The Daily COVID-19 Literature Surveillance Team Report

July 24, 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 meta-analysis of 2,765 patients in 6 studies conducted by authors at Lanzhou University in China found that tuberculosis (TB) was neither associated with increased mortality risk in COVID-19 patients (odds ratio [OR]=1.40, 95% CI: 0.10-18.93, p=0.80, I^2=31%) nor associated with an increased risk of developing severe COVID-19 (odds ratio [OR]=2.10, 95% CI: 0.61-7.18, p=0.24, I^2=36%), suggesting TB may not predispose individuals to COVID-19 related mortality, but based on having previous lung disease those with TB might have a higher chance of serious COVID-19.

Understanding the Pathology

- A cross sectional study from 23 March to 12 May 2020 found that a majority of serologic testing samples across 10 US states (n=16,025) were negative for SARS-CoV-2 antibodies, with positive results ranging from 1.0% in San Francisco Bay to 6.9% in New York City, but the number of infections was still much greater than number of reported cases at all testing sites. Authors suggest those with asymptomatic or mild infections may not seek healthcare and are often unaware of SARS-CoV-2 infection, so the general public should continue taking preventive measures (i.e. wearing cloth face coverings, social distancing, washing hands, and staying home when sick) to reduce COVID-19 transmission.

Transmission & Prevention

- The Infectious Disease Surveillance Center and National Institute of Infectious Disease in Japan investigated the Diamond Princess cruise ship COVID-19 outbreak between January and February 2020 and 58 of 601 environmental surface samples from cabins with COVID-19 patients remained positive for SARS-CoV-2 RNA for up to 17 days after cabin was vacated with no statistical difference between symptomatic and asymptomatic individuals. However, there was no evidence of viable transmission through air or wastewater samples, and no viral isolates were obtained from any sample suggesting proper disinfection and hygiene precautions are important in preventing direct and surface transmission during COVID-19 outbreaks.

Managements

- Guidelines and recommendations for management of COVID-19 patients include a clinical algorithm for determining appropriate therapeutic strategies for concomitant atrial fibrillation

Adjusting Practice During COIVD-19

- Guidelines and recommendations for adjusting practice during the pandemic include a set of triage algorithms and symptomatic management guidelines for geriatric patients diagnosed with or suspicious for COVID-19 infection.
- Researchers from Spain assessed data on COVID-19 outcomes in an ongoing randomized controlled trial comparing the use of ramipril to standard care following transcatheter aortic valve replacement and found that of 102 participants (50 ramipril, 52 control), 11 developed COVID-19 (5 ramipril, 6 control), yielding a hazard ratio of 1.150 (95% CI 0.351 - 3.768) for COVID-19 development with ramipril and found no difference in mortality between groups. Since ramipril did not result in higher COVID-19 incidence or mortality, the authors conclude that discontinuation of ACE-inhibitors as a precautionary measure may actually result in increased cardiovascular mortality.
    - Another study of 157 COVID-19 cases from Wuhan City, China found that the use of angiotensin converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs) had no significant impact on the prognosis or severity of COVID-19 in hypertensive patients when compared to use of calcium channel blockers (CCBs). They report no differences between in-hospital mortality (p=0.191), chest CT improvement time (p=0.87), nucleic acid conversion time (p=0.18), or in-hospital time (p=0.83), and efficacy was similar between both anti-hypertensive groups, suggesting there was no support for increased viral entry and replication of SARS-CoV-2 into host cells with

the use of ACEIs/ARBs. Authors recommend their continued use for the treatment of hypertension in COVID-19 patients.

- An observational study of healthcare personnel (n=5) found that wearing powered air-purifying respirators (PAPR) impaired hearing threshold (4.5 ± 3.6 to 38.6 ± 5.6 decibels in hearing level, P≤0.001) and decreased word discrimination (mean decrease from 100% to 48% ± 14%, P≤0.001), while positioning of PAPR did not alter either, suggesting a need for additional communication strategies, such as closed loop communication, for healthcare providers wearing PAPR to maintain patient and worker safety during the COVID-19 pandemic.

TABLE OF CONTENTS

ASSOCIATION BETWEEN TUBERCULOSIS AND COVID-19 SEVERITY AND MORTALITY: A RAPID SYSTEMATIC REVIEW AND META-ANALYSIS

Gao Y, Liu M, Chen Y, Shi S, Geng J, Tian J.. J Med Virol. 2020 Jul 20. doi: 10.1002/jmv.26311. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

A meta-analysis of 2,765 patients in 6 studies (Table 1) conducted by authors at Lanzhou University in China found that tuberculosis (TB) was not associated with increased mortality risk in COVID-19 patients (odds ratio [OR]=1.40, 95% CI: 0.10-18.93, p=0.80, I^2=31%) and not clearly associated with an increased risk of developing severe COVID-19 (odds ratio [OR]=2.10, 95% CI: 0.61-7.18, p=0.24, I^2=36%) (Figure 1). Authors suggest TB may not predispose individuals to COVID-19 related mortality, but based on having previous lung disease those with TB might have a higher chance of serious COVID-19, however further research is needed to confirm this association.

ABSTRACT

Coronavirus Disease 2019 (COVID-19) has become a pandemic and the number of infected cases continues to rise. As of July 8, 2020, a total of 11,669,259 laboratory-confirmed cases were reported worldwide, with a mortality rate of 4.6% 1 .

FIGURES

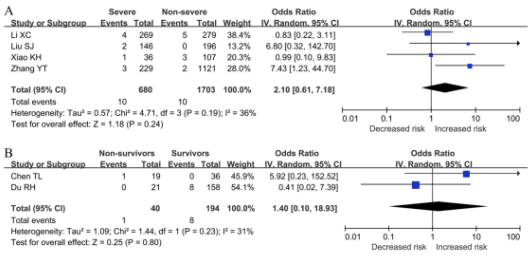


Figure 1. (A) Association between tuberculosis and COVID-19 severity, (B) Association between tuberculosis and COVID-19 mortality.

Study	Country	Language	Recruitment time frame	Sample	Sex (Male)	Age*	Tuberculosis	NOS
Li XC 2020 [7]	China	English	2020.1.26-2020.2.5	548	279(50.91%)	60 (48-69)	9(1.64%)	7
Liu SJ 2020 [8]	China	Chinese	2020.1.23-2020.2.12	342	183(53.51%)	56(45-67)	2(0.58%)	6
Xiao KH 2020 [9]	China	Chinese	2020.1.23-2020.2.8	143	73(51.05%)	45.13±1.04	4(2.80%)	7
Zhang YT 2020 [10]	China	Chinese	2020.1.15-2020.3.4	1350	664(49.19%)	44.1±17.9	5(0.37%)	6
Chen TL 2020 [11]	China	English	2020.1.1-2020.2.10	203	108(53.20%)	54(41-68)	1(2.33%)	6
Du RH 2020 [12]	China	English	2019.12.25-2020.2.7	179	97(54.19%)	57.6±13.7	8(4.47%)	8

*Age data presented as median (IQR) or mean±SD.

Table 1. Characteristics of included studies.

