The Daily COVID-19 Literature Surveillance Summary

November 30, 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

- There is higher prevalence of pulmonary macrothrombi in SARS-CoV-2 than in influenza A. A comparative analysis by pathologists at University Hospital Zurich in Switzerland assessed pulmonary macrothrombi autopsy findings in 411 patients who died from the Influenza A pandemic in 1918/1919, 12 from Influenza A in 2009-2020, and 75 for COVID-19. They found COVID-19 patients had significantly higher occurrences of grossly visible pulmonary thrombosis despite empiric thrombophylaxis due to in situ clot formation associated with SARS-CoV-2. Authors suggest a specific COVID-19 coagulopathy may be linked to higher mortality rate seen in COVID-19 compared to the seasonal flu.

Understanding the Pathology

- In vivo demonstration of microvascular thrombosis in severe COVID-19 was found in one study where researchers in the Department of Internal Medicine, Ribeirão Preto School of Medicine in Brazil conducted imaging via video capillaroscopy of 13 severe COVID-19 positive patients requiring mechanical ventilation to assess sublingual microcirculation for evidence of microthrombi. They found microthrombi in 11/13 (85%) of patients and acute thromboembolic occlusion in 5/13 (38%) of patients. This evidence suggests that microvascular thrombosis could be considered a hallmark of COVID-19 and that these microvascular thrombotic events occur systemically, affecting many organ systems.

Management

- Dosing of thromboprophylaxis and mortality in critically ill COVID-19 patients were explored by investigators in Stockholm, Sweden. They analyzed thromboprophylaxis and 28-day mortality among 156 patients with COVID-19-associated respiratory failure admitted to 2 local ICUs. Dosing was dependent on changes in regional guidelines over time and not patient severity. Results illustrated the following:
  - 67 patients on low-dose thromboprophylaxis had a mortality rate of 38.8%
  - 48 patients on medium-dose thromboprophylaxis had a mortality rate of 25%
  - 37 patients on high-dose thromboprophylaxis had the lowest mortality rate of 13.5%

  These findings suggest that starting critically ill patients on high-dose thromboprophylaxis maybe a beneficial strategy in reducing thromboembolic events and mortality.

- Point-of-Care Ultrasound (POCUS) can be useful in managing ICU Patients with COVID-19. In a guideline article, physicians at Prisma Health USC Medical Group in Charleston, South Carolina provide benefits of using POCUS on critically-ill COVID-19 patients at various diagnostic stages, in order to provide accurate and efficient care, while also attempting to decrease contamination of additional instrumentation and reduce viral transmission to hospital staff. They advocate for POCUS as a safe and valuable imaging modality to manage patients throughout the entire ICU course and suggest that it may provide benefits over other modalities for various diagnostic protocols.

Adjusting Practice During COVID-19

- Fewer motor vehicle collisions and higher alcohol involvement were seen in COVID-19 Pandemic trauma presentations in one trauma center. Medical students and physicians from the Medical College of Georgia compared trauma activations at their level 1 trauma center between March 1 and June 15, 2020 to trauma activations from the same time frame in the previous 5 years (2015-2019). While there was no difference in the number and distribution of trauma cases, they found fewer motor vehicle collisions (MVCs) ($p=0.009704$), higher incidence of alcohol involvement in traumas ($p=2.26 \times 10^{-7}$), and longer average length of hospital stay (3.87 vs 5.39; $p=8.488 \times 10^{-6}$) in 2020 compared to pre-pandemic years. Authors suggest the decreased number of MVCs is attributable to fewer drivers during pandemic-related lockdowns but recommend further investigation into factors influencing the observed increase in alcohol related trauma and longer hospital stays to better identify areas of potential preventative interventions.

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IMPACT OF COVID-19 ON WOMEN AND CHILDREN AND THE NEED FOR A GENDERED APPROACH IN VACCINE DEVELOPMENT

Vora KS, Sundararajan A, Saiyed S, Dhama K, Natesan S.. Hum Vaccin Immunother. 2020 Nov 11:1-6. doi: 10.1080/21645515.2020.1826249. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review of 56 papers conducted by public health specialists in Gandhinagar, India assessed gender disparities during the COVID-19 pandemic. They found that during the pandemic, women had increased rates of late preterm birth and abortion but less access to reproductive health services due to facility shut downs. Additionally, women had an overall higher risk of contracting the virus than men in certain countries due to caretaking responsibilities. Authors suggest a gendered approach to vaccine development given that pregnant women and their newborns may be more vulnerable to adverse health consequences due to SARS-CoV-2 infection, and advocate for further research on gender-specific indicators of mortality and morbidity.

ABSTRACT

The COVID-19 pandemic has imposed unprecedented health and socioeconomic challenges on public health, disrupting it on a global scale. Given that women and children are widely considered the most vulnerable in the times of emergency, whether in war or during a pandemic, the current pandemic has also severely disrupted access to reproductive and child health services. Despite this, data on the effect of the pandemic on pregnant women and newborns remain scarce, and gender-disaggregated indicators of mortality and morbidity are not available. In this context, we suggest the implementation of a gendered approach to ensure the specific needs of women and their newborns are considered during the development of COVID-19 vaccines. Taking into account gender-based biological differences, the inclusion of pregnant and lactating mothers in clinical trials for the development of COVID-19 vaccines is of vital importance.

HIGHER PREVALENCE OF PULMONARY MACROTHROMBI IN SARS-COV-2 THAN IN INFLUENZA A: AUTOPSY RESULTS FROM 'SPANISH FLU' 1918/1919 IN SWITZERLAND TO CORONAVIRUS DISEASE 2019

Burkhard-Koren NM, Haberecker M, Maccio U, Ruschitzka F, Schuepbach RA, Zinkernagel AS, Hardmeier T, Varga Z, Moch H.. J Pathol Clin Res. 2020 Nov 13. doi: 10.1002/cjp2.189. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A comparative analysis by pathologists at University Hospital Zurich in Switzerland assessed pulmonary macrothrombi autopsy findings between patients who died from the Influenza A pandemic in 1918/1919 (n=411), Influenza A in 2009-2020 (n=12), and COVID-19 (n=75). They found COVID-19 patients had significantly higher occurrences of grossly visible pulmonary thrombosis despite empiric thrombophylaxis due to in situ clot formation associated with SARS-CoV-2 (Figure 3, Table 1). Authors suggest a specific COVID-19 coagulopathy may be linked to higher mortality rate seen in COVID-19 compared to the seasonal flu.

ABSTRACT

Similar to the influenza A pandemic in 1918/1919, the new Coronavirus disease 2019 (COVID-19) has spread globally. The causes of death in COVID-19 are frequently compared to a seasonal influenza outbreak. Complete COVID-19 autopsy studies were almost non-existent in the first months of the outbreak and are still rare with respect to the number of deaths. It has been recently reported that capillary microthrombi are significantly more prevalent in patients with COVID-19 than in patients with influenza A. To date, the contribution of macrothrombi, i.e. visible thrombi in pulmonary arteries, to the death of patients with influenza A in comparison to COVID-19 remains unaddressed. Here, we report autopsy findings in 411 patients who died from the 'Spanish' influenza A pandemic between May 1918 and April 1919 at the University Hospital Zurich, Switzerland. We compare these results with influenza A autopsies from 2009 to 2020, other influenza A autopsy series and all COVID-19 autopsies published to date. No descriptions of any macroscopic thromboembolic events were mentioned in influenza A autopsy reports. In 75 published COVID-19 autopsies, pulmonary artery thrombosis/embolism was reported in 36%. The direct comparison of macroscopic autopsy findings suggests a significantly greater degree of grossly visible pulmonary macrothrombi in patients with COVID-19 in comparison to influenza A autopsies even though most patients received empiric thromboprophylaxis. This is consistent with the concept of a SARS-related de novo coagulopathy with generalised in situ clot formation, which could explain the high incidence of pulmonary thrombosis/embolism with or without underlying deep vein thrombosis and in the absence of a history of venous thromboembolic events.

Table 1. Autopsy findings in 411 influenza A patients from 1918/1919, 12 influenza A patients from 2009 to 2020 and 75 published COVID-19 patients.

