A preliminary study on the joint parameter Lym% and HGB for the prediction of severe and nonsevere COVID-19

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Research article

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Abstract

Objectives

The aim of this study was to identify the parameters in routine blood tests that can be used to evaluate the severity of coronavirus disease 2019 (COVID-19) and thus assist in clinically predicting the extent of progression.

Methods

This study retrospectively analyzed the epidemiological, clinical symptom and laboratory examination data of 159 COVID-19 patients. The percentage of lymphocytes (Lym%) and hemoglobin (HGB) were integrated into a joint parameter, Lym%&HGB, by binary logistic regression.

Results

Both Lym% and HGB gradually decreased with disease progression whereas the joint parameter Lym%&HGB increased gradually with disease progression. When using Lym%, HGB, and Lym%&HGB to predict COVID-19 severity, the area under the receiver operating characteristic (ROC) curve (AUC) was 0.89, 0.79, and 0.92, respectively. The dynamic change curves showed that Lym% and HGB continued to decline while Lym%&HGB continued to increase with disease progression in patients with severe COVID. The change in Lym%&HGB was more prominent than the changes in Lym% and HBG.

Conclusions

The joint parameter Lym%&HGB can serve as a good tool to differentiate severe and nonsevere COVID-19, and it has a higher sensitivity and specificity than either Lym% or HGB alone.

Introduction

At present, coronavirus disease 2019 (COVID-19) is spreading rapidly worldwide. In a short period of four months, 1,353,361 cases have been confirmed globally, and 79,235 deaths and a mortality rate of 5.84% have been reported as of April 9, 2020 [1][2][3][4]. Similar to clinical manifestations of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), COVID-19 quickly causes fever, dry cough, fatigue and dyspnea and might progress to severe life-threatening situations [5][6][7] [8].

Recent studies on clinical characteristics of COVID-19 patients have revealed that those with mild or common COVID-19 can quickly recover after appropriate clinical intervention; however, patients with severe COVID-19, especially elderly patients or those with underlying diseases, may deteriorate rapidly, leading to a higher mortality [9][10][11][12][13][14][15]. Dehkordi found that approximately 14% of COVID-19

patients were severely ill and 5% were critically ill; the remaining 80% of infected patients had a mild or common form of the illness [16]. The treatment methods for severe and nonsevere COVID-19 patients are different. Patients with mild disease often gradually recover after isolation and symptomatic treatment, while patients with severe disease may require treatment with antiviral drugs, hormones, antibiotics, immunotherapy, etc., and may even need to be admitted into an intensive care unit (ICU) for comprehensive treatment and nursing care [6][7][9][10]. Therefore, differential diagnosis between severe and nonsevere COVID-19 is critical. A rapid and accurate severity assessment of the disease can guide clinical interventions in a timely manner and facilitate the rationale allocation of medical resources, thus effectively reducing mortality. However, laboratory tests (e.g., imaging examinations, nucleic acid detection, molecular sequencing, and microbial culture), which can accurately determine disease severity, treatment efficacy, and disease outcomes, are relatively complicated and time-consuming; as a result, they cannot detect, in a timely manner, disease progression. Hence, it is urgent for clinical laboratory experts to develop rapid, convenient, and effective indicators that can differentiate severe and nonsevere COVID-19 to meet clinical needs.

According to the *Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Trial Version 6)* issued by the National Health Commission of the People' s Republic of China and the study conducted by Li *et al*., the progressive declination of peripheral blood lymphocytes in adult COVID-19 patients is an early warning of progression from mild to severe disease [17] [18]. In addition, clinical studies conducted by Lippi and Zhang *et al*. found that hemoglobin (HGB) levels declined in COVID-19 patients with progression to severe disease [19][20][21]. However, there is insufficient evidence supporting the direct use of Lym% and HGB to guide the diagnosis and treatment of COVID-19 [18][21]. We hypothesize that a joint parameter obtained through the integration of Lym% and HGB can predict severe COVID-19, potentially improving the diagnosis and treatment efficiency in patients with severe disease. Lymphocyte count and peripheral blood hemoglobin concentration can be obtained from routine blood tests. A complete blood count (CBC) is the most effective, economical and common test in clinical laboratories. If the proposed joint parameter can provide accurate information regarding disease progression and outcomes of COVID-19 patients, doctors will be able to identify patients with severe disease and take appropriate measures in a timely manner.

