CLINICAL PRESENTATION AND MANAGEMENT

Automatic pleural line extraction and COVID-19 scoring from lung ultrasound data

The authors used the hidden Markov model and Viterbi Algorithm methods to propose an automatic and unsupervised method for detecting and localizing the pleural line in lung ultrasounds piloted on in vivo lung ultrasound images from patients in Italian hospitals. Ultrasound is non-invasive and relatively inexpensive, and distinct artifacts known as A-lines and B-lines in ultrasound images of the lungs can be used in COVID-19 diagnostics. The authors claim that by using an automated ultrasound diagnostic and scoring system, fast and accurate diagnoses can be made without the assistance of a trained expert. To classify the pathological conditions of the lung, a scoring system from zero to three was created, with zero indicating a normal pleural line and three indicating a completely permeable and discontinuous pleural line. Convex and linear ultrasound probes resulted in 84% and 94% accuracy in detecting the pleura, respectively. Additionally, support vector machine (SVM) supervised classification system was used to develop an automated method to score lung ultrasound images and estimate COVID-19 severity and resulted in about 88% and 94% accuracy in evaluating the severity of changes in the pleural line due to COVID-19 for convex and linear probes, respectively. The authors claim that the algorithms used for this model are relatively simple, which would facilitate the introduction of the classification program directly into ultrasound scanners.

PATHOPHYSIOLOGY

Diaphragm pathology in critically ill patients with COVID-19 and postmortem findings from 3 medical centers

This study investigated the effects of COVID-19 on respiratory muscles, particularly the diaphragm, in critically ill patients. Autopsy diaphragm specimens from 26 patients in the Netherlands that had been critically ill with COVID-19 (COVID-19-ICU) were compared with 8 diaphragm specimens from patients who had been critically ill without COVID-19. Both COVID-19-ICU patients and control patients received invasive mechanical ventilation and stayed in the ICU for comparable amounts of time. Compared to the control samples, diaphragm samples from COVID-19-ICU patients displayed increased expression of fibrosis pathways. Epimysial and perimysial fibrosis were 2-fold greater in COVID-19-ICU diaphragms compared to controls. The authors noted that the causal pathway between SARS-CoV-2 infection and diaphragm myopathy has not yet been established. They hypothesized that fibrosis of the diaphragm that is associated with COVID-19 might lead to ventilator complications, dyspnea, and fatigue in patients after their time in the ICU.

NON-CLINICAL TRENDS

Healthcare disparities among anticoagulation therapies for severe COVID-19 patients in the multi-site VIRUS registry

The authors analysed mortality differences associated with the use of different anticoagulants among patients with severe COVID-19 being treated in intensive care units (ICU). After controlling for potential confounding factors, such as demographic information, comorbidities, and oxygenation method, the mortality rate was higher among patients who received unfractionated heparin (41%) compared to those given enoxaparin (15%). More complications were seen among those taking unfractionated heparin compared to those given enoxaparin, such as kidney injury (35% vs 26%), acute cardiac injury (6.2% vs 2.5%),
septic shock (18% vs. 12%) and anemia (13% vs. 7.6%). Race-based differences were also found in anticoagulant administration, with more African Americans receiving unfractionated heparin compared to Caucasian patients (31% vs. 24%). The authors suggest that these findings warrant future studies on potential social disparities within the use of anticoagulants to treat severe COVID patients.

Estimation of US Children’s Educational Attainment and Years of Life Lost Associated With Primary School Closures During the Coronavirus Disease 2019 Pandemic

A decision analytical model was used to conduct an analysis of publicly available data to estimate the number of expected years of life lost (YLL) due to COVID-19 in the United States conditioned on primary schools being closed or remaining open. This comparison was made under two different scenarios: 1) the early phase of primary schools closing due to the COVID-19 pandemic and 2) an unobserved scenario based on the counterfactual decision to allow primary schools to remain open. A total of 24.2 million children (ages 5-11) attended public schools that closed during the pandemic, losing a median 54 days of instruction. Missed instruction was associated with a mean loss of 0.31 and 0.21 years of final educational attainment for boys and girls, respectively. Across the population, a total 5.53 million YLL may be associated with primary school closures. The CDC reported a total of 88,241 US deaths from COVID-19 through the end of May 2020, with an estimated 1.50 million YLL as a result. The authors estimate an additional 1.47 million YLL could have been expected if primary schools remained open. Comparing the YLL under both scenarios found a 98.1% probability that primary school openings would have been associated with a lower total YLL than when primary schools closed. These findings highlight the potential consequences of primary school closures during the early phases of the COVID-19 pandemic, with the authors noting that loss of life will likely be inequitable across children across different races/ethnicities, genders, and socioeconomic statuses.