	Influenza A (1918/1919)	Influenza A (2009–2020)	COVID-19 (2019/2020)
Mean age (range), years	28 (1–85)	46 (1–84)	70 (34–96)
Male patients (%)	255 of 411 (62)	3 of 12 (25)	51 of 71 (72)
Obesity (%)*	53 of 333‡ (16)	0	25 of 60‡ (42)
Underweight (%)†	107 of 333‡ (32)	0	1 of 60‡ (2)
Bronchopneumonia (%)	411 (100)	11 of 12 (92)	25 of 75 (33)
Pulmonary arterial thrombosis/embolism (%)	0	0	27 of 75 (36)
Pulmonary infarction (%)	0	0	14 of 75 (19)
DVT (%)	NA	NA	9 of 25‡ (36)
Acute myocardial infarction (%)	0	0	2 of 71‡ (3)
Mesenteric infarction (%)	0	0	3 of 39‡ (8)

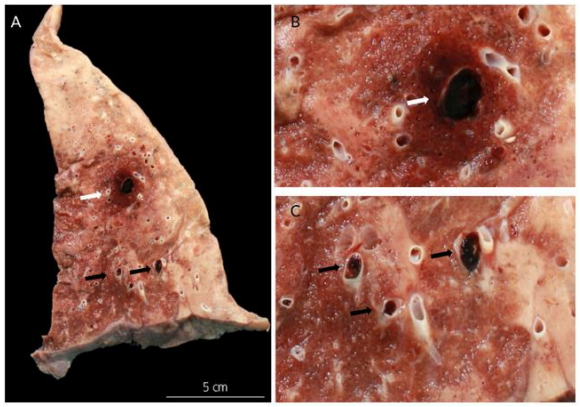


Figure 3. Post-mortem pulmonary gross findings in a COVID-19 patient. (A) Lung of a 81-year old male patient with coronary heart disease and arterial hypertension showing several thrombotic occlusions of large (white arrow) and medium sized (black arrows) arteries. Higher power views of thrombotic occlusion of (B) a large pulmonary artery (white arrow) and (C) medium sized arteries (black arrows).

PREGNANT PERSONS

THE EFFECTS OF PREGNANCY ON WOMEN WITH COVID-19: MATERNAL AND INFANT OUTCOMES

Schwartz DA.. Clin Infect Dis. 2020 Nov 19;71(16):2042-2044. doi: 10.1093/cid/ciaa559.
Level of Evidence: Other - Review / Literature Review

BLUF

A physician from the Medical College of Georgia reviews the potential threat that COVID-19 presents to maternal and newborn outcomes. The author presents studies that may evidence SARS-CoV-2 contributing to complications in pregnant women, such as cardiomyopathy, pneumonia, and even death. Another study, Li et al. (2020), suggests a higher occurrence of premature delivery in COVID-19-positive, pregnant women and states no evidence for intrauterine SARS-CoV-2 transmission. The author suggests that further investigation is warranted to understand maternal and infant outcomes related to COVID-19.

UNDERSTANDING THE PATHOLOGY

IN VIVO DEMONSTRATION OF MICROVASCULAR THROMBOSIS IN SEVERE COVID-19

do Espírito Santo DA, Lemos ACB, Miranda CH.. J Thromb Thrombolysis. 2020 Aug 13. doi: 10.1007/s11239-020-02245-x. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

Researchers in the Department of Internal Medicine, Ribeirão Preto School of Medicine in Brazil conducted imaging via video capillaroscopy of 13 severe COVID-19 positive patients requiring mechanical ventilation (table 1) to assess sublingual microcirculation for evidence of microthrombi and found microthrombi in 11/13 (85%) of patients and acute thromboembolic occlusion in 5/13 (38%) of patients (Fig. 1). This evidence suggests that microvascular thrombosis could be considered a hallmark of COVID-19 and that these microvascular thrombotic events occur systemically, affecting many organ systems.

ABSTRACT

Several autopsy studies showed microthrombi in pulmonary circulation of severe COVID-19 patients. The major limitation of these investigations is that the autopsy provided static information. Some of these alterations could be secondary to the disseminated intravascular coagulation (DIC) observed as the final standard route to the multisystem organ failure exhibited in critically ill patients. We report preliminary results of an in vivo evaluation of sublingual microcirculation in thirteen patients with severe COVID-19 requiring mechanical ventilation. We observed multiple filling defects moving within the microvessels indicative of thrombi in most of the cases 11/13 (85%). This is the first imaging documentation of microvascular thrombosis in living severe COVID-19 patients since the beginning of the hospitalization. The clinical relevance of microvascular thrombosis in this disease requires further research.

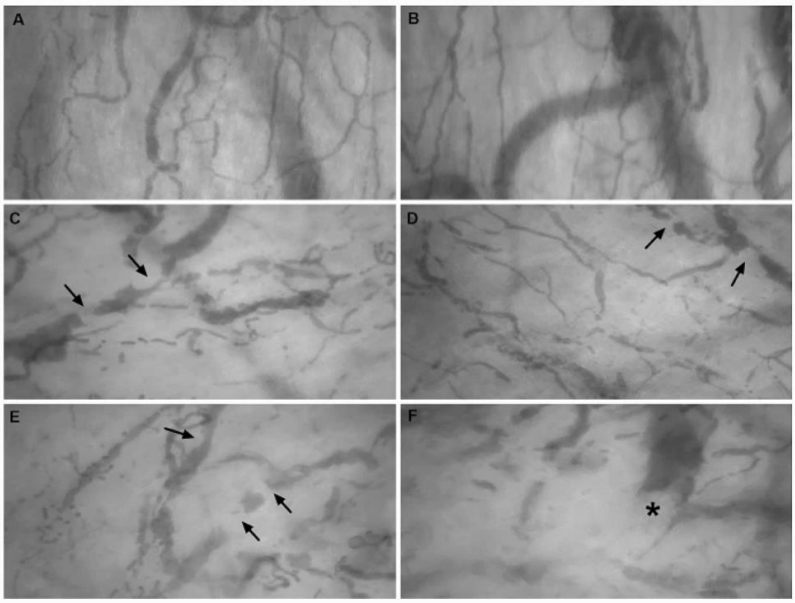
Table 1 Characteristics of the COVID-19 patients in whom sublingual microcirculation was assessed

From: In vivo demonstration of microvascular thrombosis in severe COVID-19

Parameters	n = 13
Demographic	
Age (years), mean ± sd	58 ± 11
Male, n (%)	10 (77)
Clinical presentation	
Fever, n (%)	11 (85)
Cough, n (%)	12 (92)
Dyspnea, n (%)	13 (100)
Myalgia, n (%)	7 (54)
Duration of symptoms (days), median (IQR)	6 (4–9)
Risk factors	
Diabetes mellitus, n (%)	4 (31)
Hypertension, n (%)	4 (31)
Cardiovascular disease, n (%)	1 (08)
Immunocompromise, n (%)	1 (08)
BMI (Kg/m^2), mean ± sd	34 ± 9
Physical Examination	
Systolic blood pressure (mmHg), mean ± sd	120 ± 23
Diastolic blood pressure (mmHg), mean ± sd	74 ± 11
Heart rate (beats per minute), mean ± sd	79 ± 19
Mechanical ventilation, n (%)	13 (100)
Tidal volume (ml), mean ± sd	374 ± 66
PEEP (cm of water), mean ± sd	12 ± 3
Plateau pressure (cm of water), mean ± sd	24 ± 4
Static compliance (ml/cm of water), mean ± sd	33 ± 8
Respiratory rate (cycles/min), mean ± sd	24 ± 4
FiO2 (%), range (min-max)	0.55–1.00
Drugs	
Norepinephrine, n (%)	6 (46)
Midazolam, n (%)	13 (100)
Fentanyl, n (%)	13 (100)
Neuromuscular blocking agent, n (%)	13 (100)
Hydroxychloroquine, n (%)	3 (23)
Macrolide antibiotic, n (%)	13 (100)
Corticosteroids, n (%)	9 (69)
Antiplatelet agents, n (%)	0 (00)
Therapeutic LMWH, n (%)	6 (46)
Prophylactic LMWH, n (%)	7 (54)
Laboratory test	
Hemoglobin (g/dl), mean ± sd	13 ± 2
White-cell count (per microliter), mean ± sd	8232 ± 4149
Platelets count (per microliter), mean ± sd	234,231 ± 55,853
Creatinine clearance (ml/min), mean ± sd	69 ± 18
Creatinine (mg/dl), mean ± sd	1.2 ± 0.3
D-Dimer (µg/L), median (IQR)	1830 (1120–2320)
Fibrinogen (mg/dl), median (IQR)	767 (672–843)
aPTT (Ratio), median (IQR)	1.16 (1.06–1.20)
Prothrombin time (INR), median (IQR)	1.06 (1.03–1.18)
C-reactive protein (mg/L), mean ± sd	18 ± 8
Lactate (mg/dl), mean ± sd	1.7 ± 0.4
PaO2/FiO2 ratio, mean ± sd	128 ± 32
Chest radiography with bilateral opacities, n (%)	13 (100)
Scores, median (IQR)	
SOFA	10 (8–11)
SAPS 3	56 (49–68)
DIC score (ISTH)	2(2–3)
SIC score	2 (2–2)
ARDS classification	
Severe, n (%)	2 (15)
Moderate, n (%)	11 (85)