In this study, two parameters, percentage of lymphocytes (Lym%) and HGB, as well as the joint parameter, Lym%&HGB, in peripheral blood were compared between patients with severe and nonsevere COVID-19 in order to assess the effectiveness of these parameters in differentiating patients with severe and nonsevere COVID-19 for clinical guidance.

Materials And Methods

Patients

A retrospective analysis was conducted on 159 COVID-19 patients who were admitted to The Third People's Hospital of Shenzhen, China between January 23, 2020, and March 21, 2020. Diagnosis and clinical classification were performed according to the *Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Trial Version 6)* issued by the National Health Commission of the People's Republic of China. The clinical classification of COVID-19 is as follows: 1) mild – clinical symptoms are mild, and no imaging manifestations of pneumonia are observed; 2) common – clinical symptoms, including fever and respiratory symptoms, and imaging manifestations of pneumonia; 3) severe – any of the following manifestations: a) shortness of breath and respiratory rate (RR) ≥ 30 times/minute; b) oxygen saturation at rest ≤ 93%; c) arterial partial oxygen pressure (PaO_2)/oxygen absorption concentration (FiO_2) ≤ 300 mmHg (1 mmHg = 0.133 kPa); and d) lung imaging showing a > 50% remarkable increase in lesions within 24–48 hours; and 4) critically severe – any of the following conditions: a) respiratory failure, requiring mechanical ventilation; b) shock; and c) complicated with other organ failure, requiring ICU monitoring and treatment. To simplify the statistical analysis and for an intergroup comparison, 101 patients with mild or common COVID-19 were combined into the nonsevere patient group, and 58 patients with severe and critically severe COVID-19 were combined into the severe patient group. This study was approved by the ethics committee of the hospital and granted a waiver for obtaining signed informed consent because of the retrospective nature of the study.

Data Collection

The electronic medical records of COVID-19 patients were retrieved from the hospital information system (HIS). Data related to epidemical characteristics, previous medical history, clinical manifestations, diagnosis and treatment, imaging findings, and laboratory test results of patients were collected. Respiratory tract swabs, including samples from the upper respiratory tract, throat, and alveolar lavage fluid, were collected from patients during hospital admission and sent to Shenzhen Center for Disease Control and Prevention for laboratory testing. The 159 COVID-19 patients received 1,503 CBC tests during their hospital stay. According to the real-time disease condition and recovery status of patients, the CBC data were divided into two groups: the nonsevere sample group (662 tests) and the severe sample group (841 tests).

Statistical Methods

Age and number of days are expressed as medians and ranges. Categorical variables are expressed as absolute numbers and percentages. The chi-square test and Fisher's exact test were performed for comparisons between two groups. The Kolmogorov-Smirnov test was used to test the normal distribution of continuous variables; data with a normal distribution are expressed as the mean and standard deviation (SD) and were compared between two groups using Student’s t-tests; data without a normal distribution are expressed as the median and interquartile range (IQR value) and were compared between two groups using the Mann-Whitney U test. A two-sided *p* value less than 0.05 indicated a statistically

significant difference. Logistic regression was performed to integrate two parameters into a joint parameter, Lym%&HGB, for the differential diagnosis of nonsevere and severe COVID-19. To evaluate the effectiveness of the abovementioned parameters for estimating COVID-19 severity in patients, a receiver operating characteristic curve (ROC) was established and the area under the ROC (AUC) was calculated. After the optimal cutoff value for each parameter was determined based on the Youden index and scenarios of clinical use, the sensitivity and specificity of Lym%, HGB, and the joint parameter Lym%&HGB were compared. SPSS statistical software (version 21.0) was used for analysis, and GraphPad Prism (version 8.0) was used to plot graphs.

