The Daily COVID-19 Literature Surveillance Summary

June 15, 2020

UW Medicine
UW SCHOOL OF MEDICINE

THE UNIVERSITY OF ARIZONA
COLLEGE OF MEDICINE PHOENIX

BNITM

U.S. AIR FORCE

wildernessdoc.com

UNIVERSITY OF NEW ENGLAND COLLEGE OF OSTEOPATHIC MEDICINE

ICOM

MANIPAL ACADEMY of HIGHER EDUCATION
(Deemed to be University under Section 3 of the UGC Act, 1956)
INSPIRED BY LIFE

WESTERN UNIVERSITY OF HEALTH SCIENCES
The College of Osteopathic Medicine OF THE PACIFIC

MEDICAL UNIVERSITY OF THE AMERICAS
Nevis, West Indies

NOW LIVE!

Daily audio summaries of the literature in 10 minutes or less.
https://www.covid19lst.org/podcast/

COVID-19 LST

COVID-19 Daily Literature Surveillance

COVID19LST

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

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

Climate
- A case report of an ectopic pregnancy presenting late--after 15 days of abdominal pain--highlights the [dangers of avoiding care due to fear of contracting COVID-19](#)
- Investigators in South Africa discuss the effects of lockdowns on [low- and middle-income countries](#) and recommend that governments ensure health and resource information is both easily accessible and effectively disseminated to their populations by providing resources such as e-banking, water, food, and sanitation, as well as forming community partnerships.

Epidemiology
- A retrospective cohort study at the Cleveland Clinic found that the pandemic has significantly decreased the daily number of patients presenting to the hospital and requiring emergent transfer in general (4.5 patients per day to 2.4) and specifically with ST-elevation myocardial infarction and stroke. These results add to the evidence that patients may be [reluctant to seek care during the pandemic](#), leading to an increase in mortality and morbidity outside of the hospital.
- Physicians from New York report six patients hospitalized with COVID-19 who developed [hyperpyrexia](#) with peak body temperatures of 107.2 – 109.2°F and onset 6-12 days following admission, and universal mortality within two days of onset. The authors propose hyperpyrexia may result from SARS-CoV-2-related brain injury, immune system dysfunction, and/or hypercoagulability leading to thrombus formation.

Understanding the Pathology
- Researchers reviewed two prospective multicenter cohorts of children hospitalized with [bronchiolitis pre-COVID-19](#) and found that 12% had one of the endemic coronaviruses, 85% of whom had co-infection with another virus. While co-infection was not associated with severity of the disease, higher coronavirus viral load was associated with more severe illness.
- A molecular and genetic analysis of SARS-CoV-1, SARS-CoV-2, and MERS-CoV found that key changes in the nuclear localization sequence and distinct insertions in the spike glycoprotein of the virus may be responsible for the [high pathogenicity of SARS-CoV-](#)2 compared to SARS-CoV-1 and MERS-CoV

Transmission & Prevention
- Researchers from Beijing measured the [size-dependent filtration efficacy of air purifiers](#) with fine filters (F6 class) and particulate air filters (HEPA, H12 class) and found purifiers with F6 filters removed 54% of aerosols that could carry airborne COVID-19 while those with H12 filters removed 83%.
- A literature review found that povidone-iodine (PVP-I) can be safely administered in the nose at concentrations up to 1.25% and in the mouth at concentrations up to 2.5% for up to 5 months suggesting that [PVP-I as a topical solution, may be a safe and effective agent against some coronaviruses](#).

Management
- A meta-analysis of 14 clinical studies found that the odds of mortality in patients treated with a combination of Hydroxychloroquine and Azithromycin was significantly higher than in patients treated with supportive care alone. Additionally, there was [no significant difference in mortality between patients who received hydroxychloroquine](#) alone versus supportive care or patients who received a combination of hydroxychloroquine and Azithromycin versus hydroxychloroquine alone.
- A group of researchers argue [that early initiation of mechanical ventilation and intubation](#) to prevent more severe lung injury in COVID-19 patients is not substantiated and may in fact, cause fatal complications.
- A retrospective of 84 COVID-19 patients found that [quantitative analysis programs for CT scans](#) could be used to predict severity of COVID-19 related pneumonia with severe cases exhibiting significantly higher ground-glass opacity scores, consolidation scores, and total lesion scores than the non-severe group.

Adjusting Practice During COVID-19
- Guidelines and recommendations for practice during the pandemic include:
  - Workflow recommendations for [radiology departments](#)

- - A method for [extubating patients that limits aerosolization](#)
  - [Epilepsy](#) management
  - Risk stratification and care guidelines for patients with [adult congenital heart disease](#)
  - [GI motility and function testing](#)
- Dental professionals in Saudi Arabia believe the current recommendation to delay [dental treatment on COVID-19](#) positive patients 14 days after onset of symptoms is too short of a period based on reports of several cases of COVID-19 reactivation well beyond 14 days. To mitigate the risk of transmission, the authors recommend extending the recommendation to 28 days of quarantine after onset of symptoms to ensure adequate time for recovery.
- A review indicates that [transcatheter aortic valve replacement](#) is a safe and efficient alternative to surgical aortic valve replacement, and that a modified version of the procedure can be performed during the COVID-19 pandemic to limit potential exposure.

R&D: Diagnosis and Treatments
- A cross-sectional study of 34 CT images from RT-PCR-positive COVID-19 showed typical COVID-19 pneumonia abnormalities in 94% of patients, and 29% showed abnormalities with an initial negative RT-PCR test. Authors support use [of CT analysis for diagnosis of COVID-19](#), even if RT-PCR is negative, and for monitoring disease progression and prognosis.
- A data analysis conducted in Italy found [that 19.4% of confirmed COVID-19 patients (84 out of 433) had a false negative test](#) reading on reverse transcriptase (RT)-PCR at some point in their series of swabs.

Mental Health and Resilience Needs
- Authors from the Cleveland Clinic report an overview of [ethical issues that are causing moral distress in healthcare workers](#) during the COVID-19 pandemic. Areas of distress highlighted include visitation restrictions impacting patients' well-being, risk for safety to self and loved ones, reduced provision of healthcare services and limited allocation of resources.
- Data from 217 participants using [smartphone mobile sensing](#) concluded an increase in sedentary time, depression, and anxiety during the pandemic versus the same time frame in the previous term suggests that there has been an impact on mental health and behavior for this population during the COVID-19 pandemic.

TABLE OF CONTENTS

THE IMPORTANCE OF PROPER DEATH CERTIFICATION DURING THE COVID-19 PANDEMIC

BLUF

In this expert opinion piece, two American physicians believe that physicians need to be extremely attentive when filling out death certificate data during the COVID-19 pandemic, as the specifics of cause of death may be extremely important for future public health policy. The authors also argue that physicians who usually complete death certificates are often improperly trained to do so and provide an example of how a death certificate might be filled out for a deceased COVID-19 patient (Figure).

FIGURES

Figure. Example of a US Death Certificate. There are 58 fields total in US death certificates, with only the 9 related to cause of death shown here. The key fields are cause (part I), contributing conditions (part II), manner, dates of birth and death, sex, race/ethnicity, and locations of residence and death.

EPIDEMIOLOGY

IMPACT OF COVID-19 PANDEMIC ON CRITICAL CARE TRANSFERS FOR ST-ELEVATION MYOCARDIAL INFARCTION, STROKE, AND AORTIC EMERGENCIES

Khot UN, Reimer AP, Brown A, Hustey FM, Hussain MS, Kapadia SR, Svensson LG.. Circ Cardiovasc Qual Outcomes. 2020 Jun 11. doi: 10.1161/CIRCOUTCOMES.120.006938. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective cohort study utilizing the Critical Care Transport System patient registry at the Cleveland Clinic during "baseline" (1 January 2019 to 8 March 2020) and "pandemic" (9 March 2020 to 6 May 2020) found that the pandemic has significantly decreased the daily number of patients presenting to the hospital and requiring emergent transfer in general (4.5 patients per day to 2.4) and specifically with ST-elevation myocardial infarction (STEMI) and stroke (p<0.001 for all three analyses; Figure 1), as measured by the decreased volume of activation of emergent transfers for emergent care and/or procedures. These results suggest that patients may be reluctant to seek care during the pandemic, leading to an increase in mortality and morbidity outside of the hospital. The authors call for increased public education on the importance of seeking care for these events.

ABSTRACT

The COVID-19 pandemic has dramatically impacted healthcare delivery worldwide. In hotspot areas such as Wuhan, Lombardy, and New York City, the disease has forced hospitals to focus on COVID-19 patients. Anecdotal reports have suggested that the pandemic has led to a decrease in patients presenting to these hospitals with serious cardiovascular and neurologic diseases such as ST-elevation myocardial infarction (STEMI) and stroke. We sought to measure the impact of the COVID-19 pandemic on emergency transfers for STEMI, stroke, and acute aortic emergencies within our regional health system.

FIGURES
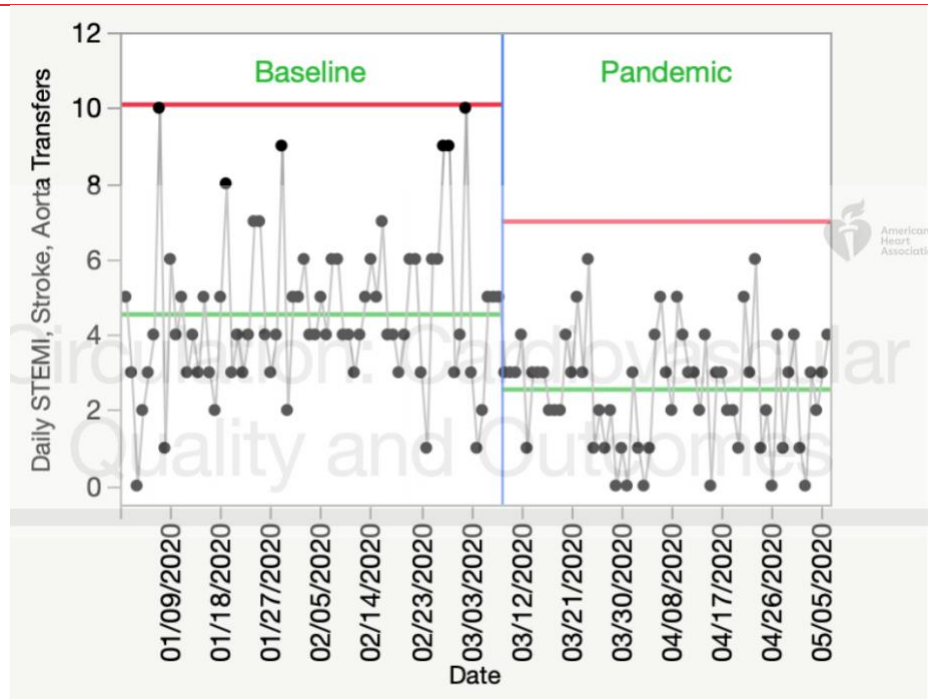
Figure 1: Daily Critical Care Transfer Volumes Between Baseline and Pandemic Time Periods in 2020. In 2020, daily transfer volumes showed a 44% reduction comparing baseline and pandemic (4.5±2.1 vs. 2.5±1.5, P<0.001). (green line = mean, red line = upper confidence level of 3σ)

ADULTS

SMELL AND TASTE DISORDERS DURING COVID-19 OUTBREAK: A CROSS-SECTIONAL STUDY ON 355 PATIENTS

BLUF

A cross-sectional study conducted at Novara University Hospital in Italy from 3/10/2020 - 3/30/2020 focused on 355 patients with confirmed SARS-CoV-2 to further investigate the prevalence and severity of smell and taste disorders. Data showed 66% of patients experienced a change in smell perception and 65.4% experienced a change in taste, 70% experienced one or both of the symptoms, and about half the patients regained these senses after two weeks (p-value less than 0.001)(Figures 1 & 2). The results suggest symptoms of anosmia and ageusia have a high prevalence in COVID-19 patients, and could be an early sign for COVID-19 infection.

