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Description of COVID-19 Scoring System for detection of Severity

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first isolated from several cases of pneumonia of unknown etiology connected to the cluster of acute respiratory illness cases in Wuhan. COVID-19 spreads from person to person mainly through the respiratory route. A new infection occurs when virus-containing particles exhaled by an infected person, either respiratory droplets or aerosols, get into the mouth, nose, or eyes of other people who are in close contact with the infected person. The severity of COVID-19 varies. The disease may take a mild course with few or no symptoms, resembling other common upper respiratory diseases such as the common cold. Some studies suggest 10% to 20% of people with COVID-19 will experience symptoms lasting longer than a month. Complications may occur including pneumonia, acute respiratory distress syndrome (ARDS), Cardiovascular complications, multi-organ failure, septic shock, and death.

Keywords: COVID-19, Scoring System

Background

Coronaviruses (CoVs) are a highly diverse family of enveloped positive-sense single-stranded RNA viruses. They infect humans, other mammals and avian species causing respiratory, enteric, hepatic and neurological diseases **(1)**. Within the order of Nidovirales and the suborder of Coronavirineae lies the family Coronaviridae. The latter is further specified into the subfamily of Orthocoronavirinae, which consists of four genera: alphacoronavirus, betacoronavirus, gammacoronavirus and deltacoronavirus. Whereas alphacoronaviruses and betacoronaviruses exclusively infect mammalian species, gammacoronaviruses and deltacoronaviruses have a wider host range that includes avian species **(2)**.

-Human (Pathogenic) Coronaviruses

Two Alphacoronavirus strains: HCoV-229E and HCoV-NL63 and five Betacoronaviruses: HCoV-HKU1, HCoV-OC43, SARS-CoV, MERS-CoV, and SARS-

CoV-2 have so far been recognized as Human Coronaviruses (HCoVs) **(3)**. HCoVs have long been known to spread in the world population. Two zoonotic HCoVs: MERS-CoV and SARS-CoV along with recently emerged SARS-CoV-2 are highly pathogenic strains **(4)**. These strains have been thought to have emerged into the human population from wildlife through spillover events, causing severe illnesses of lower respiratory tract **(3)**.

1. SARS-CoV

In November 2002, an epidemic caused by a betacoronavirus (SARS-CoV) began in South China and quickly spread from China to other Asian countries. There were also a small number of cases in several other 29 countries. The SARS pandemic was eventually brought under control in July 2003, following a policy of isolating people suspected of having the condition and screening all passengers travelling from affected countries for signs of the infection **(5)**. The SARS outbreak caused ~8,000 infections and 774 deaths before it was contained in July 2003, with a case fatality rate (CFR) of 9.6% (the CFR was ~50% among patients 65 years or older). However, since 2004, there have not been any SARS cases reported anywhere in the world **(6).**

2. MERS-CoV

MERS-CoV is a zoonotic virus that originated from dromedary camels. However, the exact route of transmission to humans remains unknown. As the name implies, this disease is relatively prominent in the Middle East region as compared to other parts of the world **(7)**.

In September 2012, Saudi Arabia reported the first case of Middle East respiratory syndrome (MERS). where a man was diagnosed with pneumonia and kidney failure. Soon, MERS had spread to neighbouring countries such as Qatar and Iran, eventually spreading to the rest of the globe **(8)**. The Republic of South Korea was the first country with the largest outbreak outside of the Middle East region; and had reported its first case in the year 2015, which eventually led to a major outbreak in the region. MERS-CoV spread to 27 countries and caused 2,519 infections and 866 deaths by January 2020, with a (CFR) of 34.4% **(7)**.

3. SARS-CoV-2 (COVID-19)

The highly infectious coronavirus disease 2019, COVID-19, is caused by the RNA virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first identified in Wuhan, China in December 2019 and declared a pandemic by the World Health Organization (WHO) in March 2020 **(9)**. Consequently, the impact of the pandemic on healthcare is unprecedented endangering healthcare professionals as one in seven has been infected. **(10)**.

