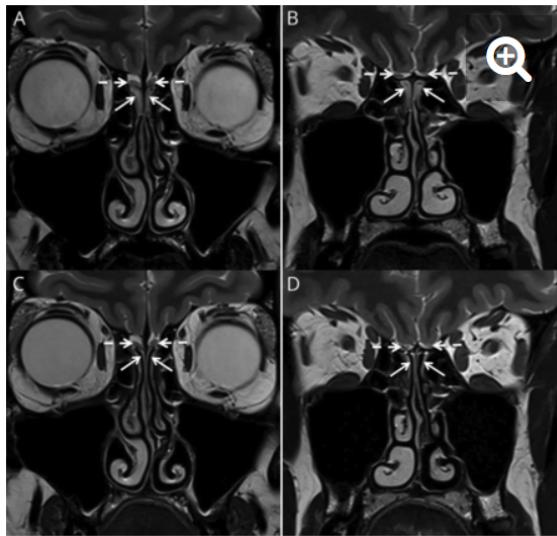


Figure 4. Patient 11: 38-year-old woman with severe acute respiratory syndrome coronavirus 2 infection. Coronal section of the olfactory clefts (OC) and bulbs on MRI on 2D T2-weighted sequences. (A and B) On the first MRI, the olfactory bulbs (white dotted arrow) are normal (right 38.1 mm³, left 42.1 mm³), while a bilateral inflammatory obstruction (white arrow) of the OC is observed below the olfactory bulbs (A, white dotted arrow) and olfactory tracts (B, white dotted arrow). (C and D) At the 1-month follow-up, the volume of the olfactory bulbs (white dotted arrow) remains normal (right 29.2 mm³, left 39.3 mm³), and no inflammatory obstruction of the OC is observed within the (A) anterior and (B) posterior parts of the OC. The olfactory score at the first consultation and the 1-month follow-up was 0 and 10, respectively.

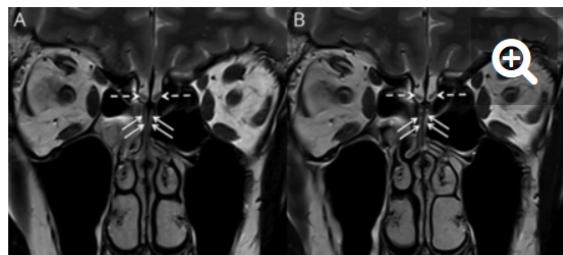


Figure 5. Patient 8: 53 year-old man with severe acute respiratory syndrome coronavirus 2 infection. Coronal section of the olfactory clefts and bulbs on MRI on 2D T2-weighted sequences. (A and B) On the first MRI, the olfactory bulbs (white dotted arrow) are normal (right 33.2 mm³, left 39.1 mm³), while a bilateral inflammatory obstruction (white arrow) of the olfactory clefts is observed. (C and D) At the 1-month follow-up, the volume of the olfactory bulbs (white dotted arrow) remains normal (right 38.2 mm³, left 41.9 mm³), but an inflammatory obstruction of the OC (white arrow) is still observed. The olfactory score at the first consultation and the 1-month follow-up was 0 and 5, respectively.

HOW SARS-COV-2 (COVID-19) SPREADS WITHIN INFECTED HOSTS - WHAT WE KNOW SO FAR

Sanyal S.. Emerg Top Life Sci. 2020 Dec 11;4(4):371-378. doi: 10.1042/ETLS20200165.

Level of Evidence: 5 - Review / Literature Review

BLUF

A physician from the University of Oxford, UK explains the biology of the infectious cycle of SARS-CoV-2 and the immunopathology behind the clinical symptoms of the virus. Notably, cells that express the ACE2 receptor and TMPRSS2 serine protease are more susceptible to SARS-CoV-2 infection, disease progression is related to both an abnormal immune response and viral spread, and the lymphopenia and cytokine storms seen in COVID-19 are due to down-regulation of major histocompatibility complex 1 restricted antigen presentation and increased secretion of pro-inflammatory cytokines (Figure 1). Understanding the immunopathology of the virus may help provide better treatment and care to patients around the world.

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of the ongoing pandemic of coronavirus disease 2019 (COVID-19), belongs to the betacoronavirus genus and shares high homology to the severe acute respiratory syndrome coronavirus (SARS-CoV) that emerged in 2003. These are highly transmissible and pathogenic viruses which very likely originated in bats. SARS-CoV-2 uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as SARS-CoV, and spreads primarily through the respiratory tract. Although several trials for vaccine development are currently underway, investigations into the virology of SARS-CoV-2 to understand the fundamental biology of the infectious cycle and the associated immunopathology underlying the clinical manifestations of COVID-19 are crucial for identification and rational design of effective therapies. This review provides an overview of how SARS-CoV-2 infects and spreads within human hosts with specific emphasis on key aspects of its lifecycle, tropism and immunopathological features.

FIGURES

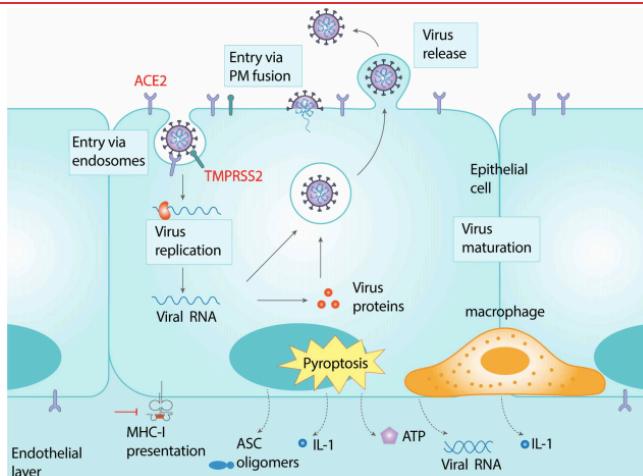


Figure 1. Schematic of the intracellular lifecycle of SARS-CoV-2 and associated immunopathology. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects cells expressing the surface receptors angiotensin-converting enzyme 2 (ACE2) and TMPRSS2, resulting in entry of the virus via the endocytic machinery or upon fusion at the plasma membrane. The viral genome is released into the cytosol upon fusion of the viral and host membranes and undergoes replication, transcription, translation and assembly to form viral progenies that are released into the extracellular space via unknown mechanisms.

Amplification and release of the virus leads to host cell pyroptosis and release of damage-associated molecular patterns, including ATP, nucleic acids and ASC oligomers. This is accompanied by secretion of pro-inflammatory cytokines and chemokines culminating in a cytokine storm. On the other hand MHC-I restricted antigen presentation is downregulated most likely by binding of the viral Orf8 protein, resulting in attenuated T-cell activation, thereby contributing to the common clinical feature of lymphopenia.

IN VITRO

LIPID DROPLETS FUEL SARS-COV-2 REPLICATION AND PRODUCTION OF INFLAMMATORY MEDIATORS

Dias SDSG, Soares VC, Ferreira AC, Sacramento CQ, Fintelman-Rodrigues N, Temerozo JR, Teixeira L, Nunes da Silva MA, Barreto E, Mattos M, de Freitas CS, Azevedo-Quintanilha IG, Manso PPA, Miranda MD, Siqueira MM, Hottz ED, Pão CRR, Bou-Habib DC, Barreto-Vieira DF, Bozza FA, Souza TML, Bozza PT.. PLoS Pathog. 2020 Dec 16;16(12):e1009127. doi: 10.1371/journal.ppat.1009127. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Brazilian immunologists conducted an in-vitro investigation to better understand how host pathways support SARS-CoV-2 replication. They found SARS-CoV-2 modulates lipid metabolism by inducing the expression of regulatory proteins CD36, PPAR- γ , and SREBP-1 (Figure 1) and increasing lipid droplet (LD) production in monocytes, lung epithelial cells, and microvascular endothelial cells. Treatment with A922500, an inhibitor of DGAT-1 (a key enzyme in LD formation), inhibited viral replication, particle assembly, and production of inflammatory mediators (Figures 3, 4). Authors suggest therapeutics targeting DGAT-1 or other lipid metabolic pathways may offer a new strategy to combat SARS-CoV-2.

ABSTRACT

Viruses are obligate intracellular parasites that make use of the host metabolic machineries to meet their biosynthetic needs. Thus, identifying the host pathways essential for the virus replication may lead to potential targets for therapeutic intervention. The mechanisms and pathways explored by SARS-CoV-2 to support its replication within host cells are not fully known. Lipid droplets (LD) are organelles with major functions in lipid metabolism, energy homeostasis and intracellular transport, and have multiple roles in infections and inflammation. Here we described that monocytes from COVID-19 patients have an increased LD accumulation compared to SARS-CoV-2 negative donors. In vitro, SARS-CoV-2 infection were seen to modulate pathways of lipid synthesis and uptake as monitored by testing for CD36, SREBP-1, PPARgamma, and DGAT-1 expression in monocytes and triggered LD formation in different human cell lines. LDs were found in close apposition with SARS-CoV-2 proteins and double-stranded (ds)-RNA in infected Vero cells. Electron microscopy (EM) analysis of SARS-CoV-2 infected Vero cells show viral particles colocalizing with LDs, suggestive that LDs might serve as an assembly platform. Pharmacological modulation of LD formation by inhibition of DGAT-1 with A922500 significantly inhibited SARS-CoV-2 replication as well as reduced production of mediators pro-inflammatory response. Taken together, we demonstrate the essential role of lipid metabolic reprogramming and LD formation in SARS-CoV-2 replication and pathogenesis, opening new opportunities for therapeutic strategies to COVID-19.

FIGURES

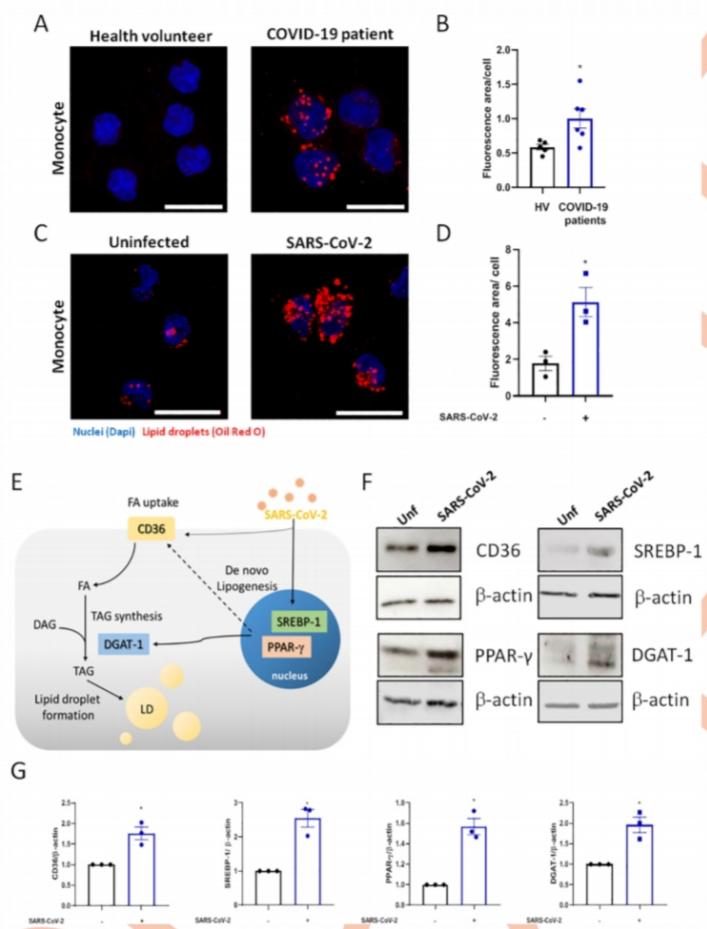


Figure 1. "SARS-CoV-2 infection modulates the lipid metabolism in human monocytes.

