New Research
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COVID-19 related publications by Providence caregivers – see Digital Commons

Clinical Syndrome


Findings: The COVID-19 pandemic is an unprecedented healthcare emergency causing mortality and illness across the world. Although primarily affecting the lungs, the SARS-CoV-2 virus also affects the cardiovascular system. In addition to cardiac effects, e.g. myocarditis, arrhythmias, and myocardial damage, the vasculature is affected in COVID-19, both directly by the SARS-CoV-2 virus, and indirectly as a result of a systemic inflammatory cytokine storm. This includes the role of the vascular endothelium in the recruitment of inflammatory leucocytes where they contribute to tissue damage and cytokine release, which are key drivers of acute respiratory distress syndrome (ARDS), in disseminated intravascular coagulation, and cardiovascular complications in COVID-19. There is also evidence linking endothelial cells (ECs) to SARS-CoV-2 infection including: (i) the expression and function of its receptor angiotensin-converting enzyme 2 (ACE2) in the vasculature; (ii) the prevalence of a Kawasaki disease-like syndrome (vasculitis) in COVID-19; and (iii) evidence of EC infection with SARS-CoV-2 in patients with fatal COVID-19. Here, the Working Group on Atherosclerosis and Vascular Biology together with the Council of Basic Cardiovascular Science of the European Society of Cardiology provide a Position Statement on the importance of the endothelium in the underlying pathophysiology behind the clinical presentation in COVID-19 and identify key questions for future research to address. We propose that endothelial biomarkers and tests of function (e.g. flow-mediated dilatation) should be evaluated for their usefulness in the risk stratification of COVID-19 patients. A better understanding of the effects of SARS-CoV-2 on endothelial biology in both the micro- and macrovasculature is required, and endothelial function testing should be considered in the follow-up of convalescent COVID-19 patients for early detection of long-term cardiovascular complications.

Findings: We reported a case series of 26 HIV-infected patients with COVID-19. Nineteen subjects were men, the median age was 54 years, 73% of patients had one or more comorbidities. Only 5 patients with interstitial pneumonia were hospitalized, but there were no admissions to intensive care unit and no deaths. In our experience, COVID-19 associated with HIV infection had a clinical presentation comparable to the general population and was frequently associated with chronic comorbidities.


FINDINGS: A sudden, severe, isolated loss of smell and/or taste, in the absence of other upper airway inflammatory diseases (allergic rhinitis, chronic rhinosinusitis, nasal polyposis), should alert individuals and physicians on being potentially affected by COVID-19. The evaluation of smell/taste disorders with a visual analogue scale or an individual olfactory or gustatory test, at the hospital or by telemedicine, to prevent contamination might facilitate an early detection of infected patients and reduce the transmission of SARS-CoV-2. During the COVID-19 outbreak, patients with sudden loss of smell should initiate social distancing and home isolation measures and be tested for SARS-CoV-2 diagnostic test when available. Olfactory training is recommended when smell does not come back after 1 month but can be started earlier.


Findings: We seek to systematically review the available evidence regarding the anticoagulation approach to prevent venous thromboembolism (VTE) among COVID-19 patients admitted to intensive care units. Electronic databases were searched for studies reporting venous thromboembolic events in patients admitted to the intensive care unit receiving any type of anticoagulation (prophylactic or therapeutic). The pooled prevalence (and 95% confidence interval [CI]) of VTE among patients receiving anticoagulant were calculated using the random-effects model. Subgroup pooled analyses were performed with studies reported prophylactic anticoagulation alone and with studies reported mixed prophylactic and therapeutic anticoagulation. We included twelve studies (8 Europe; 2 UK; 1 each from the US and China) in our systematic review and meta-analysis. All studies utilized LMWH or unfractionated heparin as their pharmacologic thromboprophylaxis, either prophylactic doses or therapeutic doses. Seven studies reported on the proportion of patients with the previous history of VTE (range 0-10%). The pooled prevalence of VTE among ICU patients receiving prophylactic or therapeutic anticoagulation across all studies was 31% (95% CI 20-43%). Subgroup pooled analysis limited to studies reported prophylactic anticoagulation alone and mixed (therapeutic and prophylactic anticoagulation) reported pooled prevalences of VTE of 38% (95% CI 10-70%) and 27% (95% CI 17-40%) respectively. With a high prevalence of thromboprophylaxis failure among COVID-19
patients admitted to intensive care units, individualised rather than protocolised VTE thromboprophylaxis would appear prudent at interim.


   Findings: We describe a patient with COVID-19 who developed simultaneous pulmonary, intracardiac and peripheral arterial thrombosis. A 58-year-old man, without major comorbidity, was admitted with a 14-day history of breathlessness. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection was confirmed by laboratory testing. Initial imaging revealed COVID-19 pneumonia but no pulmonary thromboembolism (PTE) on CT pulmonary angiography (CTPA). The patient subsequently developed respiratory failure and left foot ischaemia associated with a rising D-dimer. Repeat CTPA and lower limb CT angiography revealed simultaneous bilateral PTE, biventricular cardiac thrombi and bilateral lower limb arterial occlusions. This case highlights a broad range of vascular sequelae associated with COVID-19 and the fact that these can occur despite a combination of prophylactic and treatment dose anticoagulation.


   Findings: We report neurological manifestations in 404 consecutive patients with COVID-19 seen in outpatient clinics and hospitalized between February 20, 2020 and May 4, 2020 at Evergreen Hospital, Kirkland, Washington, USA. This hospital was among the first to report cases and deaths of COVID-19 patients in the United States. COVID-19 is caused by SARS-CoV-2. Most neurological manifestations of COVID-19 have been reported from non-USA health systems for hospitalized patients.


   Findings: A total of 11 cohort studies were included. Among hospitalized COVID-19 patients, 23.9% developed VTE despite anticoagulation. PE and DVT were detected in 11.6% and 11.9% of patients, respectively. Patients in the ICU had a higher risk for VTE (30.4%) than those in the ward (13.0%). The mortality was estimated at 21.3%. COVID-19 patients who developed VTE had higher D-dimer levels than those who did not develop VTE. The heightened and heterogeneous risk of VTE in COVID-19 despite prophylactic anticoagulation calls into research on the pathogenesis of thromboembolic complications and strategy of thromboprophylaxis and risk stratification. Prominent elevation of D-dimer may be associated with VTE development and can be used to identify high-risk subsets.