SEROPREVALENCE OF ANTIBODIES TO SARS-COV-2 IN 10 SITES IN THE UNITED STATES, MARCH 23-MAY 12, 2020

Havers FP, Reed C, Lim T, Montgomery JM, Klena JD, Hall AJ, Fry AM, Cannon DL, Chiang CF, Gibbons A, Krapiunaya I, Morales-Betoulle M, Roguski K, Rasheed MAU, Freeman B, Lester S, Mills L, Carroll DS, Owen SM, Johnson JA, Semenova V, Blackmore C, Blog D, Chai SJ, Dunn A, Hand J, Jain S, Lindquist S, Lynfield R, Pritchard S, Sokol T, Sosa L, Turabelidze G, Watkins SM, Wiesman J, Williams RW, Yendell S, Schiffer J, Thornburg NJ.. JAMA Intern Med. 2020 Jul 21. doi: 10.1001/jamainternmed.2020.4130. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross sectional study conducted by U.S. authors from 23 March to 12 May 2020 found a majority of serologic testing samples across 10 states (n=16,025; Figure 2) were negative for SARS-CoV-2 antibodies (determined via enzyme-linked immunosorbent assay [ELISA]), with positive results ranging from 1.0% in San Francisco Bay to 6.9% in New York City (Figures 1, 2 and Table 3), but the number of infections was still much greater than number of reported cases at all testing sites. Authors suggest those with asymptomatic or mild infections may not seek healthcare and are often unaware of SARS-CoV-2 infection, so the general public should continue taking preventive measures (i.e. wearing cloth face coverings, social distancing, washing hands, and staying home when sick) to reduce COVID-19 transmission.

ABSTRACT

Importance: Reported cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection likely underestimate the prevalence of infection in affected communities. Large-scale seroprevalence studies provide better estimates of the proportion of the population previously infected. Objective: To estimate prevalence of SARS-CoV-2 antibodies in convenience samples from several geographic sites in the US. Design, Setting, and Participants: This cross-sectional study performed serologic testing on a convenience sample of residual sera obtained from persons of all ages. The serum was collected from March 23 through May 12, 2020, for routine clinical testing by 2 commercial laboratory companies. Sites of collection were San Francisco Bay area, California; Connecticut; south Florida; Louisiana; Minneapolis-St Paul-St Cloud metro area, Minnesota; Missouri; New York City metro area, New York; Philadelphia metro area, Pennsylvania; Utah; and western Washington State. Exposures: Infection with SARS-CoV-2. Main Outcomes and Measures: The presence of antibodies to SARS-CoV-2 spike protein was estimated using an enzyme-linked immunosorbent assay, and estimates were standardized to the site populations by age and sex. Estimates were adjusted for test performance characteristics (96.0% sensitivity and 99.3% specificity). The number of infections in each site was estimated by extrapolating seroprevalence to site populations; estimated infections were compared with the number of reported coronavirus disease 2019 (COVID-19) cases as of last specimen collection date. Results: Serum samples were tested from 16 025 persons, 8853 (55.2%) of whom were women; 1205 (7.5%) were 18 years or younger and 5845 (36.2%) were 65 years or older. Most specimens from each site had no evidence of antibodies to SARS-CoV-2. Adjusted estimates of the proportion of persons seroreactive to the SARS-CoV-2 spike protein antibodies ranged from 1.0% in the San Francisco Bay area (collected April 23-27) to 6.9% of persons in New York City (collected March 23-April 1). The estimated number of infections ranged from 6 to 24 times the number of reported cases; for 7 sites (Connecticut, Florida, Louisiana, Missouri, New York City metro area, Utah, and western Washington State), an estimated greater than 10 times more SARS-CoV-2 infections occurred than the number of reported cases. Conclusions and Relevance: During March to early May 2020, most persons in 10 diverse geographic sites in the US had not been infected with SARS-CoV-2 virus. The estimated number of infections, however, was much greater than the number of reported cases in all sites. The findings may reflect the number of persons who had mild or no illness or who did not seek medical care or undergo testing but who still may have contributed to ongoing virus transmission in the population.

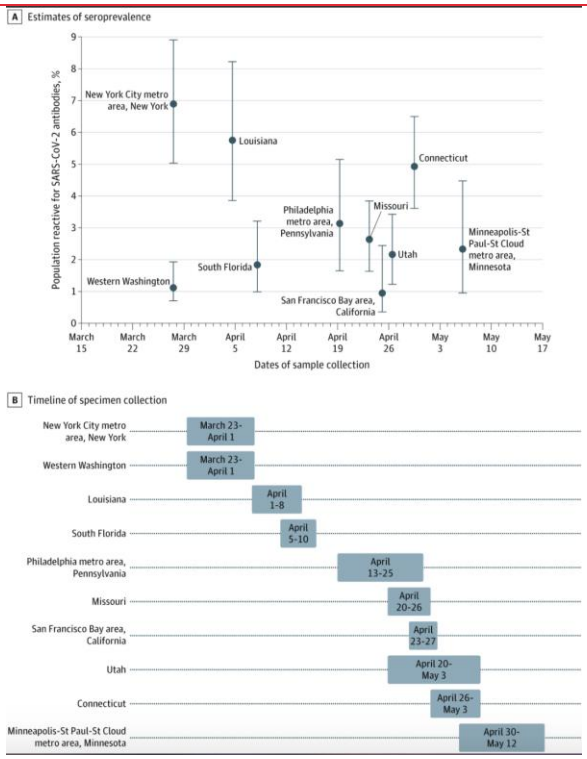


Figure 1. Estimates of Seroprevalence to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies and Timeline of Specimen Collection. A. Estimates are shown with 95% CIs for 10 geographic sites from which residual clinical specimens were collected. Seroprevalence estimate is shown at the midpoint of the specimen collection date range. B. Timeline with specimen collection dates for each site.

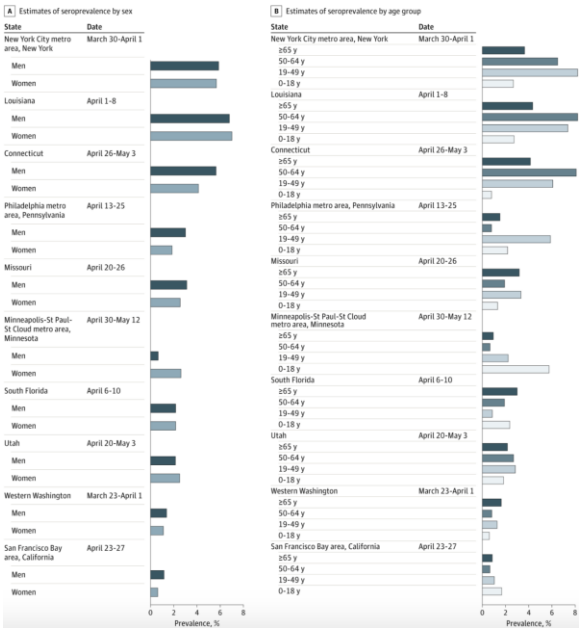


Figure 2. Strata-Specific Estimates of Seroprevalence to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in 10 Geographic Sites. A. Estimates of seroprevalence to SARS-CoV-2 antibodies by sex, from highest to lowest overall seroprevalence. B. Strata-specific estimates of seroprevalence to SARS-CoV-2 antibodies by age group, from highest to lowest overall seroprevalence.