(A and C) LDs were captured by fluorescent microscopy after Oil Red O staining (Red) and nuclei stained with DAPI (Blue). (A) Representative images of monocytes from COVID-19 patients and health volunteers. (C) Representative images of human monocytes obtained from PBMC infected by SARS-CoV-2 with MOI of 0.01 for 24 hours. Scale bar 20 μ m. (B and D) LDs were evaluated by ImageJ software analysis by the measurement of the fluorescent area. (E) Representative scheme of the increase of proteins associated with lipid metabolism by SARS-CoV-2 infection in monocyte can regulate the lipid droplet formation. (F) Monocytes were infected by SARS-CoV-2 with MOI of 0.01 during 24h. Cell lysates were collected for the detection of CD36, PPAR- γ , SREBP-1, DGAT-1 by Western blotting. β -actin levels were used for control of protein loading. (G) Densitometric evaluation of data of panel 1F. Data are expressed as mean \pm SEM of five healthy volunteers (HV) and six COVID-19 patients for ex vivo experiments and three healthy donors for LDs staining and western blot. *p < 0.05 versus health volunteers or uninfected cells".

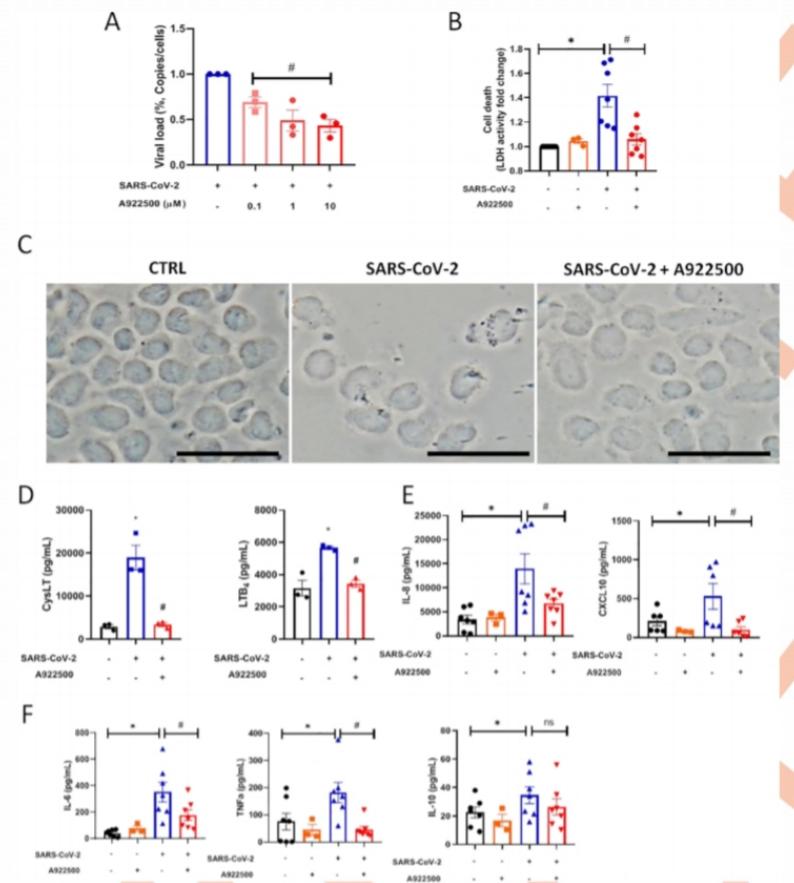


Figure 3. "DGAT-1 Inhibitor A922500 decreases the pro-inflammatory profile and cell death induced by SARS-CoV-2 infection and reduces the viral load in human monocyte. Monocytes were pre-treated with DGAT-1 inhibitor A922500 in different concentrations (0.1, 1 and 10 μM) for 2 hours before the infection with SARS-CoV-2 with MOI of 0.01 during 24h in presence of the inhibitor. (A) Cell death was measured in the supernatant by LDH activity fold change in relation to the uninfected cell. (B) Viral load by qPCR. Monocytes of each sample were counted for normalization. (C) Images of phase contrast from monocytes. Scale bar 20 μm. (D-F) The inflammatory cytokines were measured in supernatants by ELISA (D) leukotrienes: CysLT and LTB4, (E) chemokines: IL-8 and CXCL10, (F) inflammatory cytokines: IL-6, TNF-α and IL-10. Data are expressed as mean ± SEM obtained in three independent donors for viral replication, leukotrienes and the group A922500 alone, and seven independent donors for the other groups. * p <0.05 versus uninfected cells and #p <0.05 versus infected cells".

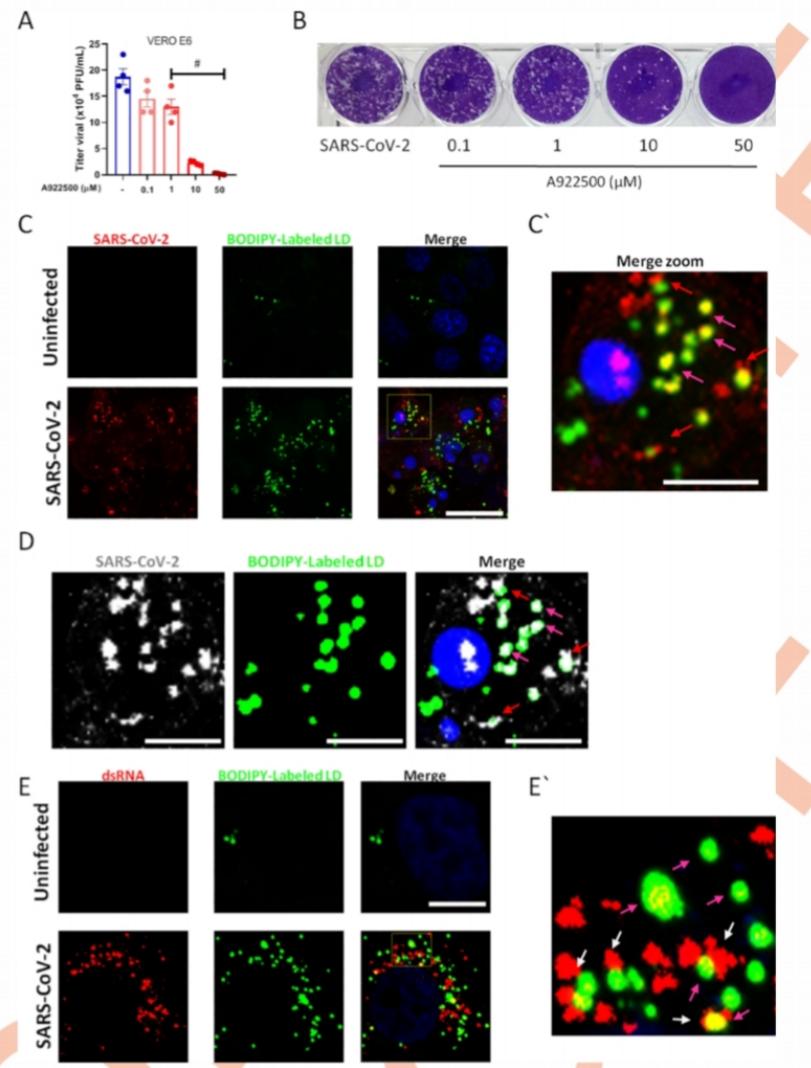


Figure 4. "Lipid droplets are necessary for SARS-CoV-2 replication in VERO E6. VERO E6 were pre-treated with DGAT-1 inhibitor A922500 with different concentrations (0.1, 1, 10 and 50 μM) for 2 hours before the infection with SARS-CoV-2 with MOI of 0.01 for 24h in presence of the inhibitor. (A) Viral replication was determined by Plaque assay. (B) Representative Plaque assay. (C-E) Immunofluorescence analyses of VERO E6 after SARS-CoV-2 infection with MOI of 0.01 for 48h. (C) The virus was detected by indirect immunofluorescence using convalescent donor serum (Red or white) or (E) the double strain RNA was detected by indirect immunofluorescence by J2 antibody (Red), the lipid droplets were stained with BODIPY 493/503 (Green) and nuclei stained with DAPI (Blue). (C' and E') Representative zoom images. Data are expressed of four independent experiments for SARS-CoV-2 replication and three for immunofluorescent analyses. # $p < 0.05$ versus infected cells. Scale bar 20 μm".

TRANSMISSION & PREVENTION

DEVELOPMENTS IN TRANSMISSION & PREVENTION

D614G SPIKE MUTATION INCREASES SARS COV-2 SUSCEPTIBILITY TO NEUTRALIZATION

Weissman D, Alameh MG, de Silva T, Collini P, Hornsby H, Brown R, LaBranche CC, Edwards RJ, Sutherland L, Santra S, Mansouri K, Gobeil S, McDanal C, Pardi N, Hengartner N, Lin PJC, Tam Y, Shaw PA, Lewis MG, Boesler C, Şahin U, Acharya P, Haynes BF, Korber B, Montefiori DC.. Cell Host Microbe. 2020 Dec 1:S1931-3128(20)30634-X. doi: 10.1016/j.chom.2020.11.012. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Investigators from various institutions across the US, UK, and Germany analyzed serum from 10 mice, 5 nonhuman primates (macaques), and 5 humans that were immunized for SARS-CoV-2 neutralizing antibodies against spike proteins, in order to determine effectiveness against two spike mutations that have been globally dominant during the pandemic: viral spikes G614 and D614. The results revealed all three serum experiments (mice: Figure 1, macaques: Figure 2, humans: Figure 3) had more susceptible antibody neutralization of G614 spike than D614 spike, suggesting the immunological and pharmacological role in targeting G614 for ongoing vaccine developments.

ABSTRACT

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein acquired a D614G mutation early in the pandemic that confers greater infectivity and is now the globally dominant form. To determine whether D614G might also mediate neutralization escape that could compromise vaccine efficacy, sera from spike-immunized mice, nonhuman primates, and humans were evaluated for neutralization of pseudoviruses bearing either D614 or G614 spike. In all cases, the G614 pseudovirus was moderately more susceptible to neutralization. The G614 pseudovirus also was more susceptible to neutralization by receptor-binding domain (RBD) monoclonal antibodies and convalescent sera from people infected with either form of the virus. Negative stain electron microscopy revealed a higher percentage of the 1-RBD "up" conformation in the G614 spike, suggesting increased epitope exposure as a mechanism of enhanced vulnerability to neutralization. Based on these findings, the D614G mutation is not expected to be an obstacle for current vaccine development.

FIGURES

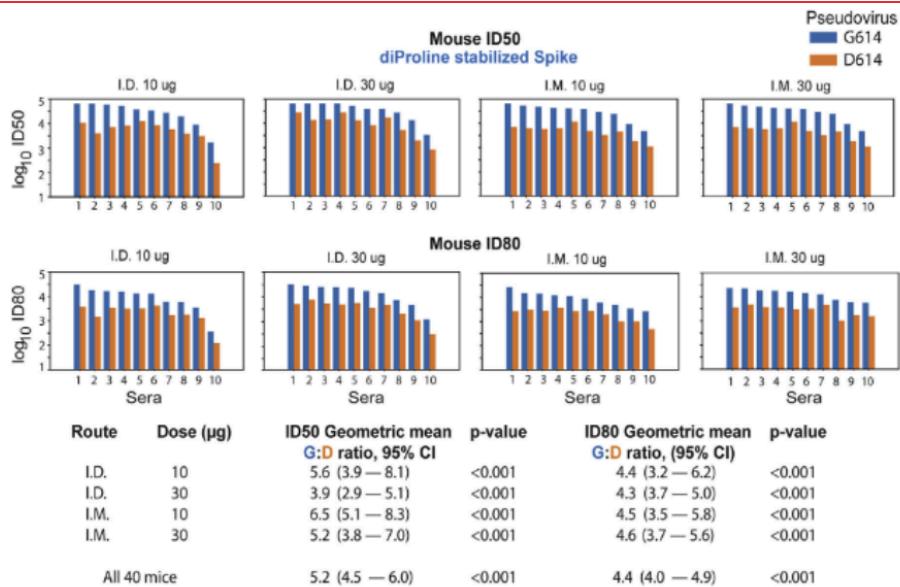


Figure 1. The G614 Spike Is Neutralized More Potently than the D614 Spike by Mouse Sera.