Findings: Eighty-six COVID-19-positive stroke cases were identified (mean age, 67.4 years; 44.2% women). Ischemic stroke (83.7%) and nonfocal neurological presentations (67.4%) predominated, commonly involving multivascular distributions (45.8%) with associated hemorrhage (20.8%). Compared with controls (n=499), COVID-19 was associated with in-hospital stroke onset (47.7% versus 5.0%; P<0.001), mortality (29.1% versus 9.0%; P<0.001), and Black/multiracial race (58.1% versus 36.9%; P=0.001). COVID-19 was the strongest independent risk factor for in-hospital stroke (odds ratio, 20.9 [95% CI, 10.4-42.2]; P<0.001), whereas COVID-19, older age, and intracranial hemorrhage independently predicted mortality. COVID-19 is an independent risk factor for stroke in hospitalized patients and mortality, and stroke presentations are frequently atypical.


Findings: A total of 18 patients reported in 14 papers were included in this review. All the patients were symptomatic for COVID-19, with cough and fever as the most frequently reported symptoms. The interval between the onset of symptoms of COVID-19 and the first symptoms of GBS ranged from -8 to 24 days (mean 9 days; median 10 days). Most of the patients had a typical GBS clinical form predominantly with a demyelinating electrophysiological subtype. Mechanical ventilation was necessary in 8 (44%) patients. Two (11%) patients died. Published cases of GBS associated with COVID-19 report a sensorimotor, predominantly demyelinating GBS with a typical clinical presentation. Clinical features and disease course seem similar to those observed in GBS related to other etiologies. These results should be interpreted with caution since only 18 cases have been heterogeneously reported so far.


Findings: 140 patients were aged in median of 62 years old, with a median SAPSII of 49 points. Neurological examination was normal in 22 patients (15.7%). One hundred eighteen patients (84.3%) developed a delirium with a combination of acute attention, awareness, and cognition disturbances. Eighty-eight patients (69.3%) presented an unexpected state of agitation despite high infusion rates of sedative treatments and neuroleptics, and 89 (63.6%) patients had corticospinal tract signs. Delirium/neurological symptoms in COVID-19 patients are a major issue in ICUs, especially in the context of insufficient human and material resources.

Findings: Fifty-one patients were reviewed. The mean age of 45 years; 38/51 (74.5%) were men. All patients had severe COVID-19 pneumonitis, and 18/51 (35.3%) had macroscopic thrombosis (15 with associated ischaemia); however, 13/51 (25.5%) patients had ischaemia without associated thrombus. The majority of patients with COVID-19 who received ECMO had areas of ischaemia within consolidated lungs, almost half of these without subtending pulmonary artery thrombosis. Although the prognostic significance of these findings is unclear, they are highly suggestive of lung ischaemia due to isolated microvascular immune thrombosis.


Findings: We characterized the coagulation and fibrinolysis profiles of patients with COVID-19 with ARDS. Findings suggest that the systemic inflammatory response is a major contributor to COVID-19–associated coagulopathy, supporting the concept of thromboinflammation.


Findings: We describe 3 patients without previous neurologic or autoimmune disorders who were diagnosed with myasthenia gravis after the onset of COVID-19.

**Diagnostics & Screening**


Findings: The Elecsys® Anti-SARS-CoV-2 immunoassay (Roche Diagnostics) was developed to provide accurate, reliable detection of antibodies to SARS-CoV-2. We evaluated sensitivity, specificity, cross-reactivity, and agreement with a vesicular stomatitis virus-based pseudo-neutralisation assay for the Elecsys Anti-SARS-CoV-2 immunoassay. Sensitivity and agreement between the Elecsys Anti-SARS-CoV-2 immunoassay and pseudo-neutralisation assay measurements were evaluated using samples from patients with PCR-confirmed SARS-CoV-2 infection, a majority of whom were hospitalised. Specificity was evaluated using samples from routine diagnostic testing/blood donors collected pre-December 2019 and thus deemed negative for SARS-CoV-2-specific antibodies. Cross-reactivity was evaluated using samples containing a wide range of potentially cross-reacting analytes, purchased from commercial vendors. For sensitivity and specificity, point estimates and 95% confidence intervals (CIs) were calculated. Agreement between the Elecsys Anti-SARS-CoV-2 immunoassay and pseudo-neutralisation assay was calculated. Sensitivity of the Elecsys Anti-SARS-CoV-2 immunoassay in patients with prior PCR-confirmed SARS-CoV-2 infection was 99.5% (95% CI 97.0-100.0) at ≥14 days post-PCR confirmation. Overall specificity (n=10,453) was 99.80% (99.69-99.88). Only
4/792 samples containing potential cross-reacting analytes were reactive with the Elecsys Anti-SARS-CoV-2 immunoassay, resulting in an overall specificity in this cohort of 99.5% (98.6-99.9). Positive, negative and overall agreement (n=46) between Elecsys Anti-SARS-CoV-2 immunoassay and a pseudo-neutralisation assay were 86.4% (73.3-93.6), 100% (34.2-100) and 87.0% (74.3-93.9), respectively. The Elecsys Anti-SARS-CoV-2 immunoassay demonstrated high sensitivity (99.5% at ≥14 days post-PCR confirmation) and specificity (99.80%), supporting its use as a tool for identification of past SARS-CoV-2 infection, including in populations with low disease prevalence.


Findings: Overall, 160 of the 217 (74%) participants tested positive for Covid-19 based on saliva, NPS, or both testing methods. The detection rate for SARS-CoV-2 was higher in saliva compared to NPS testing (93.1%, 149/160 vs 52.5%, 84/160, p<0.001). The concordance between the two tests was 45.6% (virus was detected in both saliva and NPS in 73/160), while 47.5% were discordant (87/160 tested positive for one while negative for the other). The Ct values for E and RdRp genes were significantly lower in saliva specimens compared to NP swab specimens. Our findings demonstrate that saliva is a better alternative specimen for detection of SARS-CoV-2. Taking into consideration, the simplicity of specimen collection, shortage of PPE and the transmissibility of the virus, saliva could enable self-collection for an accurate SARS-CoV-2 surveillance testing.


