The Daily COVID-19 Literature Surveillance Summary

August 7, 2020

DISCLAIMER

This free and open source document represents a good faith effort to provide real time, distilled information for guiding best practices during the COVID-19 pandemic. This document is not intended to and cannot replace the original source documents and clinical decision making. These sources are explicitly cited for purposes of reference but do not imply endorsement, approval or validation.

This is not an official product or endorsement from the institutions affiliated with the authors, nor do the ideas and opinions described within this document represent the authors' or their affiliated institutions' values, opinions, ideas or beliefs. This is a good faith effort to share and disseminate accurate summaries of the current literature.

NOW LIVE!

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

COVID-19 Daily Literature Surveillance

COVID19LST

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

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Climate

- Dr. Melina R. Kibbe from UNC Chapel Hill in the Department of Surgery argues that the COVID-19 pandemic has disproportionately affected female parents working in academic and/or clinical environments with reduction in female manuscript authorship, citing drops in female-first authors (4%), female-last authors (6%), and female-corresponding authors (7%) from 2019 to 2020 in terms of published JAMA Surgery articles. She suggests that protocols should be put in place to alleviate this disparity, such as extending grant end-dates, incorporating offsetting work shifts, and increasing allowances for part-time work.

Transmission & Prevention

- Canadian researchers investigated the effectiveness of performing asymptomatic SARS-CoV-2 testing of hospitalized patients in Hamilton, Ontario during April 2020 when incidence of new daily cases in the community was 1.9 per 100,000 people. Of the 125 hospitalized adults who were tested, only a single patient tested positive (0.8%) and this patient had reported two weeks of fevers and cough, suggesting asymptomatic testing has "minimal utility" in populations with low prevalence of COVID-19.

Management

- A retrospective collaborative study by multiple specialties at First People's Hospital of Tianmen and Fudan University of 183 COVID-19-positive patients found that increased time from symptom onset to admission (HR=0.829), use of corticosteroids (HR=0.496; Figure 2), and use of oseltamivir (HR=0.416) were associated with a longer duration for viral shedding, while use of arbidol (HR=2.605) was associated with a shorter period of shedding. These findings suggest need for early admission and therapy, cautious use of corticosteroids and oseltamivir, and clinical studies on the efficacy of arbidol.
- A case report from the Department of Cardiology, Hospital Universitario de La Princesa in Madrid, Spain examined a 66-year-old male recently diagnosed with COVID-19 pneumonia who presented with acute inferolateral ST segment elevation due to coronary vasospasm (CV) that was detected via optical coherence tomography and invasive vasospasm (ergonovine provocation) test and reversed after intracoronary nitroglycerin administration. Authors suggest COVID-19 induced inflammation may result in CV and myocardial damage, which could also be a viable mechanism in patients with normal coronary arteries on angiogram.
- A case report from Pennsylvania State University College of Medicine of a 49-year-old SARS-CoV-2-positive patient with chronic lymphocytic leukemia (CLL; Rai stage IV, Binet stage C) explores the patient's inability to produce SARS-CoV-2 antibodies. Despite a multifaceted serological approach to detect antibodies within the target period for normal production (1 to 6 weeks of infection), the patient did not mount an antibody response, suggesting that antibody testing in immunocompromised patients may have limited value due to resulting hypogammaglobulinemia so both nucleic acid and antigen tests should be performed in this population.

R&D: Diagnosis & Treatments

- Biomedical engineers and medical researchers from the University of California have pioneered a 3D-printable portable imaging platform, TinyArray imager, for rapid use in reading coronavirus antigen microarrays (CoVAMs). It achieved results equivalent to the commercial microarray reader ArrayCAM 400-S in probing and imaging of coronavirus microarrays with COVID-19-positive and -negative sera, suggesting that the TinyArray imager will help to increase serosurveillance in tandem with containment and therapeutic developments.