Table 3. Estimated Number of Infections Based on Seroprevalence Estimates and Comparison With the Number of Reported Cases as of the Last Date of Specimen Collection for 10 Sites

Site	Catchment description	Catchment population, No.	Estimated seroprevalence, % (95% CI)[a]	Cases reported by date of last specimen collection, No.[b,c]	Estimated cumulative infections, No. (95% CI)	Estimated infections/reported cases, No. (range)[d]
Western Washington	King, Snohomish, Pierce, Kitsap, Grays Harbor counties	4 273 548	1.1 (0.7-1.9)	4308	48 291 (29 915-82 907)	11.2 (6.9-19.2)
New York City metro area (New York)	Manhattan, Bronx, Queens, Kings, Nassau counties	9 260 870	6.9 (5.0-8.9)	53 803	641 778 (464 896-826 070)	11.9 (8.6-15.4)
Louisiana	Statewide	4 644 049	5.8 (3.9-8.2)	17 030	267 033 (179 725-382 205)	15.7 (10.6-22.4)
South Florida	Miami-Dade, Broward, Palm Beach, Martin counties	6 345 345	1.9 (1.0-3.2)	10 525	117 389 (63 453-204 955)	11.2 (6.0-19.5)
Philadelphia metro area (Pennsylvania)	Bucks, Chester, Cumberland, Delaware, Lancaster, Montgomery, Philadelphia counties	4 910 139	3.2 (1.7-5.2)	22 987	156 633 (82 981-254 836)	6.8 (3.6-11.1)
Missouri	Statewide	6 110 800	2.7 (1.7-3.9)	6794	161 936 (100 828-235 877)	23.8 (14.8-34.7)
Utah	Adults aged ≥19 y (statewide)	2 173 082	2.2 (1.2-3.4)	4493[e]	47 373 (26 294-74 537)	10.5 (5.5-15.5)
San Francisco Bay area (California)	Alameda, Contra Costa, San Francisco, San Mateo, Marin, Santa Clara counties	6 662 454	1.0 (0.3-2.4)	7151	64 626 (22 652-162 564)	9.0 (3.2-22.7)
Connecticut	Statewide	3 562 989	4.9 (3.6-6.5)	29 287	176 012 (128 624-232 307)	6.0 (4.3-7.8)
Minneapolis-St Paul-St Cloud metro area (Minnesota)	Anoka, Benton, Carver, Chisago, Dakota, Goodhue, Hennepin, Isanti, Le Sueur, McLeod, Mille Lacs, Ramsey, Rice, Scott, Sherburne, Stearns, Steele, Washington, Wright counties	3 857 479	2.4 (1.0-4.5)	8880	90 651 (37 803-173 587)	10.2 (4.3-19.5)

FIBRINOLYSIS AND COVID-19: A TALE OF TWO SITES?

Keragala CB, Medcalf RL, Myles PS.. J Thromb Haemost. 2020 Jul 21. doi: 10.1111/jth.15017. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

In this letter researchers in Melbourne, Australia discuss the results of a study performed by Tang et al. (2020)** and suggest that future studies should additionally examine blood clotting in the lung parenchyma, which uses urokinase instead of t-PA for the activation of plasmin formation, in order to compare the variation from other physiologic clotting processes. The results of Tang et al. and their idea for this future study on clotting in lung parenchyma secondary to COVID-19 would enhance current knowledge on the physiologic effects of COVID-19 and may help determine whether treatment with anticoagulants is appropriate for such patients.

SUMMARY

** Tang et al. found that non-survivors of severe COVID-19 had higher thrombin-antithrombin (TAT) levels compared to survivors after 7 days, indicating greater thrombin (blood clotting promoter) formation. After 14 days, however, TAT levels were near baseline in both survivors and non-survivors, while D-dimer and tPA-PAI-1 complex levels were increased and plasmin-antiplasmin (PAP) levels were decreased in non-survivors. These results indicate that fibrinolysis is initiated and then later suppressed, with a reduction in plasminogen (precursor for plasmin, a blood clot degrader) activation, in severe COVID-19.

ABSTRACT

We thank Tang et al. for their perspective on the possible limitation of D-dimer levels guiding anticoagulant treatment in patients with COVID-19 [1]. Although there is a clear association with elevated D-dimer and severity of COVID-19 disease, it is important to highlight the fact that D-dimer has always been utilised in conjunction with clinical pre-test probability, as a predictive tool to help exclude a possible diagnosis of venous thromboembolism. It has never been validated to guide clinical treatment or anticoagulation. It has recently been noted that a significant proportion of the recent literature concerning D-dimer in COVID-19 is fraught with variable, poor or incomplete reporting which further muddies its role in the management of COVID-19 related coagulopathy[2].

ENVIRONMENTAL SAMPLING FOR SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 DURING COVID-19 OUTBREAK IN THE DIAMOND PRINCESS CRUISE SHIP

Yamagishi T, Ohnishi M, Matsunaga N, Kakimoto K, Kamiya H, Okamoto K, Suzuki M, Gu Y, Sakaguchi M, Tajima T, Takaya S, Ohmagari N, Takeda M, Matsuyama S, Shirato K, Nao N, Hasegawa H, Kageyama T, Takayama I, Saito S, Wada K, Fujita R, Saito H, Okinaka K, Griffith M, Parry AE, Barnetson B, Leonard J, Wakita T.. J Infect Dis. 2020 Jul 21:jiaa437. doi: 10.1093/infdis/jiaa437. Online ahead of print.
Level of Evidence: 3 - Mechanism-based reasoning

BLUF

A mechanism-based study from the Infectious Disease Surveillance Center and National Institute of Infectious Disease in Japan investigated the Diamond Princess cruise ship COVID-19 outbreak between January and February 2020 with surface, air, and wastewater samples analyzed for presence of both SARS-CoV-2 RNA and viral isolates. 58 of 601 environmental surface samples from cabins with COVID-19 patients remained positive for SARS-CoV-2 RNA via real-time reverse transcriptase polymerase chain reaction (rRT-PCR) for up to 17 days after cabin was vacated with no statistical difference between symptomatic and asymptomatic individuals. However, there was no evidence of viable transmission through air or wastewater samples, and no viral isolates were obtained from any sample suggesting proper disinfection and hygiene precautions are important in preventing direct and surface transmission during COVID-19 outbreaks.

ABSTRACT

A COVID-19 outbreak occurred in the Diamond Princess cruise ship and we sampled environmental surfaces after passengers and crews vacated the cabins. SARS-CoV-2 RNA was detected from 58 out of 601 samples (10%) from case-cabins 1-17 days after the cabins were vacated, but not from non-case-cabins. There was no difference in the detection proportion between cabins for symptomatic (15%, 28/189, Cq: 29.79-38.86) and asymptomatic cases (21%, 28/131, Cq: 26.21-38.99). No SARS-CoV-2 virus was isolated from any of the samples. Transmission risk of SARS-CoV-2 from symptomatic and asymptomatic patients may be similar and environmental surfaces could be involved in viral transmission.