Epidemiology

The COVID-19 epidemic expanded in early December from Wuhan, China's 7th most populous city, throughout China and was then exported to a growing number of countries. The first confirmed case of COVID-19 outside China was diagnosed on 13th January 2020 in Bangkok (Thailand) **(11)**. It was declared a global pandemic by the WHO on the 11th of March 2020. The number of confirmed cases is constantly increasing worldwide and after Asian and European regions, a steep increase in cases is being observed in low-income countries **(12)**.

Scoring system

Scoring systems are standard tools used in critical care research as study inclusion criteria and to demonstrate equivalence of patient groups. Clinically, they are used to objectively quantify condition severity, risk stratify patients for clinical prognostication and, at the unit level, they can serve as a tool for assessing the impact of quality variables (staffing, organization, management, protocol changes) on patient outcomes **(12)**.

Early risk prediction and effective treatment can reduce mortality and morbidity as well as relieve resource shortages **(11)**. Risk stratification methods have been effectively used in previous viral outbreaks such as the Ebola epidemic in 2014 to reduce casualties. With COVID-19 being a novel disease, no pre-existing risk stratification methods were available, so traditional scoring systems were adapted in the early stages of the pandemic **(13)**.

Categories of ICU clinical scoring systems

Scoring systems commonly applied to critically ill patients can be broadly classified into disease specific scoring systems (such as the CHA_2DS_2-VASc score to predict thromboembolic risk in atrial fibrillation), *injury scoring systems* (such as the Glasgow Coma Scale [GCS]) and severity scoring systems **(14)**. The latter category can be further subdivided into: 1) severity scoring systems which predict risk of in-hospital mortality based on degree of physiologic derangement at time of ICU admission **(13)** (such as the Acute Physiology and Chronic Health Evaluation [APACHE] system, the Simplified Acute Physiology Score [SAPS], and the Mortality Probability Models [MPM]), and 2) severity scoring systems developed to *assess and characterize current degree of organ dysfunction (*such as the Multiple Organ Dysfunction Score [MODS], the Sequential Organ Failure Assessment [SOFA], and the Logistic Organ Dysfunction Score [LODS]) **(10)**.

Several disease severity scoring systems are often used to guide the management of patients with pneumonia, such as the Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Function Assessment (SOFA), quick Sequential Organ Function Assessment (qSOFA), Pneumonia Severity Index (PSI), Combination of

Confusion, Urea, Respiratory Rate, Blood Pressure, and Age ≥65 (CURB-65), Modified Early Warning Score (MEWS) and the Systemic Inflammatory Response Syndrome Criteria (SIRS). All these scoring systems have been proven to be useful for predicting the outcome of patient's with pneumonia **(14)**

1. The Sequential Organ Failure Assessment (SOFA)

SOFA score is one of the scoring systems used to evaluate organ failure and can predict the severity and outcome of the disease. The SOFA scoring performance is based on the evaluation of the following 6 major organ functions: circulation, respiration, liver, renal function, central nervous system, and coagulation function. The score of each organ is between 0 and 4. It is an easy-to-use tool for systematically and continuously evaluating organ functions during hospitalization and traditionally be calculated on admission to ICU and at each 24-h period that follows **(15)**.

Table 1 The criteria for assessment of the Sequential Organ Failure Assessment (SOFA) score **(15)**

Respiratory system	
PaO_2/FiO_2 (mmHg)	**SOFA score**
> 400	0
< 400	1
< 300	2
< 200 with respiratory support	3
< 100 with respiratory support	4
Nervous system	
Glasgow Coma Scale	**SOFA score**
15	0
13–14	1
10–12	2
6–9	3
< 6	4
Cardiovascular system	
Mean arterial pressure (MAP) OR administration of vasopressors required	**SOFA score**
MAP > 70 mmHg	0
MAP < 70 mm/Hg	1
Dopamine ≤ 5 µg/kg/min or dobutamine (any dose)	2
Dopamine > 5 µg/kg/min OR epinephrine ≤ 0.1 µg/kg/min OR norepinephrine ≤ 0.1 µg/kg/min	3