ABSTRACT

BACKGROUND: As reported by increasing literature, a significant number of patients with SARS-CoV-2 infection developed smell/taste disorders. Aim of this study is to determine the prevalence and severity of these symptoms among laboratory-confirmed SARS-CoV-2 patients. Secondary objective is to determine their onset/recovery time.
METHODS: This cross-sectional study was conducted from March 10 to 30, 2020 at Novara University Hospital during the COVID-19 Italian outbreak. The 355 enrolled patients answered a questionnaire at 14th (or more) days after proven infection.
RESULTS: The overall population prevalence of both smell/taste or one of the two disorders was 70%. They were first symptoms in 31 (8,7%) patients. Most patients reported a complete loss that in half of the cases (49.5%) was fully recovered after 14 days, with a median recovery time of 10 days.
CONCLUSION: This study confirms a high prevalence of smell/taste disorders in COVID-19 infection with self-recovery for half cases after about 2 weeks.

FIGURES
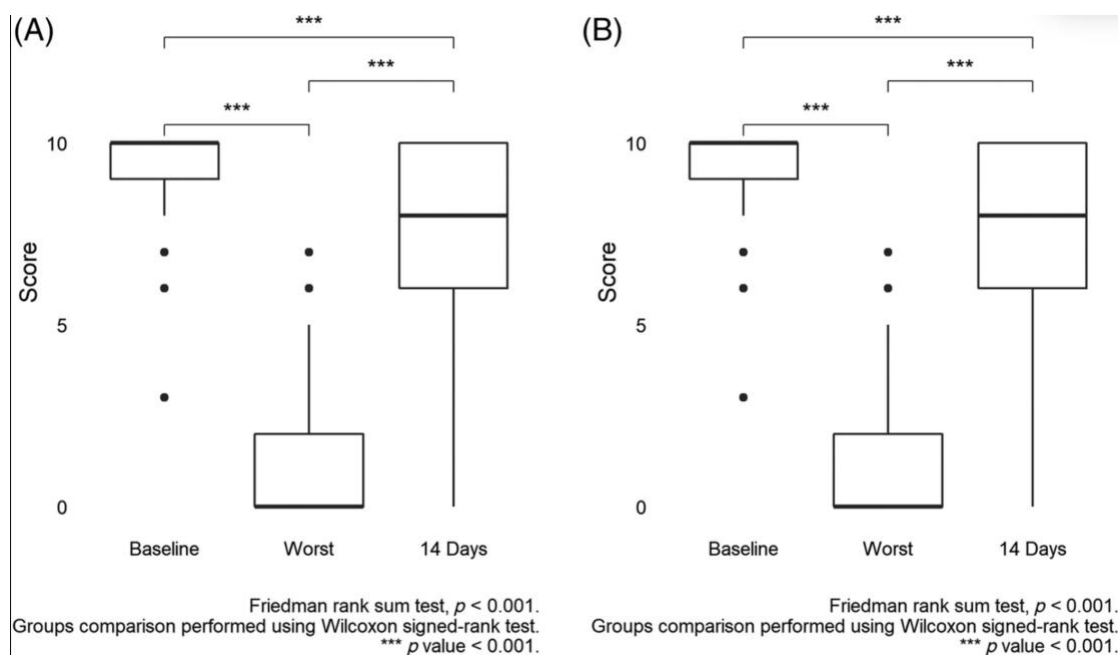
Figure 1. Smell, A, and taste, B, perception (score) before developing symptoms (baseline), at the highest intensity of symptoms (worst) and after 2 weeks from their onset (14 days).
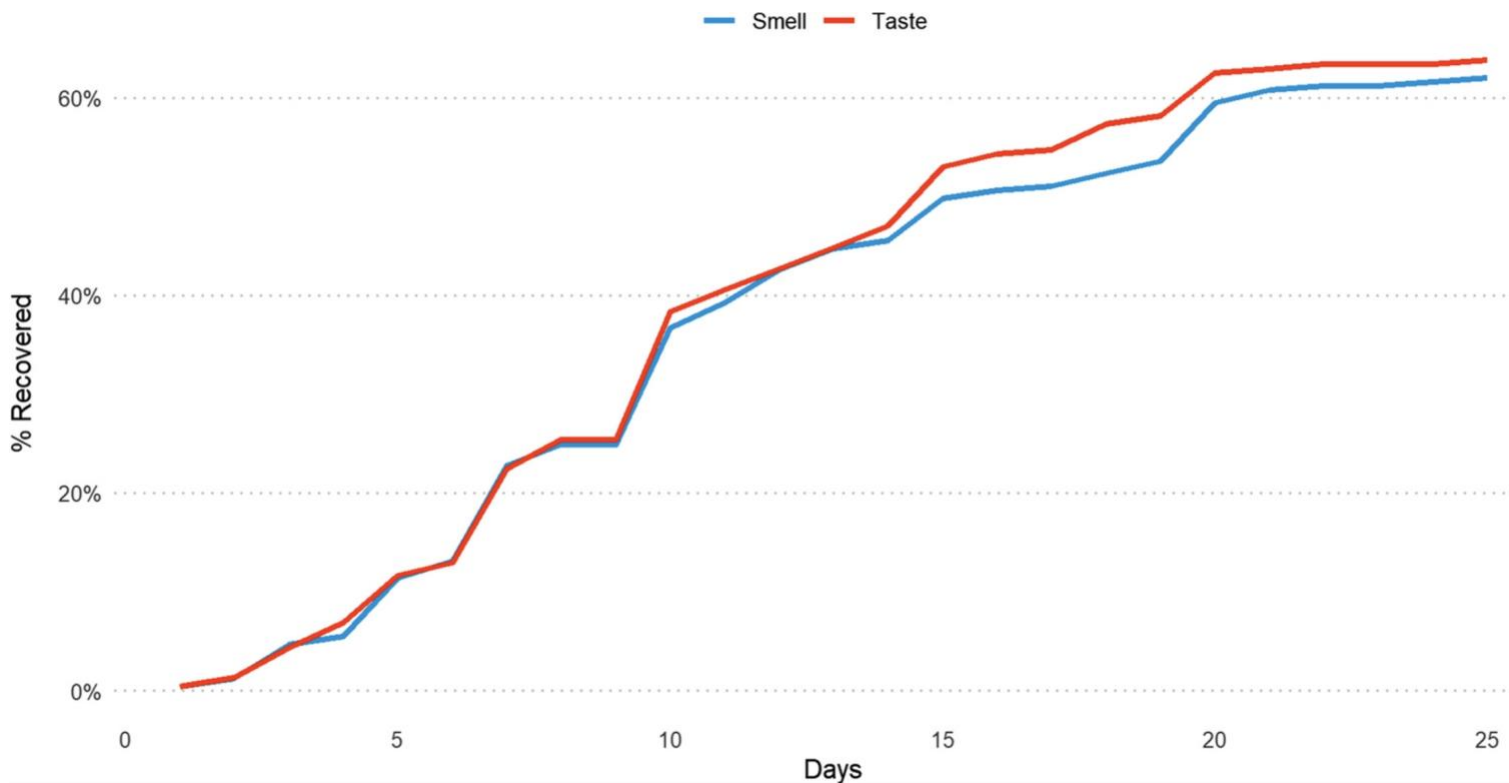
Figure 2. Daily rate of recovery for both smell (blue) and taste disorders (red) [Color figure can be viewed at wileyonlinelibrary.com].

HYPERPYREXIA IN COVID-19 PATIENTS

BLUF

In a case series, physicians from New York report six patients hospitalized with COVID-19 who developed hyperpyrexia. Clinical features include peak body temperature of 107.2 – 109.2°F with onset 6-12 days following admission, and universal mortality within two days of onset (Figure 2). The authors propose hyperpyrexia may be used as an indicator of poor prognosis and suggest it may result from SARS-CoV-2-related brain injury, immune system dysfunction, and/or hypercoagulability leading to thrombus formation.

ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global health emergency, in which its effective treatment and prevention remain obscured. Hyperpyrexia is an elevation of body temperature (BT) above 106.7 F (41.5 C) due to an abnormally increased hypothalamic thermo-regulatory set. The pathophysiology, impact, and outcomes of hyperpyrexia in COVID-19 patients have not yet been studied. Herein, we present clinical features and outcomes of six COVID-19 patients who had developed hyperpyrexia during hospitalization. All patients expired shortly after the onset of hyperpyrexia. Hyperpyrexia seems to adversely impact the outcomes and mortality in patients with COVID-19. The underlying mechanisms of developing hyperpyrexia in COVID-19 are mysterious. We propose it may be caused by SARS-CoV-2 related brain injury, exuberant immune response, and thrombus formation. More research is needed to verify our results. Understanding the association between hyperpyrexia and SARS-CoV-2 will help to elucidate the COVID-19 pathogenesis, which is mandatory for developing effective treatment strategies.

FIGURES

Figure 2: The dynamic changes of measured BT (°F) of each patient
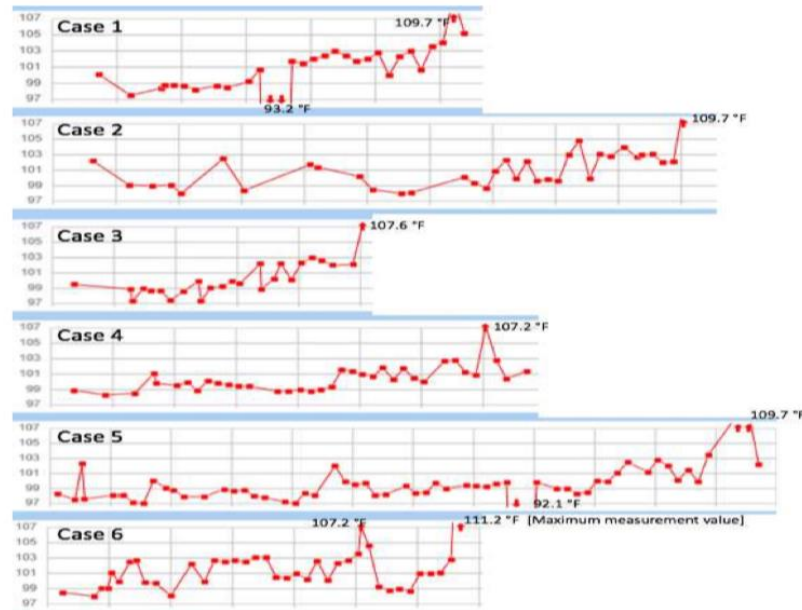
Figure 2: The dynamic changes of measured [body temperature] (°F) of each patient

PEDIATRICS

RASH AS A PRESENTING COMPLAINT IN A CHILD WITH COVID-19

BLUF

Pediatricians in Wales present the case of a 13-year-old boy who presented in April 2020 with pain on the soles of his feet, as well as a 24-hour history of fever, myalgia, and headache, and was subsequently diagnosed with COVID-19 on reverse transcriptase (RT)-PCR. He was noted to have maculopapular lesions on his axilla, the plantar surfaces of his feet, and scattered petechiae on the lower extremities (Figures 1 and 2), suggesting pediatricians should consider a diagnosis of COVID-19 in children presenting with these or similar dermatological findings.