TABLE OF CONTENTS

CONSEQUENCES OF THE COVID-19 PANDEMIC ON MANUSCRIPT SUBMISSIONS BY WOMEN

Kibbe MR.. JAMA Surg. 2020 Aug 4. doi: 10.1001/jamasurg.2020.3917. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

An opinion piece by Dr. Melina R. Kibbe from UNC Chapel Hill in the Department of Surgery argues that the COVID-19 pandemic has disproportionately affected female parents working in academic and/or clinical environments. This claim is supported by observed reduction in female manuscript authorship, citing drops in female-first authors (4%), female-last authors (6%), and female-corresponding authors (7%) from 2019 to 2020 in terms of published JAMA Surgery articles (Table 1). She concludes by suggesting that protocols should be put in place to alleviate this disparity, such as extending grant end-dates, incorporating offsetting work shifts, and increasing allowances for part-time work.

FIGURES

Table. Manuscripts With Male or Female First, Last, or Corresponding Authorship Submitted to *JAMA Surgery* in April and May of 2019 and 2020[a]

Table. Manuscripts With Male or Female First, Last, or Corresponding Authorship Submitted to *JAMA Surgery* in April and May of 2019 and 2020[a]

Characteristic	No. (%) 2019	2020	Absolute change, %
Manuscripts, No.	366	702	NA
First author			
Female	119 (33)	205 (29)	−4
Male	247 (67)	494 (70)	3
Last author			
Female	98 (27)	148 (21)	−6
Male	267 (73)	551 (78)	5
Corresponding author			
Female	105 (29)	156 (22)	−7
Male	260 (71)	542 (77)	6

Abbreviation: NA, not applicable.

[a] Authorship sex was not able to be identified in 0% to 0.57% of authorship sex categories.

ADULTS

CAN ALDOSTERONE INCREASE INTERLEUKIN-6 LEVELS IN COVID-19 PNEUMONIA?

Campana P, Flocco V, Aruta F, Cacciatore F, Abete P.. J Med Virol. 2020 Aug 4. doi: 10.1002/jmv.26382. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

A case report by researchers from the University of Federico II, Italy examines a 47-year-old COVID-19-positive patient with concomitant pneumonia, primary hyperaldosteronism (secondary to right adrenal adenoma, Figure 1A), and Guillian-Barre Syndrome (specifically, Acute Motor Sensitivity Neuropathy (AMSAN)). The patient developed high IL-6 (402 pg/ml) and IL-6 soluble receptor (greater than 1900 pg/ml) levels in conjunction with significant lung damage (Figure 1B), and was successfully treated with tocilizumab and spironolactone. The authors pose that
1) hyperaldosteronism may be related to severe COVID-19 pneumonia, specifically through its IL-6 production
2) hyperaldosteronism may assist neurological manifestations like AMSAN
3) tocilizumab may be an appropriate treatment for patients with hyperaldostonism, severe COVID-19 pneumonia, and high IL-6 levels

ABSTRACT

In the last months, the importance of identifying pathophysiological mechanisms for future therapies has emerged with the rapid spread of Covid-19 pandemic. As matter of fact, several evidences suggest the critical role of Interleukin-6 (IL-6) in the cytokine storm induced by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) infection and its correlation with the severity of acute lung injury (1, 2).

FIGURES

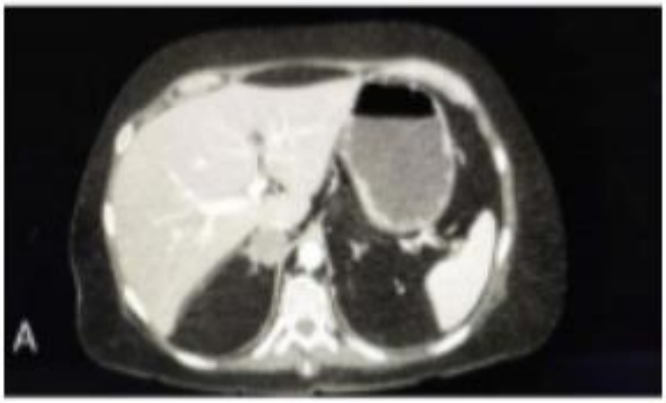

Figure 1 (A) Abdominal computed tomography (CT) scan showing a right adrenal adenoma (B) Thoracic CT scan with diffuse fibrosis and ground glass alterations in both lungs

ACE2 AND SARS-COV-2 INFECTION: MIGHT GLP-1 RECEPTOR AGONISTS PLAY A ROLE?