CARDIOLOGY

GUIDANCE ON SHORT-TERM MANAGEMENT OF ATRIAL FIBRILLATION IN CORONAVIRUS DISEASE 2019

Rattanawong P, Shen W, El Masry H, Sorajja D, Srivathsan K, Valverde A, Scott LR.. J Am Heart Assoc. 2020 Jul 21;9(14):e017529. doi: 10.1161/JAHA.120.017529. Epub 2020 Jun 9.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

A review conducted by the Department of Cardiovascular Diseases at the Mayo Clinic in Arizona reviewed the potential adverse drug-drug interactions from antiarrhythmic drug (AAD) and anticoagulants in atrial fibrillation with emerging COVID-19 medication therapies (Figure 2 and 3) and included a clinical algorithm for determining appropriate therapeutic strategies (Figure 1). The authors recommend that clinicians review the potential effects of potassium channel blockade, CYP450 enzyme inhibition/induction, and P-glycoprotein inhibition when managing atrial fibrillation in COVID-19 patients.

ABSTRACT

Atrial fibrillation is a common clinical manifestation in hospitalized coronavirus disease of 2019 (COVID-19) patients. Medications used to treat atrial fibrillation such as antiarrhythmic drugs and anticoagulants may have significant drug interactions with emerging COVID-19 treatments. Common unintended non-therapeutic target effects of COVID-19 treatment include IKr blockade, CYP450 isoenzyme inhibition or activation, and P-glycoprotein inhibition. Drug-drug interactions with antiarrhythmic drugs and anticoagulants in these patients may lead to significant bradycardia, ventricular arrhythmias, or severe bleeding. It is important for clinicians to be aware of these interactions, drug metabolism changes, and clinical consequences when choosing antiarrhythmic drugs and anticoagulants for COVID-19 patients with atrial fibrillation. The objective of this review is to provide a practical guide for clinicians who are managing COVID-19 patients with concomitant atrial fibrillation.

FIGURES

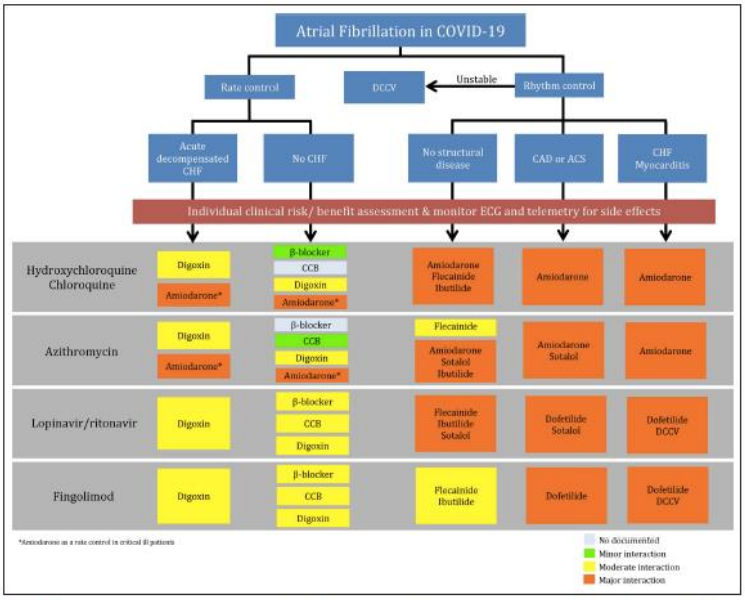


Figure 1. Management guidance algorithm for atrial fibrillation and concomitant coronavirus disease 2019 (COVID-19). ACS indicates acute coronary syndrome; CAD, coronary artery disease; CCB, calcium channel blocker; CHF, congestive heart failure; and DCCV, direct current cardioversion.

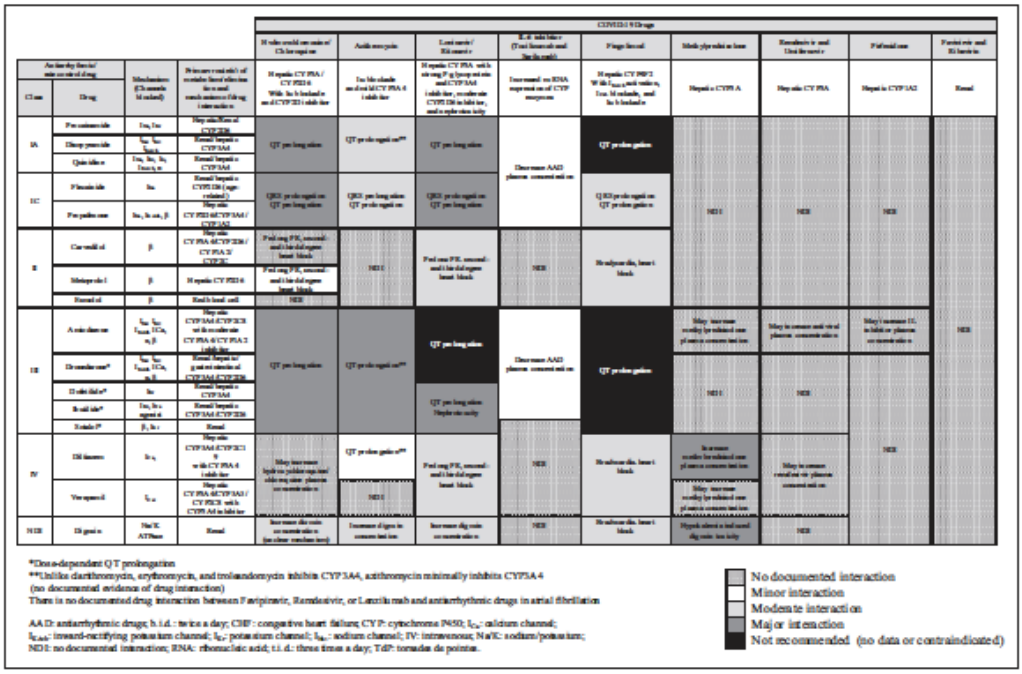


Figure 2. **AADs Used in AF and Their Drug Interaction With COVID-19 Therapy.**

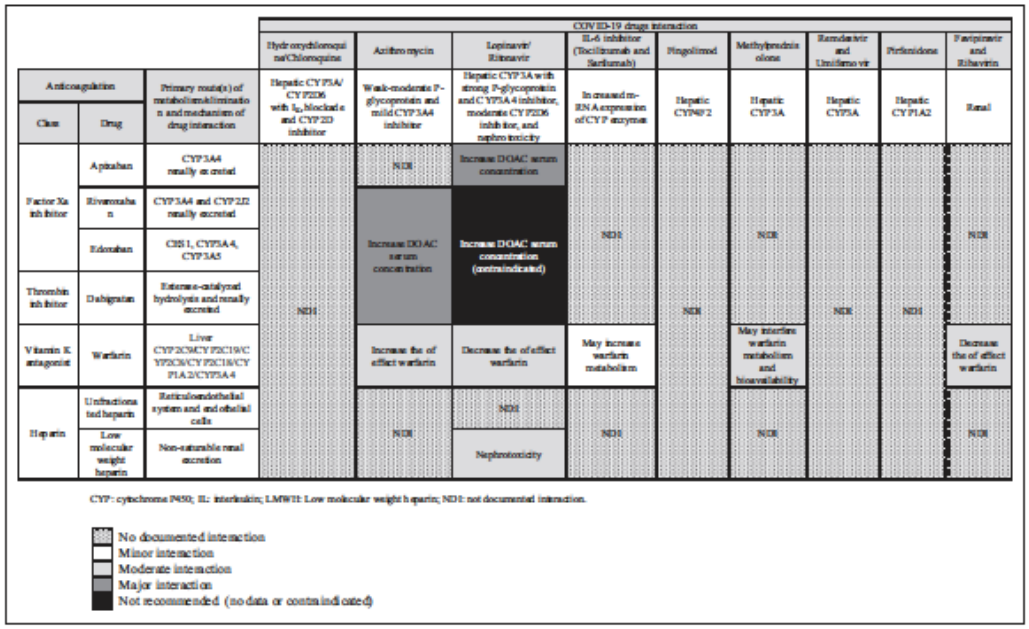


Figure 3. **Anticoagulation Drugs Used in AF and Potential Drug-Drug Interactions With COVID-19 Therapy.**