Results

Epidemiological and clinical characteristics of COVID-19 patients

This study enrolled 159 COVID-19 patients, including 101 (63.5%) in the nonsevere patient group and 58 (36.5%) in the severe patient group. The median age of all enrolled patients was 53 years (37–63 years); patients in the severe group had a median age of 63 years (54–66 years), significantly higher than the median age of patients in the nonsevere group (47 years (34–58 years); $P < 0.01$). Among the 159 COVID-19 patients, 82 (51.6%) were male, and 77 (48.4%) were female; 129 patients (81.1%) had been to Wuhan within two weeks, 25 patients (15.7%) had a contact history with patients with suspected COVID-19, and 36 patients (22.6%) had a contact history with patients with confirmed COVID-19. With regard to clinical symptoms, 115 patients (72.3%) had fever, 62 (39.0%) had cough, 12 (7.5%) had myalgia, and 12 (7.5%) had pharyngeal redness or pharyngalgia. Higher percentages of patients had fever and dry cough in the severe group than in the nonsevere group, and the differences in the occurrence rates of fever and dry cough between the two groups were statistically significant ($p < 0.05$). Except for fever and dry cough, there were no significant differences in other symptoms between the two groups ($p > 0.05$). With regard to underlying diseases, 21 (13.2%) patients had hypertension, 7 (4.4%) had diabetes mellitus, and 6 (0.6%) had cardiovascular disease; there were no significant differences between the groups ($p > 0.05$) (Table 1).

Table 1
Epidemiological and clinical characteristics of confirmed COVID19 patients

Characteristics	Total (N = 159)	Nonsevere (N = 101)	Severe (N = 58)	*p* value
Age, median (IQR), years	53 (37–63)	47 (34–58)	63 (54–66)	0.001
Sex – No. (%)				
Male	82 (51.6)	39 (38.6)	43 (74.1)	0.000
Female	77 (48.4)	62 (61.4)	15 (25.9)	
Exposure History within 2 weeks – No. (%)				
Wuhan travel history	129 (81.1)	87 (86.1)	42 (72.4)	0.033
Suspected patient contact within 2 weeks	25 (15.7)	12 (11.9)	13 (22.4)	0.079
Confirmed patient contact within 2 weeks	36 (22.6)	28 (27.7)	9 (15.7)	0.049
Signs and symptoms - No. (%)				
Fever	115 (72.3)	63 (62.4)	52 (89.7)	0.000
Dry cough	62 (39.0)	33 (32.7)	29 (50.0)	0.031
Myalgia	12 (7.5)	9 (8.9)	3 (5.2)	0.584
Pharyngalgia	12 (7.5)	10 (9.9)	2 (3.4)	0.242
Dyspnea	10 (6.3)	5 (5.0)	5 (8.6)	0.563
Fatigue	9 (5.7)	5 (5.0)	4 (6.9)	0.877
Diarrhea	7 (4.4)	3 (3.0)	4 (6.9)	0.259
Stuffy or runny nose	5 (3.1)	2 (2.0)	3 (5.2)	0.355
Headache or dizziness	4 (2.5)	1 (1.0)	3 (5.2)	0.138
Nausea or vomiting	2 (1.3)	2 (2.0)	0 (0.0)	0.534
Chills	1 (0.6)	0 (0.0)	1 (1.7)	0.365
Comorbidity - No. (%)				
Hypertension	21 (13.2)	10 (9.9)	11 (19.0)	0.104
Diabetes	7 (4.4)	6 (5.9)	1 (1.7)	0.424
Cardiovascular disease	6 (3.8)	4 (4.0)	2 (3.4)	0.618
Cancer	1 (0.6)	0 (0.0)	1 (1.7)	0.365
Other	15 (9.4)	6 (5.9)	9 (15.5)	0.087

Establishment Of The Joint Parameter Lym%&hgb By Logistic Regression

By combining Lym% and HGB, the joint parameter Lym%&HGB was formed by binary logistic regression for subsequent evaluation. Taking 101 patients with nonsevere COVID-19 as the reference group and 58 patients with severe COVID-19 as the comparison group, binary logistic regression was conducted to evaluate the impact of Lym% and HGB on the odds of developing severe COVID-19 (Table 2). Lastly, the logistic model obtained by omnibus tests was statistically significant ($P < 0.001$), and its ability to correctly recognize the grouped data was 84.4% (1268/1503) when using a prediction probability of 0.5 as the cutoff point. The two independent variables Lym% and HGB in the model were statistically significant ($p < 0.001$). With each unit Lym% decreased, the risk of progressing to severe disease increased by 17.3% (OR = 0.827, 0.811–0.845); with each unit HGB decreased, the risk increased by 4.9% (OR = 0.958, 0.951–0.965).

