Development of a Novel Scoring System for Comprehensive COVID-19 Patient Evaluation: An Evidence-based Systematic Review

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Abstract

Context: In the era of the SARS-CoV-2 virus pandemic, new scoring systems need to be developed to estimate the risk of COVID-19 complications aiding in the accurate prognosis. Improved scoring systems by combining multiple variables allow clinicians to optimize the allocation of limited medical resources for the best clinical outcomes.

Methods: Published articles were selected that assessed the relationship between clinical, para-clinical, demographics, co-morbidities, and outcomes of COVID-19 patients in a systematic review to develop a novel scoring system.

Results: In this study, by summarizing the results of 97 studies and the experiences of experts, prognostic factors were determined and divided into four groups: Age, clinical symptoms, co-morbidities, and tests. Twenty-three published articles met the selection criteria and were included in this study. Accordingly, by the opinion of experts, prognostic factors were categorized into four main groups: Age, clinical symptoms, co-morbidities, and specific test results.

Conclusions: This novel scoring model helps physicians to early identify critical COVID-19 patients and optimize patient management based on recent comprehensive data of the most significant predictive factors.

Keywords: SARS-CoV-2, COVID-19, Scoring System, Prediction, Severity

1. Context

The SARS-CoV-2 virus has spread worldwide since its outbreak in early December 2019 in a Chinese province and is now an emergent threat to global health. The number of confirmed patients in more than 210 countries has exceeded 38 million, and more than 1,000,000 people have died from COVID-19-related causes (up to 15 Oct 2020) (1). The COVID-19 pandemic is known as the biggest global health crisis of the past century, affecting all aspects of human life.

Due to the very recent emergence of SARS-CoV-2, physicians and researchers often have very little information about the accurate diagnosis and best regimens in the treatment of COVID-19. In many cases, trial and error methods are used to manage patients. In this situation, one of the most important practical tools to help clinicians to take the best step at the best time is to use valid scoring systems to optimize patient management based on the risk of disease progression to critical stage and death.

The prompt and accurate diagnosis of disease and modulating prediction rules are essential to reduce the burden of disease not only in any population but also in healthcare systems. By combining several variables to estimate the risk and prognosis, such forecasting models help physicians in proper triage and early identification of critical patients, and allow them to allocate restricted resources rationally. This proper allocation of resources is es-

pecially important for intensive care units and ventilators (2). The high impact of accurate predictive models on reducing mortality during a pandemic is due to its influence on timely adjusting the best clinical management plan (3).

So far, several scoring systems, such as SOFA and CALL, have been developed for COVID-19. In each of them, a limited number of variables have been used to score and classify patients in high, moderate, and low-risk groups (4-6). Thus, identifying the prognostic factors by multivariate analysis and preparing a prediction rule is more than useful.

2. Methods

To develop a scoring system for the prediction of COVID-19 severity, three databases of PubMed, Scopus, and Google Scholar were searched. To make these searches extensive and sensitive, the following keywords were used [(COVID-19) OR (SARS-CoV-2)] AND [(scor*) OR (predict*)] OR (severity). To obtain more results, the following keywords were added and searched in parallel in Google Scholar: [COVID-19] AND [scor*] AND [severity] AND [predicting factor] AND [co-morbidities] AND [lab tests] AND [%]. All searches were limited to studies from 2019 to September 7, 2020.

2.1. Study Selection and Appraisal

In this review, all articles that assessed the clinical or para-clinical findings, individual characteristics, and co-morbidities in the form of quantitative indicators to predict the disease severity were included in the study. To be included in this review, the articles were needed to divide the patients into severe and mild groups based on clear and valid criteria. As the only important outcome was the patient's final condition as a severe or mild illness, studies that examined this association in the form of hazard ratio (HR) were excluded. No evaluation of bias was performed.

2.2. Data Extraction

From the reported indices, cases with the highest statistical accuracy (lowest confidence interval) were selected. Risk factors were ranked based on the magnitude of OR, and according to experts, a threshold was selected to divide them into major and minor criteria.

3. Results

3.1. Included Studies

Based on the inclusion and exclusion criteria, a total number of 97 articles were identified. After excluding duplicate studies and those with insufficient data, 23 studies were selected (Appendix table in Supplementary File),

and the data from these studies were extracted in an Excel spreadsheet.

3.2. Host Factors

3.2.1. Age

In all articles included in this analysis, age was an important factor influencing the severity of COVID-19 disease with significant p values (< 0.001) (7). Most of these articles targeted adults. The ages above 65, 75, and 80 years, with odds ratios of 8.55, 6.06, and 3.43, respectively, were the most important factors to predict the severity of the disease. In only one article, it was reported that among the 4 age groups (0-14-, 15-44-, 45-64-, and 65-74-year-old), disease severity and disease related admission was highest in the 45-64-year-old age group (36%). There were very fewer articles in the pediatric population than in adults. In pediatrics, age groups were only noted; but, the relationship with the severity of the disease was not reported.