Ethnicity and Clinical Outcomes in COVID-19: A Systematic Review and Meta-analysis

Sze et al. conducted a systematic review and meta-analysis of the relationship between ethnicity and clinical outcomes during the pandemic by searching databases for reports published between December 1, 2019 and August 31, 2020 on COVID-19 outcomes based on ethnicity. Outcomes of interest were risk of infection, intensive therapy unit (ITU) admission, and death. Of the sample population, 77% were White, 7% were Asian, 3% were Black, 8% were Hispanic, <1% were Native American, 2% were Mixed, and 3% were of Other ethnic groups. Compared to White individuals, Black and Asian Individuals had a higher risk of COVID-19 infection (pooled adjusted RR for Black: 2.02, 95% CI 1.67-2.44; pooled adjusted RR for Asian: 1.50, 95% CI 1.24-1.83). Additionally, this analysis shows Asians may be at a higher risk of ITU admission compared to White patients (pooled adjusted RR 1.97 95% CI 1.342.89) and death (pooled adjusted RR/HR 1.22 [0.991.50]); however, the authors recognize there were no studies included that assessed ITU admission risk among Asian cohorts. These findings provide information to inform interventions to reduce morbidity and mortality amongst ethnic minority groups.

Mental Health

Real-time suicide mortality data from police reports in Queensland, Australia, during the COVID-19 pandemic: an interrupted time-series analysis

This study evaluated changes in suicide mortality rate and suspected motives before and after the COVID-19 pandemic in Queensland, Australia. The analysis found no significant difference in mortality rates between suicide before and after the pandemic (14.85 vs. 14.07
deaths per 100,000 population). Data on suspected motives, including domestic violence, relationship problems, job loss, or financial problems, also did not show significant differences. The authors emphasize that regions with a higher COVID-19 burden might expect an increased effect of COVID-19 on death by suicide rates, and thus recommend proactive mental health promotion and suicide prevention efforts, especially for individuals with pre-existing mental health conditions.

TRANSMISSION PATTERNS

Unexpected detection of SARS-CoV-2 antibodies in the prepandemic period in Italy
Apolone et al. used a custom receptor-binding domain (RBD)-based ELISA to investigate the presence of SARS-CoV-2 RBD-specific antibodies in blood samples of 959 asymptomatic individuals in Italy originally enrolled in a lung cancer screening trial from September 2019 to March 2020. SARS-CoV-2 RBD-specific antibodies were found in 111 of 959 individuals, with samples from as early as September 2019 and a cluster of positive cases in the second week of February 2020. The majority (53.2%) of the 111 positive samples was found in Lombardy, the region most affected by the pandemic. This unexpected circulation of SARS-CoV-2 among asymptomatic individuals many months before the first patient was identified in Italy helps clarify the onset and spread of the COVID-19 pandemic in the country. The authors suggest that a better understanding of the COVID-19 history and epidemiology could improve screening strategies and help contain the effects of a possible second wave.

An Outbreak of Covid-19 on an Aircraft Carrier
Kasper et al conducted a study of SARS-CoV-2 infection in a young, healthy population of 4779 crew members on a nuclear-powered aircraft, the U.S.S Theodore Roosevelt. The crew was made up of mostly young men (mean age 27 years) who were racially and ethnically diverse. Of this cohort, 26.6% tested positive for the virus between the dates of March 23, and May 18, 2020. 43% of those who tested positive were asymptomatic throughout the breakout, 30.5% were presymptomatic, and 22% were symptomatic at the point in time that they tested positive. Only 55% were symptomatic at any point in time during the clinical course. Those who worked in tight and contained spaces on the aircraft had higher odds of infection, and most of the men who were infected were asymptomatic during testing, meaning that they were mostly likely major contributors to the outbreak. It was also noted that those crew members that were symptomatic and required hospital care often had coexisting conditions such as hypertension, asthma, and liver-disease. One crew member died in the ICU from cardiovascular complications. Current policies to reduce COVID-19 transmission in ships and aircrafts have been implemented by the Navy: all members of the crew must quarantine for 14 days before deployment and must receive a negative rRT-PCR COVID-19 test. The authors conclude that policies described previously and mitigation strategies such as mask-use, social distancing, small-group cohorting, and cleaning of common space would help prevent major outbreaks from happening in other organizations that require groups of people to interact for sustained periods of time.

Secondary attack rate and family clustering of SARS-CoV-2 infection in children of healthcare workers with confirmed COVID-19
Ladhani et al. investigated the secondary attack rate (SAR) of SARS-CoV-2 by measuring serum SARS-CoV-2 antibodies in 215 children from 126 families of healthcare workers in London, England. Of the 126 families, 21 reported at least one parent who had symptomatic SARS-CoV-2 infection, likely being the index cases in their households. Nine of the 21 families with an infected healthcare worker parent had at least one child who was positive for SARS-CoV-2 IgG. There was strong evidence of family clustering; the SAR was 95.2%
in the nine families with at least one seropositive child, while none of the 23 children in the remaining 12 families had seroconverted.