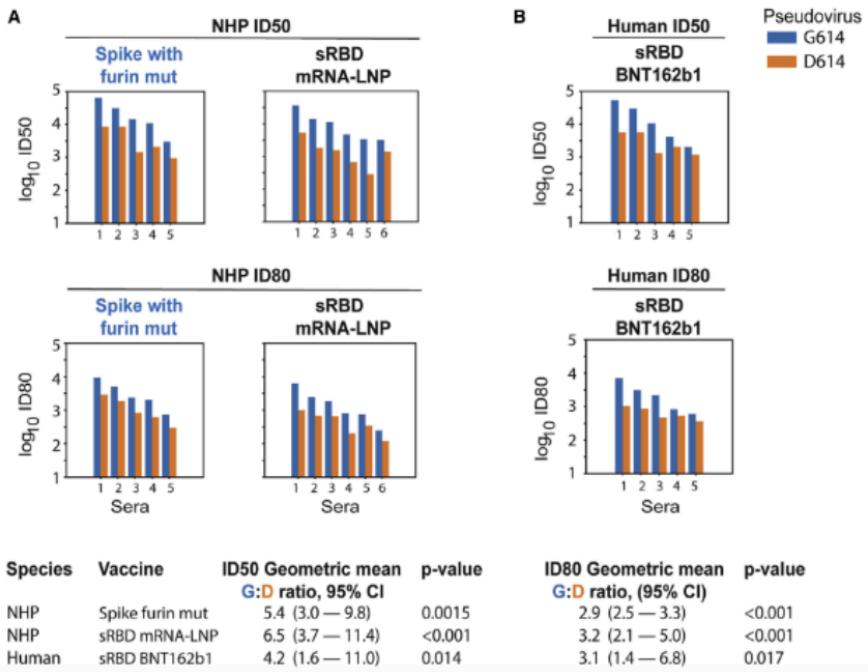


Figure 2. The G614 Spike Is Neutralized More Potently than the D614 Spike by NHP Sera

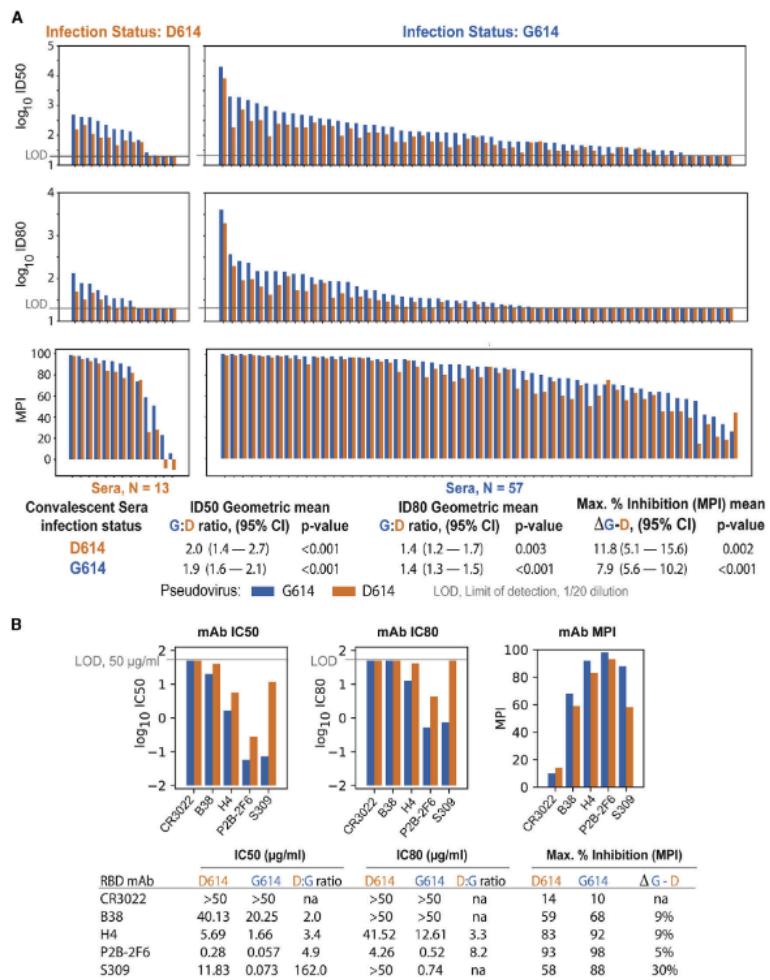


Figure 3. G614 Spike-Pseudotyped Virus Is Neutralized More Potently than D614 Spike-Pseudotyped Virus by Human Sera and mAbs.

MANAGEMENT

REGN-COV2, A NEUTRALIZING ANTIBODY COCKTAIL, IN OUTPATIENTS WITH COVID-19

Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H, Bhore R, Musser BJ, Soo Y, Rofail D, Im J, Perry C, Pan C, Hosain R, Mahmood A, Davis JD, Turner KC, Hooper AT, Hamilton JD, Baum A, Kyratsous CA, Kim Y, Cook A, Kampman W, Kohli A, Sachdeva Y, Gruber X, Kowal B, DiCioccio T, Stahl N, Lipsitch L, Braunstein N, Herman G, Yancopoulos GD; Trial Investigators.. N Engl J Med. 2020 Dec 17. doi: 10.1056/NEJMoa2035002. Online ahead of print.

Level of Evidence: 2 - Randomized trial or observational study with dramatic effect

BLUF

Investigators from Regeneron Pharmaceuticals report results from their ongoing, randomized, double-blind, phase 1–3 trial of their neutralizing antibody cocktail (REGN-COV2) in non-hospitalized patients with COVID-19 (Figure 1) between June 16 and August 13, 2020. They found the least-squares mean difference in SARS-CoV-2 viral load at seven days between the REGN-COV2 dose group (n=182) and the placebo group (n=93) was $-0.41 \log_{10}$ copies/mL (95% CI: -0.71 to -0.10), with a more significant reduction in subjects who had not mounted an antibody response at the time of randomization (Figure 2). No significant adverse effects were reported (Table 3). The authors concluded the REGN-COV2 antibody cocktail reduced viral load without significant adverse effects but, because there was no formal hypothesis testing, recommend further analysis of this ongoing trial to confirm these results.

ABSTRACT

BACKGROUND: Recent data suggest that complications and death from coronavirus disease 2019 (Covid-19) may be related to high viral loads. **METHODS:** In this ongoing, double-blind, phase 1–3 trial involving nonhospitalized patients with Covid-19, we investigated two fully human, neutralizing monoclonal antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein, used in a combined cocktail (REGN-COV2) to reduce the risk of the emergence of treatment-resistant mutant virus. Patients were randomly assigned (1:1:1) to receive placebo, 2.4 g of REGN-COV2, or 8.0 g of REGN-COV2 and were prospectively characterized at baseline for endogenous immune response against SARS-CoV-2 (serum antibody-positive or serum antibody-negative). Key end points included the time-weighted average change from baseline in viral load from day 1 through day 7 and the percentage of patients with at least one Covid-19-related medically attended visit through day 29. Safety was assessed in all patients. **RESULTS:** Data from 275 patients are reported. The least-squares mean difference (combined REGN-COV2 dose groups vs. placebo group) in the time-weighted average change in viral load from day 1 through day 7 was $-0.56 \log_{10}$ copies per milliliter (95% confidence interval [CI], -1.02 to -0.11) among patients who were serum antibody-negative at baseline and $-0.41 \log_{10}$ copies per milliliter (95% CI, -0.71 to -0.10) in the overall trial population. In the overall trial population, 6% of the patients in the placebo group and 3% of the patients in the combined REGN-COV2 dose groups reported at least one medically attended visit; among patients who were serum antibody-negative at baseline, the corresponding percentages were 15% and 6% (difference, -9 percentage points; 95% CI, -29 to 11). The percentages of patients with hypersensitivity reactions, infusion-related reactions, and other adverse events were similar in the combined REGN-COV2 dose groups and the placebo group. **CONCLUSIONS:** In this interim analysis, the REGN-COV2 antibody cocktail reduced viral load, with a greater effect in patients whose immune response had not yet been initiated or who had a high viral load at baseline. Safety outcomes were similar in the combined REGN-COV2 dose groups and the placebo group. (Funded by Regeneron Pharmaceuticals and the Biomedical and Advanced Research and Development Authority of the Department of Health and Human Services; ClinicalTrials.gov number, NCT04425629.).

FIGURES

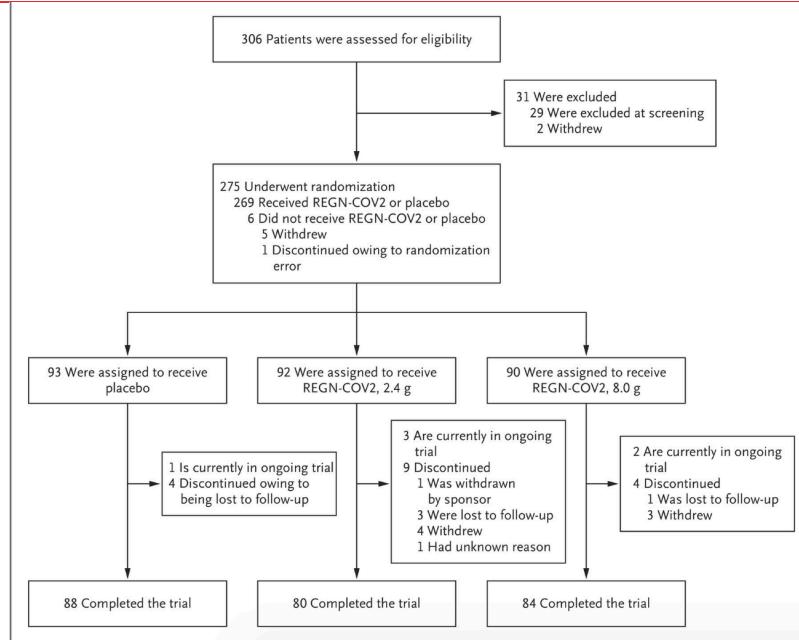


Figure 1. Screening, Randomization, and Treatment.

One patient underwent randomization in error, and Regeneron requested that the patient withdraw from the trial. Four patients in the low-dose REGN-COV2 group withdrew consent: one patient could not participate in the follow-up period, one patient could not have blood drawn and an intravenous line placed, and two patients withdrew consent with no additional information available. Three patients in the high-dose REGN-COV2 group withdrew consent: one patient could not participate in the follow-up period, one patient could not have blood drawn and an intravenous line placed, and one withdrew consent with no additional information available.

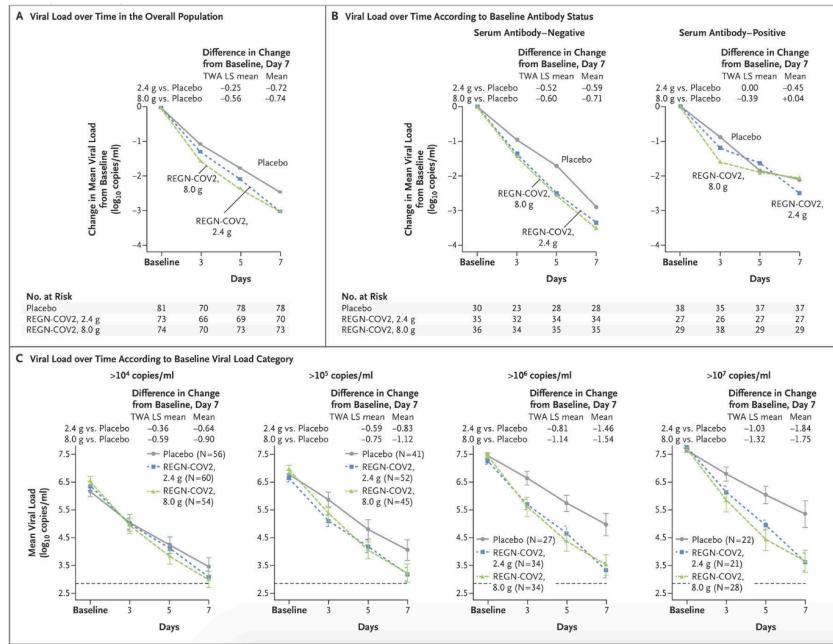


Figure 2. SARS-CoV-2 Viral Load over Time.