Table 2
Binary logistic regression of indicators in COVID19 patients

	B	S.E	Wals	df	Sig.	OR	95% CI	
Lym%	-0.189	0.010	329.807	1	0.000	0.827	0.811	0.845
HGB	-0.43	0.004	132.113	1	0.000	0.958	0.951	0.965
Content	8.572	0.502	291.088	1	0.000			

Parameter Differences Between Patients With Severe And Nonsevere Covid-19

Using 662 results from nonsevere patients and 841 results from severe patients, Mann-Whitney U tests were performed for intergroup comparisons. As shown in Table 3, Lym% and HGB were significantly lower in the severe group than in the nonsevere group ($p < 0.001$), but Lym%&HGB in the severe group was significantly higher than that in the nonsevere group ($p < 0.001$). In Figs. 1A-C, the boxplots present the differences in these parameters between the severe and nonsevere groups.

Table 3
Mann-Whitney U test results for the severe and nonsevere groups

	Total (N = 1503)	Nonsevere (N = 662)	Severe (N = 841)	Z Value	P Value
Lym (%)	15.5 (7.9–25.7)	26.2 (19.7–33.1)	9.4 (5.6–14.9)	-26.311	0.000
HGB (g/L)	116 (97–134)	130 (117–141)	102 (91–119)	-19.010	0.000
Lym%&HGB	0.661 (0.160–0.927)	0.128 (0.032–0.394)	0.903 (0.735–0.959)	-28.178	0.000

Subsequently, ROC analysis was performed, and the AUC was calculated to evaluate the effectiveness of these parameters in identifying patients with severe and nonsevere COVID-19. After the optimal cutoff value was determined based on the Youden index (sensitivity + specificity-1) and scenarios of clinical use, diagnostic sensitivity and specificity were calculated (Fig. 1-D). When Lym%, HGB, and Lym%&HGB were used to identify patients with severe COVID-19, the AUCs were 0.89, 0.79, and 0.92, respectively. When the cutoff values for Lym%, HGB, and Lym%&HGB were, respectively, 18.8%, 116 g/L and 0.481, the sensitivity rates were 85.6%, 71.1% and 88.9%, and the specificity rates were 77.5%, 77.2% and 79.8%, respectively (Table 4). A joint parameter ≥ 0.481 (0.481 is the optimal cutoff point) indicated a high risk of deteriorating to severe COVID-19. The AUC results suggested that the diagnostic effectiveness of the joint parameter Lym%&HGB was superior to that of either single parameter.

Table 4
ROC analysis results for the three parameters

Parameter	AUC	95% CI	Cutoff	Sensitivity	Specificity	Predict value (+)	Predict value (-)
Lym (%)	0.89	0.88–0.91	18.8	85.6%	77.5%	0.83	0.81
HGB (g/L)	0.79	0.76–0.81	116	71.1%	77.2%	0.80	0.68
Lym%&HGB	0.92	0.91–0.94	0.481	88.9%	79.8%	0.85	0.85

Figure 2 shows the two-dimensional scatter plot of Lym% and HGB for the two groups of patients, vividly demonstrating the high effectiveness of combining Lym% and HGB. The data points for patients with severe COVID-19 are mainly distributed in the lower left area of the figure, which can be clearly distinguished from the data points for patients with nonsevere COVID-19 in the upper right area. The dashed line represents the optimal cutoff value for Lym%&HGB obtained by ROC analysis. The data points for patients with severe and nonsevere COVID-19 are mostly distributed on the different sides of the dashed line, indicating that the joint parameter Lym%&HGB obtained by integration can serve as a good tool for differentiating severe and nonsevere COVID-19.

Dynamic profiles of the three parameters over time in COVID-19 patients

To explore the relationships among the three parameters (Lym%, HGB, and Lym%&HGB) and disease progression, dynamic change curves were created using the number of days after disease onset, i.e., the date when the patient complained of fever, dry cough, dyspnea, chest tightness, and other symptoms, as the horizontal axis and using the median parameter value for each group as the vertical axis. The change patterns and trends for the three parameters in patients with severe and nonsevere COVID-19 were analyzed. As Fig. 3-A shows, Lym% was significantly lower in patients with severe COVID-19 than in patients with nonsevere COVID-19 throughout the entire disease course, and the median Lym% in patients with severe COVID-19 was lower than the cutoff level of 18.8% on the 4th day after disease onset, providing an indication of progression to severe disease. In addition, HGB declined progressively since the end of the second week, decreasing by 24% from 133 g/L to 100 g/L, and the median value was lower than the cutoff point of 116 g/L in the third week. This suggested disease progression, likely to the severe stage (Fig. 3-B). HGB was significantly lower in the severe group than in the nonsevere group during the entire disease course. The joint parameter showed an increasing trend with disease progression in both groups, and it was significantly higher in the severe group than in the nonsevere group during the entire disease course (Fig. 3-C).