SUMMARY

The authors describe the physical exam findings as "an erythematous papular eruption in the axillae with axillary and cervical lymphadenopathy, all nodes measuring < 1cm. On the plantar surface of his feet were multiple tender, erythematous papules each measuring approximately 1 cm (Figure 1). There were no vesicles or pustules. Erythematous macules with associated scattered petechiae, located in close proximity to the macules, were also present on the child's distal lower extremities (Figure 2)."

ABSTRACT

Cutaneous manifestations are becoming increasingly well-documented in adults with COVID-19. There is now also a growing body of literature regarding skin involvement in children, with reports of papulovesicular, petechial and widespread macular and papular lesions, as well as chilblains (pernio). We describe the case of a thirteen-year-old boy with confirmed COVID-19 in the United Kingdom who presented with skin findings localized to the plantar aspects of the feet, axillae and lower limbs. The morphology was predominantly maculopapular but also included petechiae and annular lesions.

Figure 1: Feet - Multiple erythematous, tender papules, each measuring approximately 1 cm were present on the plantar aspects of the feet.

Figure 2: Lower limbs - A macular rash with associated scattered petechiae was present on the lower limbs at presentation. An annular lesion developed following discharge.

ADVANCED AGE

URTICARIA (ANGIOEDEMA) AND COVID- 19 INFECTION

BLUF

An elderly man presented with generalized pruritic hives, angioedema (Figure 1), fever, and malaise and was clinically diagnosed with COVID-19, supported by labs showing lymphopenia and a chest CT showing pneumonia with ground glass opacification suggestive of COVID-19 (Figure 2). The authors from the United Kingdom and Iran indicate that this case study suggests urticaria may be an early manifestation of COVID-19.

ABSTRACT

The novel coronavirus, otherwise known as COVID-19 has fast become a major health concern.1 2 It has been reported that in addition to the conventional respiratory symptoms, patients also display skin manifestations such as Urticaria and angioedema.3 Here we present a case study of an elderly man who first presented with generalised pruritic hives ranging from 1.5 to 8.0 cm in diameter on the 5th of March 2020. The patient was investigated for another differential diagnosis of Urticaria such as parasitic and bacterial infection, for which negative results were found. On the 5th of March 2020 the patient-reported these symptoms plus general malaise, fatigue, 37.90C temperature and sore throat. Initial biochemical tests showed that the patient presented with low numbers of white blood cells (WBC) (WBC=2.75x103).
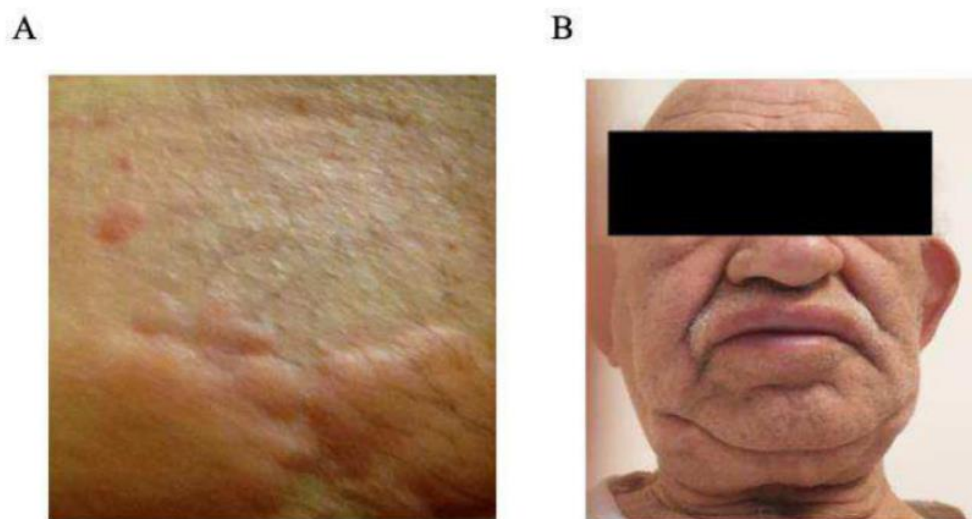
Figure 1. (A) Cutaneous manifestation of urticaria. (B) Male patient displaying angioedema.
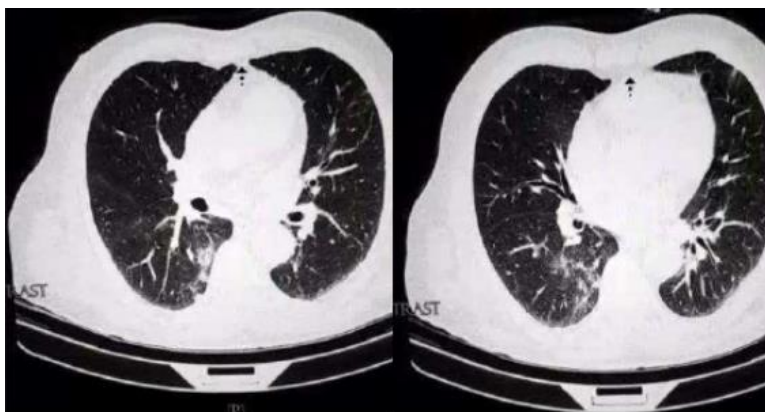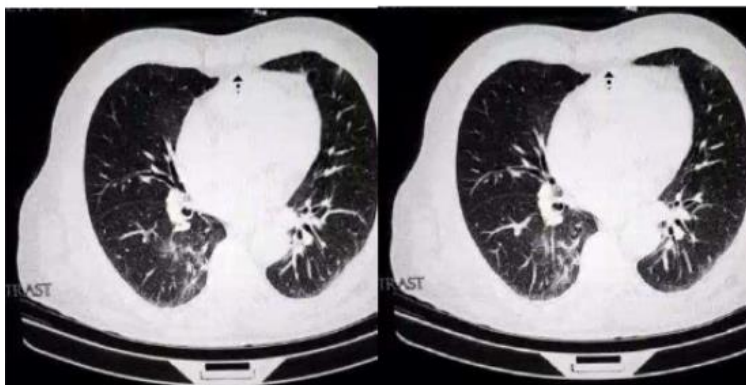

Figure A

Figure B

Figure 2. Patient CT chest at the time of hospital admission (A-D).

WORSE PROGRESSION OF COVID-19 IN MEN: IS TESTOSTERONE A KEY FACTOR?

BLUF

A review of literature from 1996 to May 19, 2020 found that Testosterone (T), in conjunction with the RAAS system, and transmembrane serine protease 2 may facilitate SARS-CoV-2 transmission and internalization explaining a possible link between worse prognosis for men with COVID-19 infection as compared to women. Furthermore, somewhat contrarily, low serum T levels were found to be associated with "impaired viral clearance and systemic inflammation" predisposing patients to "endothelial dysfunction, thrombosis and defective immune response."

ABSTRACT

BACKGROUND: The novel Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) disease 2019 (COVID-19) seems to have a worse clinical course among infected men compared to women, thus, highlighting concerns about gender predisposition to serious prognosis. Therefore, androgens, particularly testosterone (T), could be suspected as playing a critical role in driving this excess of risk. However, gonadal function in critically ill men is actually unknown, mainly because serum T concentration is not routinely measured in clinical practice, even more in this clinical context.
OBJECTIVE: To overview on possible mechanisms by which serum T levels could affect the progression of COVID-19 in men.
METHODS: Authors searched PubMed/Medline, Web of Science, EMBASE, Cochrane Library, Google, and Institutional websites for medical subheading terms and free text words referred to "SARS-CoV-2", "COVID-19", "testosterone", "male hypogonadism", "gender" "immune system", "obesity", "thrombosis" until May 19th 2020.
RESULTS: T, co-regulating the expression of angiotensin-converting enzyme 2 and transmembrane protease serine 2 in host cells, may facilitate SARS-CoV-2 internalization. Instead, low serum T levels may predispose to endothelial dysfunction, thrombosis and defective immune response, leading to both impaired viral clearance and systemic inflammation. Obesity, one of the leading causes of severe prognosis in infected patients, is strictly associated with functional hypogonadism, and may consistently strengthen the aforementioned alterations, ultimately predisposing to serious respiratory and systemic consequences.
DISCUSSION AND CONCLUSION: T in comparison to estrogen may predispose men to a widespread COVID-19 infection. Low serum levels of T, which should be supposed to characterize the hormonal milieu in seriously ill individuals, may predispose men, especially aged men, to poor prognosis or death. Further studies are needed to confirm these pathophysiological assumptions and to promptly identify adequate therapeutic strategies.

COVID 19: A CLUE FROM INNATE IMMUNITY

BLUF

A literature review from Salerno, Italy discusses various components of the innate immune system - specifically toll-like receptors, complement proteins, monocytes/macropages, neutrophils, and interferons - that appear to play a role in the development of the cytokine storm in SARS-CoV-2 infection. The authors indicate that understanding the role of innate immunity in COVID-19 is critical for identifying potential targets for treatment and to properly comprehend the pathogenesis of this viral illness.

SUMMARY

Specific topics discussed in this literature review include:

- Toll-like receptors (TLR), specifically TLR4, TLR 7/8, and TLR3, that may promote cytokine and interferon production in COVID-19 infection by indirectly activating downstream transcription factors (i.e. NF-kB, IRF3, IRF7) (Figure 1).

- Evidence suggesting complement system involvement in COVID-19 infections and early data suggesting that treatments such as Eculizumab, a human monoclonal antibody against C5a/C5b, and C3 inhibitor AMY-101 contribute to improvement in patients with COVID-19.
- The role of Open Reading Frame 8 (ORF-8) in SARS-CoV, which promotes macrophage activation of the multiprotein complex inflammasome that indirectly activates pro-inflammatory cytokines. Since the COVID-19 genome has high analogy with the ORF-8 region in SARS-CoV, this process may occur similarly in COVID-19 infection.
- Interleukin 1 (IL-1) release from macrophages during the cytokine storm of COVID-19, which has prompted trials with Anakinra, a recombinant IL-1 receptor.
- The role of neutrophils as early recruiters of inflammatory cells or as contributors to tissue damage through promotion of pro-inflammatory cytokines.
- Several studies on type 1 interferons (IFN) that illustrate their possible protective effect against COVID-19 illness.

ABSTRACT

The recent COVID-19 pandemic has had a significant impact on our lives and has rapidly expanded to reach more than 4 million cases worldwide by May 2020. These cases are characterized by extreme variability, from a mild or asymptomatic form lasting for a few days up to severe forms of interstitial pneumonia that may require ventilatory therapy and can lead to patient death. Several hypotheses have been drawn up to understand the role of the interaction between the infectious agent and the immune system in the development of the disease and the most severe forms; the role of the cytokine storm seems important. Innate immunity, as one of the first elements of guest interaction with different infectious agents, could play an important role in the development of the cytokine storm and be responsible for boosting more severe forms. Therefore, it seems important to study also this important arm of the immune system to adequately understand the pathogenesis of the disease. Research on this topic is also needed to develop therapeutic strategies for treatment of this disease.