Shown is the change in mean viral load (in log10 copies per milliliter) from baseline at each visit through day 7 in the overall population (modified full analysis set, which excluded patients who tested negative for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] by qualitative reverse-transcriptase polymerase chain reaction at baseline) and in groups defined according to baseline antibody status and baseline viral load. I bars in Panel C indicate the standard error. The least-squares mean difference between the groups in the time-weighted average change in viral load (TWA LS mean) from baseline through day 7, expressed as log10 copies per milliliter, was based on analysis-of-covariance models with treatment group, risk factor, and baseline antibody status as fixed effects and baseline viral load and treatment group-by-baseline viral load as covariates.

The lower limit of detection (dashed line) is 714 copies per milliliter ($2.85 \log_{10}$ copies per milliliter).

Table 3. Serious Adverse Events and Adverse Events of Special Interest in the Safety Population.

| Event | REGN-COV2 | | | Placebo (N=93) |
|---|-----------------|-----------------|---------------------|-------------------|
| | 2.4 g (N=88) | 8.0 g (N=88) | Combined (N=176) | |
| number of patients (percent) | | | | |
| Any serious adverse event | 1 (1) | 0 | 1 (1) | 2 (2) |
| Any adverse event of special interest* | 0 | 2 (2) | 2 (1) | 2 (2) |
| Any serious adverse event of special interest* | 0 | 0 | 0 | 0 |
| Grade ≥2 infusion-related reaction within 4 days | 0 | 2 (2) | 2 (1) | 1 (1) |
| Grade ≥2 hypersensitivity reaction within 29 days | 0 | 1 (1) | 1 (1) | 2 (2) |
| Adverse events that occurred or worsened during the observation period† | | | | |
| Grade 3 or 4 event | 1 (1) | 0 | 1 (1) | 1 (1) |
| Event that led to death | 0 | 0 | 0 | 0 |
| Event that led to withdrawal from the trial | 0 | 0 | 0 | 0 |
| Event that led to infusion interruption* | 0 | 1 (1) | 1 (1) | 1 (1) |

* Events were grade 2 or higher hypersensitivity reactions or infusion-related reactions.

† Events listed here were not present at baseline or were an exacerbation of a preexisting condition that occurred during the observation period, which is defined as the time from administration of REGN-COV2 or placebo to the last study visit.

REHABILITATION AND COVID-19: A RAPID LIVING SYSTEMATIC REVIEW 2020 BY COCHRANE REHABILITATION FIELD. UPDATE AS OF OCTOBER 31ST, 2020

Negrini F, De Sire A, Andrenelli E, Lazzarini SG, Patrini M, Ceravolo MG; International Multiprofessional Steering Committee of Cochrane Rehabilitation REH-COVER action.. Eur J Phys Rehabil Med. 2020 Dec 2. doi: 10.23736/S1973-9087.20.06723-4. Online ahead of print.

Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

This article is the fourth monthly update on a larger living systematic review by the International Multiprofessional Steering Committee of Cochrane Rehabilitation REH-COVER Action looking at evidence related to COVID-19 from a rehabilitation perspective. This PRISMA-guided update, including 22 articles, indicates a general lack research with high level of evidence (Figure 1, Table 1) and a need for more high quality research to better understand the effectiveness of rehabilitation in COVID-19 patients. A few key points this report outlines include the possible association of heterotopic ossification in hospitalized COVID-19 patients and the importance of speech-language treatment for COVID-19 patients in the ICU.

SUMMARY

The systematic review also concludes:

- There is a possible association of COVID-19 with the pathophysiology of heterotopic ossification (abnormal bone growth in non-skeletal tissue), which was seen in hips and shoulders in four severe COVID-19 patients after 30-40 days in the hospital suggesting the possible need for an early monitoring of joint mobility and careful mobilization of patients in the acute phase.
- There is possible efficacy of speech-language treatment in COVID-19 patients in ICU to improving swallowing. This indicates the importance of an adequate assessment and management of oropharyngeal dysphagia in these patients.
- More data is needed concerning chronic sequelae of COVID-19

ABSTRACT

INTRODUCTION: This living systematic review presents the monthly update of the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER Action Steering Committee. The aim of this study was to update the monthly COVID-19 and rehabilitation literature research up to October 31th, 2020.

EVIDENCE ACQUISITION: Methodology described in the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER action was applied. PubMed, Embase, CINAHL, Scopus, Web of Science, and PEDro databases were searched, and papers related to COVID-19 and rehabilitation were retrieved and summarized descriptively.

EVIDENCE SYNTHESIS: The database search retrieved 2704 publications. Duplicates were removed, and 1185 unique records were screened for inclusion. After screening titles, abstracts and full-texts, 22 papers were included in the present review.

According to OCEBM 2011 Levels of Evidence table, 17 studies (77%) fall within the level of evidence 4 category, while the

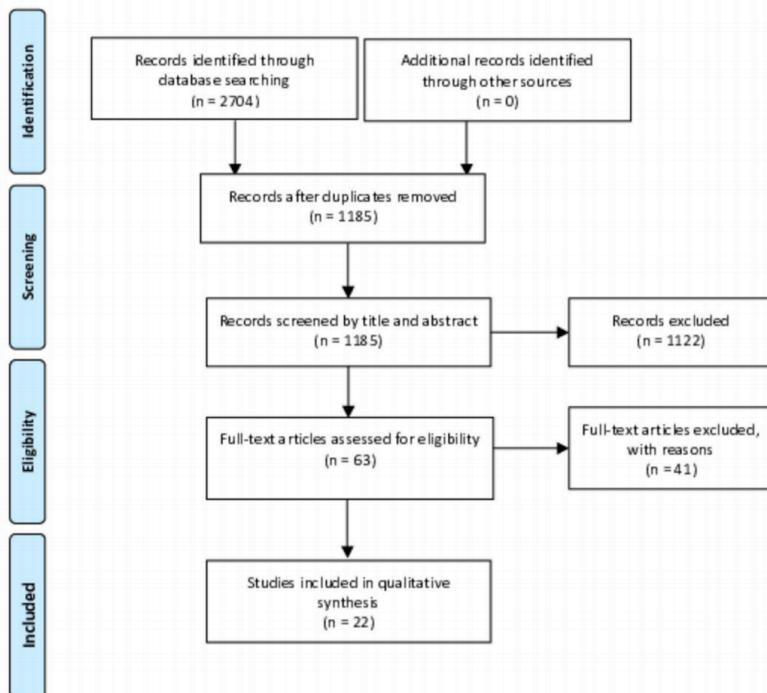
remainder (23%) are categorized as level of evidence 3. Most studies (N.=19; 86%) provided epidemiological data about the disease natural history/determining factor or the clinical presentation of COVID-19 infection, while only two studies focused on health service organization and intervention efficacy. CONCLUSIONS: The most recent published COVID-19 research relevant to rehabilitation primarily provides data on the clinical course and the clinical presentation of the pathology, rather than on rehabilitation interventions or service delivery. Studies with high levels of evidence regarding the efficacy of interventions, long-term monitoring, or new health service organization models are lacking.

FIGURES

| Parameters | Level 1 | Level 2 | Level 3 | Level 4 | Total |
|--|---------|---------|-----------|-------------------|------------|
| Epidemiology – clinical presentation | 0 | 0 | 0 | 6 (27.3%) | 6 (27.3%) |
| Epidemiology – prevalence | 0 | 0 | 0 | 1 (4.5%) | 1(4.5%) |
| Epidemiology - natural history/determining and modifying factors | 0 | 0 | 4 (18.2%) | 9 (40.9%) | 13 (59.1%) |
| Micro – interventions (efficacy/harms) | 0 | 0 | 1 (4.5%) | 0 | 1 (4.5%) |
| Meso level | 0 | 0 | 0 | 1 (4.5%) | 1 (4.5%) |
| Macro level | 0 | 0 | 0 | 0 | 0 |
| Total | 0 | 0 | 5 (22.7%) | 17 (77.3 %) | 22 (100%) |

Table 1. Level of evidence of the studies included in the present rapid living systematic review.

Figure 1. PRISMA Flow Diagram



CRITICAL CARE

THROMBOEMBOLIC COMPLICATIONS IN CRITICALLY ILL COVID-19 PATIENTS ARE ASSOCIATED WITH IMPAIRED FIBRINOLYSIS

Kruse JM, Magomedov A, Kurreck A, Münch FH, Koerner R, Kamhieh-Milz J, Kahl A, Gotthardt I, Piper SK, Eckardt KU, Dörner T, Zickler D.. Crit Care. 2020 Dec 7;24(1):676. doi: 10.1186/s13054-020-03401-8.

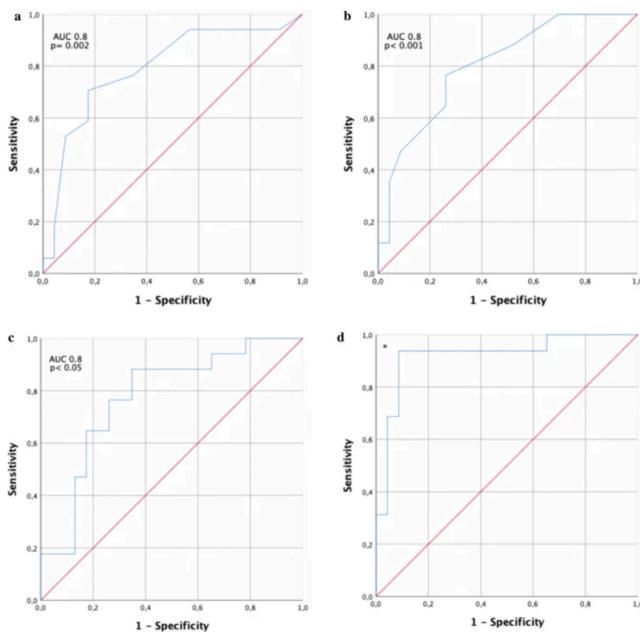
Level of Evidence: 4 - Local non-random sample

BLUF

Researchers from Charité-Universitätsmedizin Berlin hospital performed viscoelastic tests via rotational thromboelastometry (ROTEM, Figure 4) on 40 critically ill COVID-19 patients between March 25 and May 11, 2020 and found that COVID-19 patients had hypofibrinolysis, causing a hypercoagulable state. This, combined with increased D-dimer, was predictive of thromboembolic events (Figure 3), suggesting that ROTEM could be beneficial in identifying patients who may benefit from anticoagulation therapy.

ABSTRACT

BACKGROUND: There is emerging evidence for enhanced blood coagulation in coronavirus 2019 (COVID-19) patients, with thromboembolic complications contributing to morbidity and mortality. The mechanisms underlying this prothrombotic state remain enigmatic. Further data to guide anticoagulation strategies are urgently required. **METHODS:** We used viscoelastic rotational thromboelastometry (ROTEM) in a single-center cohort of 40 critically ill COVID-19 patients. **RESULTS:** Clear signs of a hypercoagulable state due to severe hypofibrinolysis were found. Maximum lysis, especially following stimulation of the extrinsic coagulation system, was inversely associated with an enhanced risk of thromboembolic complications. Combining values for maximum lysis with D-dimer concentrations revealed high sensitivity and specificity of thromboembolic risk prediction. **CONCLUSIONS:** The study identifies a reduction in fibrinolysis as an important mechanism in COVID-19-associated coagulopathy. The combination of ROTEM and D-dimer concentrations may prove valuable in identifying patients requiring higher intensity anticoagulation.