Findings: A total of 104 (54 positive and 50 negative) clinical nasopharyngeal samples were tested by both assays. Using the Panther Fusion as a reference standard, the Xpert demonstrated an overall agreement of 99.0% (95% confidence interval (CI): 94.8 - 100), positive percent agreement of 98.1% (95% CI: 90.1 - 100), and a negative percent agreement of 100% (95% CI: 94.2 - 100). The kappa coefficient was 0.98 (95% CI: 0.94 - 1.0). One sample positive by the Panther Fusion with a cycle threshold (Ct) of 38.6 was found to be reproducibly negative by the Xpert assay. The Cepheid Xpert Xpress SARS-CoV-2 assay provides test performance to the Hologic Panther Fusion SARS-CoV-2 assay while offering laboratories rapid, on-demand testing capacity.


Findings: Of the 81 included samples, there were 19 positives and 62 negatives in viral media and 18 positives and 63 negative in the MRSA swabs. Amongst all included samples, there was
concordance between the COPAN ESwabs® 480C and the viral swabs in 78 (96.3%). We found a high rate of concordance in test results between COPAN ESwabs® 480C in Amies solution and BD H192(07) nasopharyngeal swabs in in 3 mL of Universal Viral Transport medium viral media. Clinicians and laboratories should feel better informed and assured using COPAN ESwabs® 480C to help in the diagnosis of COVID-19.

Findings: A large majority of participants (>84%) reported that collecting, packing and shipping of saliva, OPS, and DBS specimens were acceptable. Nearly nine in 10 (87%) reported being confident or very confident that the specimens they collected were sufficient for laboratory analysis. There were no differences in acceptability for any specimen type, packing and shipping, or confidence in samples, by gender, age, race/ethnicity, or educational level. Self-collection of specimens for SARS-CoV-2 testing, and preparing and shipping specimens for analysis, were acceptable in a diverse group of US adults. Further refinement of materials and instructions to support self-collection of saliva, OPS and DBS specimens for COVID-related testing is needed.

Findings: We compared the analytical sensitivity (lower limit of detection, LOD) of seven commonly used qualitative SARS-CoV-2 molecular assays: the Abbott Molecular RealTime SARS-CoV-2 assay, the NeuMoDx™ SARS-CoV-2 assay, the Roche Cobas® SARS-CoV-2 assay, the BD SARS-CoV-2 reagents for BD MAX™ system, the Hologic Aptima® SARS-CoV-2 assay, the Xpert Xpress SARS-CoV-2 test, and the GenMark ePlex SARS-CoV-2 test. The comparison was performed utilizing a single positive clinical specimen that was serially diluted in viral transport media and quantified by the EUA approved SARS-CoV-2 droplet digital PCR (ddPCR) assay. Replicate samples were prepared and evaluated for reproducibility across different molecular assays with multiple replicates per assay. Our data demonstrated that the seven assays could detect 100 % of replicates at a nucleocapsid gene concentration of (N1 = 1,267 and N2 = 1,392) copies/mL. At a one log less concentration, the Abbott, the Roche, and the Xpert Xpress assays detected 100 % of the tested replicates.

Findings: We found diagnostically relevant differences in specificities for the anti-SARS-CoV-2 antibody assays by Abbott, Roche, and DiaSorin that have a significant impact on the positive predictive values of these tests.

**Epidemiology & Public Health**


Findings: The COVID-19 pandemic has had the unfortunate effect of amplifying health inequity in vulnerable populations. African Americans, who make up approximately 12% of the US population are reportedly being diagnosed with COVID-19 and dying at disproportionately higher rates. Viewed holistically, multiple factors are contributing to the perfect storm: 1) Limited availability of public testing, 2) A dramatic increase in low wage worker unemployment/health insurance loss especially in the service sector of the economy, 3) High rates of preexisting chronic disease states/reduced access to early healthcare and 4) Individual provider and structural healthcare system bias. Indeed, COVID-19 represents a pandemic superimposed on a historic epidemic of racial health inequity and healthcare disparities. Therapeutic solutions are not expected in the near term. Thus, identifying the genesis and magnitude of COVID-19's impact on African American communities is the requisite first step toward crafting an immediate well designed response. The mid and long term approach should incorporate population health based tactics and strategies.


Findings: 46,117 Northwell HCP were tested as of June 23, 2020. A 13.7% prevalence of SARS-CoV-2 antibodies in this large cohort study of HCP in the greater NYC area was similar to that among adults randomly tested in New York State (14.0%) but higher than among adults in Los Angeles (4.1%). HCP in a single hospital in Belgium had lower seroprevalence (6.4%), which was significantly associated only with household contact. In this study, high levels of HCP-reported suspicion of virus exposure and prior positive PCR testing results were most strongly associated with seropositivity.


Findings: Coronavirus disease 2019 (COVID-19) has resulted in over 1.5 million infections and 100,000 deaths in the USA. Early reports indicated that communities with high proportions of racial and ethnic minorities may be disproportionately affected. However, existing evidence is limited to studies that examined simple correlations without adjustments for potential confounders or compared counties in a single state (Massachusetts). Another recent study sought to answer this question by using national county-level data, but compared counties with
disproportionately high numbers of Black residents—which are predominantly (91%) located in the South—versus counties with a lower proportion of Black residents across states. Therefore, the study effectively compared the South versus other regions of the USA. More importantly, states vary substantially in their responses to the COVID-19 pandemic; therefore, not accounting for state characteristics may lead to biased estimates of the relationship between the proportion of Black residents and the impact of COVID-19 outbreaks.


https://pediatrics.aappublications.org/content/pediatrics/early/2020/08/03/peds.2020-009951.full.pdf

Findings: Of 1000 children tested for SARS-CoV-2 infection, 20.7% tested positive. In comparison to non-Hispanic (NH)-whites (7.3%), minority children had higher rates of infection (NH-black: 30.0%; adjusted OR 2.3 [95% CI 1.2, 4.4]; Hispanic: 46.4%; adjusted OR 6.3 [95%CI 3.3, 11.9]). In comparison to children in the highest MFI quartile (8.7%), infection rates were higher among children in quartile 3 (23.7%; adjusted OR 2.6 [95% CI 1.4, 4.9]); quartile 2 (27.1%; adjusted OR 2.3 [95% CI 1.2, 4.3]), and quartile 1 (37.7%; adjusted OR 2.4 [95% CI 1.3,4.6]). Rates of reported exposure to SARS-CoV-2 also differed by race/ethnicity and socioeconomic status. In this large cohort of children tested for SARS-CoV-2 through a community based testing site, racial/ethnic minorities and socioeconomically disadvantaged children carry the highest burden of infection. Understanding and addressing the causes of these differences are needed to mitigate disparities and limit the spread of infection.