Discussion

At present, the most difficulty challenge in treating patients and saving lives is the extreme shortage of medical resources, especially critical care resources. Therefore, the differentiation of patients with severe and nonsevere COVID-19 is key to providing treatment at different levels as needed [18][20][21]. The rational allocation of medical resources is an important means of improving diagnosis and treatment efficiency and reducing patient mortality. The use of routine blood testing, an economical and simple-to-operate tool with a short turnaround time, to determine disease severity can largely accelerate the pace and reduce the cost of COVID-19 diagnosis and treatment. The proposed approach uses a common laboratory parameters to assist clinicians in preliminarily classifying COVID-19 patients and properly allocating medical resources. This will ensure that patients with early-stage severe COVID-19 can be treated in a timely manner.

In the present study, the investigation of the epidemiology and clinical symptoms of COVID-19 patients revealed that, consistent with previous reports, patients with severe disease were older than those with nonsevere disease. This may be related to the weakening of the body's defense system caused by the declination of immune function or the presence of underlying diseases (e.g., hypertension, chronic renal failure, and diabetes mellitus) in elderly patients [6][7][8][12]. Therefore, clinicians should closely monitor the disease progression of middle-aged and elderly patients to avoid missing the optimal treatment time. In addition, 72.3% of the 159 COVID-19 patients developed clinical symptoms, including fever, and patients with severe COVID-19 were more likely to develop fever than those with nonsevere COVID-19.

In this study, two parameters, Lym% and HGB, were integrated to form a joint parameter Lym%&HGB by binary logistic regression. Both Lym% and HGB were statistically significant when used as independent variables in the model ($p < 0.001$, Table 2), indicating that both parameters had a significant impact on the possibility of developing severe COVID-19. The joint parameter Lym%&HGB obtained by integrating the above two parameters had an accuracy of 84.4% in identifying the data of different groups, suggesting great potential of this parameter in the differential diagnosis of severe and nonsevere COVID-19.

The grouping analysis of the results from 1503 routine blood tests found that Lym% and HGB continued to decline and the joint parameter Lym%&HGB continued to rise as the disease progressed in COVID-19 patients. The data from 1503 routine blood tests were divided into the severe sample group and the nonsevere sample group and were subject to Mann-Whitney U nonparametric tests. Compared with that in the nonsevere sample group, Lym% and HGB were significantly lower while the joint parameter Lym%&HGB was significantly higher in the severe sample group ($p < 0.001$). This indicated that the number of lymphocytes and the concentration of hemoglobin gradually decreased with disease progression. Therefore, Lym%, HGB, and the joint parameter Lym%&HGB are all potential tools for distinguishing severe from nonsevere COVID-19.

Subsequently, ROC analysis was conducted to assess the diagnostic performance of the three parameters in identifying patients with severe or nonsevere COVID-19. The results showed that both Lym% and HGB were good predictors, as evidenced by the AUCs of 0.89 and 0.79, respectively. When using 18.8% as the cutoff point for Lym% and 116 g/L for HGB, the sensitivity rates were 85.6% and 71.1%, and the specificity rates were 77.5% and 77.2%, respectively; moreover, the AUC for Lym%&HGB was 0.92. When using 0.481 as the cutoff point for Lym%&HGB, the sensitivity was 88.9%, and the specificity was 79.8%, suggesting that Lym%&HGB has advantages in distinguishing patient with severe COVID-19 from those with nonsevere COVID-19.

To more intuitively present the effectiveness of the joint parameter Lym%&HGB in distinguishing patients with severe COVID-19 from those with nonsevere COVID-19, a two-dimensional scatter plot of the results from 1503 tests was generated with Lym% as the horizontal axis and HGB as the vertical axis. As Fig. 2 shows, the data points for patients with severe disease are scattered mostly below the cutoff for Lym%&HGB, while those for patients with nonsevere disease are mostly above the line, indicating that the joint parameter, as a predictor, is superior to the single parameters Lym% and HBG for distinguishing patients with severe disease from those with nonsevere disease.