3.2.2. Gender

In many studies, the prevalence was higher in males than in females, but the p value for the correlation of the severity of disease with sex was insignificant (8-11).

3.2.3. Clinical Findings

In most studies, multiple variables (such as cough, dyspnea, gastrointestinal signs and symptoms, and vital signs) were noted concerning the severity of the disease. However, a vital sign was the only variable with significantly different frequencies between mild and severe disease groups (5, 8).

3.3. Comorbidities

In all studies, the presence of underlying disease was significantly higher in severe disease than in mild-to-moderate disease (P-value < 0.001; Table 1) (9, 11).

3.4. Laboratory Tests

In several articles, the results of different lab tests were compared between severe-to-critical disease and mild-to-moderate disease. Among them, the higher odds ratio was related to lymphopenia, LDH, CRP, and AST (Table 1) (5, 7-10, 12, 13). They also evaluated hemoglobin, albumin, BUN, prothrombin time, interleukin-6, procalcitonin, total bilirubin, platelet count, D-dimer, glucose, fibrinogen, ferritin, and CPK. In some studies, these test values were significantly higher among patients with mild-to-moderate symptoms than in patients with severe or critical status (5, 13).

Table 1. Odds Ratio and Confidence Interval of Predictive Factors

Predictive Factor	Result	OR	CI
Sickle cell disease		20% ICU admission	
LDH	> 500	17.33	4.3 - 42.9
CRP, mg/L	> 41.8	10.53	1.92 - 10.03
Age		6.06	3.98 - 9.22
Serious cardiovascular disease		5.19	3.25 - 8.29
Elevated liver enzyme (AST), U/L	> 40	4.00	2.46 - 6.52
Cerebrovascular disease		3.89	
Obesity (body mass index ≥30)		3.68	1.54 - 8.83
Type 2 diabetes mellitus		3.68	2.68 - 5.03
Chronic liver disease		3.55	1.23 - 10.24
Chronic obstructive pulmonary disease		3.37	
LDH	245 - 500	3.34	2.1 - 8.5
Lymphopenia		3.14	0.22 - 0.36
Chronic kidney disease		3.03	1.09 - 8.47
CRP, mg/L	> 8.2	6.17	1.22 - 34.70
Hypertension		2.72	1.60 - 4.64
Smoking		2.51	1.39 - 3.32
Pulmonary fibrosis		0.66	0.06 - 7.65
Cancer		0.15	0.01 - 1.78
Asthma (moderate to severe)		Not significant	

3.5. Development of a Novel Scoring System

From the ORs reported in the selected articles, the ones with the highest accuracy were considered (Table 1). Then, a cutoff was determined based on experts' opinions according to OR = 3.14 to determine the risk (Table 2).

3.6. Expert Consensus

The risk factors were divided into four groups (Table 2), and different combinations were provided to the experts to judge the participation of each of the major and minor risk factors in creating the final situation. Based on this judgment, each of the risk factors was scored, and finally, a threshold was set according to which patients were divided into two groups (high-risk and low-risk). Accordingly, a score of 2 was considered for the factors whose ORs were above the given threshold, and those who had ORs below the threshold were given a score of 1.

3.7. Evaluating Different Combinations

Based on the experts' opinions, in patients with the sudden onset of fever and cough or at least three or more

symptoms such as fever, headache, cough, fatigue, muscle aches, sore throat, rhinorrhea, shortness of breath, anorexia, nausea, vomiting, and diarrhea, the diagnosis of COVID-19 was relevant. Therefore, a score was given based on Table 2. If the patient presents with a combination of the above symptoms or has warning signs such as a decreased level of consciousness, hemodynamic instability, distress or resting shortness of breath, inability to eat or drink, abnormally large abdomen, refractory frequent vomiting, dysentery, acute abdomen, hematuria, swelling under the eyes, edema, lack of communication when awake, sudden movement disorder, seizures, weakness, and severe lethargy or bleeding in various parts of the body, it is necessary to refer directly to the hospital. Accordingly, scoring for the predicting factors was done, as follows (Table 3):

1) If the total score of the patient in the early evaluation (host factors, clinical manifestations, and comorbidities) is equal to or less than 5, home care is recommended by prescribing supportive medication, besides teaching the patient about warning signs and follow-up based on patient condition.