Findings: Black patients were generally younger than white, were more often female, and had larger numbers of comorbidities. Compared to white patients with COVID-19, black patients had 1.4 times the risk of hospitalization, and almost twice the risk of requiring ICU care or ventilatory support after adjusting for covariates. Black patients saw a 1.36 times increased risk of death compared to white. Disparities between black and white outcomes increased with advanced age. Despite the initial descriptions of COVID-19 being a disease that affects all individuals, regardless of station, our data demonstrate the differential racial effects in the United States. This current pandemic reinforces the need to assess the unequal effects of crises on disadvantaged populations to promote population health.

Healthcare Delivery & Healthcare Workers

Findings: Healthcare workers (HCWs) have a theoretically increased risk of contracting SARS-CoV-2 given their occupational exposure. We tested 2167 HCWs in a London Acute Integrated Care Organisation for antibodies to SARS-CoV-2 in May and June 2020 to evaluate seroprevalence. We found a seropositivity rate of 31.6% among HCWs.


Findings: This cross-sectional study found important changes in AMI hospitalization rates and worse outcomes during the early and later COVID-19 periods. Future studies are needed to identify contributors to the increased mortality rate among patients with STEMI.


Findings: 71% of the 13,167 nursing homes that reported COVID-19 data as of June 14 had at least one case among residents and/or staff. Of those, 27% experienced an outbreak. Higher RN hours are associated with a higher probability of experiencing any cases. However, among facilities with at least one case, higher nurse aide and total nursing hours are associated with a lower probability of experiencing an outbreak and with fewer deaths. The strongest predictor of cases and outbreaks in nursing homes is per capita cases in the county. Prevalence of COVID-19 in the community remains the strongest predictor of COVID-19 cases and deaths in nursing homes, but higher nurse aide and total nursing hours may help to contain the number of cases and deaths.


Findings: This paper outlines key pathophysiological principles that relate to the patient with early infection treated at home. Therapeutic approaches based on these principles include: 1) reduction of reinoculation, 2) combination antiviral therapy, 3) immunomodulation, 4) antiplatelet/antithrombotic therapy 5) administration of oxygen, monitoring, and telemedicine. Future randomized trials testing the principles and agents discussed in this paper will undoubtedly refine and clarify their individual roles, however we emphasize the immediate need for management guidance in the setting of widespread hospital resource consumption, morbidity, and mortality.


Findings: The aim of this study was to investigate the prevalence of previously undiagnosed SARS-CoV-2 infection in health professionals from two tertiary-level maternity units in London,
UK, and to determine associations between healthcare workers' characteristics, reported symptoms and serological evidence of prior SARS-CoV-2 infection. In total, 200 anaesthetists, midwives and obstetricians, with no previously confirmed diagnosis of COVID-19, were tested for immune seroconversion using laboratory IgG assays. Comprehensive symptom and medical histories were also collected. Five out of 40 anaesthetists, 7/52 obstetricians and 17/108 midwives were seropositive, with an overall total of 29/200 of maternity healthcare workers testing positive for IgG antibodies against SARS-CoV-2. Of those who had seroconverted, 10/29 (35.5%) were completely asymptomatic. Fever or cough were only present in 6/29 (21%) and 10/29 (35%) respectively. Anosmia was the most common symptom occurring in 15/29 (52%) seropositive participants and was the only symptom that was predictive of positive seroconversion. Of those who were seropositive, 59% had not self-isolated at any point and continued to provide patient care in the hospital setting. This is the largest study of baseline immune seroconversion in maternity healthcare workers conducted to date and reveals that one out of six were seropositive, of whom one out of three were asymptomatic. This has significant implications for the risk of occupational transmission of SARS-CoV-2 for both staff and patients in maternity units. Regular testing of staff, including asymptomatic staff should be considered to reduce transmission risk.


https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769442?resultClick=1

Findings: The findings of the present study indicate that the rate of SARS-CoV-2 infection among health care workers is lower than what has been reported for the general public in the surrounding region. Given that health care workers in hospitals are exposed to a much higher density of the virus, this is strong evidence that current PPE practices are protective, easing health care workers’ concern and psychological distress.


Findings: Nursing home residents undergoing dialysis might be at a higher risk for SARS-CoV-2 infection because of exposures to staff members and community dialysis patients. Attention to infection control practices and surveillance in nursing homes and dialysis centers is critical to preventing nursing home COVID-19 outbreaks.

**Prognosis**


Findings: We included 344 patients. Neurological comorbidities accounted for 22.4% of cases, with cerebrovascular diseases and cognitive impairment being the most frequent. Neurological comorbidity resulted independently associated with severe COVID-19 (OR 2.305; p = 0.012), as
well as male gender ($p = 0.001$), older age ($p = 0.001$), neoplastic diseases ($p = 0.039$), and arterial hypertension ($p = 0.045$). When neurological comorbidity was associated with non-neurological comorbidities, the OR for severe COVID-19 rose to $7.394$ ($p = 0.005$). Neurological patients received more respiratory support indication. Neurological comorbidities represent a significant determinant of COVID-19 severity, deserving a thorough evaluation since the earliest phases of infection. The vulnerability of patients affected by neurological diseases should suggest a greater attention in targeting this population for proactive viral screening.