FIGURES**Fig. 3**

ROC analysis of **a** maximum lysis (ML) in EXTEM, **b** D-dimer and **c** ML INTEM **d** difference of ML in EXTEM and max. D-dimer for prediction of thromboembolic events in our cohort [*AUC of 0.92 (p < 0.001)]

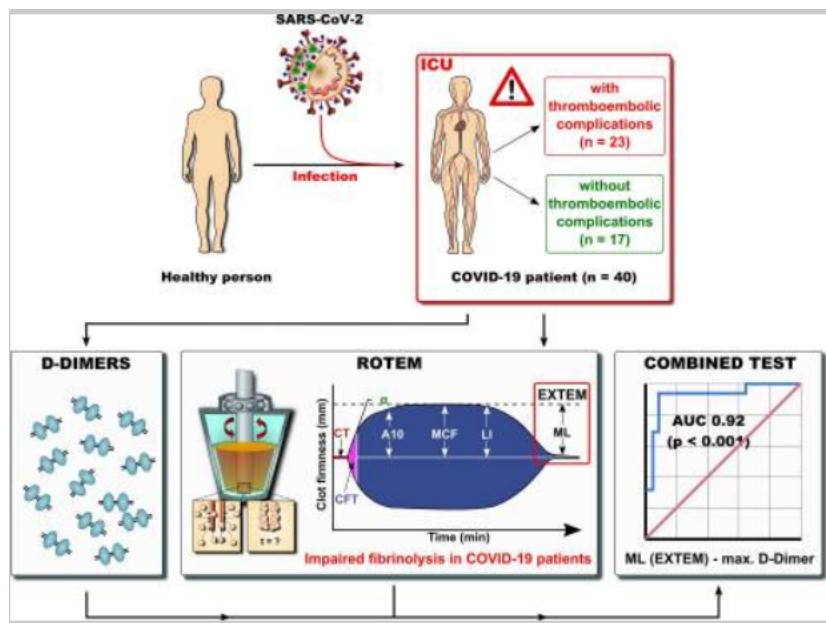


Figure 4. Summary of the study and the ROTEM technique.

ADJUSTING PRACTICE DURING COVID-19

EMERGENCY MEDICINE

OUTCOMES FOR OUT-OF-HOSPITAL CARDIAC ARREST IN THE UNITED STATES DURING THE CORONAVIRUS DISEASE 2019 PANDEMIC

Chan PS, Girotra S, Tang Y, Al-Araji R, Nallamothu BK, McNally B. JAMA Cardiol. 2020 Nov 14. doi: 10.1001/jamacardio.2020.6210. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

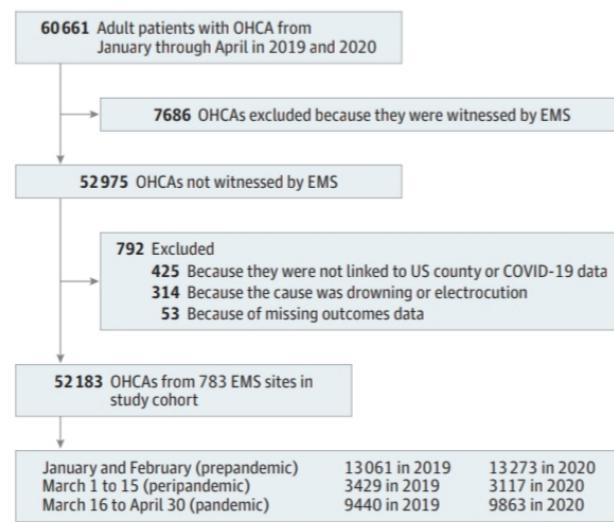
BLUF

A team of American cardiologists and emergency medicine physicians used a US registry (CARES) of out-of-hospital cardiac arrest (OHCA) to compare outcomes between March 16 and April 30, 2020 to the same period in 2019 (Figure 1). They found lower rates of sustained return of spontaneous circulation (ROSC) during the COVID-19 pandemic compared to 2019 (23.0% vs 29.8%; $p < 0.001$), with higher incidence of OHCA in communities with high (adjusted mean difference [AMD], 38.6 [95% CI, 37.1-40.1] per million residents) and very high (AMD, 28.7 [95% CI, 26.7-30.6] per million residents) COVID-19 mortality. Survival to discharge after OHCA was also lower during the pandemic than in 2019 (6.6% vs 9.8%, $p = 0.048$) (Figures 2, 3). Authors suggest the lower rates of sustained ROSC indicates a need to better understand potential underlying causes, such as the impact of infection prevention protocols implemented early in the pandemic, and care-seeking behaviors in the community.

ABSTRACT

Importance: Recent reports from communities severely affected by the coronavirus disease 2019 (COVID-19) pandemic found lower rates of sustained return of spontaneous circulation (ROSC) for out-of-hospital cardiac arrest (OHCA). Whether the pandemic has affected OHCA outcomes more broadly is unknown. **Objective:** To assess the association between the COVID-19 pandemic and OHCA outcomes, including in areas with low and moderate COVID-19 disease burden. **Design, Setting, and Participants:** This study used a large US registry of OHCA to compare outcomes during the pandemic period of March 16 through April 30, 2020, with those from March 16 through April 30, 2019. Cases were geocoded to US counties, and the COVID-19 mortality rate in each county was categorized as very low (0-25 per million residents), low (26-100 per million residents), moderate (101-250 per million residents), high (251-500 per million residents), or very high (>500 per million residents). As additional controls, the study compared OHCA outcomes during the prepandemic period (January through February) and peripandemic period (March 1 through 15). **Exposure:** The COVID-19 pandemic. **Main Outcomes and Measures:** Sustained ROSC (≥ 20 minutes), survival to discharge, and OHCA incidence. **Results:** A total of 19 303 OHCA occurred from March 16 through April 30 in both years, with 9863 cases in 2020 (mean [SD] age, 62.6 [19.3] years; 6040 men [61.3%]) and 9440 in 2019 (mean [SD] age, 62.2 [19.2] years; 5922 men [62.7%]). During the pandemic, rates of sustained ROSC were lower than in 2019 (23.0% vs 29.8%; adjusted rate ratio, 0.82 [95% CI, 0.78-0.87]; $P < .001$). Sustained ROSC rates were lower by between 21% (286 of 1429 [20.0%] in 2020 vs 305 of 1130 [27.0%] in 2019; adjusted RR, 0.79 [95% CI, 0.65-0.97]) and 33% (149 of 863 [17.3%] in 2020 vs 192 of 667 [28.8%] in 2019; adjusted RR, 0.67 [95% CI, 0.56-0.80]) in communities with high or very high COVID-19 mortality, respectively; however, rates of sustained ROSC were also lower by 11% (583 of 2317 [25.2%] in 2020 vs 740 of 2549 [29.0%] in 2019; adjusted RR, 0.89 [95% CI, 0.81-0.98]) to 15% (889 of 3495 [25.4%] in 2020 vs 1109 of 3532 [31.4%] in 2019; adjusted RR, 0.85 [95% CI, 0.78-0.93]) in communities with very low and low COVID-19 mortality. Among emergency medical services agencies with complete data on hospital survival (7085 total patients), survival to discharge was lower during the pandemic compared with 2019 (6.6% vs 9.8%; adjusted RR, 0.83 [95% CI, 0.69-1.00]; $P = .048$), primarily in communities with moderate to very high COVID-19 mortality (interaction $P = .049$). Incidence of OHCA was higher than in 2019, but the increase was largely observed in communities with high COVID-19 mortality (adjusted mean difference, 38.6 [95% CI, 37.1-40.1] per million residents) and very high COVID-19 mortality (adjusted mean difference, 28.7 [95% CI, 26.7-30.6] per million residents). In contrast, there was no difference in rates of sustained ROSC or survival to discharge during the prepandemic and peripandemic periods in 2020 vs 2019. **Conclusions and Relevance:** Early during the pandemic, rates of sustained ROSC for OHCA were lower throughout the US, even in communities with low COVID-19 mortality rates. Overall survival was lower, primarily in communities with moderate or high COVID-19 mortality.

FIGURES



The number of patients in the 3 study periods for 2020 and 2019 are depicted. COVID-19 indicates coronavirus disease 2019; EMS, emergency medical services; OHCA, out-of-hospital cardiac arrest.

Figure 1. "Definition of the Study Cohort"

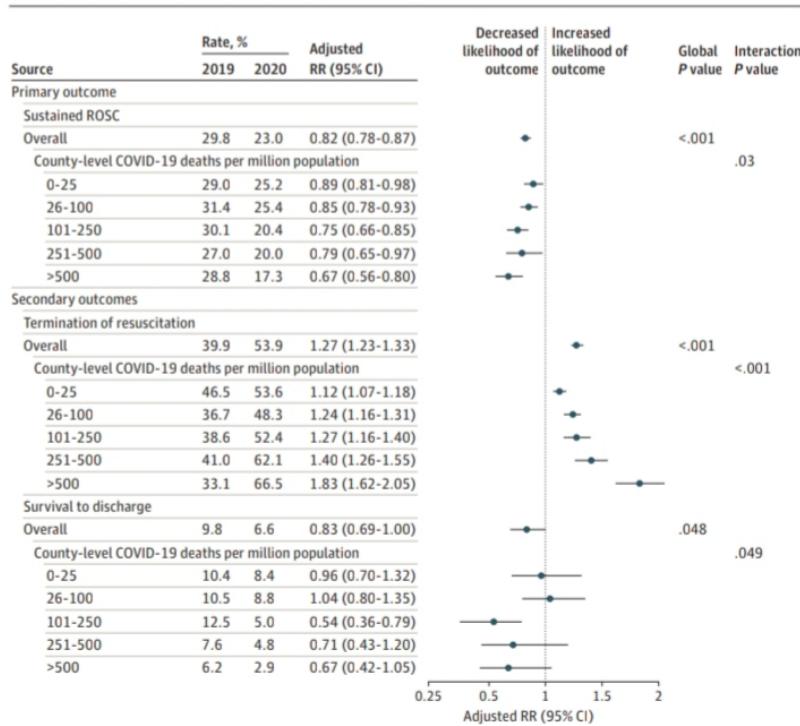
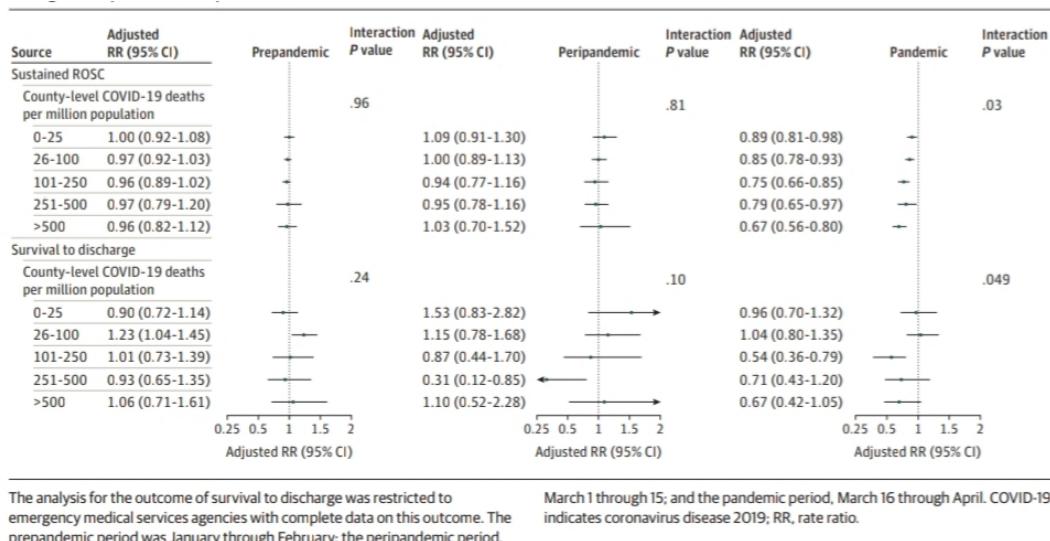


Figure 2. "Rates of Sustained Return of Spontaneous Circulation(ROSC), Termination of Resuscitation, and Survival to Discharge During the 2020 Pandemic Period vs 2019."