FIGURES
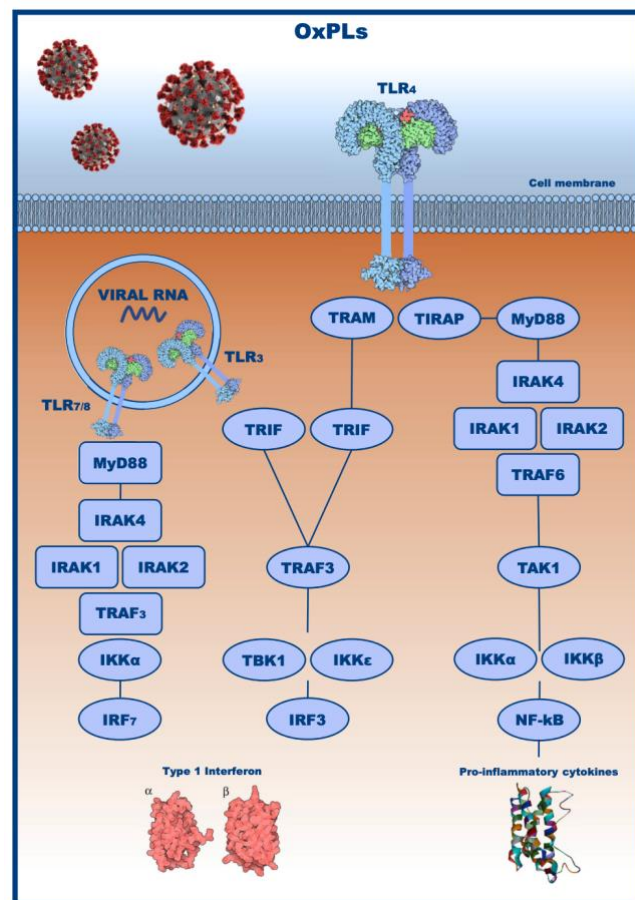
Figure 1. Role of toll-like receptor in response to coronavirus infection. TLR4 is involved in the response triggered by oxidized phospholipids (OxPLs) induced by SARSCoV2 infection, with activation, through MyD88 and TRIF, of the production of type I Interferon and inflammatory cytokines such as IL6 and TNF. TLR3 and TLR7/8 recognize viral RNA at the endosome and through MyD88 and TRIF, activate interferon regulatory factor (IRF3 and IRF7)

RATIONING SOCIAL CONTACT DURING THE COVID-19 PANDEMIC: TRANSMISSION RISK AND SOCIAL BENEFITS OF US LOCATIONS

BLUF

A research study sponsored by Massachusetts Institute of Technology used mobility data from smartphone devices as well as data from a consumer survey and the US Census Statistics of US Businesses to analyze the potential risk of exposure to COVID-19 versus the economic importance of twenty-six location categories including banks, universities, gyms, dentists, and fast-food restaurants. They highlighted numerous relationships between the various interrogated locations (Figure 1), demonstrated a strong positive relationship between the risk of exposure at a specific location type and its economic benefit (Figure 2A), and found an overall decrease in visitation to locations deemed to offer the highest benefit of closing between February and March 2020 (Figure 2B). Overall, their findings may be useful for government officials when making decisions about location closures and re-openings during the pandemic.

ABSTRACT

To prevent the spread of coronavirus disease 2019 (COVID-19), some types of public spaces have been shut down while others remain open. These decisions constitute a judgment about the relative danger and benefits of those locations. Using mobility data from a large sample of smartphones, nationally representative consumer preference surveys, and economic statistics, we measure the relative transmission reduction benefit and social cost of closing 26 categories of US locations. Our categories include types of shops, entertainments, and service providers. We rank categories by their trade-off of social benefits and transmission risk via dominance across 13 dimensions of risk and importance and through composite indexes. We find that, from February to March 2020, there were larger declines in visits to locations that our measures indicate should be closed first.

FIGURES
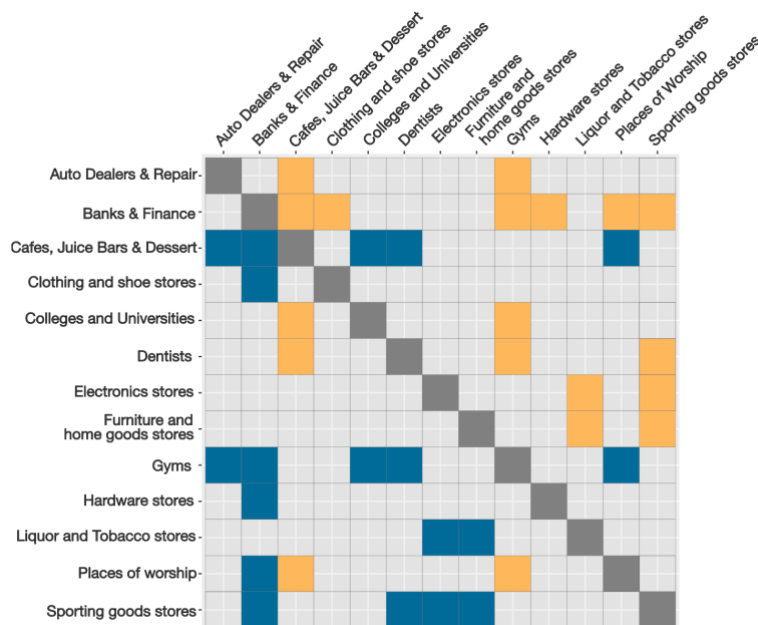
Figure 1: Grid indicating dominating and dominated categories. A cell is gold if the row category is better on all nine risk and four importance dimensions than the column category, and blue for the converse. [Per article, dominating locations refer to "locations that dominate another in all dimensions of lower transmission danger and higher importance."]
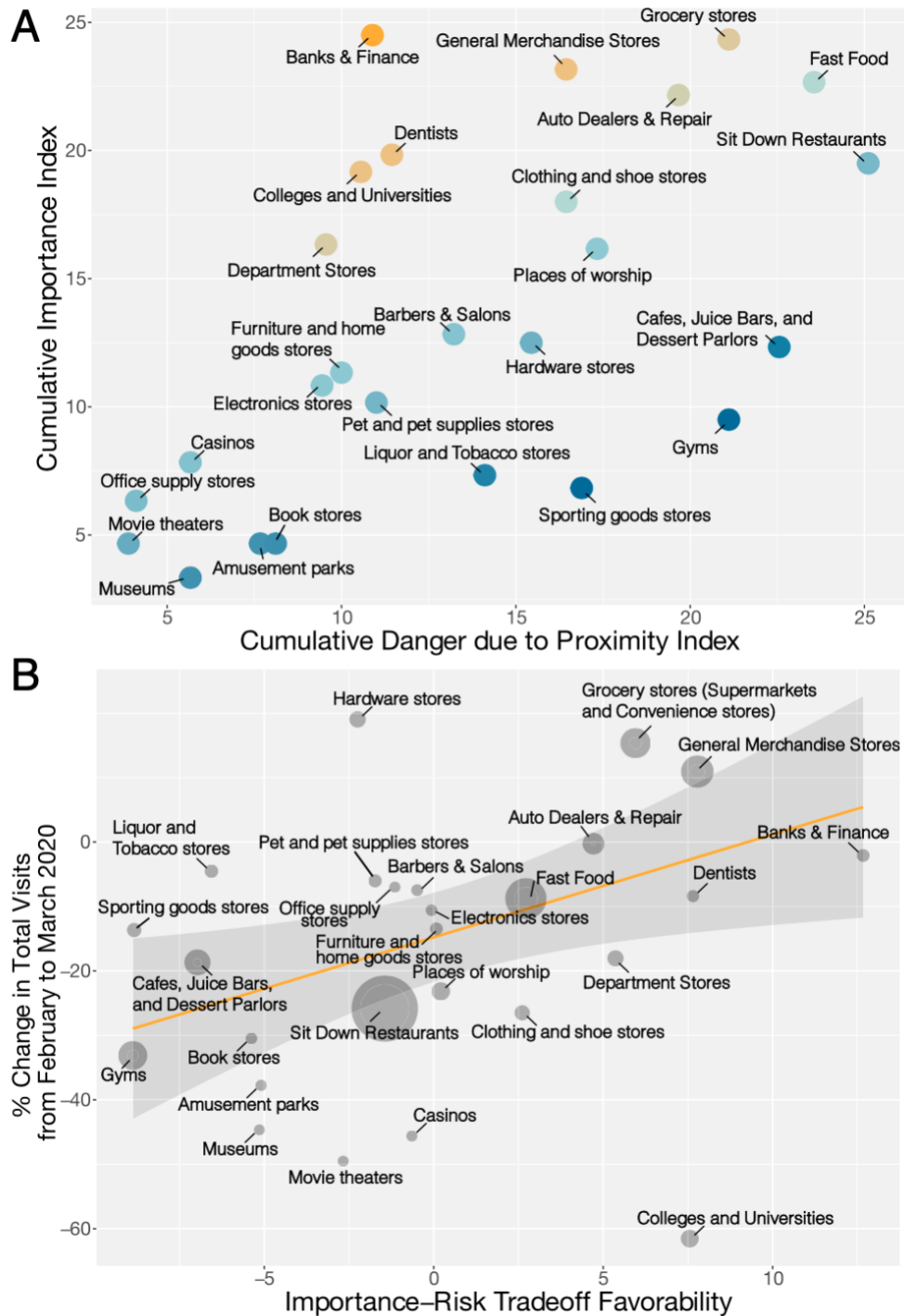
Figure 2: (A) Category cumulative importance index and cumulative danger index. The color scale reflects the residuals, by category, of a linear regression of the importance index on the danger index. Golden categories have disproportionately high importance for their risk, and blue categories have disproportionately low importance. (B) Change in location category visits versus the category importance–risk residual. Marker sizes are proportional to total visits in February 2020.

DOES ADDING OF HYDROXYCHLOROQUINE TO THE STANDARD CARE PROVIDE ANY BENEFIT IN REDUCING THE MORTALITY AMONG COVID-19 PATIENTS?: A SYSTEMATIC REVIEW

BLUF

This systematic review identified 14 clinical studies (3 randomized and 11 non-randomized) that analyzed the effect of Hydroxychloroquine on mortality in COVID-19 patients. Meta-analysis found that the odds of mortality in patients treated with a combination of Hydroxychloroquine and Azithromycin was significantly higher than in patients treated with supportive care alone (odds ratio (OR) = 2.34, 95% confidence interval (CI): 1.63-3.34) (Figure 4). Additionally, there was no significant difference in mortality between patients who received Hydroxychloroquine alone versus supportive care alone (OR = 1.25, 95% CI: 0.65-2.38) or patients who received a combination of Hydroxychloroquine and Azithromycin versus Hydroxychloroquine alone (OR = 1.07, 95% CI: 0.58-1.98) (Figure 5). Authors conclude that current evidence suggests Hydroxychloroquine produces no improvement in mortality outcomes in COVID-19 patients.

ABSTRACT

Hydroxychloroquine has been promoted for its use in treatment of COVID-19 patients based on in-vitro evidences. We searched the databases to include randomized and observational studies evaluating the effect of Hydroxychloroquine on mortality in COVID-19 patients. The outcome was summarized as odds ratios (OR) with a 95% confidence interval (CI).We used the inverse-variance method with a random effect model and assessed the heterogeneity using I2 test. We used ROBINS-I tool to assess methodological quality of the included studies. We performed the meta-analysis using 'Review manager software version 5.3'. We identified 6 observational studies satisfying the selection criteria. In all studies, Hydroxychloroquine was given as add on to the standard care and effect was compared with the standard care alone. A pooled analysis observed 251 deaths in 1331 participants of the Hydroxychloroquine arm and 363 deaths in 1577 participants of the control arm. There was no difference in odds of mortality events amongst Hydroxychloroquine and supportive care arm [1.25 (95% CI: 0.65, 2.38); I2 = 80%]. A similar trend was observed with moderate risk of bias studies [0.95 (95% CI: 0.44, 2.06); I2 = 85%]. The odds of mortality were significantly higher in patients treated with Hydroxychloroquine + Azithromycin than supportive care alone [2.34 (95% CI: 1.63, 3.34); I2 = 0%]. A pooled analysis of recently published studies suggests no additional benefit for reducing mortality in COVID-19 patients when Hydroxychloroquine is given as add-on to the standard care. Graphical Abstract.