Findings: The study included 158 consecutive patients. The mean age was 57 years, and 61% were women. The mean (SD) of BMI was 33.2 (8.6) kg/m². Overall, patients admitted to the ICU were older (62 vs. 55 years, $P = 0.003$) and had higher BMI (36.5 kg/m² vs. 31.9 kg/m², $P = 0.002$). In unadjusted and adjusted analysis, the factors most associated with ICU admission in this sample were age (adjusted odds ratio [aOR]: 1.073; 95% CI: 1.033-1.114), BMI (aOR: 1.115; 95% CI: 1.052-1.182), and lung disease (aOR: 3.097; 95% CI: 1.137-8.437). This study identified risk factors for severe disease in COVID-19, specifically in an African American population. Further inclusive research aimed at optimizing clinical care relevant to the African American population is critical to ensure an equitable response to COVID-19.


Findings: To determine whether conditions associated with dysregulated complement or coagulation systems impact disease, we performed a retrospective observational study and found that history of macular degeneration (a proxy for complement-activation disorders) and history of coagulation disorders (thrombocytopenia, thrombosis and hemorrhage) are risk factors for SARS-CoV-2-associated morbidity and mortality—effects that are independent of age, sex or history of smoking. Transcriptional profiling of nasopharyngeal swabs demonstrated that in addition to type-I interferon and interleukin-6-dependent inflammatory responses, infection results in robust engagement of the complement and coagulation pathways. Finally, in a candidate-driven genetic association study of severe SARS-CoV-2 disease, we identified putative complement and coagulation-associated loci including missense, eQTL and sQTL variants of critical complement and coagulation regulators. In addition to providing evidence that complement function modulates SARS-CoV-2 infection outcome, the data point to putative transcriptional genetic markers of susceptibility. The results highlight the value of using a multimodal analytical approach to reveal determinants and predictors of immunity, susceptibility and clinical outcome associated with infection.

Findings: Obese have steatosis, impaired hepatic function, compromise immune response and higher inflammation. In addition, they have a reduced prognostic nutritional index (PNI), nutritional survival index for ICU patients. We underlined obese characteristic with likely poorly prognosis and an important misclassification of obesity. A not negligible number of patients with normal BMI could actually have an excess of adipose tissue and therefore have an unfavorable outcome such as an obese.

FINDINGS: Out of a total of 3009 citations, 17 articles (22 studies, 21 from China and one study from Singapore) with 3396 ranging from 12 to1099 patients were included. Our meta-analyses showed a significant decrease in lymphocyte, monocyte, and eosinophil, hemoglobin, platelet, albumin, serum sodium, lymphocyte to C-reactive protein ratio (LCR), leukocyte to C-reactive protein ratio (LeCR), leukocyte to IL-6 ratio (LeIR), and an increase in the neutrophil, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, blood urea nitrogen (BUN), creatinine (Cr), erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP), Procalcitonin (PCT), lactate dehydrogenase (LDH), fibrinogen, prothrombin time (PT), D-dimer, glucose level, and neutrophil to lymphocyte ratio (NLR) in the severe group compared with the non-severe group. No significant changes in white blood cells (WBC), Creatine Kinase (CK), troponin I, myoglobin, IL-6 and K between the two groups were observed. This meta-analysis provides evidence for the differentiation of severe cases of COVID-19 based on laboratory test results at the time of ICU admission. Future well-methodologically designed studies from other populations are strongly recommended.

Findings: Of the 4,035 patients, males accounted for 2,433/3,987 (61.0%), the median age was 70 years, and 2,539/3,439 (73.8%) had >1 comorbidity. The most common symptoms were a history of fever, cough, malaise, and dyspnoea. During hospitalization 1,255/3,979 (31.5%) patients developed acute respiratory distress syndrome, 736/3,992 (18.5%) were admitted to intensive care units, and 619/3,992 (15.5%) underwent mechanical ventilation. Viral or host-targeted medications included lopinavir/ritonavir 2,820/4,005 (70.4%), hydroxychloroquine 2,618/3,995 (65.5%), interferon-beta 1,153/3,950 (29.2%), corticosteroids 1,109/3,965 (28.0%), and tocilizumab 373/3,951 (9.4%). Overall 1,131/4,035 (28%) patients died. Mortality increased with age (85.6% occurring in older than 65 years). Seventeen factors were independently associated with an increased hazard of death, the strongest among them included advanced age, liver cirrhosis, low age-adjusted oxygen saturation, higher concentrations of C-reactive protein, and lower estimated glomerular filtration rate.

Findings: Four hundred eighty-two SOT recipients from >50 transplant centers were included: 318 (66%) kidney or kidney/pancreas, 73 (15.1%) liver, 57 (11.8%) heart, and 30 (6.2%) lung. Median age was 58 (IQR 46-57), median time post-transplant was 5 years (IQR 2-10), 61% were male, and 92% had ≥1 underlying comorbidity. Among those hospitalized (376 [78%]), 117 (31%) required mechanical ventilation, and 77 (20.5%) died by 28 days after diagnosis. Specific underlying comorbidities (age >65 [aOR 3.0, 95%CI 1.7-5.5, p<0.001], congestive heart failure [aOR 3.2, 95%CI 1.4-7.0, p=0.004], chronic lung disease [aOR 2.5, 95%CI 1.2-5.2, p=0.018], obesity [aOR 1.9, 95% CI 1.0-3.4, p=0.039]) and presenting findings (lymphopenia [aOR 1.9, 95%CI 1.1-3.5, p=0.033], abnormal chest imaging [aOR 2.9, 95%CI 1.1-7.5, p=0.027]) were independently associated with mortality. Multiple measures of immunosuppression intensity were not associated with mortality. Mortality among SOT recipients hospitalized for COVID-19 was 20.5%. Age and underlying comorbidities rather than immunosuppression intensity-related measures were major drivers of mortality.


Findings: six hundred and sixty-four patients were classified according to CFS. Two hundred and seventy-one died, during a mean follow-up of 34.3 days. Worse frailty at baseline was associated with increased mortality risk, even after full adjustment (p = 0.004). Patients with CFS 4 and CFS 5 had non-significant increased mortality risks, compared to those with CFS 1-3. Patients with CFS 6 had a 2.13-fold (95% CI 1.34-3.38) and those with CFS 7-9 had a 1.79-fold (95% CI 1.12-2.88) increased mortality risk, compared to those with CFS 1-3 (p = 0.001 and 0.016, respectively). Older age, male sex and acute illness severity were also associated with increased mortality risk. Frailty is associated with all-cause mortality risk in older inpatients with COVID-19.