RAMIPRIL IN HIGH-RISK PATIENTS WITH COVID-19

Amat-Santos IJ, Santos-Martinez S, López-Otero D, Nombela-Franco L, Gutiérrez-Ibanes E, Del Valle R, Muñoz-García E, Jiménez-Diaz VA, Regueiro A, González-Ferreiro R, Benito T, Sanmartin-Pena XC, Catalá P, Rodríguez-Gabella T, Delgado-Arana JR, Carrasco-Moraleja M, Ibañez B, San Román JA.. J Am Coll Cardiol. 2020 Jul 21;76(3):268-276. doi: 10.1016/j.jacc.2020.05.040. Epub 2020 May 26.
Level of Evidence: 2 - Individual randomized trial or (exceptionally) observational study with dramatic effect

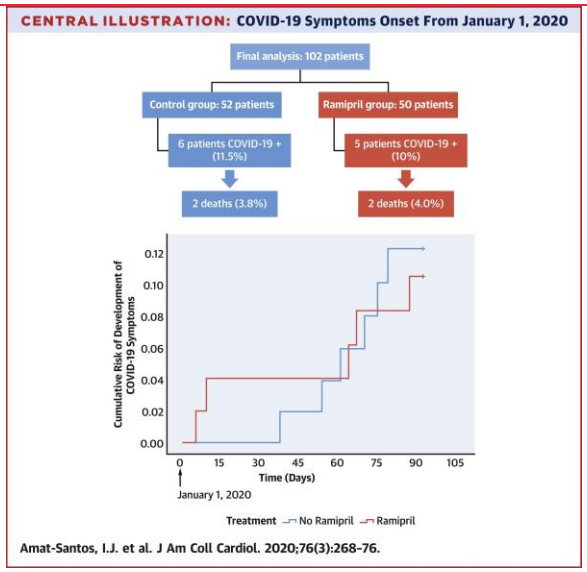
BLUF

To investigate the risk of angiotensin-converting enzyme (ACE)-inhibitor use in COVID-19, researchers from Spain assessed data on COVID-19 outcomes in an ongoing randomized controlled trial comparing the use of ramipril to standard care following transcatheter aortic valve replacement. Of 102 participants (50 ramipril, 52 control), 11 developed COVID-19 (5 ramipril, 6 control), yielding a hazard ratio of 1.150 (95% CI 0.351 - 3.768) for COVID-19 development with ramipril (see Central Illustration); there was also no difference in mortality between groups. As ramipril did not result in higher COVID-19 incidence or mortality, the authors conclude that discontinuation of ACE-inhibitors as a precautionary measure may actually result in increased cardiovascular mortality.

ABSTRACT

BACKGROUND: The coronavirus disease 2019 (COVID-19) is caused by SARS-CoV2 that interfaces with the renin-angiotensin-aldosterone system (RAAS) through angiotensin-converting enzyme 2 (ACE-2). This interaction has been proposed as a potential risk factor in patients treated with RAAS-inhibitors. OBJECTIVES: To analyze if RAAS-inhibitors modify the risk for COVID-19. METHODS: RASTAVI (NCT03201185) is an ongoing randomized clinical trial randomly allocating Ramipril or control after successful transcatheter aortic valve replacement at 14 centers is Spain. We performed a non-pre-specified interim analysis to evaluate its impact on COVID-19 risk in this vulnerable population. RESULTS: As in April 1st 2020, 102 patients (50 Ramipril and 52 controls) were included in the trial. Mean age was 82.3+-6.1 years, 56.9% males. Median time of Ramipril treatment was 6 months [IQR:2.9-11.4]. Eleven patients (10.8%) have been diagnosed with COVID-19 (6 in control group and 5 receiving Ramipril, HR=1.150 [95%CI: 0.351-3.768]). The risk of COVID-19 was increased in older patients (p=0.019), those with atrial fibrillation (p=0.066), lower hematocrit (p=0.084), and more comorbidities according to Society of thoracic surgeons score (p=0.065). Admission and oxygen supply was required in 4.9% (2 patients in the Ramipril and 3 in control), and 4 of them died (two in each randomized group). A higher body mass index was the only factor increasing the mortality rate (p=0.039). CONCLUSIONS: In a high risk population of old patients with cardiovascular disease, randomization to Ramipril had no impact in the incidence or severity of COVID-19. This analysis supports the maintenance of RAAS-inhibitor treatment during COVID-19 crisis.

FIGURES



Central Illustration. COVID-19 symptoms onset from January 1st, 2020.

EFFECT OF POWERED AIR-PURIFYING RESPIRATORS ON SPEECH RECOGNITION AMONG HEALTH CARE WORKERS

Kempfle JS, Panda A, Hottin M, Vinik K, Kozin ED, Ito CJ, Remenschneider AK.. Otolaryngol Head Neck Surg. 2020 Jul 21:194599820945685. doi: 10.1177/0194599820945685. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Authors in Massachusetts, United States conducted an observational study of healthcare personnel (n=5) and found wearing powered air-purifying respirators (PAPR) impaired hearing threshold (4.5 ± 3.6 to 38.6 ± 5.6 decibels in hearing level, P≤0.001) and decreased word discrimination (mean decrease from 100% to 48% ± 14%, P≤0.001), while positioning of PAPR did not alter either (Figures 1, 2). Authors suggest a need for additional communication strategies, such as closed loop communication, for healthcare providers wearing PAPR to maintain patient and worker safety during the COVID-19 pandemic.

ABSTRACT

Powered air-purifying respirators (PAPRs) are used as personalized protective equipment for health care personnel. PAPRs offer health care workers added protection when dealing with patients who have high-risk infectious disease such as COVID-19. Unfortunately, PAPRs can produce notable levels of background noise. We hypothesize that PAPR use may be associated with increased hearing thresholds and impaired word discrimination and may ultimately have a negative impact on effective communication. Herein, we (1) determined sound levels generated by PAPRs and (2) measured hearing thresholds and word discrimination with and without operational PAPRs. All participants had normal hearing. When the PAPR was operational, mean +- SD thresholds increased from 4.5 +- 3.6 to 38.6 +- 5.6 dB HL (P < .001). Word discrimination dropped from 100% in all participants in quiet to a mean 48% +- 14% with operational PAPR (P < .001). Thus, we find that use of PAPR hoods results in hearing impairment comparable to moderate to severe hearing loss, and we suspect that users will experience communication difficulties as a result.Level of Evidence. Prospective study.