Monda VM, Porcellati F, Strollo F, Gentile S.. Diabetes Ther. 2020 Aug 4. doi: 10.1007/s13300-020-00898-8. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Authors within the fields of Internal Medicine and Endocrinology review several in-vivo animal studies to support the hypothesis that glucagon-like peptide 1 receptor agonists (GLP-1 RAs), a drug class used in the treatment of type 2 diabetes mellitus, may have a protective role in COVID-19. The authors propose that GLP-1 RAs may increase surfactant protein synthesis and indirectly promote the ACE2/Angiotensin-(1–7)/Mas Receptor Axis, a pathway that has anti-inflammatory and anti-thrombotic effects, through increasing ACE2 expression (Figure 1). Based on the current evidence and their proposed mechanism, the authors urge for clinical studies to investigate the relationship between GLP-1 RAs and ACE2.

FIGURES

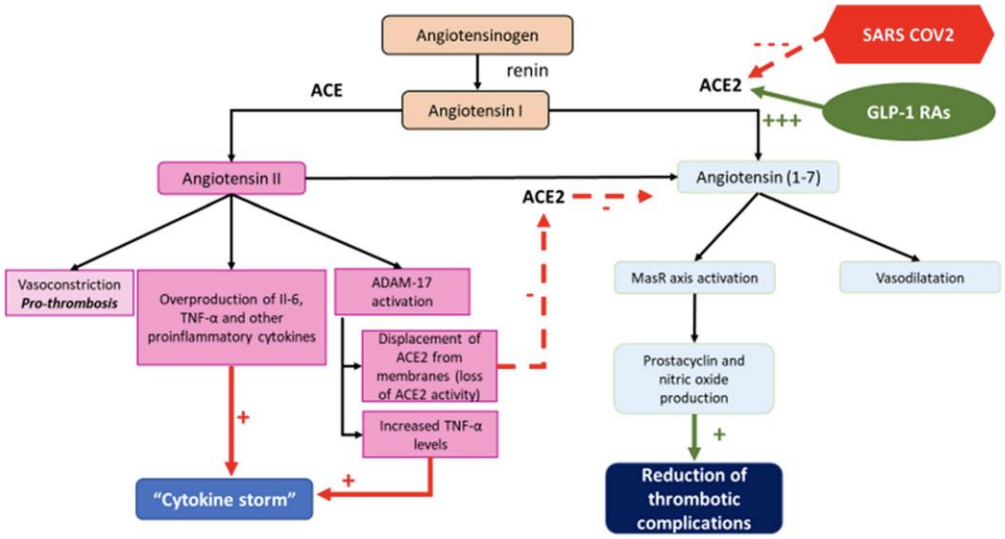

Fig. 1 Possible role of dysregulation of RAS during SARS-CoV-2 infection at lung level and potential beneficial effects of GLP-1 RA_S therapy (see text for details)

UTILITY OF ASYMPTOMATIC INPATIENT TESTING FOR COVID-19 IN A LOW PREVALENCE SETTING: A MULTI-CENTER POINT PREVALENCE STUDY

Bai AD, Li X, Alsalem M, Khan S, Smieja M, Mertz D, Chagla Z.. Infect Control Hosp Epidemiol. 2020 Jul 22:1-11. doi: 10.1017/ice.2020.349. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

In this article Canadian researchers investigated the effectiveness of performing asymptomatic SARS-CoV-2 testing of hospitalized patients in Hamilton, Ontario during April 2020 when incidence of new daily cases in the community was 1.9 per 100,000 people. Of the 125 hospitalized adults who were tested, only a single patient tested positive (0.8%) and this patient had reported two weeks of fevers and cough. The authors argue that their results indicate asymptomatic testing has "minimal utility" in populations with low prevalence of COVID-19.

CORTICOSTEROID, OSELTAMIVIR, AND DELAYED ADMISSION ARE INDEPENDENT RISK FACTORS FOR PROLONGED VIRAL SHEDDING IN PATIENTS WITH CORONAVIRUS DISEASE 2019

Hu F, Yin G, Chen Y, Song J, Ye M, Liu J, Chen C, Song Y, Tang X, Zhang Y.. Clin Respir J. 2020 Aug 4. doi: 10.1111/crj.13243. Online ahead of print.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

A retrospective collaborative study by multiple specialties at First People's Hospital of Tianmen and Fudan University identified various risk factors independently associated with duration of viral shedding in 183 COVID-19-positive patients admitted before February 9, 2020. Increased time from symptom onset to admission (HR=0.829; Figure 1), use of corticosteroids (HR=0.496; Figure 2), and use of oseltamivir (HR=0.416) were associated with a longer duration for viral shedding, while use of arbidol (HR=2.605; Figure 3) was associated with a shorter period of shedding. These findings suggest need for early admission and therapy, cautious use of corticosteroids and oseltamivir, and clinical studies on the efficacy of arbidol.

ABSTRACT

INTRODUCTION: Coronavirus Disease 2019 (COVID-19) has spread worldwide, and it has reached to more than 14.5 million cases. Although Hubei province is the epicenter of China, little is known about epidemiological and clinical features of COVID-19 in other areas in Hubei province around Wuhan. In addition, the virological data, particularly the factors associated with viral shedding of COVID-19 has not been well described. OBJECTIVE: To describe the epidemiological and clinical features of patients with COVID-19 in Tianmen city, and identify risk factors associated with prolonged viral shedding of COVID-19. METHODS: Inpatients with COVID-19 admitted before February 9, 2020 were included. Characteristics were compared between patients with early and late viral RNA shedding. Multivariate cox regression model was used to investigate variables associated with prolonged viral shedding. RESULTS: 183 patients were included. 8.2% patients were categorized as critical degree of severity. All patients received antiviral therapy, with arbidol and interferon being the commonest. 38.3% and 16.9% patients were treated with corticosteroid and immunoglobulin, respectively. Time from onset to admission (HR=0.829, P<0.001), and administration of corticosteroid (HR=0.496, P=0.002), arbidol (HR=2.605, P=0.008), and oseltamivir (HR=0.416, P<0.001) were independently associated with duration of viral shedding. CONCLUSION: Symptoms of patients from Tianmen are relatively mild. Treatment should be started as early as possible, but corticosteroid and oseltamivir should be initiated with caution. In addition, clinical trials on arbidol should be conducted to demonstrate its effectiveness.

FIGURES

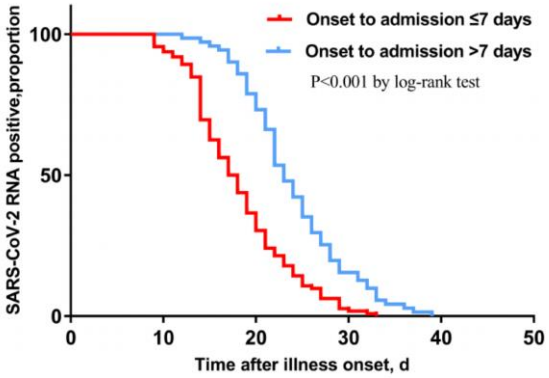

Figure 1. Cumulative proportion of patients with detectable SARS-CoV-2 RNA by day after illness onset between patients who admitted to the hospital of less than 7 days and those who didn't. (P less than 0.001 by log-rank test)

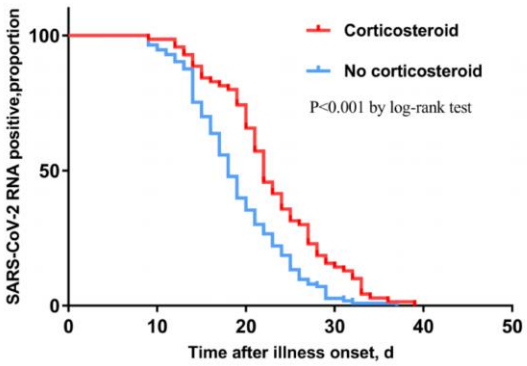

Figure 2. Cumulative proportion of patients with detectable SARS-CoV-2 RNA by day after illness onset between patients who received corticosteroid and those who not. (P less than 0.001 by log-rank test)