Findings: This is a multicentric kidney transplant cohort including 104 hospitalized patients between Mar 4 and Apr 17, 2020. Risk factors for death and ARDS were investigated, and clinical and laboratory data was analyzed. The mean age was 60 years. Forty-seven patients (54.8%) developed ARDS. Obesity was associated to ARDS development. Significant age differences were not found among patients developing and not developing ARDS (61.3yr vs 57.8yr, p=0.16). Seventy-six (73%) patients were discharged while 28 (27%) died. Death was more common among the elderly (55yr and 70.8yr, p<0.001) and those with preexisting pulmonary disease. At admission, higher baseline lactate dehydrogenase (257 IU/ml vs 358 IU/ml, p=0.001) or ARDS conferred higher risk of death (HR 2.09, p=0.044). In our cohort, ARDS
was equally present among young and old kidney recipients. However, the elderly might be at higher risk of death, along with those showing higher baseline LDH at admission.

**Survivorship & Rehabilitation**


Findings: We conducted a retrospective observational cohort study of discharged patients with confirmed COVID-19 not receiving anticoagulation. The cohort included 163 patients with median time from discharge to last recorded follow up of 30 days (IQR 17-46). The median duration of index hospitalization was 6 days (IQR 3-12) and 26% required intensive care. The cumulative incidence of thrombosis (including arterial and venous events) at day 30 following discharge was 2.5% (95% CI 0.8-7.6); the cumulative incidence of venous thromboembolism alone at day 30 post-discharge was 0.6% (95% CI 0.1-4.6). The 30-day cumulative incidence of major hemorrhage was 0.7% (95% CI 0.1-5.1) and clinically relevant non-major bleeds was 2.9% (95% CI 1.0-9.1). We conclude that the rates of thrombosis and hemorrhage appear to be similar following hospital discharge for COVID-19, emphasizing the need for randomized data to inform recommendations for universal post-discharge thromboprophylaxis.

**Therapeutics**


Findings: In this randomized clinical trial that included 103 patients and was terminated early, the hazard ratio for time to clinical improvement within 28 days in the convalescent plasma group vs the standard treatment group was 1.40 and was not statistically significant. Among patients with severe or life-threatening COVID-19, convalescent plasma therapy added to standard treatment, compared with standard treatment alone, did not result in a statistically significant improvement in time to clinical improvement within 28 days. Interpretation is limited by early termination of the trial, which may have been underpowered to detect a clinically important difference.


Findings: This review aims to assess the risk of drug-drug interactions in the severely ill COVID-19 patient. A total of 2378 records were retrieved from ClinicalTrials.gov, which yielded 249 drugs that met inclusion criteria. Thirteen primary compounds were screened against 512 comedications. A full database of these interactions is available at [www.covid19-](http://www.covid19)
Experimental therapies for COVID-19 present a risk of drug-drug interactions, with lopinavir/ritonavir, chloroquine and hydroxychloroquine posing the greatest risk. With management, these risks can be mitigated. We have published a drug-drug interaction resource to facilitate medication review for the critically ill patient.


Findings: We performed 1,461 surgical (81.3%) and 429 percutaneous tracheostomies. Median timing of tracheostomy was 12 days (4-42 days) since orotracheal intubation. A close follow-up of 1616/1890 (85.5%) patients at the cut-off time of 1-month follow-up showed that in 842 (52.1%) patients, weaning was achieved, while 391 (24.2%) were still under mechanical ventilation and 383 (23.7%) patients had died from COVID-19. Decannulation among those in whom weaning was successful (n = 842) was achieved in 683 (81%) patients. To the best of our knowledge, this is the largest cohort of COVID-19 patients undergoing tracheostomy. The critical focus is the unprecedented amount of tracheostomies: 1890 in 7 weeks. Weaning could be achieved in over half of the patients with follow-up. Almost one out of four tracheotomized patients died from COVID-19.


Findings: Forty-two health-care workers (11.4%) tested positive for infection, but only three of them required hospitalisation. Data are reported for all patients (69.3% male), whose mean age was 68 (sd 13) years. The PaO2/FiO2 ratio at baseline was 152±79, and the majority of patients (49.3%) were treated with CPAP. The overall unadjusted 30-day mortality rate was 26.9% with 16%, 30%, and 30%, while the total ETI rate was 27% with 29%, 25% and 28%, for HFNC, CPAP, and NIV, respectively, and the relative probability to die was not related to the NRS used after adjustment for confounders. ETI and length of stay were not different among the groups. Mortality rate increased with age and comorbidity class progression. The application of NRS outside the ICU is feasible and associated with favourable outcomes. Nonetheless, it was associated with a risk of staff contamination.


Findings: The rate of CPAP failure (either intubation or death) in COVID-19 patients seems to be higher in our study compared with the one recently reported in a multicenter, observational study which enrolled non-COVID-19 pneumonia patients with comparable severity. Nevertheless, the overall mortality rate of our cohort was comparable to that recently reported in ICU patients [10]. A total of 55.4% of our patients with a median PaO2:FiO2 ratio of 136 and
treated with helmet CPAP avoided intubation, and, then, were successfully weaned to oxygen therapy.


**FINDINGS:** From an initial screen of 80 identified studies, 24 studies provided clinical outcome data on the use of immunotherapies for the treatment of COVID-19 patients, including convalescent plasma therapy (33 patients), monoclonal antibodies (55 patients), interferon (31 patients), mesenchymal stem cell therapy (8 patient), and immunoglobulin (63 patients). Except for nine severe patients who died after treatment, most patients were recovered from COVID-19 with improved clinical symptoms and laboratory assessment. Based on the available evidence, it seems that treatment with immunotherapy along with other standard cares could be an effective and safe approach to modulate the immune system and improvement of clinical outcomes.


**Findings:** In this monograph, we review the procedures and methods to safely care for COVID-19 patients who require tracheostomy, gastrostomy, weaning from mechanical ventilation, and final decannulation. The guiding principles consist of modifications in the methods of airway care, to safely prevent iatrogenesis and promote safety in patients severely affected by COVID-19, including mitigation of aerosol generation to minimize risk for healthcare workers.