Dopamine > 15 µh/kg/min OR epinephrine > 0.1 µg/kg/min OR norepinephrine > 0.1 µg/kg/min	4
Liver	
Bilirubin (mg/dl) [µmol/L]	**SOFA score**
< 1.2 (< 20)	0
1.2–1.9 [20–32]	1
2.0–5.9 [33–101]	2
6.0–11.9 [102–204]	3
> 12.0 [> 204]	4
Coagulation	
Platelets ×10^3/ml	**SOFA score**
> 150	0
< 150	1
< 100	2
< 50	3
< 20	4
Kidneys	
Creatinine (mg/dl) [µmol/L]; urine output	**SOFA score**
< 1.2 [< 110]	0
1.2–1.9 [110–170]	1
2.0–3.4 [171–299]	2
3.5–4.9 [300–440] (or urine output < 500 ml/day)	3
> 5.0 [> 440]; urine output < 200 ml/day	4

The respiratory SOFA component

Assessment of the respiratory SOFA score relies on invasive arterial monitoring to measure arterial partial pressure of oxygen followed by calculation of the PaO_2/FiO_2 ratio. **(16)**.

In addition to fixed performance (venturi) oxygen masks, many patients will be treated at some stage in their care with conventional nasal cannula, standard facemasks or a mask with reservoir bag, all of which deliver oxygen at variable flow rates and inspired oxygen percentage. An approximation of the FiO_2 associated with their use may be employed for SOFA score calculation **(15)**. For patients on nasal cannula oxygen, an estimated FiO_2 may be calculated by multiplying the litre flow/minute by 0.03 and adding that to 0.21. The SOFA score calls for patients to receive a score of 3 or 4 if they reach a PaO_2/FiO_2 ratio of less than 200 or less than 100 respectively and are receiving respiratory support. In addition to invasive and non-invasive ventilators, high flow rate

oxygen delivered at a controlled percentage via a dedicated nasal cannula has become more prevalent in the years since the development of the SOFA score **(16)**.

SOFA Score and COVID

Gupta et al.**(16)** summarized the clinical characteristics of SARS-CoV-2 infection, which could not only cause severe lung injury but also damaged the heart, liver, kidney, nervous system, endocrine system, blood system, and skin, resulting in arrhythmia, acute coronary syndrome, thrombosis, gastrointestinal symptoms, hyperglycemia, and skin rash **(16)**. Thus, the SOFA score can comprehensively assess multiple organ dysfunction caused by SARS-CoV-2.

Raschke et al. (17)study reported that the discriminant accuracy of the SOFA score for mortality prediction in patients prior to intubation for COVID-19 pneumonia was poor. This finding has several potential explanations. The SOFA score was designed for patients with sepsis and only 3 of the 6 equally weighted organ system sub scores (respiratory, renal, and hepatobiliary) are associated with mortality in COVID-19. Also they showed that SOFA scores are not a good discriminator of probable mortality in patients with COVID-19 pneumonia requiring mechanical ventilation because the study was conducted in critically ill patients admitted to the ICU for treatment and requiring mechanical ventilation **(17)**.

However, **Martinez et al., (18)** showed that the increase on SOFA score in the first 48 hours after admission is associated with a significant ICU mortality in critically ill patients with COVID-19. These correlate with similar findings in no COVID19 patients. Thus, suggesting that SOFA score is an excellent tool to predict mortality in critically ill patients with COVID 19. **Zhou et al., (19)** showed that older age, higher d-dimer levels, and higher SOFA scores in COVID-19 patients at admission were associated with high in-hospital mortality.