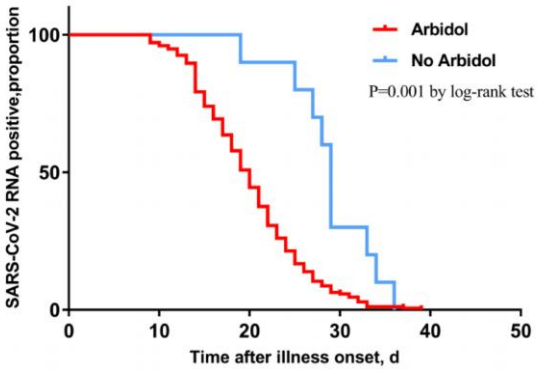

Figure 3. Cumulative proportion of patients with detectable SARS-CoV-2 RNA by day after illness onset between patients who received arbidol and those who not. (P less than 0.001 by log-rank test)

COVID-19: AN IMMUNOPATHOLOGIC ASSAULT

Munro N, Scordo KA, Richmond MM.. AACN Adv Crit Care. 2020 Jul 15:e1-e13. doi: 10.4037/aacnacc2020802. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

In this literature review, American researchers provide an overview of several COVID-19 related topics relevant to critical care clinicians:
1. The pathogenesis of coronaviruses broadly and COVID-19 specifically: The authors cite research indicating COVID19 infects host cells by using its spike glycoprotein to bind angiotensin-converting enzyme 2 receptors.
2. The clinical presentation of COVID-19, including symptomatology: Ranges from asymptomatic to septic shock with subsequent multi-organ failure.
3. Radiologic findings and diagnostic testing: Common chest CT findings include "bilateral, multiple lobular and subsegmental areas of consolidation" and key diagnostic tests include real time PCR and antibody tests. The authors provide a tiered screening approach (see Table 1).
4. Disease characteristics unique to COVID-19 like hypoxic respiratory failure, cytokine release syndrome, and hypercoagulopathy.
5. Treatment approaches, especially those related to critical care (Table 2).
6. The psychological impact of the pandemic for the public, patients, and healthcare workers.

ABSTRACT

When caring for patients with coronavirus disease 2019 (COVID-19), clinicians have noticed some unusual clinical presentations not observed before, such as profound hypoxia and severe hypotension. Scientists are probing the evidence to explain these issues and many other unanswered questions. Severe acute respiratory syndrome associated with coronavirus 2 presents an unchartered acute and critical care dilemma. Some of the theories and proposed interventions that will improve outcomes for these critically ill patients are explored in this article. Various testing procedures for COVID-19 are described so

valid results can be obtained. Clinical presentations are discussed but continue to evolve as the pandemic ravages our society. The psychological impact of this devastation is also addressed from multiple perspectives. The health care provider is faced with an unprecedented, harrowing situation that has become an internal war that also must be confronted. Professional dedication has provided a formidable response to this destructive virus.

FIGURES

Topic	Interventions
Infection control	Use of negative-pressure rooms When performing aerosol-generating procedures, fitted N95 masks recommended, as well as additional PPE if available When performing nonaerosol-generating procedures, general surgical mask recommended CDC offers guidance for managing PPE shortages at https://www.cdc.gov/coronavirus/2019-ncov/hcp/ppe-strategy/index.html
Shock (adults)	Monitor clinical status using dynamic parameters (eg, skin temperature, capillary refill time, serum lactate levels) Use conservative fluid-resuscitation strategy with buffered or balanced crystalloids First-line vasoactive agent: norepinephrine Second-line vasoactive agent: vasopressin or epinephrine Titrate vasoactive agents for MAP goal of 60-65 mm Hg (vs a higher MAP goal) Avoid routine use of colloids If cardiac dysfunction is possible despite fluid resuscitation and vasoactive agents, consider using dobutamine If refractory shock, consider low-dose steroid therapy
Acute kidney injury	Consider initiation of continuous venovenous hemofiltration Discuss dialysate disposal with institutional infection control resources

Abbreviations: CDC, Centers for Disease Control and Prevention; MAP, mean arterial pressure; PPE, personal protective equipment.
[a] Data were derived from Alhazzani et al[40] and Centers for Disease Control and Prevention.

Table 2. Brief Summary of Additional General Critical Care Interventions.