REGION-SPECIFIC LESSONS LEARNED

Seroprevalence of SARS-CoV-2 in slums versus non-slums in Mumbai, India

Malani et al conducted a study to estimate the seroprevalence of SARS-CoV-2 in six slum and non-slum communities in Mumbai, India from June 29 to July 19, 2020. A total 4,202 samples from slums and 2,702 samples from non-slums were collected. Samples were provided by women and men from four different age strata, age 12 and up, and were tested for IgG antibodies. 54.1% of samples from slums were estimated to be positive for IgG antibodies as compared to 16.1% in non-slums, and positive test proportions in both age and sex were higher in slums compared to non-slums. Proportions were also higher amongst women compared to men in both slums and non-slums. The authors suggest that there is higher asymptomatic spread of disease in slums, most likely as a result of population density, lack of social-distancing, and poor hygiene.

NON-PHARMACEUTICAL/ PUBLIC HEALTH INTERVENTIONS

Cost-effectiveness of public health strategies for COVID-19 epidemic control in South Africa: a microsimulation modelling study

Reddy et al built a model to assess the clinical outcomes and cost-effectiveness of combinations of five public health interventions during two epidemic scenarios in KwaZulu-Natal province, South Africa. The public health interventions included: health care testing only of those presenting to healthcare centers; providing isolation centers; mass symptom screening and testing for symptomatic individuals; providing quarantine centers; and contact tracing. The two epidemic scenarios were informed by current pandemic estimates in South Africa and were run for a period of 360 days; the first with an effective reproductive number (Re) of 1.5 and the second with an Re of 1.2. Scenarios resulting in an incremental cost-effectiveness ratio (ICER) below US$3250 per year of life saved (YLS) were deemed cost effective. The first epidemic scenario (Re of 1.5) demonstrated that a combination of all five interventions would provide the greatest clinical benefit, a decrease in life-years lost by 94%, a reduction in peak daily hospital bed use of 86%, and an increase in costs by 33%, which was deemed cost-effective compared to the healthcare testing alone scenario (ICER $340/YLS). Even in scenarios where quarantine centers were unavailable, health-care testing, contact tracing, isolation centers, and mass symptom screening was cost-effective when compared to healthcare testing alone (ICER $590/YLS). The second scenario (Re of 1.2) determined that health-care testing, contact tracing, and use of isolation and quarantine centers, was the least costly strategy, resulting in strong dominance. The addition of mass symptom screening would result in 48% fewer life-years lost but was not cost effective (ICER $27590/YLS). No other strategies emerged as cost-effective. The authors thus conclude that the combination of the five strategies can control COVID-19 efficiently, and in resource constrained settings, other combinations of interventions can provide a certain degree of benefit that still considers economic efficiency.

PHARMACEUTICAL INTERVENTIONS

Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial

Monk et al conducted a phase 2 pilot clinical trial to understand the efficacy of SNG001, an interferon beta-1a nebulizer solution, in comparison with a placebo. Patients from nine sites across the United Kingdom with confirmed SARS-CoV-2 infection, were delivered either
SNG001 (6 MIU dose) or a placebo via a nebulizer for up to 14 days. While in the hospital, patient vital signs, levels of consciousness, electrocardiogram assessments, blood samples, the Breathlessness, Cough and Sputum Scale (BCSS), and the WHO Ordinal Scale for Clinical Improvement (OSCI) assessments were taken and monitored daily. The study found the odds of improvement on the OSCI were over two times greater in the SNG001 group on day 15-16 (OR=2.32 [95% CI 1.07–5.04]; p=0.03). SNG001 decreased the odds of severe disease or death in the per-protocol population by 79% (OR=0.21 [95% CI 0.04–0.97]; p=0.046) and over the course of the treatment, patients in the SNG001 group were over twice as likely to recover (HR=2.19 [95% CI 1.03–4.69]; p=0.043). No significant difference was found in hospital discharge odds or time to discharge between the groups. Of the patients receiving SNG001, 54% reported treatment-emergent adverse effects, the most common being headaches, while 60% reported adverse events in the placebo group. Serious adverse events were more commonly found in the placebo group, including death. The authors call for a phase 3 trial of SNG001, as it seems to be well tolerated in COVID-19 patients, as well as an assessment of the formulation’s safety in critically ill patients.

ADDITIONAL RESOURCES
UCSF Library COVID-19 Research and Information Resources
UCSF Institute for Global Health Sciences COVID-19 Resources
UC Davis One Health Institute COVID-19 FAQs
Harvard Viswanath Lab Myths vs Facts

Note on this Document: This document was assembled by graduate and doctoral students attending the University of California, San Francisco with the intent of facilitating the rapid dissemination of information to the global community in order to help during this time. Canice Christian, Ilia Vasilopoulos, Mariam Carson, Deandra Lee, Maya Ganeshan, and Shivali Joshi contributed to these summaries. This work is volunteer based.

References:


