Develop – DeVos Cardiovascular Research Program's Emergency Letter on the Pandemic

Scientific Stream Update on the COVID-19 Pandemic – 4.9.20, 1000

Spectrum Health contact: Stefan Jovinge, MD

Article Title: Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China

https://jamanetwork.com/journals/jamacardiology/fullarticle/2763524

Source: JAMA

Clinical Field: Cardiology

Article Type: Clinical Study

Study Type: Retrospective Study

Patient Group: Hospitalized COVIDF-19 Patients

Intervention: Observational, retrospective

Reviewer	Stefan Jovinge
Study Design	Minor Concerns
Study Design Concerns	Single-center experience.
Main Results	A Cohort of 416 consecutive patients. Patients with incomplete data being excluded. Following univariate data of statistical significance were observed (Card Injury vs No Card Injury : Older age (74 vs 60) , Sore throat more common (4.9 vs 2.4), HT (59.8 vs 23.4), CAD (29.3 vs 6.0), CVD (15.9 vs 2.7), Chronic Heart Failure (14.6 vs 1.5), COPD (7.3 vs 1.8), Cancer (8.5 vs 0.6), WBC (9.4 vs 5.5), Lymphocytes (0.6 vs 1.0), Platelets (172 vs 216), CRP (10.2 vs 3.7), Procalcitonin (0.27 vs 0.06), Nt-pro BNP (1689 vs 139), Albumin (3.2 vs 3.7), Creat (1.15 vs 0.64), Unilat pneumonia (8.5 vs 29.3), Bilat pneumonia (91.5 vs 70.7). Mortality significantly higher in the cardiac injury group (51.2% vs 4.5%). In a multi-variable analysis with mortality as outcome only Cardiac Injury and ARDS stay as independent predictors. Interestingly, CVCD, Cerebrovasc Dis, Diabetes, COPD, Renal Failure doesn't survive as indepent predictor in the analysis. However renal failure could raise cardiac markers without cardiac injury.
Comments	Cardiac injury, as for many other conditions, comes with a significant increase in mortality.

Article Title: Reinfection could not occur in SARS-CoV-2 infected rhesus macaques

https://www.biorxiv.org/content/10.1101/2020.03.13.990226v1

Source: bioRxiv

Clinical Field: Infectious Disease

Article Type: Basic Science

Study Type: _____

Patient Group: Rhesus monkeys

Intervention: SARS-CoV-2 infection followed byan attempt to re-infect

Reviewer	Kathrine A. Kelly-Schuette
Study Design	Well Designed
Study Design Concerns	Small sample size, primate model. Only five monkeys and only three re-infected. No viral badge effect test was performed - non-infected monkeys infected with the same badge time at the same time as the monkeys are being re-infected.
Main Results	Rhesus monkeys do get infected with SARS-VoV-1 and the attempt to to re-infect was not successful. Would indicate that the infection provides at least short term immunity. Viral NP and anal swabs were negative for SARS-CoV-2. Necropsy of re-infected monkey demonstrated no viral replication in tissues.
Comments	Monkey #1; necropsy at day 7 demonstrated viral replication in nose, pharynx, lung, gut, spinal cord, heart, skeletal muscle, and bladder. Xray showed opacification, interstitial markings, GGO Monkeys 2, 3, and 4: tracking of the antibody against SARS-CoV-2 from day 3-28. Prior to reinfection challenge, monkeys had negative clinical symptoms, xrays, and two negative PCR tests. Primary Question: Do patients have a risk of re-infection with SARS-CoV-2 after recovery? Methods: primate subjects were used for virus challenge with SARS-CoV-2 Primates were infected via tracheal challenge and nasal, pharyngeal and viral loads were tested

	Conclusion: the results suggest that the monkeys who recover from SARS-CoV-2 could not be re-infected with the same strain and infection could be protective The monkeys with titers of 1:16 after re-infection developed elevated 1:40 titers while the monkey with titer 1:8 maintained the same titer.

Article Title: ISTH interim guidance on recognition and management of coagulopathy in COVID-19

https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14810

Source: _____

Clinical Field: Hematology

Article Type: International Document

Study Type: Other

Patient Group: N/A

Intervention: N/A

Reviewer	Stefan Jovinge
Study Design	N/A
Study Design Concerns	N/A
Main Results	Recommendation: 1. Three-fourfold increase of upper reference of d-dimer in ER patients should be hospitalized even without symptoms. 2. PT ratio is more sensitive in picking up patients at risk than INR. 3. Thrombocytopenia is an indicator of severe COVID-19 but is not at consistent prognosticator (critical disease can occur also with normal thrombocyte counts. 4. All patients hospitalized with COVID-19 without contraindication towards Thrombose prophylaxis (thrombocyte count 25 x10(9)/L, active bleeding). Kidney dysfunction not a contraindication but mandates more close monitoring. The prophylaxis given is for now is low sode LMWH.
Comments	All COVID-19 patients should be monitored with D-dimer, PT and Thrombocyte count.

Article Title: AGA Institute Rapid Recommendations for Gastrointestinal Procedures During the COVID-19 Pandemic

https://www.gastrojournal.org/article/S0016-5085(20)30458-3/fulltext

Source: Gastroenterology

Clinical Field: Gastroenterology

Article Type: National Document

Study Type: Other

Patient Group: COVID-19 with the need of endoscopy

Intervention: _____

Reviewer	Kathrine Kelly-Schuette
Study Design	Minor concerns
Study Design Concerns	Summary of the existing data and evidence- based recommendations and clinical guidelines from American Gastroenterological Association. Thorough summary with good methodology for review, inclusion, and grading of data sources. No direct studies pertaining to PPE during endoscopy in COVID 19 patients
Main Results	GI Manifestations of COVID 19: nausea, vomiting, and diarrhea in 2-14% of patients, but may be present in stool independent of diarrhea Liver Manifestations of COVID 19: liver injury has been documented, however the etiology is uncertain. Abnormal LFTs do not appear to be prognostic factor. More data is needed. Risks during endoscopy: COVID 19 is spread during droplet transmission. Endoscopic procedures can lead to aerosolization. Triaging procedures: non-urgent procedures should be rescheduled, time-sensitivity and impact on patient outcomes should be taken into decision to reschedule Recommendations 1. Upper GI procedures> N95, N99, or PAPR +PPE regardless of COVID status 2. Lower GI procedures > N95, N99, or PAPR +PPE regardless of COVID status 3. Any GI procedures in COVID positive patient> against standard surgical mask.

	*Strong recommendations, low to moderate evidence 4. Any GI procedure, regardless of COVID status. If extreme resource-constrained setting>use/re-use of N95 over surgical mask. insufficient evidence to comment on safety of reusing PPE *conditional recommendation, very low certainty of evidence 5. double gloving during any GI procedure *strong recommendation 6. Negative pressure room use for any COVID known or presumptive patient undergoing a GI procedure*conditional, very low evidence 7. Standard cleaning of endoscopes regardless of status
Comments	SARS-CoV-2 has been confirmed in stool specimens. Angiotensin converting enzyme 2 is expressed in gastric, duodenal and rectal epithelia, implicating a viral receptor and possibility of fecal-oral transmission.

Article Title: Microneedle array delivered recombinant coronavirus vaccines: Immunogenicity and rapid translational development

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(20)30118-3/fulltext

Source: Lancet

Clinical Field: Infectious Disease

Article Type: Basic Science

Study Type: Other

Patient Group: Mouse study

Intervention: A recombinant antigen from SARS-CoV- as a vaccine

Reviewer	Stefan Jovinge
Study Design	Major Concerns
Study Design Concerns	This study shows only immunization against the vaccine occurs in mice. It doesn't show that this immunization protects against the disease. Earlier study has shown that the live
Main Results	Recombinant vaccine against S1 domain in SARS-CoV- generates an immune response in mice. The sera had in vitro neutralizing effect on pathogenic effect of the virus on African Green monkey cells.
Comments	Study done with SARS-CoV-2-S1 subunit. It is important in the sense that recombinant vaccine is feasible to generate an immune response. These vaccines can be generated in a high throughput fashion early in the development of the pandemic. No direct implication for the use of this very vaccine directly in humans. Human trial would be mandated.

Article Title: Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020

https://www.cdc.gov/mmwr/volumes/69/wr/mm6913e2.htm

Source: CDC

Clinical Field: Other

Article Type: National Document

Study Type: Other

Patient Group: N/A

Intervention: N/A

Reviewer	Vinu Perinjelil
Study Design	Minor concerns
Study Design Concerns	1) preliminary analysis with significant missing data a) only 74,439 case report forms submitted to CDC which is 60.7% of total US reported cases (n=122,653) as of March 28,2020 b) out of these available case report forms, information on underlying conditions only available for 7,162 (5.8%) patients. 67,277 therefore have missing/unknown status for risk factors for adverse outcomes in resp infections c) socioeconomic status/race and geographic region not included as a risk factor, could be valuable in future 2) this report lacks sufficient information on pediatric and adolescent population cases and hospitalizations (<19 y.o.) 3) descriptive analysis only, therefore **no statistical analysis** was possible. Also no information on risk stratification based on severity of each disease so subgroups of higher risk patients can be identified 4) limited availability of COVID testing means any analysis is biased towards more severe cases
Main Results	Report on patient summary of COVID-19 patients in the USA that are: 1. Outpatients 2. Hospitalized, non-ICU 3. ICU 4. Unknown status

	This publication is a weekly report from the CDC COVID-19 response team expanding on earlier reports from China and Italy. This publication provides a preliminary analysis of the prevalent risk factors within all lab confirmed COVID 19 patients (n=122,653) in the US. Out of the confirmed cases, case report forms were submitted for 74,439 cases. Out of these forms, only 7,162 (5.8%) included data pertaining to underlying health conditions or potential risk factors. These findings suggest amongst those cases with available case report forms, 1/3 of patients (2,692, 37.6%) had at least one underlying health condition. Risk factors included lung disease (asthma, COPD), diabetes, cardiovascular disease, chronic renal disease, chronic liver disease, immunocompromised condition, neurologic disorder, intellectual disability, pregnancy, smoking status or any other chronic disease. Highest reported conditions were diabetes (784,10.9%) ,chronic lung disease (656,9.2%) and cardiovascular disease (647,9%). Among 457 ICU admissions and 1,037 non ICU hospitalizations with complete data available, 358 (78%) and 732 (71%) occurred among persons with one or more reported underlying health condition. In contrast, 27% (1,388/5143) of COVID-19 patients who were not hospitalized were reported to have an underlying health condition. No case fatality estimates could be made due to small sample size and limited available data. However, out of 184 deaths which occurred amongst the pool of COVID-19 patients with complete information available, 173 (94%) were reported to have an underlying condition. In summary, these underlying risk factors as represented in table 1 of this paper, appears to place patients with underlying health conditions at higher risk for severe COVID 19 warranting hospitalizations/ICU stays. This is congruent from earlier reports from other countries with high burdens from COVID-19.
Comments	Snapshot analysis of risk factor prevalence in cases documented from Feb 12-March 28,2020.

Article Title: Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial

https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2

Source: MedRxiv

Clinical Field: Infectious Disease

Article Type: Clinical Study

Study Type: Proper RCT

Patient Group: COVID-19+ (>+ 18, RT-PCR positive, Positive Chest CT, SaO2/SPO2 >93%, P/F >300

Intervention: Hydroxychloroquine

Reviewer	Ambaris Singh, MD
Study Design	Major Concerns
Study Design Concerns	-Control and Treatment Groups were not stratified by co-morbidities, but rather only age and sex. There is no way to determine if data findings are confounded by pre-existing conditions -Size of study (n=31 for each group) is inadequate -Unclear as to whether radiologists were blinded when evaluating post treatment/control CT scans -More people in the treatment group had exhibited symptoms on day 0 of experiment, which in turn raises the question "if they got sick earlier, then wouldn't they get better earlier, all things being equal?"
Main Results	-Fever and cough lasted for approximately one day less in the treatment group versus the control group -More control group patients had worse follow-up CT exams, and more treatment group patients had significantly improved CT exams.
Comments	-While improved cough and fever are admirable results, these are not direct attributes which lead to morbidity and mortality in COVID-19 -The publication wrongfully insinuates that people who were previously on Hydroxychloroquine treatment are somehow protected from acquiring SARS-CoV-2 infection.