sd standard deviation, *IQR* interquartile range, *BMI* body mass index, *PEEP* positive end-expiratory pressure, *PaO2* partial pressure of arterial oxygen, *FiO2* fraction of inspired oxygen, *LMWH* low-molecular-weight heparin, *aPTT* activated partial thromboplastin time, *INR* international normalized ratio, *SOFA* sequential organ failure assessment score, *SAPS 3* simplified acute physiology score 3, *DIC* International Society of Thrombosis and Hemostasis criteria for disseminated intravascular coagulation, *SIC* sepsis-induced coagulopathy score, *ARDS* acute respiratory distress syndrome

Fig. 1



Normal sublingual microcirculation in a healthy individual (**a**–**b**). Presence of several filling defects (arrows) moving inside the microvessels indicative of thrombi (**c**–**e**) in severe COVID-19 patients. Microvessel with interrupted flow showing semi-oval imaging (asterisk) in its distal extremity compatible with acute thromboembolic occlusion (**f**) in COVID-19 patient

ASPIRATION OF PERIODONTOPATHIC BACTERIA DUE TO POOR ORAL HYGIENE POTENTIALLY CONTRIBUTES TO THE AGGRAVATION OF COVID-19

Takahashi Y, Watanabe N, Kamio N, Kobayashi R, Iinuma T, Imai K.. J Oral Sci. 2020 Nov 12. doi: 10.2334/josnusd.20-0388. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review by dental specialists from Nihon University School of Dentistry in Japan discusses how aspiration of periodontopathic bacteria (such as P. gingivalis and F. nucleatum) may aggravate the COVID-19 clinical course via increased expression of angiotensin-converting enzyme 2 (ACE2; a known SARS-CoV-2 receptor), degradation of viral protein S, and release of pro-inflammatory cytokines (Figure 1). Authors suggest improved oral care and periodontitis prevention may contribute to COVID-19 aggravation, particularly in patients with poor oral hygiene lacking adequate dental care during the pandemic.

ABSTRACT

Coronavirus infectious disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic in March 2020 by the World Health Organization. Periodontitis, one of the most prevalent diseases worldwide, leads to alveolar bone destruction and subsequent tooth loss, and develops due to pro-inflammatory cytokine production induced by periodontopathic bacteria. Periodontopathic bacteria are involved in respiratory diseases, including aspiration pneumonia and chronic obstructive pulmonary disease (COPD), and other systemic diseases, such as diabetes and cardiovascular disease. Patients with these diseases have an increased COVID-19 aggravation rate and mortality. Because aspiration of periodontopathic bacteria induces the expression of angiotensin-converting enzyme 2, a receptor for SARS-CoV-2, and production of inflammatory cytokines in the lower respiratory tract, poor oral hygiene can lead to COVID-19 aggravation. Conversely, oral care, including periodontal treatment, prevents the onset of pneumonia and influenza and the exacerbation of COPD. The reduced chance of receiving professional oral care owing to long-term hospitalization of patients with COVID-19 may increase the aggravation risk of infection in the lower respiratory tract. It can be hypothesized that

periodontopathic bacteria are involved in the COVID-19 aggravation and therefore, the management of good oral hygiene potentially contributes to its prevention.

FIGURES

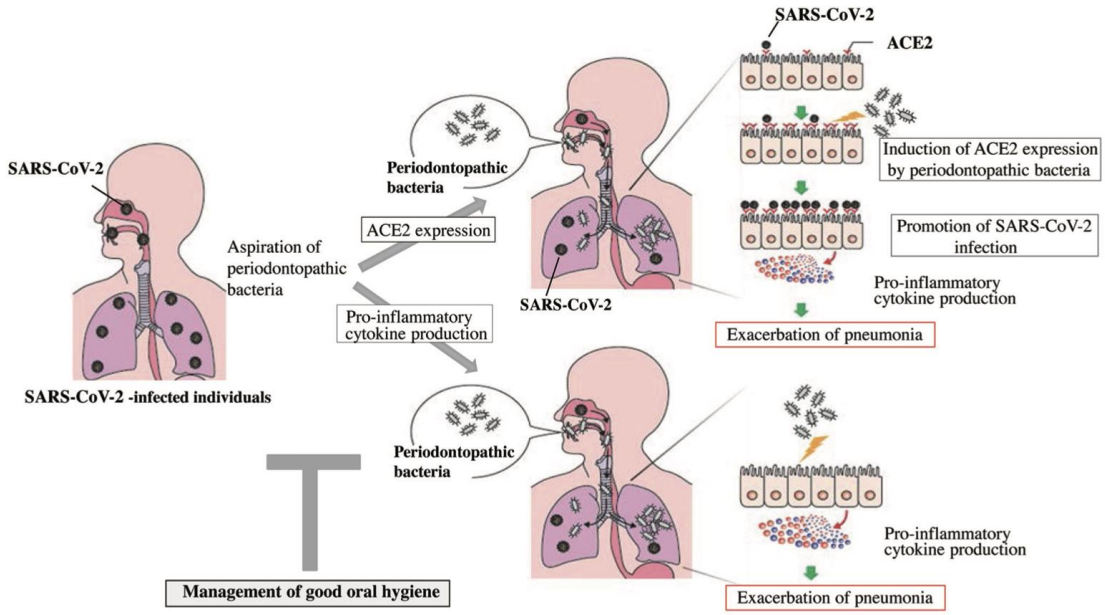


Figure 1. Involvement of periodontopathic bacteria in the aggravation of COVID-19. Aspiration of periodontopathic bacteria in patients with COVID-19 potentially leads to the aggravation of COVID-19 through the induction of inflammatory cytokine production, ACE2 expression, and cleavage of the S protein of SARS-CoV-2. Management of oral hygiene is therefore important in patients with mild COVID-19 as it may help prevent the aggravation of COVID-19.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

WEB EXCLUSIVE. ANNALS ON CALL - A PRIMER ON COVID-19 VACCINES

Centor RM, Goepfert P.. Ann Intern Med. 2020 Nov 24:OC1. doi: 10.7326/A19-0044. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Internists from the University of Alabama host an episode of the Annals On Call podcast and provide a brief overview of SARS-CoV-2 vaccines. After reviewing how vaccines function, the hosts explain the two protein targets (spike and E-proteins) and the three primary approaches for expressing target proteins (mRNA, adenovirus, and recombinant protein)(see summary). They also cover upcoming challenges in distribution and storage of vaccines, and remaining unknowns such as the need for booster doses, vaccine side effects, and efficacy in older patients (Summary). The podcast concludes by encouraging physicians to trust the US Food and Drug Administration approval process and to advocate for vaccinations.

SUMMARY

Link to Podcast:
https://www.acpjournals.org/doi/10.7326/A19-0044

Moderna and Pfitzer are both conducting phase III efficacy studies on COVID-19 vaccines using the mRNA approach. Astrazeneca and Janssen are employing the adenovirus approach and are currently enrolling patients. Novavax and Sanofi are developing vaccines with the recombinant protein approach and will be enrolling patients soon. Although efficacy studies are enrolling >25% of patients over the age of 65, the majority of patients in these studies are of the younger age range, so it is unclear if the vaccine will be effective in the older populations.

CRITICAL CARE

DOSING OF THROMBOPROPHYLAXIS AND MORTALITY IN CRITICALLY ILL COVID-19 PATIENTS

Jonmarker S, Hollenberg J, Dahlberg M, Stackelberg O, Litorell J, Everhov ÅH, Järnbert-Pettersson H, Söderberg M, Grip J, Schandl A, Günther M, Cronhjort M.. Crit Care. 2020 Nov 23;24(1):653. doi: 10.1186/s13054-020-03375-7.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

In this retrospective cohort study, investigators in Stockholm, Sweden analyzed thromboprophylaxis and 28-day mortality among 156 patients with COVID-19-associated respiratory failure admitted to 2 local ICUs in March and April, 2020. Dosing was dependent on changes in regional guidelines over time and not patient severity. Results illustrated the following (Table 2, Figure 1):
- 67 patients on low-dose thromboprophylaxis had a mortality rate of 38.8%
- 48 patients on medium-dose thromboprophylaxis had a mortality rate of 25%
- 37 patients on high-dose thromboprophylaxis had the lowest mortality rate of 13.5%

These findings suggest that starting critically ill patients on high-dose thromboprophylaxis maybe a beneficial strategy in reducing thromboembolic events and mortality.

SUMMARY

Patients in this study were placed into three groups based on the dosing of thromboprophylaxis (either tinzaparin or dalteparin):

-low (2500–4500 IU tinzaparin or 2500–5000 IU dalteparin)
-medium (greater than 4500 IU but less than 175 IU/kilogram, kg, of body weight tinzaparin or greater tahn 5000 IU but less than 200 IU/kg of body weight dalteparin)
- high dose (greater than or equal to 175 IU/kg of body weight tinzaparin or greater than or equal to 200 IU/kg of body weight dalteparin

ABSTRACT

BACKGROUND: A substantial proportion of critically ill COVID-19 patients develop thromboembolic complications, but it is unclear whether higher doses of thromboprophylaxis are associated with lower mortality rates. The purpose of the study was to evaluate the association between initial dosing strategy of thromboprophylaxis in critically ill COVID-19 patients and the risk of death, thromboembolism, and bleeding. METHOD: In this retrospective study, all critically ill COVID-19 patients admitted to two intensive care units in March and April 2020 were eligible. Patients were categorized into three groups according to initial daily dose of thromboprophylaxis: low (2500-4500 IU tinzaparin or 2500-5000 IU dalteparin), medium (> 4500 IU but < 175 IU/kilogram, kg, of body weight tinzaparin or > 5000 IU but < 200 IU/kg of body weight dalteparin), and high dose (>= 175 IU/kg of body weight tinzaparin or >= 200 IU/kg of body weight dalteparin). Thromboprophylaxis dosage was based on local standardized recommendations, not on degree of critical illness or risk of thrombosis. Cox proportional hazards regression was used to estimate hazard ratios with corresponding 95% confidence intervals of death within 28 days from ICU admission. Multivariable models were adjusted for sex, age, body mass index, Simplified Acute Physiology Score III, invasive respiratory support, and initial dosing strategy of thromboprophylaxis. RESULTS: A total of 152 patients were included: 67 received low-, 48 medium-, and 37 high-dose thromboprophylaxis. Baseline characteristics did not differ between groups. For patients who received high-dose prophylaxis, mortality was lower (13.5%) compared to those who received medium dose (25.0%) or low dose (38.8%), p = 0.02. The hazard ratio of death was 0.33 (95% confidence intervals 0.13-0.87) among those who received high dose, and 0.88 (95% confidence intervals 0.43-1.83) among those who received medium dose, as compared to those who received low-dose thromboprophylaxis. There were fewer thromboembolic events in the high (2.7%) vs medium (18.8%) and low-dose thromboprophylaxis (17.9%) groups, p = 0.04. CONCLUSIONS: Among critically ill COVID-19 patients with respiratory failure, high-dose thromboprophylaxis was associated with a lower risk of death and a

lower cumulative incidence of thromboembolic events compared with lower doses. TRIAL REGISTRATION: Clinicaltrials.gov NCT04412304 June 2, 2020, retrospectively registered.

FIGURES

	Total ($n=152$)	Initial dosing strategy of thromboprophylaxis			p-value[d]
		Low dose[a] ($n=67$)	Medium dose[b] ($n=48$)	High dose[c] ($n=37$)	
Primary outcome					
28-day mortality, No. (%)	43 (28.3)	26 (38.8)	12 (25.0)	5 (13.5)	0.02
Secondary outcomes					
ICU-free days alive during 28 days from ICU-admission, days	9 (0–21)	0 (0–20)	11 (0–19)	18 (0–26)	0.07
Thromboembolic events < 28 days, No. (%)	22 (14.5)	12 (17.9)	9 (18.8)	1 (2.7)	0.04
Pulmonary embolism, No. (%)	17 (11.2)	10 (14.9)	6 (12.5)	1 (2.7)	0.15
Deep vein thrombosis, No. (%)	4 (2.6)	1 (1.5)	3 (6.3)	0 (0.0)	0.21
Ischemic stroke, No. (%)	4 (2.7)	4 (6.0)	0 (0.0)	0 (0.0)	0.16
Other thrombotic event, No. (%)	3 (2.0)	2 (3.0)	1 (2.1)	0 (0.0)	0.79
Time to event, days	8 (6–17)	8 (6–20)	8 (6–10)	11 (11–11)	0.61
Bleeding events < 28 days, No. (%)	16 (10.5)	8 (11.9)	7 (14.6)	1 (2.7)	0.16
Cerebral parenchymal bleeding, No. (%)	2 (1.3)	2 (3.0)	0 (0.0)	0 (0.0)	0.50
WHO bleeding assessment score					
Grade I—minor, No. (%)	8 (5.3)	3 (4.5)	4 (8.3)	1 (2.7)	0.58
Grade II—moderate, No. (%)	3 (2.0)	2 (3.0)	1 (2.1)	0 (0.0)	0.79
Grade III—major, No. (%)	2 (1.3)	1 (1.5)	1 (2.1)	0 (0.0)	0.99
Grade IV—severe, No. (%)	3 (2.0)	2 (3.0)	1 (2.1)	0 (0.0)	0.79
Time to bleeding event, days	13 (8–18)	16 (6–20)	11 (10–20)	1 (1–1)	0.36
Lab characteristics					
Fibrin-D-dimer, mg/L FEU, highest	3.2 (1.2–9.9)	6.4 (2.0–14.6)	2.8 (1.2–9.4)	1.7 (0.7–3.3)	0.002
CRP, mg/L, highest	282 (183–381)	335 (200–423)	290 (201–385)	229 (162–319)	0.01
Hemoglobin, g/L, lowest	98 (85–113)	94 (80–104)	102 (94–116)	107 (95–118)	0.01
Creatinine, µmol/L, highest	82 (64–158)	100 (78–236)	78 (55–139)	66 (49–74)	< 0.001
Platelet count, 10^9/L, lowest	239 (180–322)	203 (164–282)	257 (197–290)	314 (218–370)	0.003
INR, highest	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.0 (1.0–1.1)	0.18

Primary and secondary outcomes during the first 28 days among 152 patients admitted to the intensive care unit due to COVID-19 at Södersjukhuset, Stockholm, March 6 to April 30, 2020, by initial dosing strategy with tinzaparin/dalteparin as thromboprophylaxis

Values are medians (interquartile range) unless otherwise indicated. p-values for differences across exposure categories were obtained using Fisher´s exact test for categorical, and Kruskal Wallis for continuous, data. CRP, C-reactive protein; ICU, intensive care unit; OD, once a day; IQR, interquartile range; WHO, World Health Organization

[a] Tinzaparin, 2500–4500 IU OD; or dalteparin, 2500–5000 IU OD

[b] Tinzaparin, > 4500 IU OD to < 175 IU/kg of body weight OD; or dalteparin, > 5000 IU OD to < 200 IU/kg of body weight OD

[c] Tinzaparin, ≥ 175 IU/kg of body weight OD; or dalteparin, ≥ 200 IU/kg of body weight OD

[d] p values for differences across exposure categories were obtained using Fisher's exact test for categorical and Kruskal–Wallis test for continuous data

Table 2. Outcomes by initial dosing strategy of thromboprophylaxis.