Quick Sequential Organ Failure Assessment (QSOFA)

For the rapid identification of patients with suspected infection outside of the ICU, on the other hand, Seymour et al. introduced the quick Sequential Organ Failure Assessment (qSOFA) score TheqSOFA score is a simple score consisting of three items: respiratory rate (RR) $\geq$ 22 breaths per minute, altered mentation (Glasgow Coma Scale [GCS] < 15), and systolic blood pressure (SBP) < 100 mmHg. A qSOFA score $\geq$ 2 was found to be significantly predictive of increased all-cause mortality in patients outside of the ICU The Third International Consensus Definitions for Sepsis recommends qSOFA as a simple prompt to identify infected patients outside the ICU who are likely to be septic **(15)**.

QSOFA in COVID

However, due to the threatened capacities of health care systems worldwide during the COVID-19 pandemic, there is a strong need for a validated clinical risk score to identify

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patients with confirmed SARS-CoV-2 infection at risk for severe or critical disease progression. Due to its ease of access requiring no laboratory tests, qSOFA could be a valuable tool for risk stratification in patients with COVID-19 and help clinicians with the decision upon start or escalation of therapy and the consideration of referring patients to the intensive care unit. Its predictive value for mortality and critical progression in patients with COVID-19, however, has not been sufficiently evaluated so far **(20)**.

in studies that the qSOFA score should not be the only screening tool for a risk assessment of critical disease progression in COVID-19 patients. Also confirmed that patients with a high qSOFA score or/and an impaired SO_2 (e.g., less than 94% SO_2) should be monitored more closely to initiate necessary intensive medical measures at an early stage, to look closer for affected organ systems other than the respiratory system (especially for affected renal function, neurologic impairments, and myocardial involvement) and thus to initiate the necessary instrumental diagnostics **(20)**.

The Acute Physiology And Chronic Health EvaluationAPACHE

The APACHE series is one of the most commonly used scoring systems in ICUs **(13)**. The APACHE II (acute physiology and chronic health evaluation II) scoring system is being used to evaluate the condition of patients in ICU using 12 parameters **(21)**.

It has the advantage of being able to be used on a daily basis and has similar positive and negative predictive values as the Ranson score at 48 hours after admission The APACHE-II system assigns points for 12 physiologic variables, . The 12 variables are temperature; heart rate; respiratory rate; mean arterial blood pressure; oxygenation; arterial pH; serum potassium, sodium, and creatinine; hematocrit; white blood cell (WBC); and Glasgow Coma Scale **(21)**.

Table 2. Acute physiologic and chronic health evaluation (APACHE II) **(20).**

A: Acute physiological score (12 variables)

Physiologic variable	High abnormal range				Normal range	Low abnormal range			
	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature rectal (°C)	≥41	39-40.9	-	38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.0
Mean arterial pressure (mm Hg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart rate-ventricular response	≥180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory rate per minute-non-ventilated or ventilated	≥50	35-490		25-34	12-24	10-11	6-9		≤5
Oxygen: A-a DO_2 or PaO_2 (Torr)									
FiO_2 ≥0.5 record A-a DO_2	≥500	350-499	200-349		≤200	PO_2 61-70		PO_2 55-60	PO_2 <55
FiO_2 <0.5 record only PaO_2					PO_2 >70				
Arterial pH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum HCO_3 (mmol/L)-only if no ABGs	≥52	41-51.9		32-40.9	23-31.9		18-21.9	15-17.9	<15
Serum sodium (mmoL/L)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110
Serum potassium (mmoL/L)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		≤2.5
Serum creatinine (μmoL/L)	≥350	200-340	150-190		60-140		<60		
Hematocrit (%)	≥60		50-50.9	46-49.9	30-45.9		20-29.9		≤20
White blood cell count (×1,000/mm^3)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow coma score=15 minus actual GCS									