The analysis for the outcome of survival to discharge was restricted to emergency medical services agencies with complete data on this outcome. The prepandemic period was January through February; the peripandemic period,

March 1 through 15; and the pandemic period, March 16 through April. COVID-19 indicates coronavirus disease 2019; RR, rate ratio.

Figure 3. "Comparison of 2020 vs 2019 Rates of Sustained Return of Spontaneous Circulation(ROSC) and Survival to Discharge During the Prepandemic, Peripandemic, and pandemic periods."

SURGICAL SUBSPECIALTIES

THE USE OF TELEMEDICINE TO MAINTAIN BREAST CANCER FOLLOW-UP AND SURVEILLANCE DURING THE COVID-19 PANDEMIC

Sonagli M, Cagnacci Neto R, Leite FPM, Makdissi FBA.. J Surg Oncol. 2020 Dec 17. doi: 10.1002/jso.26327. Online ahead of print.

Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A retrospective cohort study conducted by the Department of Breast Surgery at the AC Camargo Cancer Center in Sao Paulo, Brazil analyzed 77 patients who utilized telemedicine appointments for breast cancer follow-up (46.8%), breast cancer screening (26%), benign breast disease (13%), second opinion (9%), and general orientation (5.2%) (See Table 2). They found that use of telemedicine allowed for 58.4% of patient encounters to be spared from face-to-face appointments, allowing for ongoing preventative care in a timely manner while minimizing risk of COVID-19 transmission. However, the authors recommend that patients fill out a pre-visit survey (See Table 3) to determine whether a more urgent or in-person appointment is needed. This study highlights how telemedicine can be a useful option to maintain follow-up visits for breast cancer treatment and surveillance, however considerations such as lack of access to internet/technology and limited health literacy must be accounted for to prevent disparities when utilizing telemedicine.

ABSTRACT

As a result from restricted economic activities and social distancing due to the coronavirus disease-2019 (COVID-19) pandemic, we observed a 49.4% decrease in outpatient appointments at our Institution. to minimize this impact on screening and oncological follow-up of breast cancer patients, telemedicine appointments were established. The authors demonstrate how a cancer center in the largest city in Brazil has managed outpatient appointments during the COVID-19 pandemic. This is a retrospective study of patients who had their appointments through telemedicine at the AC Camargo Cancer Center between June 2020 and October 2020, during the COVID-19 pandemic. Of the 77 patients who had telemedicine appointments, 36 (46.8%) accounted for breast cancer follow-up, 20 (26%) for breast cancer screening, 10 (13%) for benign breast disease evaluation, 7 (9%) for a second opinion, and 4 (5.2%) for general orientations. Routine surveillance/follow-up exams were requested for 45 (58.4%) patients and breast image exams and a request to return for a personal appointment for 30 (39%) patients. Two (2.6%) patients were requested to schedule a personal appointment immediately for a physical exam. In conclusion, telemedicine may be a feasible alternative to reduce personal outpatient appointments for cancer follow-up and breast cancer screening during the COVID-19 pandemic.

FIGURES

TABLE 2 Medical conduct after telemedicine appointments at the AC Camargo Breast Cancer Reference Center during COVID-19 pandemic

| Reasons for telemedicine appointment | Number of patients, n (%) |
|---|---------------------------|
| Breast cancer follow-up | 36 (100%) |
| Routine surveillance/follow-up exams | 27 (75%) |
| Requested breast image exams and advised to return for an in-person appointment | 9 (25%) |
| Breast cancer screening | 20 (100%) |
| Routine surveillance/follow-up exams | 9 (45%) |
| Requested breast image exams and advised to return for an in-person appointment | 9 (45%) |
| Requested to schedule an in-person appointment immediately for a physical exam | 2 (10%) |
| Evaluation of breast benign disease | 10 (100%) |
| Routine surveillance/follow-up exams | 6 (60%) |
| Requested breast image exams and advised to return for an in-person appointment | 4 (40%) |
| Second opinion | 7 (100%) |
| Routine surveillance/follow-up exams | 1 (14.3%) |
| Requested breast image exams and advisor to return in an appointment in person | 6 (85.7%) |
| General orientation of breast diseases | 4 (100%) |
| Routine surveillance/follow-up exams | 2 (50%) |
| Requested breast image exams and advised to return for an in-person appointment | 2 (50%) |

Note: Bold text means the reason for telemedicine appointments groups and the values refer to the number of patients and percentage in each group.

TABLE 3 Suggested query to be filled by the patient before scheduling a telemedicine appointment

| | | |
|------------|---|--|
| Question 1 | Do you have any breast complain? | If Yes → schedule in-person appointment If No → continue to Question 2 |
| Question 2 | Do you have breast images exams? | If Yes → continue to Question 3 If No → You can schedule a telemedicine appointment |
| Question 3 | Any of your breast images exams have a BI-RADS® 4, 5, or 6? | If Yes → schedule in-person appointment If No → You can schedule a telemedicine appointment |
| Question 4 | Do you have problems with your internet access? | If Yes → schedule in-person appointment If No → You can schedule a telemedicine appointment |
| Question 5 | Do you have difficulty in dealing with technology (e-mail or social networking websites)? | If Yes → continue to Question 6 If No → You can schedule a telemedicine appointment |
| Question 6 | Do you have someone to help you to connect to telemedicine digital platform? | If Yes → You can schedule a telemedicine appointment If No → schedule in-person appointment |

Abbreviation: BI-RADS, breast imaging-reporting data system.

ORTHOPEDICS

EVALUATION OF THE FEASIBILITY OF A TELEMEDICAL EXAMINATION OF THE HIP AND PELVIS - EARLY LESSONS FROM THE COVID-19 PANDEMIC

Jaenisch M, Kohlhof H, Touet A, Kehrer M, Cucchi D, Burger C, Wirtz DC, Welle K, Kabir K.. Z Orthop Unfall. 2020 Dec 16.
doi: 10.1055/a-1289-0779. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

BLUF

German orthopedic surgeons evaluated 29 adult patients with hip complaints and no known hip pathology in a telemedicine visit followed by in-person examination. They found close agreement between hip inspection (mean Cohen's κ : 0.76 ± 0.37) and evaluation of hip function ($\kappa=0.61 \pm 0.26$) (Table 1) and adequate agreement with palpation ($\kappa=0.38 \pm 0.19$), range of motion testing ($\kappa=0.36 \pm 0.19$), and provocative tests ($\kappa=0.33 \pm 0.13$) (Table 1). Deviations were more likely with increased body mass index (BMI; $r=0.389$, $p<0.05$), age ($r=0.588$, $p<0.01$), and degree of disability by American Society of Anesthesiologists (ASA) physical status classification score ($r=0.396$, $p<0.05$) (Figure 2). The authors conclude that in the wake of restrictions placed on outpatient visits during the pandemic, telemedicine examinations of the hip joint and pelvis can replace in-person visits with certain limitations, though they suggest in-person visits for patients with ASA score > 3, age>75 years, or BMI > 30.

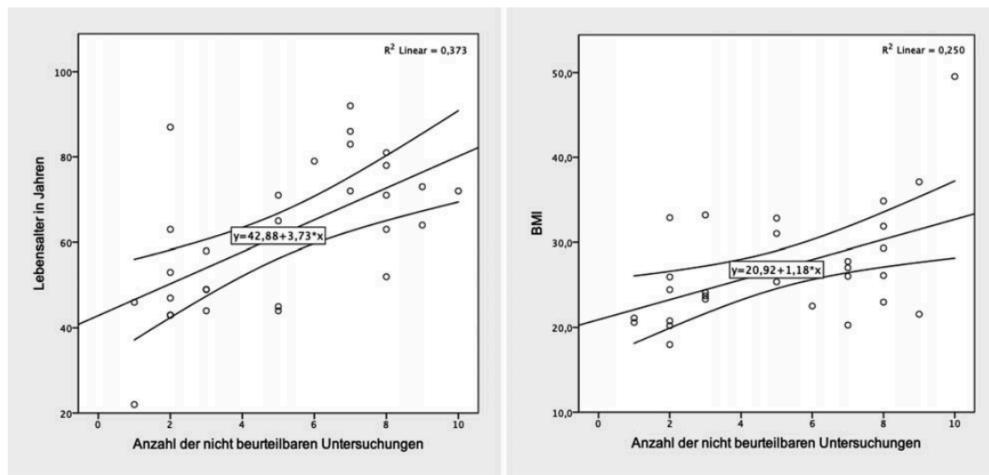
ABSTRACT

INTRODUCTION: Due to the current COVID-19 pandemic, the German Health Ministry has issued restrictions applying to the field of orthopaedics and trauma surgery. Besides postponement of elective surgeries, outpatient consultations have been drastically reduced. Parallel to these developments, an increase in telemedical consultations has reflected efforts to provide sufficient patient care. This study aims to evaluate the feasibility of a clinical examination of the hip joint and pelvis by way of a telemedical consultation. **MATERIALS AND METHODS:** Twenty-nine patients of a German university clinic were recruited and assessed in both telemedical and conventional examinations. Agreement between the two examinations was then assessed, and connections between the observed agreement and patient-specific factors such as age, BMI and ASA classification were investigated. **RESULTS:** The inspections agreed closely with a mean Cohen's kappa of 0.76 ± 0.37 . Palpation showed adequate agreement with a mean Cohen's kappa of 0.38 ± 0.19 . Function showed good agreement with a mean Cohen's kappa of 0.61 ± 0.26 and range of motion showed adequate agreement with a mean Cohen's kappa of 0.36 ± 0.19 . A significant positive correlation was observed between the number of deviations in the different examinations and age ($p = 0.05$), and a significant positive correlation was shown between the number of non-feasible examinations and age ($p < 0.01$), BMI ($p < 0.01$) and ASA classification score ($p < 0.01$). **DISCUSSION:** Inspection and function can be reliably evaluated, whereas the significance of palpation, provocation and measurement of range of motion is limited. The small sample size puts limitations on the significance of a statistically relevant correlation between patient-specific factors such as age, BMI and ASA classification score and valid and successful implementation of a telemedical examination. The authors recommend targeted patient selection. If, however, patients are being evaluated who are very old (> 75 years), obese (BMI > 30) or with multiple comorbidities (ASA 3 and above), caution is advised. Large, prospective studies are needed in the future to fully validate telemedical consultations in the fields of orthopaedics and trauma surgery. **CONCLUSION:** A telemedical examination of the hip joint and pelvis can be performed with certain limitations. Patient-specific factors such as age, BMI, and extent of comorbidities appear to have a relevant impact on validity and execution of the examination. Patients with multiple comorbidities (ASA 3 and above), advanced age (> 75 years) or obesity (BMI > 30) should, whenever possible, be examined in a conventional outpatient setting.