FIGURES

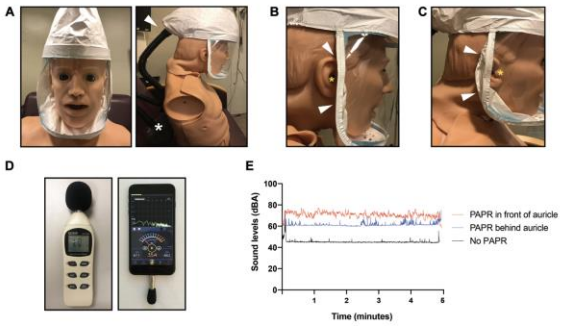


Figure 1. (A) Powered air-purifying respirator hood (arrowhead), battery (asterisk). Position (B) in front of auricle (arrowheads) or (C) behind auricle (arrowheads). Asterisks mark microphone location. (D) Sound level meter for calibration and phone setup with microphone and Decibel X app. (E) Sound levels in dBA

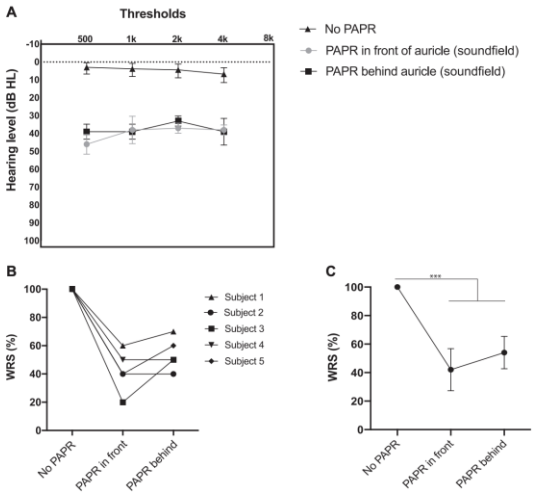


Figure 2. (A) Mean +/- SD pure tone thresholds without powered air-purifying respirator (PAPR) and soundfield measurements with operating PAPR in each condition (10 ears). (B) Word recognition score (WRS) with and without PAPR. (C) Mean +/- SD WRS. ***P .001.

MEDICAL SUBSPECIALTIES

INPATIENT MEDICINE

EFFICACY OF ACEIS/ARBS VERSUS CCBS ON THE PROGRESSION OF COVID-19 PATIENTS WITH HYPERTENSION IN WUHAN: A HOSPITAL-BASED RETROSPECTIVE COHORT STUDY

Liu X, Liu Y, Chen K, Yan S, Bai X, Li J, Liu D.. J Med Virol. 2020 Jul 20. doi: 10.1002/jmv.26315. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

In this case series and analysis (n = 157), researchers in Wuhan City, China found the use of angiotensin converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs) had no significant impact on the prognosis or severity of COVID-19 in hypertensive patients when compared to use of calcium channel blockers (CCBs). They report no differences between in-hospital mortality (p=0.191), chest CT improvement time (p=0.87), nucleic acid conversion time (p=0.18), or in-hospital time (p=0.83), and efficacy was similar between both anti-hypertensive groups (Figure 2). As such, they conclude that no data were found in their study to support increased viral entry and replication of SARS-CoV-2 into host cells with the use of ACEIs/ARBs and recommend their continued use for the treatment of hypertension in COVID-19 patients.

ABSTRACT

BACKGROUND: To evaluate the efficacy of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) versus calcium channel blockers (CCBs) on the progression of COVID-19 patients with hypertension in Wuhan. METHODS: This retrospective single-center case series analyzed COVID-19 patients with hypertension, treated with ACEIs/ACEIs or CCBs at the Tongji Hospital of Wuhan City, Chin from January 25th to March 15th, 2020. After PSM analysis, 76 patients were selected into two groups. Univariate and multivariable analyses were conducted to determine factors related to improvement measures and outcome measures by Cox proportional hazard regression models. RESULTS: Among 157 patients with confirmed COVID-19 combined hypertension, including 73 males and 84 females, a median age of 67.28 +-9.11 vs 65.39 +-10.85 years. A univariable analysis indicated that clinical classification, lymphp cyte count and interleukin-2 receptor were associated with a lengthened negative time of nucleic acid, with a significant difference between two groups (p=0.036). Furthermore, we found no obvious difference in nucleic acid conversion time between ACEIs/ARBs group and CCBs group (HR 0.70, 95% CI [0.97, 3.38], p=0.18) in the multivariable analysis as well as chest CT improved time (HR 0.73, 95% CI [0.45, 1.2], p=0.87), and hospitalization time between ACEIs/ARBs group and CCBs group (HR 1.06, 95% CI [0.44, 1.1], p=0.83). CONCLUSION: Our study provided additional evidence of no obvious difference in progress and prognosis between ACEIs/ACEIs and CCBs group, which may suggest ACEIs/ARBs may have scarcely influence on increasing the clinical severe situations of COVID-19 patients with hypertension. This article is protected by copyright. All rights reserved.

FIGURES

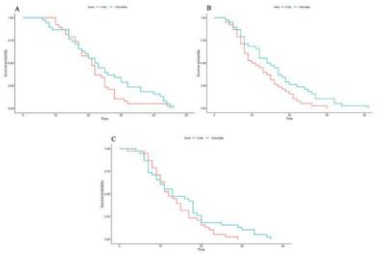


Figure 2 A: Cox regression analysis curve of nucleic acid conversion time of COVID-19 patients with hypertension (After PSM), B: Cox regression analysis curve of chest CT improved time of COVID-19 patients with hypertension (After PSM), C: Cox regression analysis curve of the hospitalization time of COVID-19 patients with hypertension (After PSM).

OBGYN

PROVIDING WOMEN'S HEALTH CARE DURING COVID-19: PERSONAL AND PROFESSIONAL CHALLENGES FACED BY HEALTH WORKERS

Green L, Fateen D, Gupta D, McHale T, Nelson T, Mishori R.. Int J Gynaecol Obstet. 2020 Jul 21. doi: 10.1002/ijgo.13313. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Researchers from Massachusetts, Washington, DC, and New York discussed the obstacles faced by medical professionals and patients in the women's health care arena during the COVID-19 crisis, reporting that patients are now restricted to telehealth services and self-monitoring, while women's health care workers have limited PPE access. Women's health care is essential, and continuous evaluation of the rapid changes of this field during the pandemic is necessary to ensure adequate patient care, as well as safety of patients and health care professionals.