B: Age points		C: Chronic health points			Apache II score
Age (years)	Points	History	Points for elective surgery	Points for emergency surgery	Sum of A+B+C
≤44	0	Liver: Biopsy-proven cirrhosis and documented portal hypertension or prior episodes of hepatic failure	2	5	A: APS
45-54	2	Cardiovascular: NYHA Class IV	2	5	B: Age points
55-64	3	Respiratory: e.g., severe COPD, hypercapnia, home O_2, pulmonary hypertension	2	5	score
65-74	5	Immunocompromised	2	5	C: Chronic health
≥75	6	Renal: Chronic dialysis	2	5	point score
Total score					

Value

Most patients survive if APACHE-II scores are 9 or less during the first 48 hours. However, patients with APACHE-II scores of 13 or more have a high likelihood of dying. **(19)**. Strong drawbacks are its complexity, its low sensitivity on admission, and the fact that at 48 hours the score is no better than other scoring systems. **(11).**.

APACHE-II scores in COVID

at the beginning of the pandemic studies showed excellent discriminative power for the APACHE II score (AUC 0.966). however, did not calibrate their model. Their primary goal was to investigate the APACHE score as a predictor for survival to facilitate end-of-life decision-making at the very beginning of the pandemic. Therefore, their study included patients admitted in Wuhan between January 10th, 2020, and February 10th, 2020.

The APACHE II score is a classic tool for assessing the severity of the disease in patients in the ICU. The higher the score, the more critical the situation, worse the prognosis, and higher the mortality**(21)**. **Wang and Li.(14)** determined that the median APACHE II score of patients with severe novel coronavirus pneumonia was 17 (10–22) **(14)**.

The Murray Score

The Murray Score is used to grade the severity of lung injury in acute respiratory distress syndrome (ARDS). The final score is obtained by dividing the collective score by the number of components that were used. A score greater than 2.5 will indicate ARDS, a score between 1-2.5 indicates mild to moderate lung injury, and a score of zero rules out lung injury The Murray Score is based on four criteria, which are hypoxemia, respiratory compliance, chest radiographic findings, and the level of positive end-expiratory pressure. Each criterion receives a score from zero to four according to condition severity and those numbers are summed to create the Murray Score **(20)**.

Table 3. The Murray Lung Injury Score **(20)**.

The lung injury score (Murray score)		
1. Chest roentgenogram score		
No alveolar consolidation		0
Alveolar consolidation confined to 1 quadrant		1
Alveolar consolidation confined to 2 quadrant		2
Alveolar consolidation confined to 3 quadrant		3
Alveolar consolidation in all 4 quadrant		4
2. Hypoxemia score		
PaO_2/FiO_2	>300	0
PaO_2/FiO_2	225–299	1
PaO_2/FiO_2	175–224	2
PaO_2/FiO_2	100–174	3
PaO_2/FiO_2	≤ 100	4
3.PEEP score (when ventilated)		
PEEP	≤ 5 cm H_2O	0
PEEP	6–8 cm H_2O	1
PEEP	9–11 cm H_2O	2
PEEP	12–14 cm H_2O	3
PEEP	> 15 cm H_2O	4
espiratory system compliance score (when availa		
Compliance	>80 ml/cmH_2O	0
Compliance	60–79 ml/cmH_2O	1
Compliance	40–59 ml/cmH_2O	2
Compliance	20–39	3

	ml/cmH_2O	
Compliance	< 19 ml/cmH_2O	4

Murray score with CXR in COVID

CXR of patients with COVID-19 pneumonia may reveal unilateral, bilateral, peripheral, and patchy opacities. In the early stage of COVID-19 pneumonia, CXR may not be able to detect abnormal findings, because CXR is not sensitive for ground-glass opacity (GGO) **(22)**.