CAUTION ABOUT EARLY INTUBATION AND MECHANICAL VENTILATION IN COVID-19

BLUF

A group of researchers argue that early initiation of mechanical ventilation and intubation to prevent more severe lung injury in COVID-19 patients is not substantiated and may in fact, cause fatal complications. In particular, the researchers claim that fear of patient self-induced lung injury via vigorous spontaneous inspiratory efforts is not enough justification to rapidly initiate these interventions, as the evidence is lacking. This contrasts an article by Marini and Gattioni published recently.

DIAGNOSTIC RADIOLOGY

CT QUANTITATIVE ANALYSIS AND ITS RELATIONSHIP WITH CLINICAL FEATURES FOR ASSESSING THE SEVERITY OF PATIENTS WITH COVID-19

BLUF

A retrospective cohort study conducted at Chongqing Three Gorges Central Hospital in China of 84 COVID-19 patients receiving care from January 23rd, 2020 to February 29th, 2020 found that quantitative analysis programs for CT scans could be used to predict severity of COVID-19 related pneumonia. The severe group had significantly higher ground-glass opacity (GGO) scores, consolidation scores, and total lesion scores than the non-severe group (Figure 2), indicating a potential application for CT quantitative analysis programs to prognosticate severity of COVID-19 illness.

ABSTRACT

OBJECTIVE: To investigate the value of initial CT quantitative analysis of ground-glass opacity (GGO), consolidation, and total lesion volume and its relationship with clinical features for assessing the severity of coronavirus disease 2019 (COVID-19). MATERIALS AND METHODS: A total of 84 patients with COVID-19 were retrospectively reviewed from January 23, 2020 to February 19, 2020. Patients were divided into two groups: severe group (n = 23) and non-severe group (n = 61). Clinical symptoms, laboratory data, and CT findings on admission were analyzed. CT quantitative parameters, including GGO, consolidation, total lesion score, percentage GGO, and percentage consolidation (both relative to total lesion volume) were calculated. Relationships between the CT findings and laboratory data were estimated. Finally, a discrimination model was established to assess the severity of COVID-19. RESULTS: Patients in the severe group had higher baseline neutrophil percentage, increased high-sensitivity C-reactive protein (hs-CRP) and procalcitonin levels, and lower baseline lymphocyte count and lymphocyte percentage ($p < 0.001$). The severe group also had higher GGO score ($p < 0.001$), consolidation score ($p < 0.001$), total lesion score ($p < 0.001$), and percentage consolidation ($p = 0.002$), but had a lower percentage GGO ($p = 0.008$). These CT quantitative parameters were significantly correlated with laboratory inflammatory marker levels, including neutrophil percentage, lymphocyte count, lymphocyte percentage, hs-CRP level, and procalcitonin level ($p < 0.05$). The total lesion score demonstrated the best performance when the data cut-off was 8.2%. Furthermore, the area under the curve, sensitivity, and specificity were 93.8% (confidence interval [CI]: 86.8-100%), 91.3% (CI: 69.6-100%), and 91.8% (CI: 23.0-98.4%), respectively. CONCLUSION: CT quantitative parameters showed strong correlations with laboratory inflammatory markers, suggesting that CT quantitative analysis might be an effective and important method for assessing the severity of COVID-19, and may provide additional guidance for planning clinical treatment strategies.
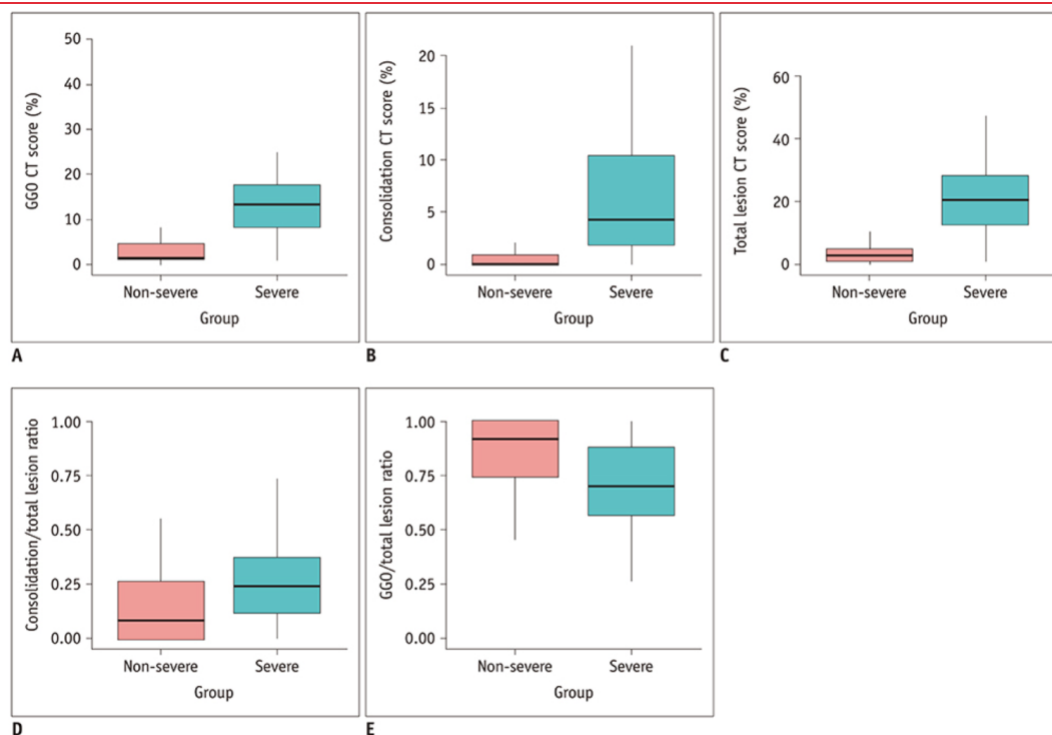
FIGURES

Figure 2. Results of GGO score (A), consolidation score (B), total lesion score (C), consolidation/total lesion ratio (D), and GGO/total lesion ratio (E) in severe and non-severe groups.

CRITICAL CARE

LOW MOLECULAR WEIGHT HEPARINS IN COVID-19 PATIENTS: BEWARE OF AUGMENTED RENAL CLEARANCE!

BLUF

This study reports the case of a 52-year-old male with augmented renal clearance (ARC) who developed pulmonary thromboembolism after a two week ICU stay due to severe COVID-19 pneumonia. The patient received enoxaparin 60 mg daily since admission, which may have been insufficient for DVT prophylaxis considering the patient's COVID-19 and ARC status. The study also quantified the incidence of ARC in ICU patients during the COVID-19 pandemic, finding 18/47 ICU patients had ARC. The authors conclude that ARC has a high incidence, and regular doses of low molecular weight heparin may not provide adequate protection from DVT and PE in COVID-19 positive patients with ARC.

OPERATIONALIZING COVID-19 TESTING: WHO, WHAT, WHEN, WHERE, WHY, AND HOW

Reddy AJ, Fraser TG, Grover P, Weathers AL, Cruise M, Foxx MA, Babiuch CM, Henricks WH, Meldon SW, Muenzenmeyer A, Pengel SL, Simon JF, Procop GW.. Cleve Clin J Med. 2020 Jun 9. doi: 10.3949/ccjm.87a.ccc048. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

The authors describe how COVID-19 testing was set up at the Cleveland Clinic Health System, and they elaborate on the technological highlights, such as the home monitoring program and electronic health record (EHR) test order integration, that aided this process. The experiences detailed provide a framework that may be used by other hospital systems in preparing a COVID-19 testing workflow.

SUMMARY

The authors review the following questions about COVID-19 testing in their system:

- What: The CDC assay (TIBMOLBIO assay) and the Xpert Xpress SARS-CoV-2 assay were chosen for their high sensitivity (95%).
- Who, When, Where: In the ED, testing was initially expedited for symptomatic high-risk patients (e.g. requiring ICU admission) and then expanded to include asymptomatic and presymptomatic patients (Figure 2). In the inpatient setting, there was more testing capacity, so tests were widely distributed and only withdrawn depending on availability. Testing was encouraged before any procedures or surgeries and was expanded to community populations, including prisons and health centers (Figure 4).
- Why: Diagnostic testing is important for prevention of COVID-19 spread.
- How: An interdisciplinary COVID-19 Testing Stewardship Committee was established to oversee the workflow. A COVID-19 Test Volume Dashboard (Figure 1) and COVID-19 Home Monitoring Program were implemented, and COVID-19 was incorporated into the EHR ordering workflow.

ABSTRACT

The authors review the rationale behind and approaches to testing for COVID-19, the quality of currently available tests, the role of data analytics in strategizing testing, and using the electronic medical record and other programs designed to steward COVID-19 testing and follow-up of patients.

FIGURES

Figure 1. COVID-19 test volume dashboard.

Figure 2. Rapid COVID-19 testing inpatient workflow for emergency surgeries and procedures.
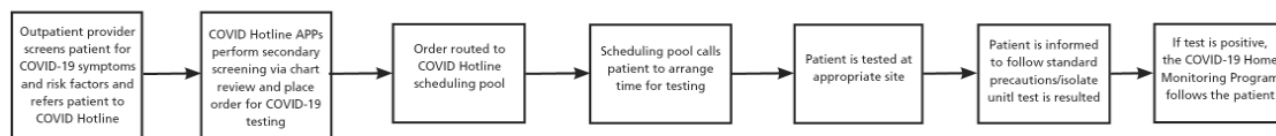

Figure 4. COVID-19 testing process for symptomatic outpatients.

ACUTE CARE

DIAGNOSTIC RADIOLOGY

INFECTION CONTROL AND MANAGEMENT STRATEGY FOR COVID-19 IN THE RADIOLOGY DEPARTMENT: FOCUSING ON EXPERIENCES FROM CHINA

BLUF

In this article, the authors outline the new workflow (Figure 3), PPE guidelines (Table 3), and control team modifications implemented in Radiology departments of non-designated hospitals for COVID-19 in Nanjing, China, in order to prevent nosocomial transmission of COVID-19 to both patients and staff. Given the importance of chest computed tomography (CT) in identifying early manifestations of COVID-19 with a high sensitivity of 97–98%, the safety, practicability, and efficiency of imaging procedures are of the utmost importance during this pandemic, and the authors suggest strict adherence to the proposed workflow and infection control measures in order to reduce the risk to staff and patients.

ABSTRACT

Coronavirus disease 2019 (COVID-19) is a new infectious disease rapidly spreading around the world, raising global public health concerns. Radiological examinations play a crucial role in the early diagnosis and follow-up of COVID-19. Cross infection among patients and radiographers can occur in radiology departments due to the close and frequent contact of radiographers with confirmed or potentially infected patients in a relatively confined room during radiological workflow. This article outlines our experience in the emergency management procedure and infection control of the radiology department during the COVID-19 outbreak.
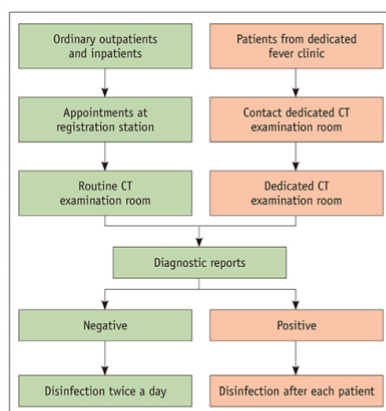
FIGURES

Fig. 3. Workflow of CT examination room in our department.
Non-COVID-19 patients and suspected COVID-19 patients were examined in routine CT rooms or dedicated CT room, respectively. Dedicated CT examination room was disinfected after each patient, while routine CT examination rooms implemented strict disinfection before next patient's examination if COVID-19 was suspected, based on diagnostic reports. CT = computed tomography

Table 3. Personal Protection Guidelines Checklist

Items	General Protection	Level 1 Protection	Level 2 Protection	Level 3 Protection
Working clothes	√	√	√	√
Mask	√ Surgical	√ N95	√ N95	√ N95
Round hat		√	√	√
Gloves		√	√	√
Gown		√	√	√
Goggles/ face guard			√	√
Shoe covers			√	√
Comprehensive respiratory apparatus				√

ANAESTHESIA

MANAGEMENT OF THE AIRWAY AND LUNG ISOLATION FOR THORACIC SURGERY DURING THE COVID-19 PANDEMIC

Greenhalgh D.. Anaesthesia. 2020 Jun 11. doi: 10.1111/anae.15167. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF
This letter from a thoracic anesthetist is a response to recent airway management recommendations for thoracic surgical patients during the COVID-19 pandemic. The author suggests a method of extubating patients that limits cough and viral spread, which includes extubating while the patient is still under anesthesia and in a lateral position to facilitate spontaneous breathing, as well as replacing the viral filter and double clamp as soon as possible after suctioning the remaining air out of the patient's lungs.