SUMMARY

- An estimated 1.6 million babies will be born during pandemic, and many more patients will have gynecological disorders, so women's health care is essential.
- In the US, some providers have reduced the number of in-person prenatal visits (from an average of 12-14 to 5) by teaching women self-monitoring and documentation for things such as number of kicks and blood pressure.
- Telehealth may be difficult for women with co-morbidities, women with limited internet access, or women who require a physical examination of breasts or genitalia.
- The pandemic has led to reductions in family planning services and in-person services for survivors of sexual violence. There has been a 10% reduction in use of contraceptives which could result in an extra 15 million unintended pregnancies. Sexual violence survivors are reduced to more telehealth services where in-person contact is not feasible and sometimes have to self-swab for DNA collection. Research must continue to evaluate these health care changes and use empirical data and experiences of health care workers and patients to guide future decision-making.
- In a worldwide survey of maternal and newborn healthcare workers, 60% of respondents reported not having access to enough PPE. There were similar findings for surveys in the UK, Bangladesh, Ethiopia, Iran, and other countries. These workers also have concerns about being forgotten about in terms of PPE access given the focus on emergency workers. The second stage of labor is considered by recent publications to be an aerosol-generating procedure leading to calls for N-95 masks, face shields, and full gowns.
- Visitor limitations during birth force women to make difficult decisions between choosing family and professional support (such as doulas) to be in the room with them during labor. Advocates are important for a good outcome, especially for low-income women and women of color, and more pressure is placed on the health care team to provide emotional support for the women. One possible solution is to consider supportive care such as doulas to be essential, not optional.

ABSTRACT

The coronavirus pandemic has reshaped the healthcare landscape, placing a strain on all healthcare workers, including those who provide critical health services for women. Around the world, healthcare workers have been facing increased workloads, shortages of personal protective equipment (PPE), harassment and violence, and ever-evolving clinical guidance on how best to care for their patients [1-4].

GERIATRICS

"PALLIATIVE PANDEMIC PLAN," TRIAGE AND SYMPTOMS ALGORITHM AS A STRATEGY TO DECREASE PROVIDERS' EXPOSURE, WHILE TRYING TO INCREASE TEAMS AVAILABILITY AND GUIDANCE FOR GOALS OF CARE (GOC) AND SYMPTOMS CONTROL

Lopez S, Decastro G, Van Ogtrop KM, Weiss-Domis S, Anandan SR, Magalee CJ, Roofeh R, Liberman TA.. Am J Hosp Palliat Care. 2020 Jul 21:1049909120942494. doi: 10.1177/1049909120942494. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

A group of geriatric and palliative (GAP) care physicians from New York state developed a set of triage algorithms and symptomatic management guidelines for patients diagnosed with or suspicious for COVID-19 infection (Figure 1, 2) to help prevent COVID-19 exposure by patient care teams and patients' families. The authors found that these guidelines helped streamline care at their institutions despite a massive increase in consults to GAP teams during first month of the pandemic (March-April). Future research is needed to evaluate the reproducibility of these algorithms in alternative contexts, such as outpatient clinics.

ABSTRACT

As the spread of the novel coronavirus disease 2019 (COVID-19) continues worldwide, health care systems are facing increased demand with concurrent health care provider shortages. This increase in patient demand and potential for provider shortages is particularly apparent for palliative medicine, where there are already shortages in the provision of this care. In response to the developing pandemic, our Geriatrics and Palliative (GAP) Medicine team formulated a 2-team approach which includes triage algorithms for palliative consults as well as acute symptomatic management for both patients diagnosed with or under investigation (PUI) for COVID-19. These algorithms provided a delineated set of guidelines to triage patients in need of palliative services and included provisions for acute symptoms management and the protection of both the patient care team and the families of patients with COVID-19. These guidelines helped with streamlining care in times of crisis, providing care to those in need, supporting frontline staff with primary-level palliative care, and minimizing the GAP team's risk of infection and burnout during the rapidly changing pandemic response.

FIGURES

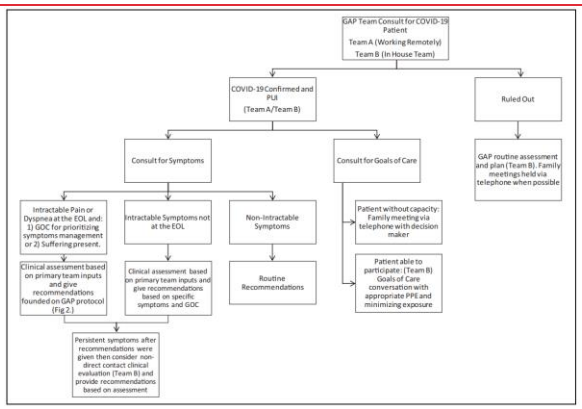


Figure 1. Algorithm for palliative care consult of patient with coronavirus disease 2019 (COVID-19) confirmed or patient under investigation (PUI) for COVID-19.

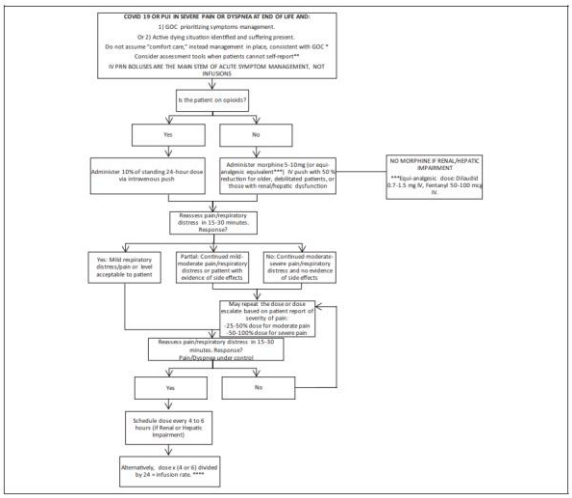


Figure 2. Algorithm for acute management of coronavirus disease 2019 (COVID-19) or patients under investigation (PUI) for COVID-19 in severe pain or dyspnea at the end of life (EOL).

* Comfort care is a non-specific term that does not define a treatment plan. Therefore, specific treatments such as intravenous fluids,
antimicrobials, and other therapies should be continued unless otherwise define by goals of care (GOC).

** Pain Assessment in Advanced Dementia Scale (PAIN AD) and Respiratory Distress Observation Scale (RDOS).

*** Opioid equi-analgesic table as per individual institutional consensus.

**** In patients with normal renal or hepatic function, adjusting the continues infusion at 8-12 hours (about five half-lives) is generally acceptable,
as the drug will be close to or at steady state. If there is organ impairment, it is reasonable to wait up to 24 hours.

PUI = Patient under investigation.

R&D: DIAGNOSIS & TREATMENTS

CURRENT DIAGNOSTICS

BREATH ANALYSIS FOR DETECTION OF VIRAL INFECTION, THE CURRENT POSITION OF THE FIELD

Gould O, Ratcliffe N, Król E, de Lacy Costello B.. J Breath Res. 2020 Jul 21;14(4):041001. doi: 10.1088/1752-7163/ab9c32.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review conducted primarily at the University of West England found little ongoing research regarding the development of virus-specific tests using volatile compounds from breathing. Current research has focused on either oxidative stress markers, which are not disease-specific, and MALDI-ToF-MS, which is effective but relies upon previous identification of the spectra of each virus or bacteria. The authors encourage development of these tests for COVID-19 to identify viral presence in the lungs after the viral presence has diminished in the nasopharynx and before serum-based antibody tests are effective.