**Findings:** The major protease (Mpro) of SARS-CoV-2 is considered a promising target, based on previous results from related CoVs with lopinavir (LPV), an HIV protease inhibitor. However, limited evidence exists for other clinically approved antiretroviral protease inhibitors. Extensive use of atazanavir (ATV) as antiretroviral and previous evidence suggesting its bioavailability within the respiratory tract prompted us to study this molecule against SARS-CoV-2. Our results show that ATV could dock in the active site of SARS-CoV-2 Mpro, with greater strength than LPV, blocking Mpro activity. We confirmed that ATV inhibits SARS-CoV-2 replication, alone or in combination with ritonavir (RTV) in Vero cells and human pulmonary epithelial cell line. ATV/RTV also impaired virus-induced enhancement of IL-6 and TNF-α levels. Together, our data strongly suggest that ATV and ATV/RTV should be considered among the candidate repurposed drugs undergoing clinical trials in the fight against COVID-19.

Findings: Novaferon inhibited the viral replication, and prevented viral infection. Results from the 89 enrolled COVID-19 patients showed that both Novaferon and Novaferon plus Lopinavir/Ritonavir groups had significantly higher viral clearance rates on day 6 than Lopinavir/Ritonavir group (50.0% vs.24.1%, p = 0.0400, and 60.0% vs.24.1%, p = 0.0053). Median time to viral clearance were 6 days, 6 days, and 9 days for three groups respectively, a 3-day reduction in both Novaferon and Novaferon plus Lopinavir/Ritonavir groups compared with Lopinavir/Ritonavir group. Novaferon exhibited anti-SARS-CoV-2 effects in vitro and in COVID-19 patients. These data justified the further evaluation of Novaferon.


Findings: In this study, one third of coronavirus disease 2019 mechanically ventilated patients have a pulmonary embolism visible on CT pulmonary angiography. High regimen thromboprophylaxis may decrease the occurrence of such complication.


Findings: The survey was completed by 166 participants from 23 countries and 82 different hospitals. Local guidelines for antibiotic use in COVID-19 patients were reported by 61.8% (n = 102) of participants and for 82.9% (n = 136) they did not differ from local community-acquired pneumonia guidelines. Clinical presentation was recognized as the most important reason for the start of antibiotics (mean score = 4.07 and SD = 1.095 on grading scale from 1 to 5). When antibiotics were started, most respondents rated as the highest the need for coverage of atypical pathogens (mean score = 2.8 and SD = 0.99), followed by Staphylococcus aureus (mean score = 2.67 and SD = 1.05 on bi-modal scale, with values 1 and 2 for disagreement and values 3 and 4 for agreement). In the patients on the ward, 29.1% of respondents chose not to prescribe any antibiotic. Combination of β-lactams and macrolides or fluoroquinolones was reported by 52.4% (n = 87) of respondents. In patients in the ICU, piperacillin/tazobactam was the most commonly prescribed antibiotic. The mean reported duration of antibiotic treatment was 7.12 (SD = 2.44) days. The study revealed widespread broad-spectrum antibiotic use in patients with COVID-19. Implementation of antimicrobial stewardship principles is warranted to mitigate the negative consequences of antibiotic therapy.

Findings: Prompt identification and treatment of COVID19-CS prior to intubation may be more important than the specific type of anti-inflammatory treatment. Randomized controlled trials of targeted anti-cytokine treatments and corticosteroids should report duration of cytokine storm in addition to clinical severity at randomization.

Findings: In our group of 117 patients meeting inclusion criteria methylprednisolone was associated with increased ventilator-free days and higher probability of extubation in a propensity-score matched cohort. Randomized, controlled studies are needed to further define methylprednisolone use in patients with COVID-19.

Transmission / Infection Control

Findings: To explore any relationship between the ABO blood group and the COVID-19 susceptibility, we compared ABO blood group distributions in 2,173 COVID-19 patients with local control populations, and found that blood group A was associated with an increased risk of infection, whereas group O was associated with a decreased risk.

Findings: In this cohort study of symptomatic and asymptomatic patients with SARS-CoV-2 infection who were isolated in a community treatment center in Cheonan, Republic of Korea, the viral shedding values in asymptomatic patients were similar to those in symptomatic patients. Isolation of asymptomatic patients may be necessary to control the spread of SARS-CoV-2.

Findings: We have demonstrated a simple optical measurement method to evaluate the efficacy of masks to reduce the transmission of respiratory droplets during regular speech. In proof-of-principle studies, we compared a variety of commonly available mask types and
observed that some mask types approach the performance of standard surgical masks, while some mask alternatives, such as neck fleece or bandanas, offer very little protection. Our measurement setup is inexpensive and can be built and operated by non-experts, allowing for rapid evaluation of mask performance during speech, sneezing, or coughing.


Findings: We propose a novel low-cost and accurate method to estimate the incubation distribution of COVID-19. We have conducted a cross-sectional and forward follow-up study by identifying those pre-symptomatic individuals at their time of departure from Wuhan and then following them until their symptoms developed. The renewal process is adopted by considering the incubation period as a renewal and the duration between departure and symptoms onset as a forward time. Such a method enhances the accuracy of estimation by reducing recall bias and utilizing the abundant and readily available data. The estimated median of incubation period is 7-76 days (95% CI: 7-02-8-53), the 90th percentile is 14-28 days (95% CI: 13-64-14-90). By taking the possibility that a small portion of patients may contract the disease on their way out of Wuhan, the estimated probability that incubation period is longer than 14 days is between 5% to 10%.


Findings: We identified 689 studies during literature searches. We included 10 full-text studies. A narrative synthesis was provided. Two on-field studies reported no difference in the rates of healthcare workers performing airway procedures during the care of critical patients with SARS-CoV-2. A single simulation trial reported a lower level of cross-contamination of participants using PAPR compared to alternative respiratory protection. There is moderate quality evidence that PAPR use is associated with greater heat tolerance but lower scores for mobility and communication ability. We identified a trend towards greater self-reported wearer comfort with PAPR technology in low-quality observational simulation studies. Field observational studies do not indicate a difference in healthcare worker infection utilizing PAPR devices versus other compliant respiratory equipment. Greater heat tolerance accompanied by lower scores of mobility and audibility in PAPR was identified. Further pragmatic studies are needed in order to delineate actual effectiveness and provider satisfaction with PAPR technology.