MEDICAL SUBSPECIALTIES

CARDIOLOGY

DISTURBING EFFECT OF LOCKDOWN FOR COVID-19 ON THE INCIDENCE OF INFECTIVE ENDOCARDITIS: A WORD OF CAUTION

BLUF

This letter to the editor outlines a single-center prospective study conducted in Belgium to evaluate the incidence of infective endocarditis (IE) during the COVID-19 lockdown period. The results show a decrease in the diagnosis of IE during the weeks of lockdown compared to the incidence of IE during pre-lockdown (Fig. 1 and 2), increasing awareness of a possible harmful effect of COVID-19 lockdown measures on the detection rate of IE.

FIGURES

Fig. 1

From: Disturbing effect of lockdown for COVID-19 on the incidence of infective endocarditis: a word of caution
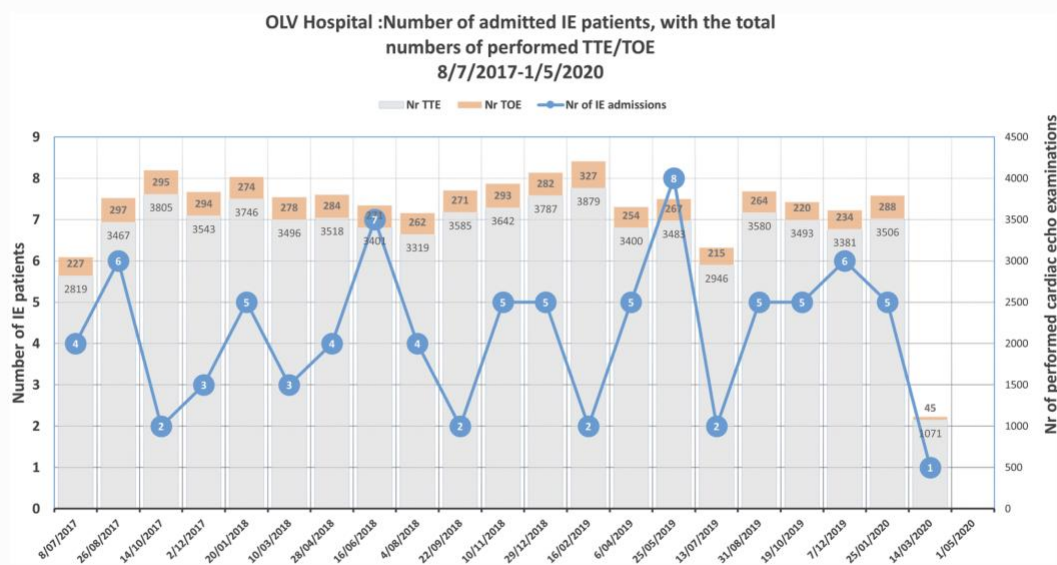
Graphical representation of the number of patients with definite IE represented by clusters of 7 weeks period. Last cluster of 7 weeks represents the lockdown period in Belgium. Superimposed are the numbers of TTE's and TOE's for each time cluster

Fig. 2

From: Disturbing effect of lockdown for COVID-19 on the incidence of infective endocarditis: a word of caution

Focus on the latest 21 weeks. Weekly numbers are shown

GASTROENTEROLOGY

EUROPEAN SOCIETY FOR NEUROGASTROENTEROLOGY AND MOTILITY (ESNM) RECOMMENDATIONS FOR CONDUCTING GASTROINTESTINAL MOTILITY AND FUNCTION TESTING IN THE RECOVERY PHASE OF THE COVID-19 PANDEMIC

BLUF

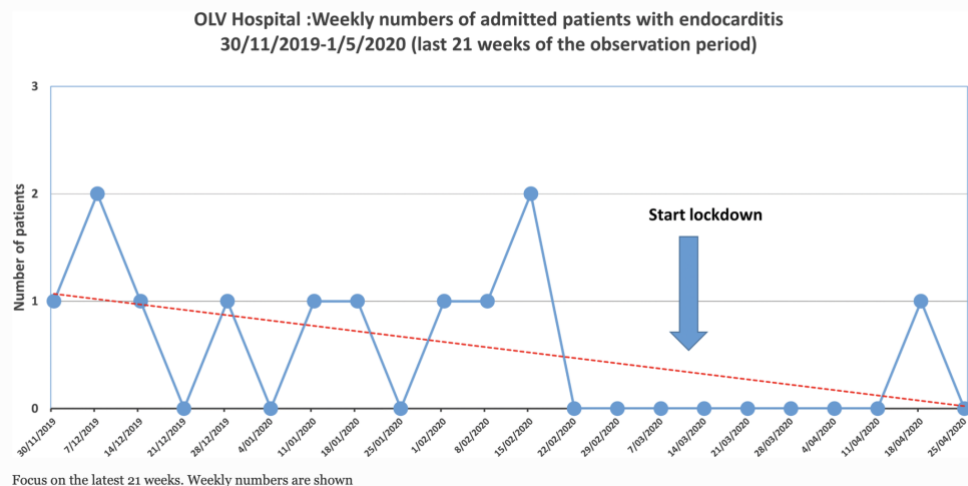In this article, a panel of experts from the European Society for Neurogastroenterology and Motility (ESNM) proposed recommendations to carry out the GI motility and function testing safely in the early recovery phase of COVID-19. Since many motility disorders are chronic and may be managed with symptomatic treatment, postponement is recommended unless an urgent procedure is indicated. The authors explained that tests including esophageal manometry, pH monitoring, and breath tests might be associated with a high risk of SARS-CoV-2 transmission through the production of aerosol droplets and recommended increased precautions during these procedures. The ESNM guidelines to carry out relevant procedures in a safe manner are summarized below.

SUMMARY

The ESNM stratified risk of the procedure based on the following scoring system (0-2: low-risk procedure, 3-4: moderate-risk and >4: high-risk procedure) and made the following recommendations:

1. Test timing: Urgent procedures were identified as "esophageal manometry for severe dysphagia with weight loss and risk of aspiration, achalasia presenting with weight loss, pH monitoring for non-cardiac chest pain with persistent regurgitation and high risk of aspiration and weight loss." See Table 1 in the article.
2. Education and Staff training: Hand washing for 20 seconds before and after the procedure, avoid touching the face, daily screening with temperature monitor, looking for new-onset COVID-19 symptoms, appropriate PPE use.
3. Protective measures for healthcare staff for various time points (before study, day of study, and management of motility units), detailed in Table 5 a, b, and c in the article.
4. Staff protection recommendations based on risk status for patient COVID-19 infection, detailed in Table 6 in the article..
5. Specific precautions that need to be followed during each procedure are shown in Table 8 in the article.

ABSTRACT

BACKGROUND: During the peak of the COronaVIrus Disease 2019 (COVID-19) pandemic, care for patients with gastrointestinal motility and functional disorders was largely suspended. In the recovery phases of the pandemic, non-urgent medical care is resumed, but there is a lack of guidance for restarting and safely conducting motility and function testing. Breath tests and insertion of manometry and pH monitoring probes carry a risk for SARS-CoV-2 spread through droplet formation.
METHODS: A panel of experts from the European Society for Neurogastroenterology and Motility (ESNM) evaluated emerging national and single center recommendations to provide the best current evidence and a pragmatic approach to ensure the safe conduct of motility and function testing for both healthcare professionals and patients.
RESULTS: At a general level, this involves evaluation of the urgency of the procedure, evaluation of the infectious risk associated with the patient, the investigation and the health care professional(s) involved, provision of the test planning and test units, education and training of staff and use of personnel protection equipment. Additional guidance is provided for specific procedures such as esophageal manometry, pH monitoring and breath tests.
CONCLUSIONS AND INFERENCES: The ESNM guidelines provide pragmatic and appropriate guidance for the safe conduct of motility and function testing in the COVID-19 pandemic and early recovery phase.

SURGICAL SUBSPECIALTIES

THORACIC SURGERY

TRANSCATHETER MANAGEMENT OF SEVERE AORTIC STENOSIS DURING THE COVID-19 PANDEMIC

BLUF

This review by authors in the United Kingdom evaluates the risks and benefits (see summary below) of performing transcatheter aortic valve implantation (TAVI) in patients diagnosed with aortic stenosis (AS) during the COVID-19 pandemic. The review indicates that TAVI is a safe and efficient alternative to surgical aortic valve replacement (SAVR) (Figures 1 and 2), and that a modified version of the procedure (Table 1) can be performed during the COVID-19 pandemic to limit potential exposure.

SUMMARY

A literature review conducted by authors in the United Kingdom weighs the risks and benefits of performing TAVI in AS patients since the COVID-19 pandemic has imposed a shutdown of all elective and non-urgent surgical procedures. The review emphasizes the following:

- The diagnosis of AS carries with it a poor prognosis with 1-year mortality rates being as high as 40% in severe symptomatic cases and 21.1% within 3 years in asymptomatic cases. Postponing treatment is a high-risk decision.
- TAVI has grown increasingly popular in recent years and has emerged as a safe and effective alternative to SAVR.
- Early intervention has shown better patient outcomes since procedures become riskier with disease progression.
- When compared with SAVR, which is a more invasive technique with longer recovery time, TAVI has shown equal efficacy in intermediate-risk patients (Figure 1) and is even favorable to SAVR in low-risk patients (Figure 2).
- TAVI has low recovery time with no required ventilation or critical care in most cases, yielding reduced risk of COVID-19 exposure.
- Studies have shown good 5-year valve durability but data beyond 5 years is lacking. This may indicate increased risk in young, low-risk patients, as they will likely require repeat procedures beyond the initial 5-year period.

Overall, the authors recommend weighing risk of COVID-19 infection and potential procedural complications versus the chance of cardiac decompensation with postponement of a simplified TAVI procedure (Table 1) on a case-by-case basis.