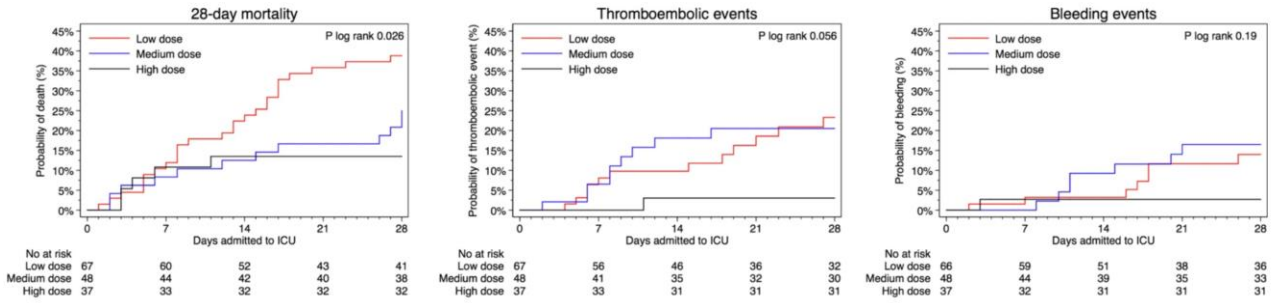


Figure 1. Kaplan–Meier plots of outcomes by initial dosing strategy of thromboprophylaxis. Kaplan–Meier plot of a 28-day survival, b thromboembolic events, and c bleeding events, among 152 patients admitted to the ICU due to COVID-19 between March 6 and April 30, 2020. By thromboprophylactic anticoagulant strategy with tinzaparin/dalteparin: The red line represent low-dose thromboprophylaxis (2500–4500 IU of tinzaparin daily, or 2500–5000 IU of dalteparin daily), the blue line represent medium-dose thromboprophylaxis (> 4500 IU to < 175 IU/kg of body weight of tinzaparin daily, or > 5000 IU to < 200 IU/kg of body weight of dalteparin daily), and the black line represent high-dose thromboprophylaxis (≥ 175 IU/kg of body weight of tinzaparin daily, or ≥ 200 IU/kg of body weight of dalteparin daily). Thromboembolic events in b are defined as pulmonary embolism, deep vein thrombosis, ischemic stroke, or peripheral arterial embolism. Hemorrhagic events in c are defined as grade 1–4 in the WHO bleeding scale

THE USE OF POCUS TO MANAGE ICU PATIENTS WITH COVID-19

Schrift D, Barron K, Arya R, Choe C.. J Ultrasound Med. 2020 Nov 11. doi: 10.1002/jum.15566. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

In this guideline article, physicians at Prisma Health USC Medical Group in Charleston, South Carolina provide benefits of using point-of-care ultrasound (POCUS) on critically-ill COVID-19 patients at various diagnostic stages, in order to provide accurate and efficient care, while also attempting to decrease contamination of additional instrumentation and reduce viral transmission to hospital staff. They advocate for POCUS as a safe and valuable imaging modality to manage patients throughout the entire ICU course, and suggest that it may provide benefits over other modalities for various diagnostic protocols (see summary).

SUMMARY

Diagnostic protocols as outlined by this article:
- Baseline scan to establish pulmonary, cardiac, and systemic vascular status
- Repeat evaluation for change in patient status
- Evaluate central venous catheter (CVC) placement
- Monitor for coagulopathies including deep vein thrombosis (DVT) and pulmonary embolism (PE)
- Weaning scans for intubated patients including 12-zone lung scan with point system to evaluate underlying respiratory failure, remaining modifiable lung pathology, and likelihood of successful extubating

ABSTRACT

Since the advent of SARS-CoV-2, the virus that causes COVID-19, clinicians have had to modify how they provide high-value care while mitigating the risk of viral spread. Routine imaging studies have been discouraged due to elevated transmission risk. Patients who have been diagnosed with COVID-19 often have a protracted hospital course with progression of disease. Given the need for close follow-up of patients, we recommend the use of ultrasonography, particularly point-of-care ultrasound (POCUS), to manage patients with COVID-19 through their entire ICU course. POCUS will allow a clinician to evaluate and monitor cardiac and pulmonary function, as well as evaluate for thromboembolic disease, place an endotracheal tube, confirm central venous catheter placement, and rule out a pneumothorax. If a patient improves sufficiently to perform weaning trials, POCUS can also help evaluate readiness for ventilator liberation.

MEDICAL SUBSPECIALTIES

ENDOCRINOLOGY

THYROID FUNCTION BEFORE, DURING AND AFTER COVID-19

Khoo B, Tan T, Clarke SA, Mills EG, Patel B, Modi M, Phylactou M, Eng PC, Thurston L, Alexander EC, Meeran K, Comninos AN, Abbara A, Dhillo WS.. J Clin Endocrinol Metab. 2020 Nov 12:dgaa830. doi: 10.1210/clinem/dgaa830. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

An observational controlled cohort study by endocrinologists in London, UK investigated thyroid function in COVID-19 patients (n=334) versus non-COVID-19 patient controls (n=122) and found COVID-19 patients had mildly reduced TSH and free T4 (FT4) on admission, but 86.6% of all patients were classified as euthyroid (Table 2) and COVID-19 patients with known baseline values showed a return to their euthymic baseline state post-recovery (Figure 3). Authors report these data may be limited by lack of free T3 (FT3) and reverse T3 measurements but suggest continuous thyroid monitoring may not be necessary in COVID-19 patients, unless the patient has preexisting thyroid disease.

ABSTRACT

CONTEXT: The effects of COVID-19 on the thyroid axis remain uncertain. Recent evidence has been conflicting, with both thyrotoxicosis and suppression of thyroid function reported. OBJECTIVE: We aimed to detail the acute effects of COVID-19 on

thyroid function and determine if these effects persisted upon recovery from COVID-19. DESIGN: Cohort observational study. PARTICIPANTS AND SETTING: Adult patients admitted to Imperial College Healthcare National Health Service Trust, London, UK with suspected COVID-19 between March 9 to April 22, 2020 were included, excluding those with pre-existing thyroid disease and those missing either free thyroxine (FT4) or TSH measurements. Of 456 patients, 334 had COVID-19 and 122 did not. MAIN OUTCOME MEASURES: TSH and FT4 measurements at admission, and where available, those taken in 2019 and at COVID-19 follow-up. RESULTS: Most patients (86 6%) presenting with COVID-19 were euthyroid, with none presenting with overt thyrotoxicosis. Patients with COVID-19 had a lower admission TSH and FT4 compared to those without COVID-19. In the COVID-19 patients with matching baseline thyroid function tests from 2019 (n=185 for TSH and 104 for FT4), both TSH and FT4 were reduced at admission compared to baseline. In a complete cases analysis of COVID-19 patients with TSH measurements at follow-up, admission and baseline (n=55), TSH was seen to recover to baseline at follow-up. CONCLUSIONS: Most patients with COVID-19 present with euthyroidism. We observed mild reductions in TSH and FT4 in keeping with a non-thyroidal illness syndrome. Furthermore, in survivors of COVID-19, thyroid function tests at follow-up returned to baseline.

FIGURES

	FT4 pmol/L	**TSH mU/L**	**All**	**COVID-19 Neg**	**COVID-19 Positive**				
	9·0-23·0	*0·30-4·20*			*COVID-19 Pos*	*Surv*	*Non-surv*	*Not ITU adm*	*ITU adm*
Euthyr	↔	↔	395 (86·6%)	106 (86·9%)	289 (86·5%)	211 (88·3%)	78 (82·1%)	258 (87·8%)	31 (77·5%)
Hyper	↑	↓	0	0	0	0	0	0	0
Hypo	↓	↑	2 (0·4%)	0	2 (0·6%)	2 (0·8%)	0	2 (0·7%)	0
SC hyper	↔	↓	26 (5·7%)	8 (6·6%)	18 (5·4%)	12 (5·0%)	6 (6·3%)	13 (4·4%)	5 (12·5%)
SC hypo	↔	↑	24 (5·3%)	7 (5·7%)	17 (5·1%)	9 (3·8%)	8 (8·4%)	15 (5·1%)	2 (5·0%)
Sec hyper	↑	↔	0	0	0	0	0	0	0
Sec hypo	↓	↔	9 (2·0%)	1 (0·8%)	8 (2·4%)	5 (2·1%)	3 (3·2%)	6 (2·0%)	2 (5·0%)
p-values				0·826		0·337		0·129	

Table 2. Thyroid diagnostic categories in patients diagnosed with COVID-19 and without COVID-19. Patients were classified into diagnostic categories according to the pattern of results falling below, within or above the indicated reference ranges. P-values calculated using Fisher's exact test for the comparison between COVID-19 negative and positive patients, COVID-19 positive survivors and non-survivors, and COVID-19 patients admitted and not admitted to ITU are shown below. Euthyr, euthyroid; Hyper, hyperthyroid; Hypo, hypothyroid; SC, subclinical; Sec, secondary.

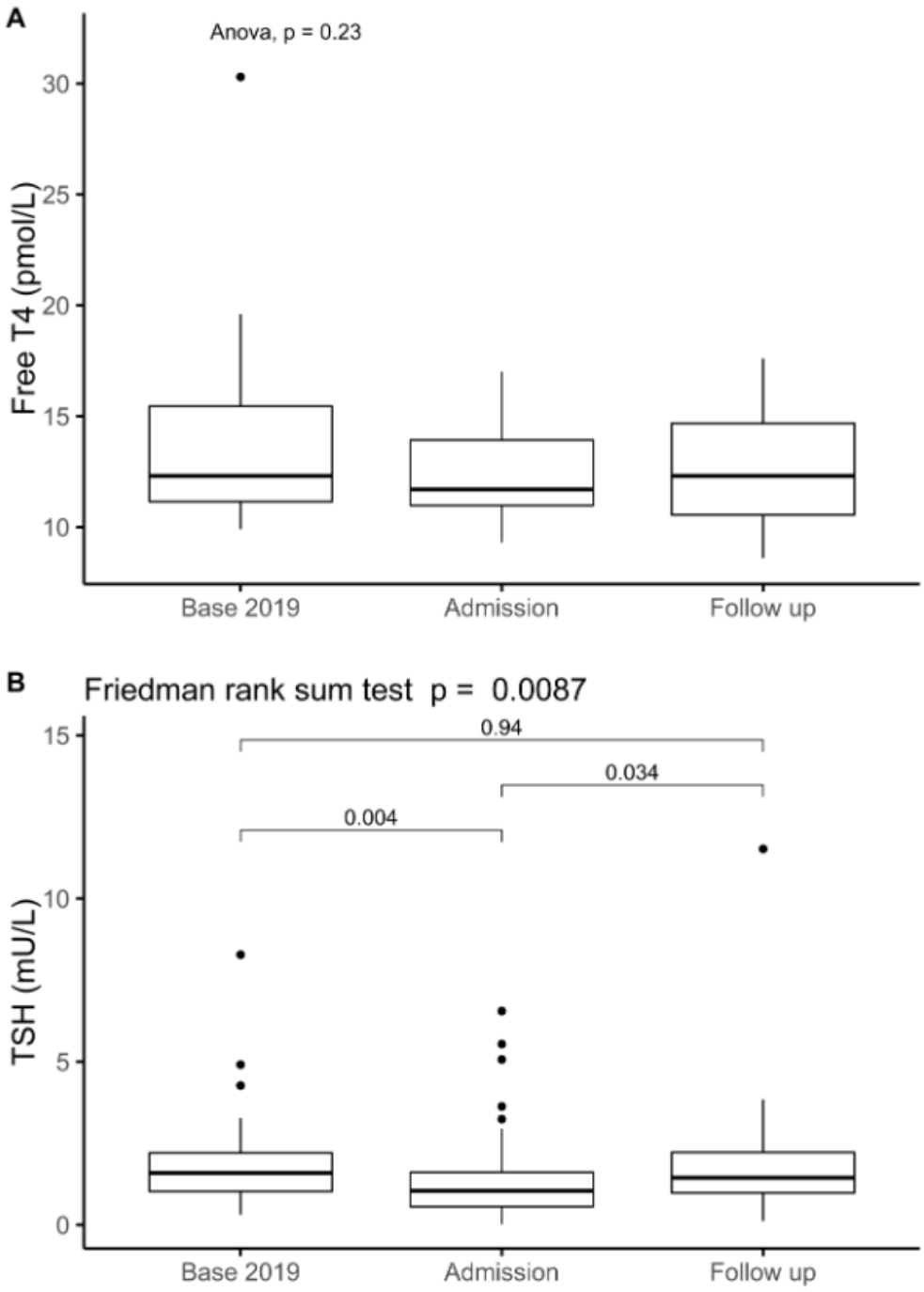


Figure 3. Longitudinal study of TSH and FT4 using 2019 baseline, admission and follow up measurements. Free T4 (A, n=20) and TSH (B, n=50) measurements are plotted against the timepoint they were taken (baseline in 2019, admission with COVID-19 and Follow up). Repeated measures one-way ANOVA or Friedman rank sum test performed as indicated. Pairwise comparisons of TSH were performed with paired Wilcoxon signed-rank tests, with Bonferroni adjustment.

EMERGENCY MEDICINE

THE EFFECTS OF THE COVID-19 PANDEMIC ON TRAUMA PRESENTATIONS IN A LEVEL ONE TRAUMA CENTER

Devarakonda AK, Wehrle CJ, Chibane FL, Drevets PD, Fox ED, Lawson AG.. Am Surg. 2020 Nov 24:3134820973715. doi: 10.1177/0003134820973715. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Medical students and physicians from the Medical College of Georgia conducted a retrospective cohort study comparing trauma activations at their level 1 trauma center between March 1 and June 15, 2020 to trauma activations from the same time frame in the previous 5 years (2015-2019). While there was no difference in the number and distribution of trauma cases, they found fewer motor vehicle collisions (MVCs)(p=0.009704), higher incidence of alcohol involvement in traumas (p=2.26 × 10^-7), and longer average length of hospital stay (3.87 vs 5.39; p=8.488 × 10^-6) in 2020 compared to pre-pandemic years (Table 1). Authors suggest the decreased number of MVCs is attributable to fewer drivers during pandemic-related lockdowns, but recommend further investigation into factors influencing the observed increase in alcohol related trauma and longer hospital stays to better identify areas of potential preventative interventions.

ABSTRACT

BACKGROUND: Over 28 million confirmed cases of COVID-19 have been reported to date, resulting in over 900 000 deaths. With an increase in awareness regarding the virus, the behavior of general population has changed dramatically. As activities such as driving and hospital presentation patterns have changed, our study aimed to assess the differences in trauma case variables before and during the COVID-19 pandemic. METHODS: Trauma data for the period of March 1st-June 15th were compared for the years 2015-2019 (pre-COVID) and 2020 (COVID). The data were analyzed across the following categories: injury severity score, injury mechanism, motor vehicle crashes (MVCs) vs. other blunt injuries, alcohol involvement, and length of hospital stay. RESULTS: The median injury severity score pre-COVID and during COVID was 9, representing no change. There was no difference in overall distribution of mechanism of injury; however, there was a significant decrease in the percentage of MVCs pre-COVID (36.39%) vs. COVID (29.6%, P < .05). Alcohol was significantly more likely to be involved in trauma during COVID-19 (P < .05). The mean hospital stay increased from 3.87-5.4 days during COVID-19 (P < .05). DISCUSSION: We saw similar results to prior studies in terms of there being no change in trauma severity. Our observation that motor vehicle collisions have decreased is consistent with current data showing decreased use of motor vehicles during the pandemic. We also observed an increase in alcohol-related cases which are consistent with the reported changes in alcohol consumption since the pandemic began.

FIGURES

Table 1. Changes in Trauma Variables Before and After COVID-19.