Priority Level	Population
Tier 1	Critically ill patients with unexplained symptoms Individuals with respiratory symptoms and who have had contact with a patient who has tested positive for COVID-19 or who have recently traveled to areas with high community transmission Individuals with fever or respiratory infections who also are immunocompromised (including those with HIV), elderly, or who have underlying chronic conditions Individuals critical to the pandemic response who have respiratory symptoms, such as health care workers, public health officials, and other essential leaders
Tier 2	Patients who are hospitalized but not in intensive care units and long-term care residents with symptoms
Tier 3	Patients in outpatient settings who meet the criteria for influenza testing, including those with select comorbid conditions such as diabetes, chronic obstructive pulmonary disease, or congestive heart failure Pregnant women Symptomatic children with additional risk factors
Tier 4	Individuals in communities being monitored by health authorities to collect data and ascertain the prevalence of COVID-19

Abbreviation: COVID-19, coronavirus disease 2019.

Table 1. Infectious Diseases Society of America Prioritization Recommendations for COVID-19 Testing.

CARDIOLOGY

SEVERE CORONARY SPASM IN A COVID-19 PATIENT

Rivero F, Antuña P, Cuesta J, Alfonso F.. Catheter Cardiovasc Interv. 2020 Aug 1. doi: 10.1002/ccd.29056. Online ahead of print.
Level of Evidence: Other - Case report

BLUF

A case report by physicians at the Department of Cardiology, Hospital Universitario de La Princesa in Madrid, Spain examined a 66-year-old male recently diagnosed with COVID-19 pneumonia who presented with acute inferolateral ST segment elevation (Figure 1a) due to coronary vasospasm (CV; Figure 1c, 1d) that was detected via optical coherence tomography and invasive vasospasm (ergonovine provocation) test and reversed after intracoronary nitroglycerin administration (Figure 2a, 2b). Authors suggest COVID-19 induced inflammation may result in CV and myocardial damage, which could also be a viable mechanism in patients with normal coronary arteries on angiogram.

ABSTRACT

Myocardial injury is frequently detected in coronavirus disease 2019 (COVID-19) patients. However, up to one-third of COVID-19 patients showing ST-segment elevation on the electrocardiogram have angiographically normal coronary arteries. We present a case of an acute coronary syndrome due to a coronary spasm in a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patient. This pathophysiological mechanism was clearly demonstrated by intracoronary imaging techniques (optical coherence tomography) and invasive vasospasm test.

FIGURES

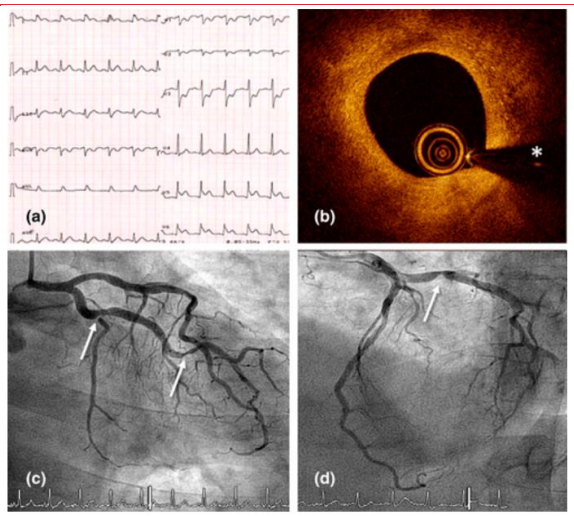

Figure 1. (a) Electrocardiogram during the chest pain episode showing elevation of the inferolateral ST-segment with specular descent in right precordial leads. (b) Optical coherence tomography intracoronary image of the proximal left circumflex coronary artery (LCX) showing the presence of a stable fibrous plaque with cellular infiltration adjacent to the site with minimal lumen area. Notably, presence of erosion or rupture as a possible trigger of acute coronary syndrome was excluded (asterisk denotes wire artifact). (c and d) Urgent coronary angiogram showing lesions in the proximal (arrow) and distal (arrow) LCX