2) If the total score of the patient in the early evaluation (host factors, clinical manifestations, and comorbidities) is between 6 and 8, the initial tests such as CBC, LDH, or CRP should be ordered. The patient should receive outpatient treatment according to national guidelines and at the discretion of the treating physician.

3) If the total score in the early evaluation (host factors, clinical manifestations, and comorbidities) or the total score in Table 2 (early and secondary evaluation) is equal to or greater than 9, the patient should be referred to the hospital.

4) The score limit that can be assigned to the total clinical findings and the total age and underlying disease is 5 points and to laboratory tests, 3 points.

4. Discussion

Articles published so far (September 15, 2020) on the scoring of patients with COVID-19 have considered a few prognostic factors, such as laboratory test results (CBC, CRP, GFR, and myoglobin), age, and several comorbidities (such as respiratory diseases, cardiac diseases, hypertension, hyperlipidemia, diabetes, kidney diseases, liver diseases, History of previous surgery). In this study, by summarizing the results of studies in this area and the experience of experts, more prognostic factors were determined and divided into four groups: Age, clinical symptoms, comorbidities, and tests.

In this review, by summarizing the results of other studies in this area and using the experience of experts,

Table 2. Predictive Scoring Measures

Predictors	Predictive Factor	Cutoff	Score
Early Evaluation			
Host factors	Age	> 60	1
		> 70	2
Clinical manifestations	Pulse rate	100 - 120/min	1
		> 120/min	2
	Respiratory rate	24 - 30/min	1
		> 30/min	2
	O$_2$ Sat.	90% - 93%	2
		< 90%	3
	Temperature	> 38.5	1
		> 38.5 for > 5 days	2
Co-morbidities	Obesity	body mass index ≥ 40	2
		body mass index = 30 - 40	1
	Diabetes mellitus	Uncontrolled	2
		Controlled	1
	Cardiovascular disease	2	
	Cerebrovascular disease	1	
	Chronic liver disease	1	
	Hypertension	Uncontrolled	2
		Controlled	1
	Chronic lung disease	Chronic obstructive pulmonary disease	2
		Other (uncontrolled asthma, pulmonary fibrosis)	1
	Immune deficiency	Bone marrow or solid organ transplant	2
		Other immunodeficiencies (HIV (CD4 < 200 OR 15%), use of corticosteroids or other immunosuppressing agents)	1
	Cancer	Under chemotherapy	2
		In remission	1
	Hemoglobinopathy	Sickle cell disease	2
		Other hemoglobinopathies	1
	Smoking	1	
	Chronic kidney disease	1	
Secondary evaluation			
Laboratory tests	Lymphopenia	< 500	2
		< 1100	1
	LDH Or CRP	> 500	2
		245 - 500	1
		> 70 mg/L	2
		40 - 70 mg/L	1

more prognostic factors were incorporated into a new, more comprehensive, and uniform clinical scoring system for COVID-19 treatment planning, encompassing four major groups of variables: Age, clinical symptoms, comorbidities, and laboratory tests. Finally, patient management guideline was developed based on predictive factors.

4.1. Limitation of Study

As COVID-19 is an emergent disease, prospective studies are needed to determine a scoring system with acceptable validity. However, these studies are time-consuming. Thus, we have an urgent need to develop a scoring system that helps physicians in decision-making and managing the patients (whether to start treatment or hospitalization). The only way to prepare a scoring system is to use the results of studies and expert opinions. On the other hand, most studies only reported the frequency of observed risk factors in patients with mild, moderate, severe, and critical symptoms for disease progression, and there were no studies that showed the presence of risk factors separately with any severity of the disease, including age, sex, underlying diseases, clinical symptoms, and test results. This led us to use the reported odds ratios for risk factors in the studies, as well as the opinions of experts in the field, to develop

Table 3. Management of Patients According to Scores

Total Score	Suggested Management
≤ 5	Outpatient supportive medication; announcing warning signs and symptoms
6 - 8	Outpatient supportive medication like naproxen; optional prescription like hydroxychloroquine sulfate[a] or azithromycin[a]; announcing warning signs and symptoms
≥ 9	Hospitalization for immediate supportive care like oxygen and correction of electrolytes; precise evaluation of disease progression; Low-dose corticosteroids[a], interferon beta-1b[a] and 1a[a], and antiviral drugs[a]; anti-coagulant drugs like enoxaparin

[a]Drugs are prescribed according to national guidelines and there is no approved drug yet.

an initial scoring system that can help physicians in the proper management of patients. Indeed, it is noteworthy that to assess the external and internal validity of this scoring system, we have started a comprehensive study nationwide to examine the impact of various risk factors on the severity of the disease in different people, which has not been completed yet.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Footnotes

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