Article Title: Convalescent Plasma in COVID-19

https://www-ncbi-nlm-nih-gov.proxy2.cl.msu.edu/pubmed/?term=Mair-Jenkins+%5Bau%5D+AND+effectiveness+%5Bti%5D

Source: Proc Natl Acad Sci USA

Clinical Field: Infectious Disease

Article Type: Clinical Study

Study Type: Case Report

Patient Group: Severe COVID-19

Intervention: Convalescent serum

Reviewer	Mohammed Al-Charakh, MD
Study Design	Major Concerns
Study Design Concerns	-Not Randomized or controlled study -Small sample -Patient received antiviral and steroid treatment in addition to receiving CP transfusions
Main Results	Design: - 10 patients with confirmed COVID 19 were enrolled prospectively. (six males and four females) were enrolled and received Convalescent plasma transfusion. - One dose of 200 mL of convalescent plasma (CP) derived from recently recovered donors with the neutralizing antibody titers above 1:640 was transfused to the patients as an addition to maximal supportive care and antiviral agents. - The primary endpoint was the safety of CP transfusion. - The second endpoints were the improvement of clinical symptoms and laboratory parameters within 3 d after CP transfusion. - The median age was 52.5 y. Four patients had underlying chronic diseases, including cardiovascular and/or cerebrovascular diseases and essential hypertension. -The median time from onset of symptoms to hospital admission and CP transfusion was 6 days (IQR, 2.5 d to 8.5 d) and 16.5 d (IQR, 11.0 d to 19.3 d), respectively. -Prior to CP treatment, three patients received mechanical ventilation, three received high-flow nasal cannula oxygenation, and two received conventional low-flow nasal cannula oxygenation. -Antibacterial or antifungal treatment was used when patients had coinfection. Six patients received intravenous (i.v.) methylprednisolone (20 mg every 24 h).

	Results : - All symptoms in the 10 patients, especially fever, cough, shortness of breath, and chest pain, disappeared or largely improved within 1 d to 3 d upon CP transfusion. -After treatment with CP, two patients were weaned from mechanical ventilation to high-flow nasal cannula, and one patient discontinued high-flow nasal cannula. one patient treated with conventional nasal cannula oxygenation, continuous oxygenation was shifted to intermittent oxygenation - An increase of SaO2 was observed (median: 93.00% vs. 96.00%) - 7 out of 10 patients showing an increase of lymphocyte counts - Inflammatory markers decreased including (CRP) (median: 55.98 mg/L vs. 18.13 mg/L), alanine aminotransferase (median: 42.00 U/L vs. 34.30 U/L), and aspartate aminotransferase (median: 38.10 U/L vs. 30.30 U/L) -The neutralizing antibody titers of five patients increased and remained at the same level after CP transfusion in four patients - SARS-CoV-2 RNA was decreased to an undetectable level in three patients on day 2, three patients on day 3, and one patient on day 6 after CP therapy. -Outcome of patients treated with CP as compared to a recent historic control group with matching baseline criteria and severity of disease showed : three cases discharged while seven cases in much improved status and ready for discharge in CP group, as compared to three deaths, six cases in stabilized status, and one case in improvement in the control group ($P <$ 0.001 - No serious adverse reactions or safety events were recorded after CP transfusion. - A better treatment outcome was observed among patients who were given CP before 14 of symptoms onset (58.3% vs. 15.6%; $P < 0.01$).
Comments	All patients received antiviral treatment despite the uncertainty of the efficacy of drugs used and some patients received glucocorticoid therapy, which might interfere with immune response and delay virus clearance. The relationship between SARS-CoV-2 RNA reduction and CP therapy, as well as the optimal concentration of neutralizing antibodies and treatment schedule, should be further clarified.

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