FIGURES

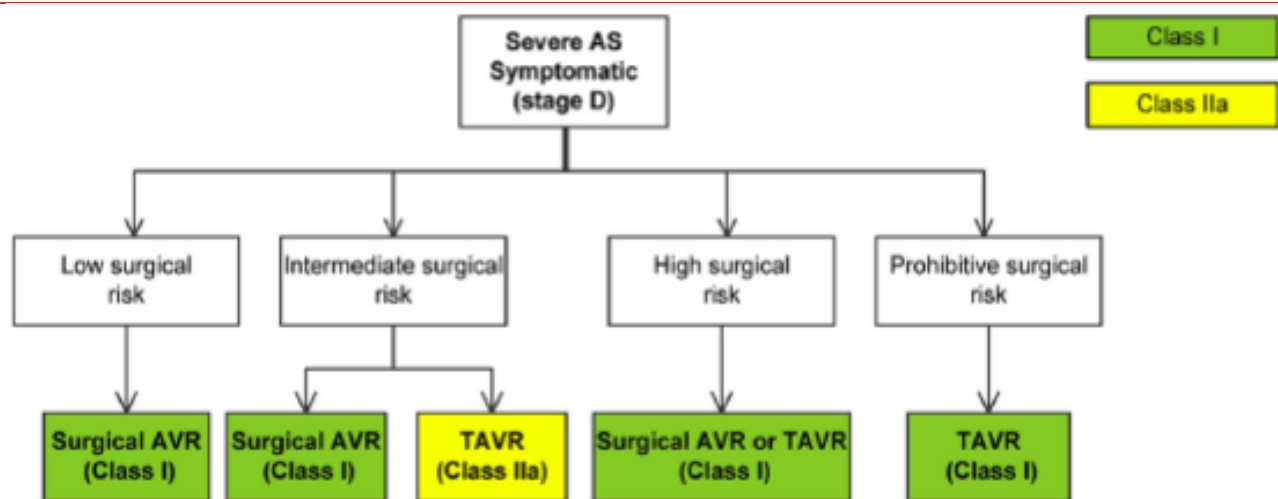Figure 1. The latest guidelines illustrate that TAVI should be considered for patients at intermediate surgical risk from: Nishimura et al, American Heart Association/American College of Cardiology (AHA/ACC) guidelines, JACC 20017;70:252–89 (TAVR: TAVI). AS, aortic stenosis; AVR, aortic value replacement; TAVI, transcatheter aortic valve implantation; TAVR, transcatheter aortic valve replacement.
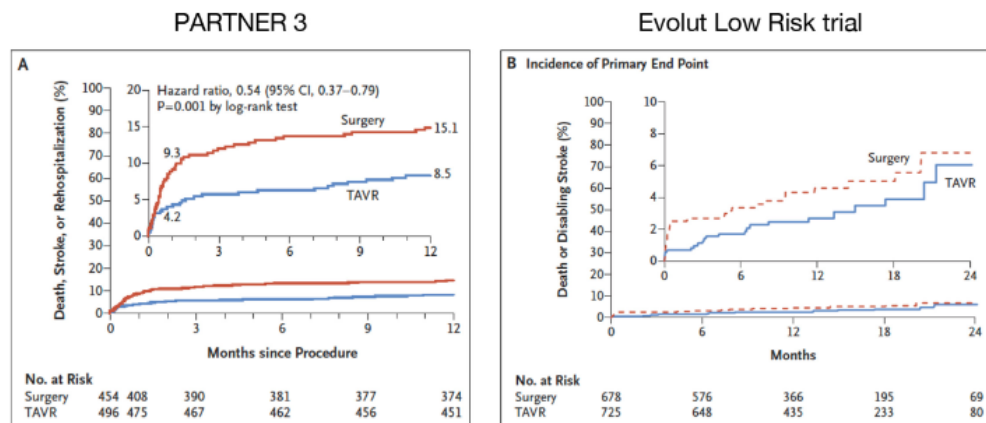
Figure 2. Both the PARTNER 3 and the Evolut Low Risk trials showed favourable performance of TAVI versus surgical aortic valve replacement (AVR) in low-risk patients (TAVR: TAVI) from refs 31 and 32. TAVI, transcatheter aortic valve implantation.

Table 1 Factors to consider doing differently along the patient pathway for AS during the COVID-19 crisis

Phase of patient pathway	Alterations to practice during the COVID-19 crisis
Case selection	Review TAVI waiting list and triage for highest risk.
	Review sAVR waiting list.
	Convert intermediate risk patients to TAVI if appropriate.
	Convert low-risk patients to TAVI only with Heart Team consensus.
	Consider risk to patient of nosocomial COVID-19 infection.
TAVI work-up	Avoid TOE.
	Use CTCA instead of invasive coronary angiography.
	Consider risk to patient of COVID-19 when attending for tests.
	Do all tests in a single attendance.
Procedure	Keep it simple.
	Use devices the operator/team is familiar with.
	Transfemoral procedures only.
	Consider appropriateness/ethics of surgical bail-out.
Post-TAVI	Early safe discharge.
	No need for follow-up echo until 6 months.

CTCA, CT coronary angiogram; sAVR, surgical valve replacement ; TAVI, transcatheter aortic valve implantation; TOE, transoesophageal echo.

TRANSPLANT SURGERY

PROLONGED SARS-COV-2 SHEDDING AND MILD COURSE OF COVID-19 IN A PATIENT AFTER RECENT HEART TRANSPLANTATION

Decker A, Welzel M, Laubner K, Grundmann S, Kochs G, Panning M, Thimme R, Bode C, Wagner D, Lother A.. Am J Transplant. 2020 Jun 9. doi: 10.1111/ajt.16133. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

A case report conducted at the University of Freiburg in Germany of a 62 year old male patient on immunosuppressive medications due to a heart transplant in November of 2019 who experienced a mild, though long, course of SARS-CoV-2 with no cardiorespiratory complications. This suggests that immunosuppressive medication regimens may be continued for patients diagnosed with COVID-19, though they may prolong viral clearing. Additional findings of the study included:

- The patient tested positive via PCR for SARS-CoV-2 on day 1 through day 35
- Symptoms included fever, tachycardia, and sore throat
- On day 7, levels of proBNP, CRP, and IL-6 increased (Figure 1)

- Patient was asymptomatic by day 20

ABSTRACT

In the coronavirus disease 2019 (COVID-19) pandemic, organ transplant recipients are considered to be at high risk for unfavorable outcome. However, in particular the role of immunosuppression in patients infected with SARS-CoV-2 remains undetermined. Here, we present a 62-year old male COVID-19 patient with recent heart transplantation who developed only mild symptoms, but had prolonged virus shedding, and summarize the available data on COVID-19 in cardiac allograft recipients. Initially the patient presented with a transient episode of fever and sore throat but no other symptoms, in particular no cough or dyspnea at rest. After diagnosis, immunosuppression was continued unchanged. On day 7, temperature increased again with concurrent mild rise of CRP, IL-6 and proBNP levels. Hydroxychloroquine was started and continued for 7 days. While the patient had no clinical symptoms anymore 20 days after initial presentation, virus culture of throat swabs on days 18 and 21 confirmed active virus replication and SARS-CoV-2 PCR remained positive on day 35 with copy numbers similar to the onset of infection. In conclusion, immunosuppression regimen in transplant recipients with mild COVID-19 associated symptoms may be continued unchanged. However, it may contribute to delayed virus PCR conversion and thus possible prolonged infectivity.
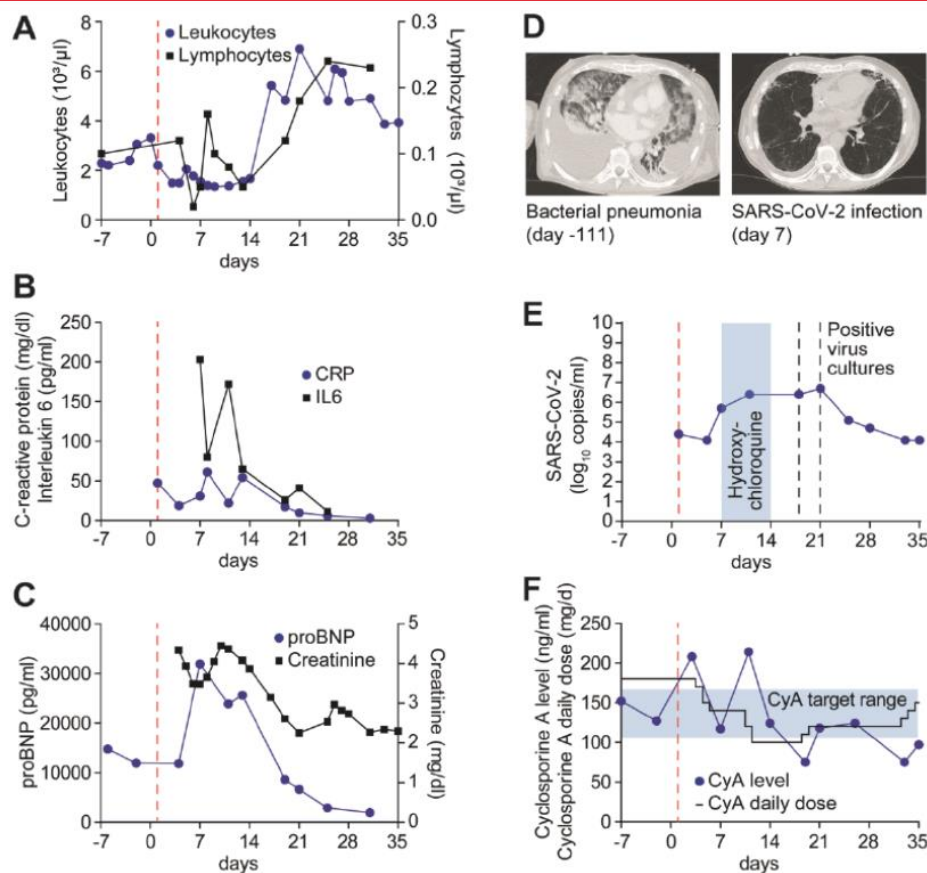
FIGURES

Figure 1: Course of COVID-19 in a heart transplant recipient: Leukocyte and lymphocyte count (A), levels of C-reactive protein (CRP) and interleukin 6 (IL6, B), proBNP and creatinine (C) were followed during the course of disease. Chest computed tomography during SARS-CoV-infection (7 days after symptom onset) revealed residues of previous bacterial pneumonia (111 days before symptom onset) but no typical signs of COVID-19 (D). SARS-CoV-2 was detected in throat swabs by RT-PCR (quantitiy shown as log10 copies/ml) and by positive virus culture (dashed black lines) before and after hydroxychloroquine treatment (blue area, E). Administered daily doses (solid black line), serum levels (blue discs), and target range (blue area) of cyclosporine A are indicated (F). Dashed red lines indicated date of first symptoms and detection of SARS-CoV-2 in throat swab in each panel

CURRENT DIAGNOSTICS

EARLY CHEST CT FEATURES OF PATIENTS WITH 2019 NOVEL CORONAVIRUS (COVID-19) PNEUMONIA: RELATIONSHIP TO DIAGNOSIS AND PROGNOSIS

BLUF

In this retrospective cross-sectional study, radiologists analyzed 34 CT images from RT-PCR-positive COVID-19 patients diagnosed between January 20 and February 4, 2020 in Hainan, China. Initial CTs showed typical COVID-19 pneumonia abnormalities in 94% of patients, and 29% showed abnormalities with an initial negative RT-PCR test. Authors support use of CT analysis for diagnosis of COVID-19, even if RT-PCR is negative, and for monitoring disease progression and prognosis.

ABSTRACT

OBJECTIVE: To determine the consistency between CT findings and real-time reverse transcription-polymerase chain reaction (RT-PCR) and to investigate the relationship between CT features and clinical prognosis in COVID-19.
METHODS: The clinical manifestations, laboratory parameters, and CT imaging findings were analyzed in 34 COVID-19 patients, confirmed by RT-PCR from January 20 to February 4 in Hainan Province. CT scores were compared between the discharged patients and the ICU patients.
RESULTS: Fever (85%) and cough (79%) were most commonly seen. Ten (29%) patients demonstrated negative results on their first RT-PCR. Of the 34 (65%) patients, 22 showed pure ground-glass opacity. Of the 34 (50%) patients, 17 had five lobes of lung involvement, while the 23 (68%) patients had lower lobe involvement. The lesions of 24 (71%) patients were distributed mainly in the subpleural area. The initial CT lesions of ICU patients were distributed in both the subpleural area and centro-parenchyma (80%), and the lesions were scattered. Sixty percent of ICU patients had five lobes involved, while this was seen in only 25% of the discharged patients. The lesions of discharged patients were mainly in the subpleural area (75%). Of the discharged patients, 62.5% showed pure ground-glass opacities; 80% of the ICU patients were in the progressive stage, and 75% of the discharged patients were at an early stage. CT scores of the ICU patients were significantly higher than those of the discharged patients.
CONCLUSION: Chest CT plays a crucial role in the early diagnosis of COVID-19, particularly for those patients with a negative RT-PCR. The initial features in CT may be associated with prognosis.
KEY POINTS: Chest CT is valuable for the early diagnosis of COVID-19, particularly for those patients with a negative RT-PCR. The early CT findings of COVID-19 in ICU patients differed from those of discharged patients.