Topic		Data					
ISS score		Average	Median	Standard deviation	N		*P*-value
	Pre-COVID	10.51	9	9.00	3032		.2018
	COVID	10.18	9	7.23	464		
Injury type		Blunt	Burn	Penetrating	Other	Total	*P*-value
	Pre-COVID	2531 (83.5%)	9 (.3%)	473 (15.6%)	19 (.62%)	3032	.3504
	COVID	409 (84.7%)	1 (.21%)	73 (15.1)	0 (0%)	483	
Blunt vs. MVC		MVC	Other blunt	Total			*P*-value
	Pre-COVID	921 (36.39%)	1610 (63.61%)	2531			.009704
	COVID	119 (29.60%)	282 (70.40%)	402			
Alcohol involvement		Yes	No	Total			*P*-value
	Pre-COVID	475	2545	3020			2.26×10^{-07}
	COVID	122	358	480			
Average length of stay		Mean	Median	Standard deviation	N		*P*-value
	Pre-COVID	3.87	2	6.04	3033		8.488×10^{-06}
	COVID	5.39	2	9.58	574		

Abbrevations: ISS, injury severity score; MVC, motor vehicle collision.

UV-PHOTOKERATITIS ASSOCIATED WITH GERMICIDAL LAMPS PURCHASED DURING THE COVID-19 PANDEMIC

Sengillo JD, Kunkler AL, Medert C, Fowler B, Shoji M, Pirakitikulr N, Patel N, Yannuzzi NA, Verkade AJ, Miller D, Slin ey DH, Parel JM, Amescua G.. Ocul Immunol Inflamm. 2020 Nov 20:1-5. doi: 10.1080/09273948.2020.1834587. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

Ophthalmologists from Bascom Palmer Eye Institute in Florida reported 7 cases of UV-associated photokeratitis after using germicidal lamps occuring between April 1 and July 19, 2020 (Figures 1, 2), the majority of whom (n=5/6, 1 lost to follow-up) reported resolution of symptoms after two to three days. Because the public continues to use UV lamps as a sterilization strategy against SARS-CoV-2 despite lack of evidence for their efficacy, authors suggest physicians should be vigilant about educating patients against misuse of germicidal lamps that can lead to eye damage.

ABSTRACT

PURPOSE: To report photokeratitis caused by the improper use of germicidal lamps purchased during the COVID-19 pandemic. METHODS: Case series. RESULTS: Seven patients presented with acute ocular surface pain after exposure to UV-emitting germicidal lamps. Visual acuity was 20/30 or better in 13 of 14 eyes (93%). Anterior segment examination revealed varying degrees of conjunctival injection and diffusely distributed punctate epithelial erosions (PEEs) in every patient. No intraocular inflammation was identified across the cohort and all fundus examinations were normal. Treatment varied by provider and included artificial tears alone or in combination with antibiotic ointments and/or topical steroids. Five patients were followed via telehealth, one patient returned for an in-office visit, and one patient was lost to follow-up. Five of six patients endorsed complete resolution of symptoms within 2-3 days. CONCLUSIONS: Patients should follow manufacturer recommendations when using UV-emitting germicidal lamps and avoid direct exposure to the ocular surface.

FIGURES

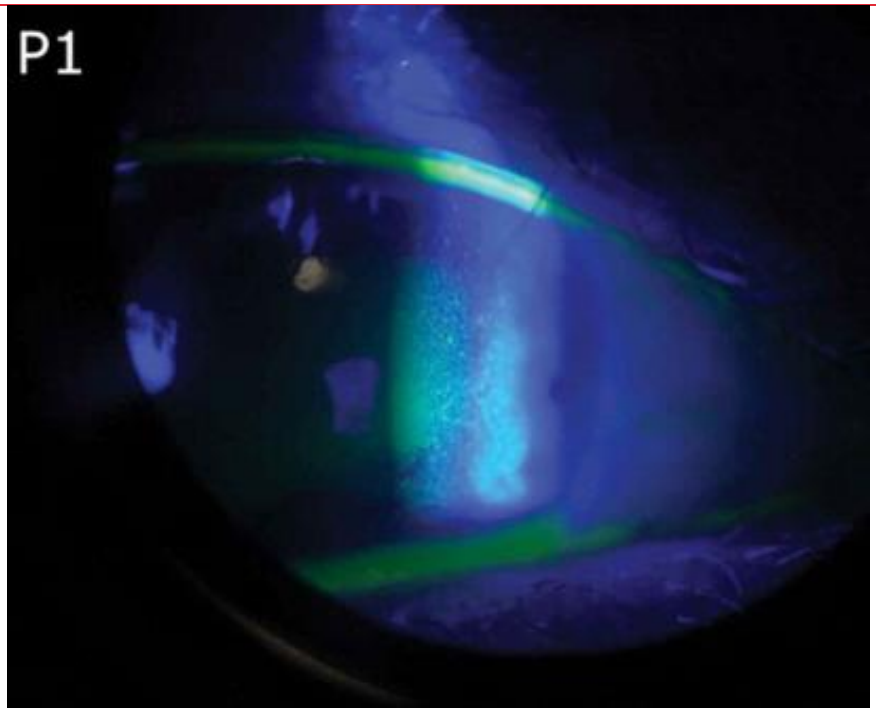


Figure 1. Slit-lamp photography of patient P1 with UV photokeratitis following exposure to a germicidal lamp. Dense confluent PEEs are seen over the central cornea with fluorescein stain under a cobalt blue filter. A characteristic limitation of injury to the interpalpebral area is observed

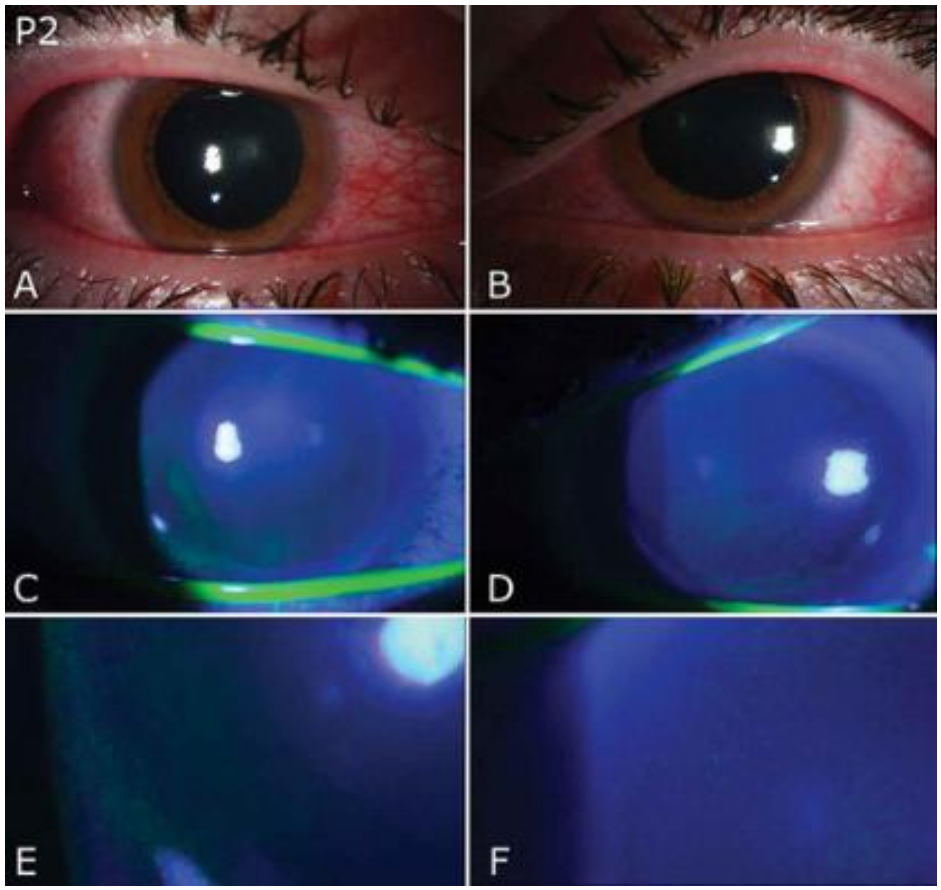


Figure 2. Slit-lamp photography of a both eyes of a patient (P2) with photokeratitis due to germicidal lamp exposure. Diffuse conjunctival injection is seen in in the right (a) and left (b) eyes. Diffuse PEEs with fluorescein stain are seen under cobalt blue light with fluorescein stain of the right (c) and left (d) eyes. High magnification of epithelial erosions of the right (e) and left (f) eyes

EFFECTIVE OPTIMIZATION OF SARS-COV-2 LABORATORY TESTING VARIABLES IN AN ERA OF SUPPLY CHAIN CONSTRAINTS

S Sahajpal N, Mondal AK, Njau A, Ananth S, Jones K, Ahluwalia PK, Ahluwalia M, Jilani Y, Chaubey A, Hegde M, Kota V, Rojiani A, Kolhe R.. Future Microbiol. 2020 Nov 12:1483-1487. doi: 10.2217/fmb-2020-0094. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

Pathologists from Augusta University in Georgia provide recommendations to optimize SARS-CoV-2 testing given the ongoing shortage of sample collection materials and test reagents. They propose that a volume reduction of RT-PCR reagents may achieve similarly reliable results (Figure 2) and discuss the utilization of various RT-PCR media compositions (Figure 1) and the use of alternative sample collection methods compatible with RT-PCR (nasopharyngeal swabs, ESwab or 3D-printed swabs preserved in viral transport media, universal transport media, 0.9% sodium chloride or Amies media). The authors acknowledge that mass population testing is limited by instrumentation and economic resources but propose these recommendations in hopes of optimizing testing capabilities during the COVID-19 pandemic.