ABSTRACT

The COVID-19 pandemic has highlighted the importance of rapid, cost effective, accurate, and non-invasive testing for viral infections. Volatile compounds (VCs) have been suggested for several decades as fulfilling these criteria. However currently very little work has been done in trying to diagnose viral infections using VCs. Much of the work carried out to date involves the differentiation of bacterial and viral sources of infection and often the detection of bacterial and viral co-infection. However, this has usually been done in vitro and very little work has involved the use of human participants. Viruses hijack the host cell metabolism and do not produce their own metabolites so identifying virus specific VCs is at best a challenging task. However, there are proteins and lipids that are potential candidates as markers of viral infection. The current understanding is that host cell glycolysis is upregulated under viral infection to increase the available energy for viral replication. There is some evidence that viral infection leads to the increase of production of fatty acids, alkanes, and alkanes related products. For instance, 2,3-butandione, aldehydes, 2,8-dimethyl-undecane and n-propyl acetate have all been correlated with viral infection. Currently, the literature points to markers of oxidative stress (e.g. nitric oxide, aldehydes etc) being the most useful in the determination of viral infection. The issue, however, is that there are also many other conditions that can lead to oxidative stress markers being produced. In this review a range of (mainly mass spectrometric) methods are discussed for viral detection in breath, including breath condensate. Currently MALDI-ToF-MS is likely to be the preferred method for the identification of viral strains and variants of those strains, however it is limited by its need for the viral strains to have been sequenced and logged in a database.

DEVELOPMENTS IN DIAGNOSTICS

THE SCENT OF COVID-19: VIRAL (SEMI-)VOLATILES AS FAST DIAGNOSTIC BIOMARKERS?

Lamote K, Janssens E, Schillebeeckx E, Lapperre TS, De Winter BY, van Meerbeeck JP.. J Breath Res. 2020 Jul 21;14(4):042001. doi: 10.1088/1752-7163/aba105.
Level of Evidence: Other - Expert Opinion

BLUF

Authors from Belgium discuss the field of breathomics and its potential as a rapid, non-invasive technique for diagnosing and prognosticating COVID-19. They suggest that analysis of the composition of an individual's breath for SARS-CoV-2 specific volatile organic compounds (VOCs) as well as non-volatile compounds in exhaled breath condensate (EBC) and aerosols (EBA) could provide an alternative method to diagnosing COVID-19 as well as predicting the stage of infection in COVID-19 patients (Figure 1). The authors note that more information on SARS-CoV-2 specific breath markers and improvements to sensitivity and specificity of such tests are needed to enable development of effective tests based on analysis of breath VOCs, EBCs, and EBAs.

ABSTRACT

The COVID-19 pandemic pressurizes the healthcare system. Protective measures against SARS-CoV-2 infection, like social distancing or isolation, are being taken too late and COVID-19 symptoms are non-specific and can resemble those from rhinoviral infection or influenza, causing a rush of anxious patients with (mild) symptoms to the hospitals. Furthermore, COVID-19 diagnosis is made by taking swabs from the upper of lower respiratory tract, which is not only an unpleasant experience for the patient, but is also time-consuming. Therefore, a fast differential diagnosis between SARS-COV-2, influenza or rhinovirus infection would allow to optimize the hospital management and hospitalize those patients with proven COVID-19 disease, where other patients can easily recover at home. Breath analysis could therefore be explored investigating both volatile organic compounds (VOC) and exhaled breath condensate (EBC) and aerosols (EBA) in a non-invasive manner, without discomforting the patient. However, breath research is highly affected since human-mediated transmission of viral particles through breath is of high concern. Nevertheless, breathomics can provide fast results and the sampling materials can be cleaned and autoclaved thoroughly, minimizing the risk for cross-contamination. Breath analysis also allows the breath sample to be taken by the patient himself, hence, considering the social distancing measures and protecting health care workers. In this article, we summarize 3 pathways in which SARS-CoV-2 could generate specific VOCs. In that way, breath analysis could allow a fast differential diagnosis as first line screening, optimizing COVID-19 management.

FIGURES

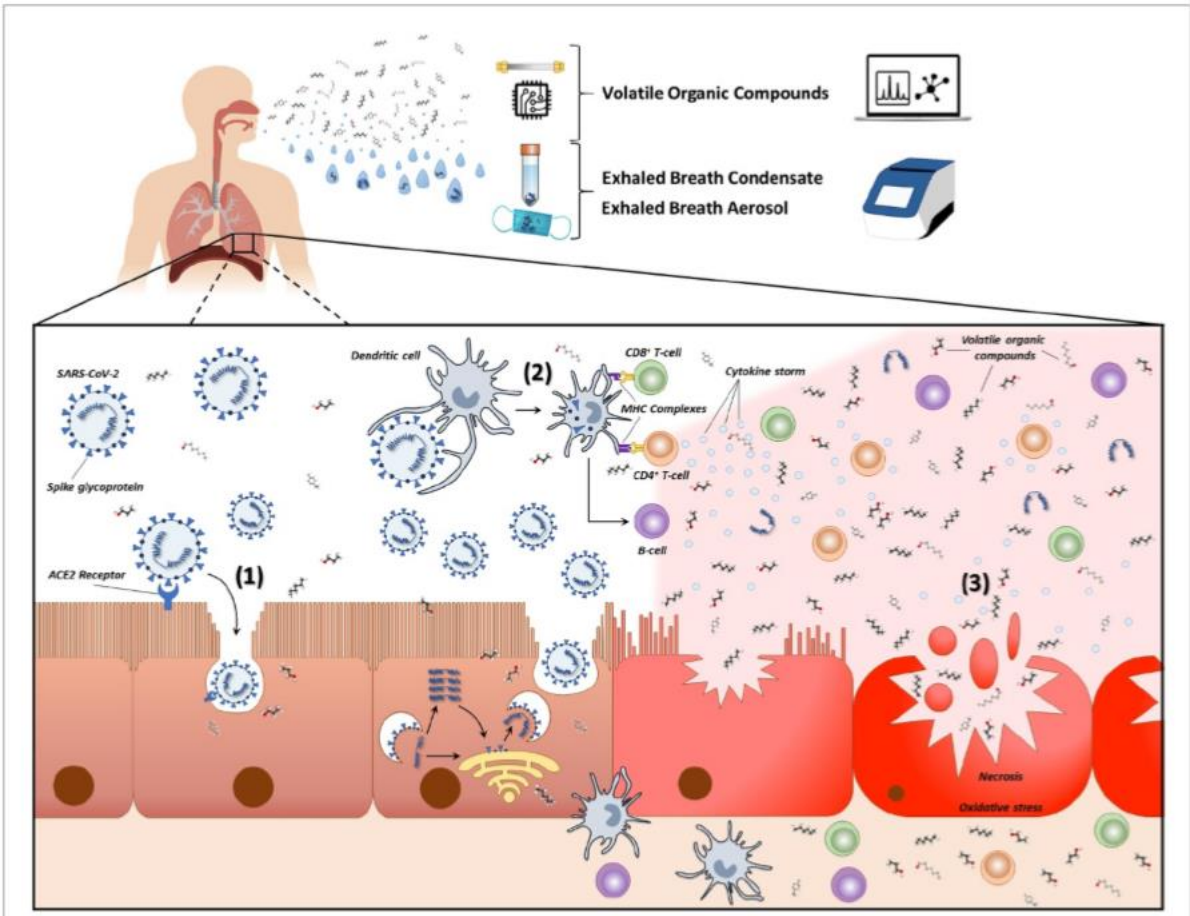


Figure 1. Breathomics to detect SARS-COV-2 infection.

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