Findings: Based on the scientific evidence accumulated to date, our view is that SARS-CoV-2 is not spread by the airborne route to any significant extent and the use of particulate respirators offers no advantage over medical masks as a component of personal protective equipment for the routine care of patients with COVID-19 in the health care setting. Moreover, prolonged use of particulate respirators may result in unintended harms. In conjunction with appropriate hand hygiene, PPE used by health care workers caring for patients with COVID-19 must be used with attention to detail and precision of execution to prevent lapses in adherence and active failures in the donning and doffing of the PPE.

### 62. Filtration Efficiency of Hospital Face Mask Alternatives Available for Use During the COVID-19 Pandemic.
[https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769443](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769443)

Findings: In this quality-improvement study of 29 fitted face mask alternatives, expired N95 respirators with intact elastic bands and masks that had been subjected to ethylene oxide and hydrogen peroxide sterilization had unchanged fitted filtration efficiencies (FFEs) of more than 95%, while the performance of N95 respirators in the wrong size resulted in decreased FFEs between 90% and 95%. As a group, surgical and procedure masks had lower FFEs relative to N95 respirators, with masks secured with elastic ear loops showing the lowest performance.

### Whole Person Care

### 63. Symptom Relief Is Possible in Elderly Dying COVID-19 Patients: A National Register Study.

Results: Breathlessness as a breakthrough symptom was more common in COVID-19 patients than in the 2019 reference population (p < 0.001) and relief of breathlessness, as well as anxiety, delirium, and death rattles was less successful in COVID-19 patients (p < 0.05 to p < 0.01 in different comparisons). Patients were older in nursing homes than in hospitals (86.6 years vs. 80.9 years, p < 0.001) and more often female (48% vs. 34%, p < 0.001). Breakthrough of breathlessness was much more frequently reported in hospital settings than in nursing homes, 73% versus 35% (p < 0.0001), and complete relief was more rarely possible in hospitals, 20% versus 42% (p < 0.01). The proportion of partial relief+complete relief was comparable, 92% versus 95% (ns). Also, anxiety and pain were more often completely relieved in nursing homes (p < 0.01 in both comparisons). Conclusion: The lower symptom prevalence in nursing homes may be explained by elderly frail residents dying already in the first phase of the COVID-19 disease, before acute respiratory distress syndrome develops.

### Women & Children

Findings: It seems unnecessary to perform chest imaging in children to diagnose COVID-19. Chest radiography can be used in symptomatic children to assess airway infection or pneumonia. CT should be reserved for when there is clinical concern to assess for possible complications, especially in children with coexisting medical conditions.


Findings: The incidences of fever, cough and positive CT findings in pregnant women with COVID-19 are less than those in the normal population with COVID-19, but the rate of preterm labor is higher among pregnant with COVID-19 than among normal pregnant women. There is currently no evidence that COVID-19 can spread through vertical transmission.


Findings: Distinguishing MIS-C from other severe infectious or inflammatory conditions poses a challenge to clinicians caring for children and adolescents. As the COVID-19 pandemic continues to expand in many jurisdictions, health care provider awareness of MIS-C will facilitate early recognition, early diagnosis, and prompt treatment.


Findings: Analysis of pediatric COVID-19 hospitalization data from 14 states found that although the cumulative rate of COVID-19–associated hospitalization among children (8.0 per 100,000 population) is low compared with that in adults (164.5), one in three hospitalized children was admitted to an intensive care unit.


Findings: A total of 107 paediatric COVID-19 index cases and 248 of their household members were identified. One pair of paediatric index-secondary household case was identified, giving a household SAR of 0.5% (95% CI 0.0% to 2.6%). The index case was self-quarantined at home after international travel, stayed in her room, but shared a meal table with the secondary case. The SAR from children to household members was low in the setting of social distancing, underscoring the importance of rigorous contact tracing and early isolation in limiting transmission within households.

Findings: In our experience of caring for newborns at a center with high incidence of maternal SARS-CoV-2, newborns did not show signs of infection after birth. Moreover, we report no short-term adverse neonatal outcomes with skin-to-skin care, rooming-in, or breastfeeding in infants of SARS-CoV-2 positive mothers in our population. In contrast to early reports from China, majority of our newborns were born via vaginal delivery [4]. And although it has been shown that SARS-CoV-2 can be detected in the stool samples of mothers, routine testing in our cohort of newborns did not show a high incidence of positive PCR results [5]. A possible explanation for both of these observations could be the high number of asymptomatic or mildly symptomatic mothers in our study.


Findings: Our study showed that imaging findings in children were often milder and more focal than adults, typically as ground-glass opacities and consolidations with unilateral lower-lobe predominance, which have been regressed during the recovery time. A balance must be struck between the risk of radiation and the need for chest CT. If still necessary, low-dose CT is more appropriate in this age group. Albeit, due to the limited number of reported pediatrics with COVID-19, and the lack of consistency in CT descriptors, further work is still needed in this regard.


Findings: We analysed viral load at the time of diagnosis in 53 children and 352 adults with COVID-19 in the first 5 days post symptom onset. No significant differences in SARS-CoV-2 RNA loads were seen between children and adults.

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**GUIDELINES & CONSENSUS STATEMENTS**


**FDA / CDC / NIH / WHO Updates**

**CDC - Criteria for Return to Work for Healthcare Personnel with SARS-CoV-2 Infection (Interim Guidance) updated August 10, 2020**
American Academy of Pediatrics and the Children’s Hospital Association -  Children and COVID-19: State-Level Data Report

WHO - Estimating mortality from COVID-19

Commentary & News

New York Times - Russia Approves Coronavirus Vaccine Before Completing Tests

Universal Masking in the United States: The Role of Mandates, Health Education, and the CDC.

We Must Take Advantage of This Pandemic to Make a Radical Social Change: The Coronavirus as a Global Health, Inequality, and Eco-Social Problem.


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