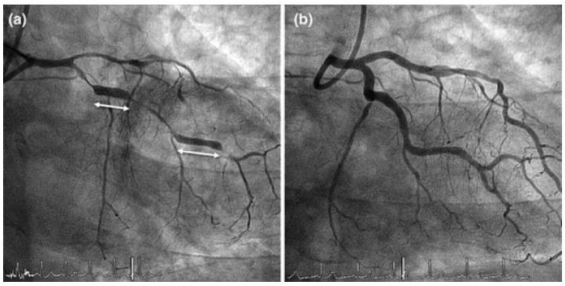

Figure 2. Coronary angiogram during invasive pharmacological coronary vasospasm (CV) provocation test. After intracoronary administration of 10 μg of ergonovine, nearly occlusive multisegment CV involving both the left anterior descending coronary artery and left circumflex coronary artery (LCX) was demonstrated. Only the two previously stented segments of the LCX (double head arrows) maintained lumen unchanged (a). After the administration of intracoronary nitroglycerin, the spasm was reversed with a recovery of the previous arterial caliber (b)

HEMATOLOGY AND ONCOLOGY

A COVID-19 PATIENT WITH REPEATEDLY UNDETECTABLE SARS-COV-2 ANTIBODIES

Goetz L, Yang J, Greene W, Zhu Y.. J Appl Lab Med. 2020 Aug 3:jfaa137. doi: 10.1093/jalm/jfaa137. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

This case report from Pennsylvania State University College of Medicine of a 49-year-old SARS-CoV-2-positive patient with chronic lymphocytic leukemia (CLL; Rai stage IV, Binet stage C) explores the patient's inability to produce SARS-CoV-2 antibodies. Despite a multifaceted serological approach (3 separate assays with discrete antigens – Roche, DiaSorin and Abbot assays) to detect antibodies within the target period for normal production (1 to 6 weeks of infection), the patient did not mount an antibody response. The authors pose that antibody testing in immunocompromised patients may have limited value due to resulting hypogammaglobulinemia, suggesting that both nucleic acid and antigen tests should be performed in this population.

A MODULAR MICROARRAY IMAGING SYSTEM FOR HIGHLY SPECIFIC COVID-19 ANTIBODY TESTING

Hedde PN, Abram TJ, Jain A, Nakajima R, Ramiro de Assis R, Pearce T, Jasinskas A, Toosky MN, Khan S, Felgner PL, Gratton E, Zhao W.. Lab Chip. 2020 Aug 3. doi: 10.1039/d0lc00547a. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Biomedical engineers and medical researchers from the University of California have pioneered a 3D-printable portable imaging platform, TinyArray imager (Figure 1), for rapid use in reading coronavirus antigen microarrays (CoVAMs). In probing and imaging of coronavirus microarrays with COVID-19-positive and -negative sera, the authors found that the TinyArray imager achieved results equivalent to the commercial microarray reader ArrayCAM 400-S (Figure 2 and 3). The authors suggest that the TinyArray imager will help to increase serosurveillance in tandem with containment and therapeutic developments.

ABSTRACT

To detect the presence of antibodies in blood against SARS-CoV-2 in a highly sensitive and specific manner, here we describe a robust, inexpensive ($200), 3D-printable portable imaging platform (TinyArray imager) that can be deployed immediately in areas with minimal infrastructure to read coronavirus antigen microarrays (CoVAMs) that contain a panel of antigens from SARS-CoV-2, SARS-1, MERS, and other respiratory viruses. Application includes basic laboratories and makeshift field clinics where a few drops of blood from a finger prick could be rapidly tested in parallel for the presence of antibodies to SARS-CoV-2 with a test turnaround time of only 2-4 h. To evaluate our imaging device, we probed and imaged coronavirus microarrays with COVID-19-positive and negative sera and achieved a performance on par with a commercial microarray reader 100x more expensive than our imaging device. This work will enable large scale serosurveillance, which can play an important role in the months and years to come to implement efficient containment and mitigation measures, as well as help develop therapeutics and vaccines to treat and prevent the spread of COVID-19.