FIGURES

► **Table 1** Cohen's kappa values grouped according to the different examination methods.

| Examination | Cohen's κ |
|-----------------------------------|------------------|
| Inspection | 0.76 ± 0.37 |
| ▪ Swelling | 0.818 |
| ▪ Redness | 1.0 |
| ▪ Atrophy | 0.220 |
| ▪ Scar/wound anomalies | 1.0 |
| Palpation | 0.38 ± 0.19 |
| ▪ Symphysis | 0.588 |
| ▪ Trochanter major | 0.223 |
| ▪ Groin | 0.209 |
| ▪ Gluteal | 0.482 |
| Function | 0.61 ± 0.26 |
| ▪ Muscle strength hip flexion | 0.473 |
| ▪ Muscle strength hip extension | 1.0 |
| ▪ Muscle strength hip abduction | 0.482 |
| ▪ Muscle strength hip adduction | 0.482 |
| ▪ Gait | 1.0 |
| ▪ Feasibility of one-legged stand | 1.0 |
| ▪ Feasibility of knee bend | 1.0 |
| Range of motion | 0.36 ± 0.19 |
| ▪ Extension/flexion | 0.380 |
| ▪ Outer rotation/inner rotation | 0.486 |
| ▪ Abduction/adduction | 0.265 |
| Provocation tests | 0.33 ± 0.13 |
| ▪ Apley test | 0.181 |
| ▪ Drehmann sign | 0.386 |
| ▪ Trendelenburg sign | 0.281 |
| ▪ Axial compression pain | 0.475 |
| ▪ Thomas test | 0.370 |
| ▪ Posterior impingement test | 0.146 |
| ▪ Ventral impingement test | 0.147 |
| ▪ Foveal impingement test | 0.045 |



► **Fig. 2** Scatter diagram of correlation between age in years and BMI with the number of non-feasible examinations.

THE ACCURACY OF HEALTHCARE WORKER VERSUS SELF COLLECTED (2-IN-1) OROPHARYNGEAL AND BILATERAL MID-TURBinate (OPMT) SWABS AND SALIVA SAMPLES FOR SARS-COV-2

Tan SY, Tey HL, Lim ETH, Toh ST, Chan YH, Tan PT, Lee SA, Tan CX, Koh GCH, Tan TY, Siau C.. PLoS One. 2020 Dec 16;15(12):e0244417. doi: 10.1371/journal.pone.0244417. eCollection 2020.

Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A multicenter prospective cohort study from Singapore compared the efficacy of "self-swabbing" pharyngeal and saliva testing done by patients vs swabs performed by healthcare workers (HCW) in 401 non-hospitalized COVID-19 patients and 100 healthy controls. Results showed that the detection rates of the HCW swab, self-swab, saliva, and combined self-swab plus saliva samples were 82.8%, 75.1%, 74.3% and 86.5% respectively (Table 1). Additionally, they found that the sensitivities of all patient-performed methods of testing are higher when the Ct (cycle threshold) is lower (Figure 1). These findings highlight a potential role that self-swabbing may have to reduce use of PPE and HCW exposure in non-hospitalized COVID-19 patients, however the accuracy of these tests decreases in this presumed less symptomatic population with higher Ct values.

ABSTRACT

BACKGROUND: Self-sampling for SARS-CoV-2 would significantly raise testing capacity and reduce healthcare worker (HCW) exposure to infectious droplets personal, and protective equipment (PPE) use. **METHODS:** We conducted a diagnostic accuracy study where subjects with a confirmed diagnosis of COVID-19 ($n = 401$) and healthy volunteers ($n = 100$) were asked to self-swab from their oropharynx and mid-turbinate (OPMT), and self-collect saliva. The results of these samples were compared to an OPMT performed by a HCW in the same patient at the same session. **RESULTS:** In subjects confirmed to have COVID-19, the sensitivities of the HCW-swab, self-swab, saliva, and combined self-swab plus saliva samples were 82.8%, 75.1%, 74.3% and 86.5% respectively. All samples obtained from healthy volunteers were tested negative. Compared to HCW-swab, the sensitivities of a self-swab sample and saliva sample were inferior by 8.7% (95%CI: 2.4% to 15.0%, $p = 0.006$) and 9.5% (95%CI: 3.1% to 15.8%, $p = 0.003$) respectively. The combined detection rate of self-swab and saliva had a sensitivity of 2.7% (95%CI: -2.6% to 8.0%, $p = 0.321$). The sensitivity of both the self-collection methods are higher when the Ct value of the HCW swab is less than 30. The specificity of both the self-swab and saliva testing was 100% (95% CI 96.4% to 100%). **CONCLUSION:** Our study provides evidence that sensitivities of self-collected OPMT swab and saliva samples were inferior to a HCW swab, but they could still be useful testing tools in the appropriate clinical settings.

FIGURES

Table 3. Detection rates of various modalities in all subjects.

| | HCW Swab | Self-Swab | Saliva | Self-Swab + Saliva |
|------------|---------------|---------------|---------------|--------------------|
| Count | 336 | 301 | 297 | 347 |
| Percentage | 83.8% | 75.1% | 74.3% | 86.5% |
| 95% CI | 79.8% - 87.3% | 70.1% - 79.2% | 69.7% - 78.5% | 82.8% - 89.7% |

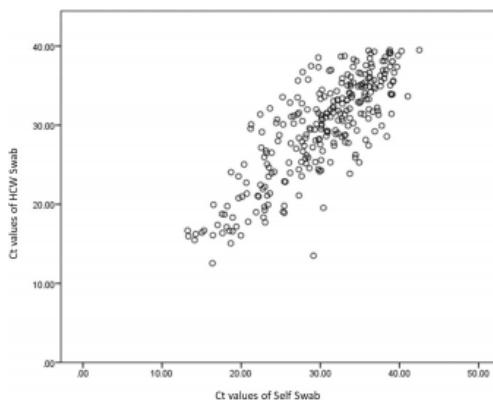


Fig 1. Correlation of Ct values of HCW swab and self-swab.

CURRENT DIAGNOSTICS

IMPACT OF LIVER INJURY ON THE SEVERITY OF COVID-19: SYSTEMATIC REVIEW WITH META-ANALYSIS

Ampuero J, Sánchez-Torrijos Y, García Lozano MDR, Maya D, Romero-Gómez M.. Rev Esp Enferm Dig. 2020 Dec 3. doi: 10.17235/reed.2020.7397/2020. Online ahead of print.

Level of Evidence: 1 - Systematic review of cross sectional studies with consistently applied reference standard and blinding

BLUF

A systematic review and meta-analysis of 26 articles (Figure 1) conducted by gastrointestinal specialists in Spain found liver injury and elevated liver function tests (LFTs) upon admission were significantly associated with higher risk of severe COVID-19. They identified markers including elevations of AST (Figure 2), ALT (Figure 3) and bilirubin, which were associated with worse outcomes (specificities of 78%, 77%, and 94% respectively). Authors suggest incorporating these laboratory markers into existing tools for COVID-19 monitoring and prognosis determination.

ABSTRACT

BACKGROUND AND AIMS: SARS-CoV-2 is mainly a respiratory virus that has relevant systemic effects. We assessed the impact of the baseline liver function (AST, ALT, and bilirubin) on COVID-19-related outcomes, including on mortality, intensive care unit admission, and non-fatal severe complications. **METHODS:** After a systematic review of the relevant studies, odds ratio, mean difference, sensitivity, specificity, and positive and negative likelihood ratios, were calculated for the prediction of relevant COVID-19 outcomes by performing a meta-analysis using fixed and random effects models. A Fagan nomogram was used to assess the clinical utility. Heterogeneity was explored by sensitivity analysis and univariable meta-regression. **RESULTS:** Twenty-six studies were included (22 studies and 5271 patients for AST, 20 studies and 5440 subjects for ALT, and 9 studies and 3542 patients for bilirubin). The outcomes of the studies were: survival (n=8), intensive care unit admission (n=4), and non-fatal severe complications (n=16). AST>ULN (OR 3.10 (95%CI 2.61-3.68)), ALT>ULN (OR 2.15 (95%CI 1.43-3.23)), and bilirubin >ULN (OR 2.78 (95%CI 1.88-4.13)) were associated with an increased prevalence of severe complications, with 78%, 77% and 94% of specificity, respectively. The mean difference between mild and severe COVID-19 was 10.7 U/L (95%CI 5.8-15.6) for AST, 8 U/L (95%CI 1.0-15) for ALT, and 0.3 mg/dL (95%CI 0.16-0.45) for bilirubin. **CONCLUSIONS:** Patients showing liver injury had significantly higher risks of developing severe COVID-19 compared to those with normal liver function tests at admission. We should include the assessment of AST, ALT, and total bilirubin routinely in patients affected by SARS-CoV-2 in order to anticipate those at risk of developing COVID-19-related outcomes.

FIGURES

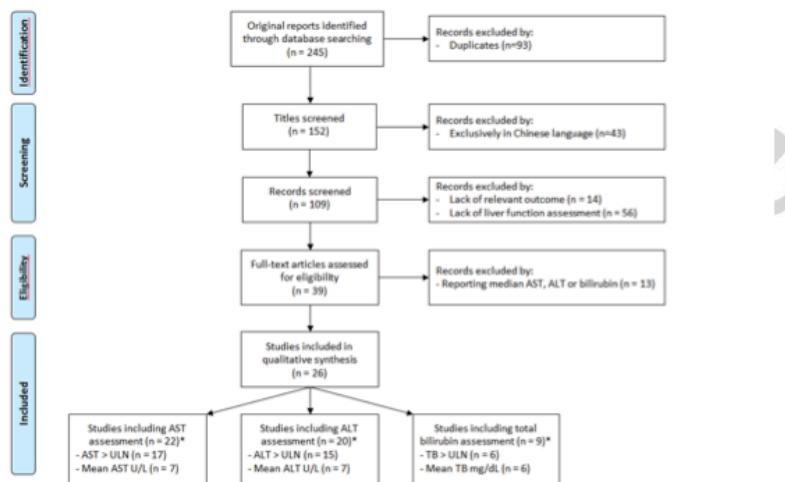


Figure 1. Flow-chart summarizing the selection of eligible studies. * Individual studies, although some of them reported simultaneously dichotomous and continuous variables..

Figure 2c

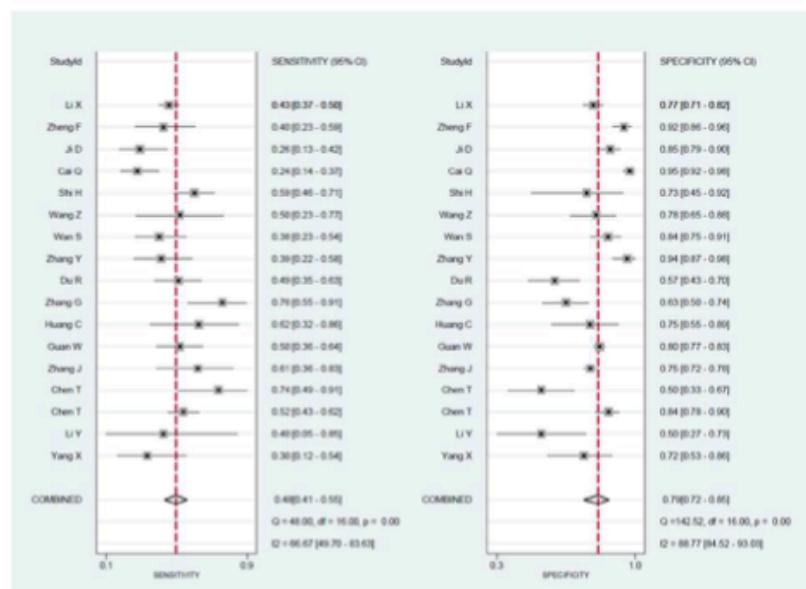


Figure 2. Forest plots of the studies assessing AST depending on the outcomes. 2c.) Sensitivity and specificity.