4c Mortality Score for COVID

The 4C mortality score is an accessible risk stratification score developed by the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC). It was derived and internally validated on a large, diverse cohort within the United Kingdom but requires external validity to confirm its generalizability creating the pragmatic 4C Mortality Score (where 4C stands for Coronavirus Clinical Characterization Consortium) The 4C score incorporates age, sex, comorbidities, respiratory rate, peripheral oxygen saturation, Glasgow Coma Scale, blood urea nitrogen, and C-reactive protein. We adapted the score to match our available data as the Glasgow Coma Scale was not collected at presentation. The 4C score ranges from 0 to 21 with risk groups defined as Low (0–3), Intermediate (4–8), High (9–14), and very high (≥ 15) **(22)**. The ISARIC4C score was mainly internally validated, and it predicted mortality only in hospitalized patients. The 4C Mortality Score performed relatively well in early risk stratification of patients with COVID-19 with good sensitivity and specificity in mortality prediction. Within the score, hypoxia, tachypnea, high BUN, and CRP were the significant independent predictors of mortality. There is a possibility to consider other important early predictors especially D-dimer. Still, there is an urgent need for a better scoring system that can be used in early stages to help in decision-making to stratify those at high risk that may require more careful assessment and earlier intervention **(22)**.

4-C score is a good predictor for the severity of the disease. The 4-C score correlates well with the elevation in BUN, ARDS progression and liver injury. Elevated 4-C scores were correlated with mortality in the COVID-19 patients. The 4-C mortality score uses patient demographics, clinical observations, and blood parameters that are commonly available at the time of hospital admission and can accurately characterize the population of hospital patients at high risk of death**(9)**.

Table 4. Final 4C Mortality Score for in-hospital mortality in patients with covid-19.

Variable	4C Mortality Score
Age (years)	
<50	—

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50-59	+2
60-69	+4
70-79	+6
≥80	+7
Sex at birth	
Female	—
Male	+1
No of comorbidities*	
0	—
1	+1
≥2	+2
Respiratory rate (breaths/min)	
<20	—
20-29	+1
≥30	+2
Peripheral oxygen saturation on room air (%)	
≥92	—
<92	+2
Glasgow coma scale score	
15	—
<15	+2
Urea (mmol/L)	
<7	—
7-14	+1
>14	+3
C reactive protein (mg/L)	
<50	—
50-99	+1
≥100	+2

Veterans Health Administration COVID-19 (VACO) Index for COVID-19 Mortality

The VACO Index estimates 30-day all mortality causes after COVID-19 infection, incorporating demographic data and pre-existing conditions. The VACO Index can be used to screen uninfected patients to identify those at a higher risk of dying should they develop COID-19. Age is the strongest predictor of risk, but the index also takes into account other factors, such as pre-existing medical conditions. People with a higher risk score can be more closely monitored for the disease and advised to take extra precautions to avoid the virus. Those with a higher score are also more likely to require hospitalization if infected, meaning the index can help with care planning **(4)**.

Among COVID-19 positive individuals, the VACO Index accurately estimates risk of short-term mortality among a wide variety of patients. While it modestly over-estimates risk in recent intervals, the Index consistently identifies those at greatest relative risk. The VACO Index could identify individuals who should continue practicing social distancing, help determine who should be prioritized for vaccination, and among outpatients who test positive for SARS-CoV-2, indicate who should receive greater clinical attention or monoclonal antibodies **(4)**.

The COVID-GRAM score

a clinical risk tool (the COVID-GRAM) was recently validated to predict the development of critical COVID-19 illness which defined as admission to the intensive care unit (ICU), requiring invasive mechanical ventilation or death—after hospital admission in a nationwide cohort in China. Risk scores, applied to 10 variables at the time of admission that were independent predictors of critical illness, were used to classify patients as having a low (0.7% probability), medium (7.3%), or high risk (59.3%) of developing a critical illness **(8)**.

Chest radiography abnormality, age, hemoptysis, dyspnea, unconsciousness, number of comorbidities, cancer history, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, and direct bilirubin were included in the COVID risk score **(23)**.

High COVID-GRAM scores at presentation could warrant increased vigilance and treatment while low scores could require only observation. The COVID-GRAM was developed among patients with a 1.5% incidence of severe pneumonia, as defined by the American Thoracic Society, and an 8.2% incidence of critical illness. Thus, the COVID-GRAM score should be replicated and validated for use in other clinical populations **(8)**.

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