FIGURES

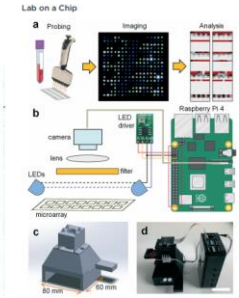

Figure 1: TinyArray imager design. (a) Workflow: after probing of the antigen microarrays, images are taken where the fluorescence intensities corresponding to the relative antibody concentration are quantified. (b) The microarray was LED-illuminated (470 nm) from the
top and imaged through long pass and band pass filters with an OmniVision OV5647 sensor module. Illumination was controlled and images were acquired with a single board computer (Raspberry Pi 4). (c) CAD design of the microarray imager. (d) 3D printed and assembled
prototype together with a Raspberry Pi 4 single board computer interfacing the camera and 75 mm × 25 mm × 1 mm microarray slide inserted into the device. Scale bars, 30 mm.

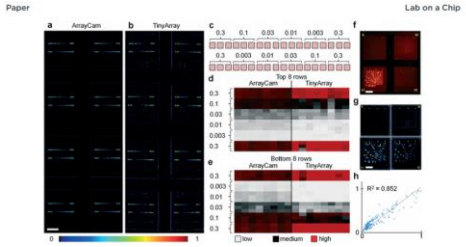

Figure 2: Fluorescence images and quantification of printed microarrays with 280 µm spaced, 150 µm-diameter dots of labeled with quantum dot probes. (a and b) Fluorescence images of 2 × 4 microarray pads (7 mm × 7 mm each) taken with the commercial ArrayCam 400-S and the TinyArray imager, respectively. Fluorescence intensity is represented on a pseudo rainbow color scale. (c) Layout and relative concentrations of the serial dilutions of QD655–streptavidin microarray dots imaged in panels (a and b). (d and e) Quantitative analysis of the background-subtracted median intensities in the top (panel d) and bottom QD655–streptavidin dot rows (panel e) of the images taken with the ArrayCam (left column) and the TinyArray imager (right column) as shown in panels (a and b). (f) Raw image of four microarray pads probed with human serum samples and developed with secondary antibodies conjugated to QD655. (g) Background-subtracted microarray image in pseudo rainbow color scale. (h) Graph and linear regression (R2 > 0.85) of the background-subtracted median fluorescence intensities of the same microarray sample as obtained with the TinyArray imager prototype and the ArrayCam 400-S. Scale bars, 2 mm.

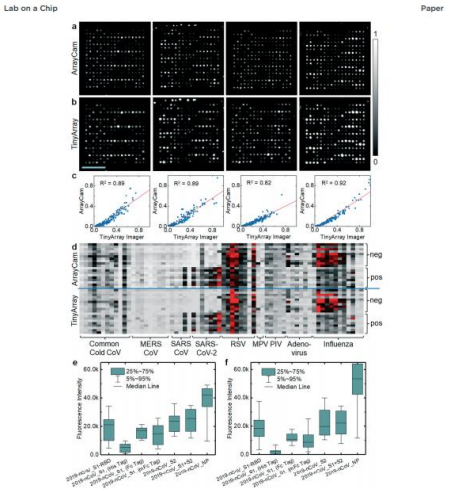

Figure 3: Fluorescence images and data analysis of CoVAM probed with positive sera and stained for human IgG. (a) Four exemplary fluorescence images acquired with the Array Cam 400-S. (b) Corresponding TinyArray images. (c) Background-subtracted median fluorescence intensities obtained for each microarray spot with the Array Cam 400-S and the TinyArray imager that were normalized and plotted against each other; linear regressions were performed and R^2 values were calculated. (d) Heat maps of 9 SARS-CoV-2-positive and 10 negative control samples generated from the Array Cam 400-S (top row) and TinyArray imager data (bottom row). Gray/black/red colors indicate low/medium/high antibody prevalence. (e and f) Statistical analysis of the seven SARS-CoV-2 antigens in the CoVAM for positive sera for the ArrayCam and the TinyArray imager data. Scale bar, 2 mm.

ACKNOWLEDGEMENTS

CONTRIBUTORS

Ben Showalter
Colin Bartz-Overman
Diep Nguyen
Shayan Ebrahimian
Tasha Ramparas
Zubair Ahmed

EDITORS

Alvin Rafou
Cameron Richards
Maggie Donovan
Michelle Arnold

SENIOR EDITORS

Allison Hansen
Avery Forrow
Kyle Ellingsen

EXECUTIVE SENIOR EDITOR

Thamanna Nishath

CHIEF EDITOR

Jasmine Rah

ADVISOR

Will Smith