Figure 3c

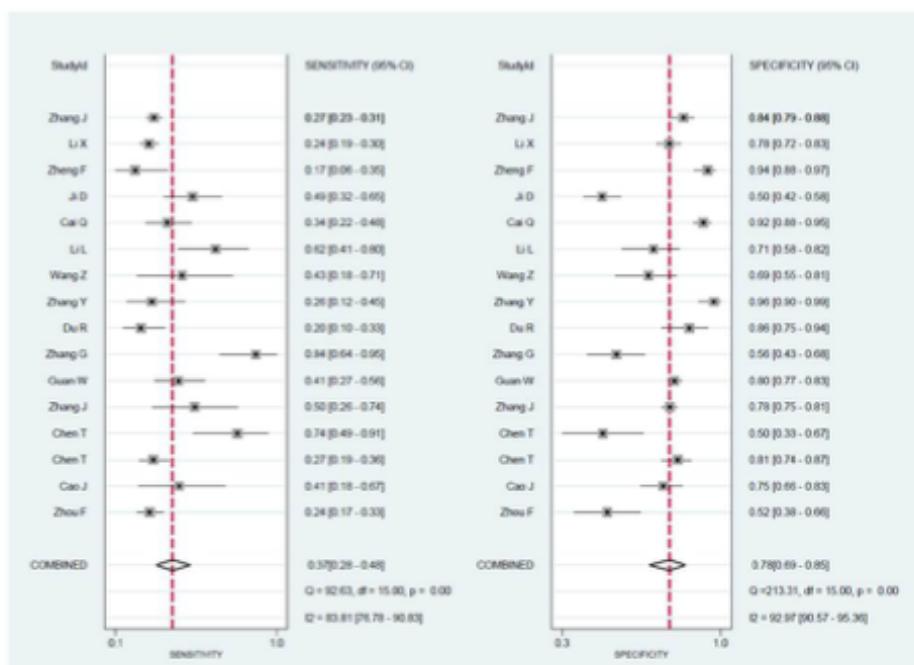


Figure 3. Forest plots of the studies assessing ALT depending on the outcomes. 3c) Sensitivity and specificity.

DEVELOPMENTS IN TREATMENTS

GLUCOCORTICOIDS WITH LOW-DOSE ANTI-IL1 ANAKINRA RESCUE IN SEVERE NON-ICU COVID-19 INFECTION: A COHORT STUDY

Borie R, Savale L, Dossier A, Ghosn J, Taillé C, Visseaux B, Jebreen K, Diallo A, Tesmoingt C, Morer L, Goletto T, Faucher N, Hajouji L, Neukirch C, Phillips M, Stelianides S, Bouadma L, Brosseau S, Ottaviani S, Pluvy J, Le Pluart D, Debray MP, Raynaud-Simon A, Descamps D, Khalil A, Timsit JF, Lescure FX, Descamps V, Papo T, Humbert M, Crestani B, Dieude P, Vicaut E, Zalcman G; Bichat & Kremlin-Bicêtre AP-HP COVID teams.. PLoS One. 2020 Dec 16;15(12):e0243961. doi: 10.1371/journal.pone.0243961. eCollection 2020.

Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A multidisciplinary team of French physicians conducted a cohort study of 171 hospitalized, non-intensive care (non-ICU) patients with severe COVID-19 who received steroids, anakinra (an interleukin-1 antagonist), or both between March 27 and April 10, 2020. They found a non-statistically significant 30% relative decrease in mortality at day 15 in patients who received corticosteroids with or without anakinra (n=108) compared to controls (n=63) (20.4% vs. 30.2%; OR: 0.9 [95%CI 0.80–1.01]; p=0.067) (Figure 2). No patients received anakinra alone. Authors suggest corticosteroids may have a mortality benefit in treating non-ICU patients with COVID-19 but recommend randomized controlled trials to better evaluate corticosteroid and anakinra treatment algorithms given limitations in methodology.

ABSTRACT

BACKGROUND: The optimal treatment for patients with severe coronavirus-19 disease (COVID-19) and hyper-inflammation remains debated. **MATERIAL AND METHODS:** A cohort study was designed to evaluate whether a therapeutic algorithm using steroids with or without interleukin-1 antagonist (anakinra) could prevent death/invasive ventilation. Patients with a ≥ 5 -day evolution since symptoms onset, with hyper-inflammation ($CRP \geq 50\text{mg/L}$), requiring 3-5 L/min oxygen, received methylprednisolone alone. Patients needing ≥ 6 L/min received methylprednisolone + subcutaneous anakinra daily either frontline or in case clinical deterioration upon corticosteroids alone. Death rate and death or intensive care unit (ICU) invasive ventilation rate at Day 15, with Odds Ratio (OR) and 95% CIs, were determined according to logistic regression and propensity scores. A Bayesian analysis estimated the treatment effects. **RESULTS:** Of 108 consecutive patients, 70 patients received glucocorticoids alone. The control group comprised 63 patients receiving standard of care. In the corticosteroid+-stanakinra group (n = 108), death rate was 20.4%, versus 30.2% in the controls, indicating a 30% relative decrease in death risk and a number of 10 patients to treat to avoid a death (p = 0.15). Using propensity scores a per-protocol analysis showed an OR for COVID-19-related death of 0.9 (95%CI [0.80-1.01], p = 0.067). On Bayesian analysis, the posterior probability of any mortality benefit with corticosteroids+/-anakinra was 87.5%, with a 7.8% probability of treatment-related harm. Pre-existing diabetes exacerbation occurred in 29 of 108 patients (26.9%). **CONCLUSION:** In COVID-19 non-ICU inpatients at the cytokine release phase, corticosteroids with or without anakinra were associated with a 30% decrease of death risk on Day 15.

FIGURES

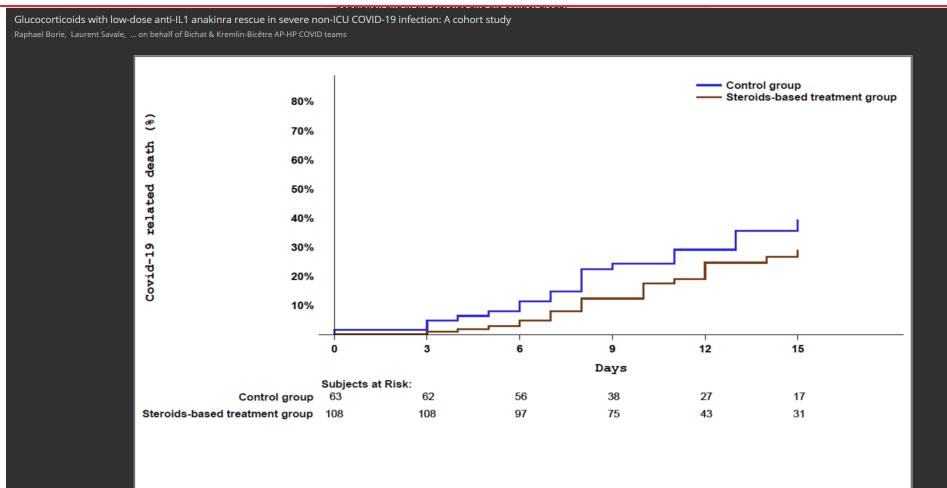


Figure 2. Kaplan Meier curves of survival of time to death from day of hospitalization.

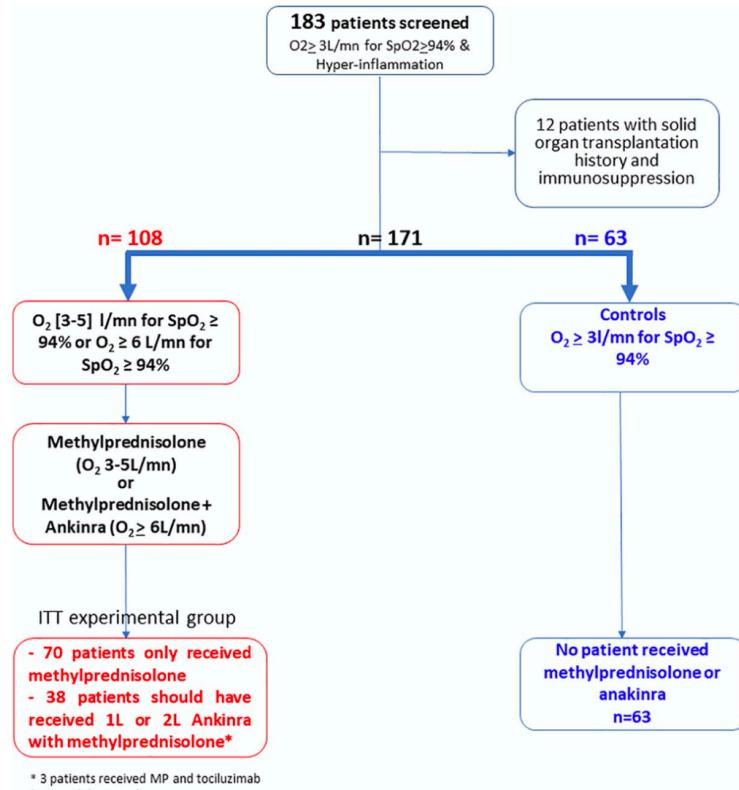


Fig 1. Flowchart of the 120 patients included in treatment algorithm group.

MENTAL HEALTH & RESILIENCE NEEDS

IMPACT ON PUBLIC MENTAL HEALTH

TRENDS IN U.S. EMERGENCY DEPARTMENT VISITS RELATED TO SUSPECTED OR CONFIRMED CHILD ABUSE AND NEGLECT AMONG CHILDREN AND ADOLESCENTS AGED <18 YEARS BEFORE AND DURING THE COVID-19 PANDEMIC - UNITED STATES, JANUARY 2019-SEPTEMBER 2020

Swedo E, Idaikkadar N, Leemis R, Dias T, Radhakrishnan L, Stein Z, Chen M, Agathis N, Holland K. MMWR Morb Mortal Wkly Rep. 2020 Dec 11;69(49):1841-1847. doi: 10.15585/mmwr.mm6949a1.

Level of Evidence: 3 - Local non-random sample

BLUF

A multidisciplinary team of researchers associated with the Centers for Disease Control and Prevention (CDC) discuss evidence of increased emergency room visits and hospitalizations for child abuse/neglect during the COVID-19 pandemic when compared to 2019. Authors attribute this trend to increases in stress, substance use, mental health issues, and financial hardships as a result of the pandemic. They advocate for increased awareness of child abuse/neglect and outline specific prevention strategies recommended by the CDC.

ABSTRACT

Heightened stress, school closures, loss of income, and social isolation resulting from the coronavirus disease 2019 (COVID-19) pandemic have increased the risk for child abuse and neglect (1). Using National Syndromic Surveillance Program (NSSP) data from January 6, 2019-September 6, 2020, CDC tabulated weekly numbers of emergency department (ED) visits related to child abuse and neglect and calculated the proportions of such visits per 100,000 ED visits, as well as the percentage of suspected or confirmed ED visits related to child abuse and neglect ending in hospitalization, overall and stratified by age group (0-4, 5-11, and 12-17 years). The total number of ED visits related to child abuse and neglect began decreasing below the corresponding 2019 period during week 11 (March 15-March 22, 2020) for all age groups examined, coinciding with the declaration of a national emergency on March 13 (2); simultaneously, the proportion of these visits per 100,000 ED visits began increasing above the 2019 baseline for all age groups. Despite decreases in the weekly number of ED visits related to child abuse and neglect, the weekly number of these visits resulting in hospitalization remained stable in 2020; however, the yearly percentage of ED visits related to child abuse and neglect resulting in hospitalization increased significantly among all age groups. Although the increased proportion of ED visits related to child abuse and neglect might be associated with a decrease in the overall number of ED visits, these findings also suggest that health care-seeking patterns have shifted during the pandemic. Hospitalizations for child abuse and neglect did not decrease in 2020, suggesting that injury severity did not decrease during the pandemic, despite decreased ED visits. Child abuse is preventable; implementation of strategies including strengthening household economic supports and creating family-friendly work policies can reduce stress during difficult times and increase children's opportunities to thrive in safe, stable, and nurturing relationships and environments (3).

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