DEVELOPMENTS IN TREATMENTS

LITHIUM AS A CANDIDATE TREATMENT FOR COVID-19: PROMISES AND PITFALLS

BLUF

The authors propose lithium as a possible therapeutic agent against SARS-CoV-2 through a summary of various in vitro and animal studies of lithium's immunomodulatory and antiviral mechanisms, including its potential effects against the cytokine storm (Table 1). The authors discuss limitations of lithium as a monotherapy for COVID-19, namely its delayed onset, narrow therapeutic index, and wide range of drug interactions. The authors suggest that more studies be conducted with lithium against SARS-CoV-2 to elucidate pharmacodynamic mechanisms and inform future therapeutic development.

ABSTRACT

The pandemic of respiratory illness caused by a novel coronavirus (SARS-nCoV-2) is a global health crisis. Despite numerous preliminary results, there is as yet no treatment of proven efficacy for this condition. In this context, the pharmacological properties of lithium, better known as a treatment for mood disorders, merit closer examination. Lithium has shown in vitro

efficacy at inhibiting the replication of coronaviruses responsible for gastrointestinal and respiratory diseases in animals. It has immunomodulatory properties that may be of additional benefit in moderating the host inflammatory response to the novel coronavirus (SARS-CoV-2). Furthermore, there is evidence that lithium may exert a protective action against upper respiratory infections and influenza-like illnesses in patients taking it for other indications. These promising reports must be balanced against the narrow therapeutic index and high risk of toxicity associated with lithium therapy, its documented interactions with several commonly used drugs, and the absence of evidence of its efficacy against coronaviruses responsible for human disease. Nevertheless, naturalistic studies of the risk of COVID-19 in patients already receiving lithium could provide indirect evidence of its efficacy, and understanding the putative antiviral and immune-regulatory mechanisms of lithium in models of SARS-CoV-2 infection may provide leads for the development of safer and more effective treatments with a specific action against COVID-19.

FIGURES

Action	Mechanism	References
Antiviral effects	Inhibition of viral RNA polymerase, probably related to blockade of co-factor phosphorylation through inhibition of GSK-3β	Harrison et al., 2007; Asenjo et al., 2008
	Protection of host cells from apoptosis triggered by viral infection	Ren et al., 2011
Immunomodulatory effects	Inhibition of NF-κB	Troib & Azab, 2015
	Inhibition of IL-6 induced activation of STAT-3, perhaps mediated through inhibition of GSK-3β	Beurel et al., 2010; Wang, Zhang, Li, et al., 2013; Minashima et al., 2014
	Inhibition of IL-1β production	Nassar & Azab, 2014
	Reduction in cyclooxygenase-2 expression	Nassar & Azab, 2014

Abbreviations: RNA, ribonucleic acid; GSK-3β, glycogen synthase kinase—3 beta; NF-κB, nuclear factor kappa B; STAT-3, signal transducer and activator of transcription 3; IL-6, interleukin-6; IL-1β, interleukin-1 beta.

Table 1. Summary of various articles and lithium mechanisms that may be useful as an antiviral agent against the COVID-19 virus.

MENTAL HEALTH AND BEHAVIOR DURING THE EARLY PHASES OF THE COVID-19 PANDEMIC: A LONGITUDINAL MOBILE SMARTPHONE AND ECOLOGICAL MOMENTARY ASSESSMENT STUDY IN COLLEGE STUDENTS

Huckins JF, DaSilva AW, Wang W, Hedlund E, Rogers C, Nepal SK, Wu J, Obuchi M, Murphy EI, Meyer ML, Wagner DD, Holtzheimer PE, Campbell AT.. J Med Internet Res. 2020 Jun 9. doi: 10.2196/20185. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

In this observational study, adapted from the ongoing longitudinal StudentLife cohort study investigating the mental health of Dartmouth College undergraduate students, the authors analyzed data from 217 participants using smartphone mobile sensing through an app and Ecological Momentary Assessments (EMAs), including a PHQ-4 to measure anxiety and depression symptoms, to determine if there was a difference during the COVID-19 pandemic compared to previous terms. Results concluded an increase in sedentary time, depression and anxiety during the pandemic versus the same time frame in the previous term (Figure 2), suggesting there has been an impact on mental health and behavior for this population during the COVID-19 pandemic.

ABSTRACT

BACKGROUND: Worldwide, the vast majority of people have been impacted by COVID-19. While millions of individuals have become infected, billions of individuals have been asked or required by local and national governments to change their behavioral patterns. Previous research on epidemics or traumatic events suggest this can lead to profound behavioral and mental health changes, but rarely are researchers able to track these changes with frequent, near real-time sampling or compare these to previous years of data on the same individuals.

OBJECTIVE: We seek to answer two overarching questions by combining mobile phone sensing and self-reported mental health data among college students participating in a longitudinal study for the past two years. First, have behaviors and mental health changed in response to the COVID-19 pandemic as compared to previous time periods within the same participants? Second, did behavior and mental health changes track the relative news coverage of COVID-19 in the US media?

METHODS: Behaviors such as the number of locations visited, distance traveled, duration of phone usage, number of phone unlocks, sleep duration and sedentary time were measured using the StudentLife mobile smartphone sensing app. Depression and anxiety were assessed using weekly self-reported Ecological Momentary Assessments (EMAs) of the Patient Health Questionnaire-4 (PHQ-4). Participants were 217 undergraduate students, with 178 students having data during the Winter 2020 term. Differences in behaviors and self-reported mental health collected during the Winter 2020 term (the term in which the coronavirus pandemic started), as compared to previous terms in the same cohort, were modeled using mixed linear models.

RESULTS: During the initial COVID-19 impacted academic term (Winter 2020), individuals were more sedentary and reported increased anxiety and depression symptoms (P<.001), relative to the previous academic terms and subsequent academic breaks. Interactions between the Winter 2020 term and week of academic term (linear and quadratic) were significant. In a mixed linear model, phone usage, number of locations visited, and week of the term, were strongly associated with increased coronavirus-related news. When mental health metrics (e.g., depression and anxiety) were added to the previous measures (week of term, number of locations visited, and phone usage), both anxiety (P<.001) and depression (P=.029) were significantly associated with coronavirus-related news.

CONCLUSIONS: Compared with prior academic terms, individuals in Winter 2020 were more sedentary, anxious, and depressed. A wide variety of behaviors, including increased phone usage, decreased physical activity, and fewer locations visited, are associated with fluctuations in COVID-19 news reporting. While this large-scale shift in mental health and behavior is unsurprising, its characterization is particularly important to help guide the development of methods that could reduce the impact of future catastrophic events on the mental health of the population.
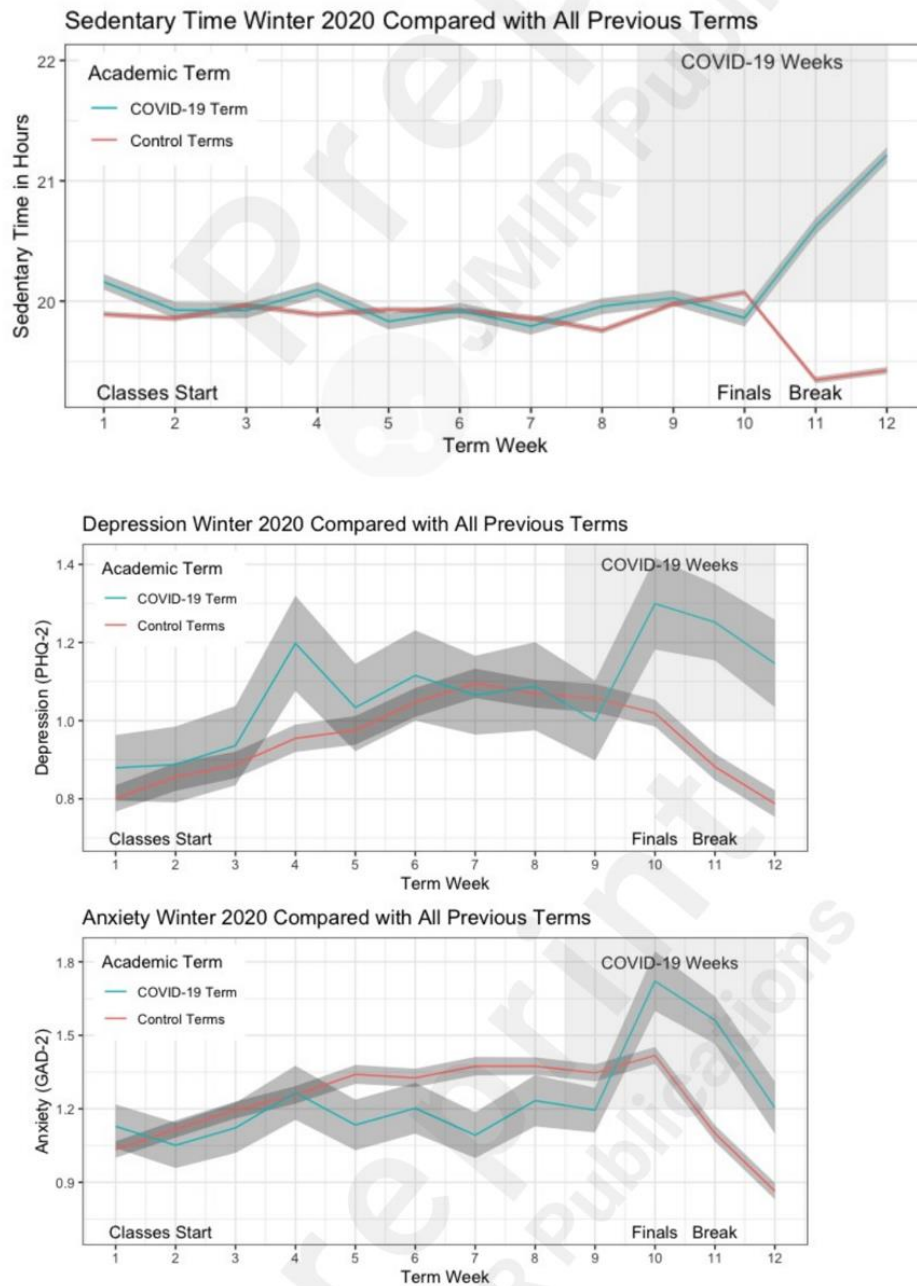
Figure 2. Sedentary time (top), depression (middle), and anxiety (bottom) scores across an academic term and the first two weeks of break, with the term influenced by the coronavirus pandemic broken out as a separate line. Shaded ribbons represent +/- standard error for each week. Weeks influenced by policy changes related to coronavirus are represented with a shaded box from weeks 9-12. Sedentary time was calculated via the StudentLife application. Depression and anxiety were measured with the PHQ-2 and GAD-2 through the StudentLife application. Control Terms include data from the same group of individuals across previous academic terms.

ACKNOWLEDGEMENTS