ABSTRACT

RT-PCR-based assays for the detection of SARS-CoV-2 have played an essential role in the current COVID-19 pandemic. However, the sample collection and test reagents are in short supply, primarily due to supply chain issues. Thus, to eliminate testing constraints, we have optimized three key process variables: RNA extraction and RT-PCR reactions, different sample types and media to facilitate SARS-CoV-2 testing. By performing various validation and bridging studies, we have shown that various sample types such as nasopharyngeal swab, bronchioalveolar lavage and saliva, collected using conventional nasopharyngeal swabs, ESwab or 3D-printed swabs and, preserved in viral transport media, universal transport media, 0.9% sodium chloride or Amies media are compatible with RT-PCR assay for COVID-19. Besides, the reduction of PCR reagents by up to fourfold also produces reliable results.

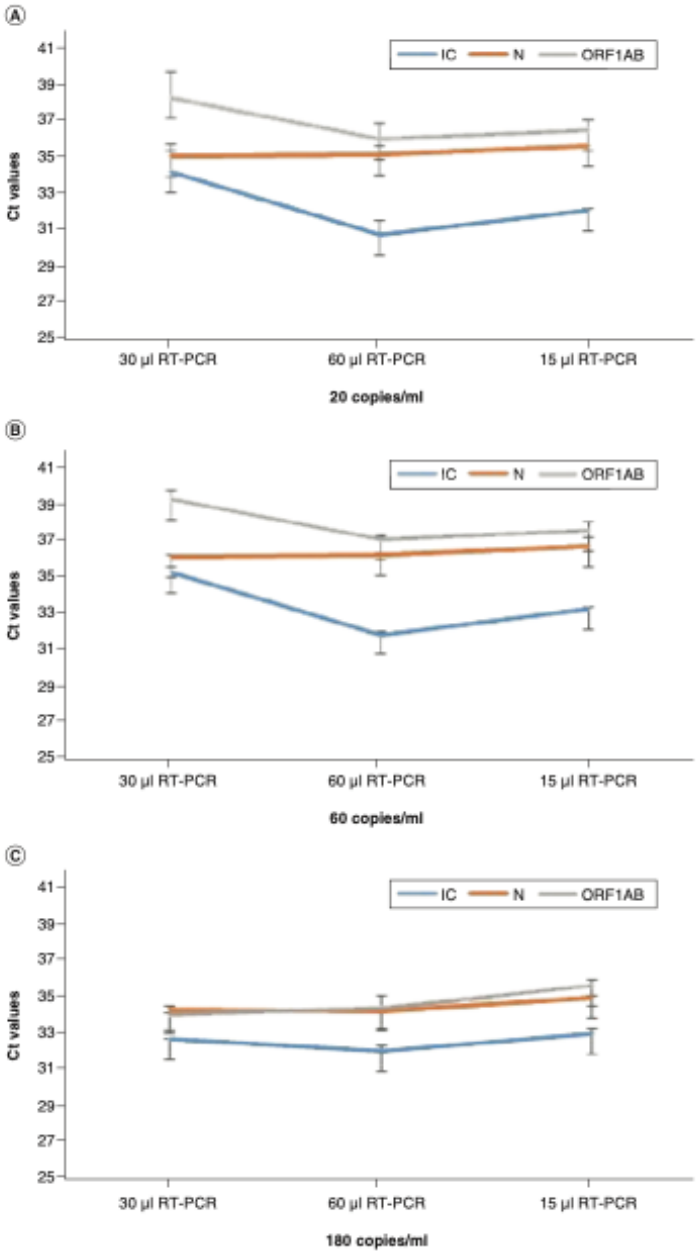


Figure 2. Optimization of RT-PCR analytical variables. Comparison of cycle threshold values of SARS-CoV-2 control **(A)** 20 copies/ml, **(B)** 60 copies/ml and **(C)** 180 copies/ml with 30 µl, 60 µl and 15 µl RT-PCR reaction volumes performed on QuantStudio 3. All data points were in triplicate.

Figure 2. Optimization of RT-PCR analytical variables. Comparison of cycle threshold values of SARS-CoV-2 control (A) 20 copies/ml, (B) 60 copies/ml and (C) 180 copies/ml with 30 µl, 60 µl and 15 µl RT-PCR reaction volumes performed on QuantStudio 3. All data points were in triplicate.

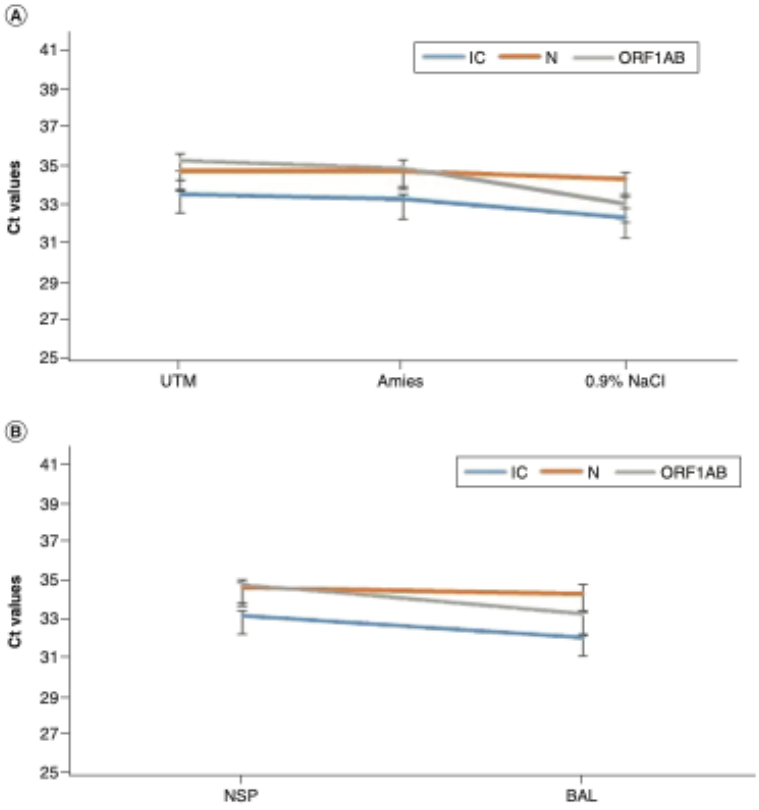


Figure 1. Representative comparison of pre-analytical process variables. (A) Comparison of cycle threshold values of SARS-CoV-2 control (60 copies/ml) in UTM versus Amies versus 0.9% NaCl. **(B)** Comparison of cycle threshold values of SARS-CoV-2 control (60 copies/ml) in negative NPS versus BAL samples. All data points were in triplicate.
BAL: Bronchioalveolar lavage; Ct: Cycle threshold; NPS: Nasopharyngeal swab; UTM: Universal transport media.

Figure 1. Representative comparison of pre-analytical process variables. (A) Comparison of cycle threshold values of SARS-CoV-2 control (60 copies/ml) in UTM versus Amies versus 0.9% NaCl. (B) Comparison of cycle threshold values of SARS-CoV-2 control (60 copies/ml) in negative NPS versus BAL samples. All data points were in triplicate. BAL: Bronchioalveolar lavage; Ct: Cycle threshold; NPS: Nasopharyngeal swab; UTM: Universal transport media.

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