The dynamic profile demonstrated that Lym% was significantly lower in the severe patient group than that in the nonsevere patient group and that the median Lym% in the severe patient group began to fall below the cutoff point of 18.8% on the 4th day after disease onset, suggesting a high possibility of developing severe disease. Similarly, HGB declined progressively beginning at the end of the second week after disease onset, and the median fell below the cutoff point of 116 g/L in the third week, showing a decrease by 24% from 133 g/L to 100 g/L. This indicated that the disease was likely to progress to a

severe stage. However, the joint parameter Lym%&HGB showed an opposite change trend to that of Lym% and HGB. Compared with patients with nonsevere COVID-19 whose Lym%&HGB slightly fluctuated and increased, patients with severe COVID-19 had a higher Lym%&HGB level, above the cutoff point of 0.481, throughout the entire disease course. This observation can help clinicians more easily identify patients with severe disease.

Lymphocytes play a decisive role in maintaining systemic immune balance and regulating the inflammatory response in the body. Currently, there are four possible explanations for the decrease in the number of lymphocytes caused by novel coronavirus infection. (1) The virus directly attacks and kills lymphocytes. In the early stage of infection, B lymphocytes produce antibodies that directly bind to and kill the virus, and T lymphocytes engulf the virus-infected cells, thereby clearing the virus. Therefore, the reduction in lymphocytes in COVID-19 patients might be attributed to the massive consumption of lymphocytes [22][23][24][25][26]. (2) The virus may directly destroy lymphatic organs. The attack of lymphatic organs, including the thymus and spleen, by the novel coronavirus affects lymphocyte production, resulting in a drastic decline in the number of lymphocytes. This view is supported by the autopsy report published by Hanley [27]. In previous reports, SARS and MERS patients showed similar changes, i.e., their lymphatic organs were attacked or even destroyed by the virus with disease progression [28][29][30][31]. (3) Inflammatory factors induce lymphocyte apoptosis. Basic research confirmed that tumor necrosis factor (TNF)-α, interleukin 6 (IL-6), and other pro-inflammatory cytokines can induce lymphocyte apoptosis, leading to an acute decrease in the number of lymphocytes [32]. (4) The metabolic molecules produced in metabolic diseases, such as hyperlactic acidemia, inhibit lymphocytes. In patients with severe COVID-19, a continuous increase in blood lactic acid levels might inhibit the proliferation of lymphocytes [33]. The abovementioned mechanisms may jointly cause lymphopenia; however, this claim requires further research. The significant change in HGB may be explained by the fact that the virus adheres to the surface of hematopoietic cells through the angiotensin converting enzyme (ACE) 2 receptor [26] and enters the hematopoietic system. The substances released by the virus, viremia, and endotoxins jointly influence the release of immune factors and immune regulatory function, affect hematopoietic stem/progenitor cells, and lead to an abnormal hematopoietic microenvironment, thereby inhibiting the hematopoietic function of bone marrow. This ultimately affects the compensatory production of HGB, causing a continuous decrease in HGB and even hematopoietic failure or aplastic anemia [34]. Among the 99 COVID-19 patients admitted to Wuhan Jinyintan Hospital, China, 51% experienced decrease in HGB [6], consistent with the finding in the present study. In this study, two parameters, Lym% and HGB, were linearly integrated into a joint parameter, Lym%&HGB, using binary logistic regression.

Conclusion

The new parameter, which is associated with the production of peripheral blood leucocytes and erythrocytes, can reflect both immune function and the overall nutritional status of the body; thus, it may serve as a superior indicator reflecting disease severity in COVID-19 patients. This study is a single-center

retrospective study based on routine blood test data of 159 COVID-19 patients in our hospital; therefore, the findings should be verified and confirmed by other centers and more samples.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due local policy but are available from the corresponding author on reasonable request.

Competing interests

All authors declared no conflicts of interest.

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Author's contribution

Wenping ZHANG and Yanting Luo has access to all data in this study and is responsible for the integrity of the data and the accuracy of the data analysis.

Wenping ZHANG and Zhongming ZHONG were responsibility for the research content, experimental design, and obtain the ethical approval.

Zhiyong YU and Jiahui ZENG took responsibility for data collection and data accuracy:

Shiyao PAN, Jin LI and Huan Qiwas in charge of the statistical analysis;

Wenping ZHANG, Shiyao PAN and Jin LI were in charge of the manuscript draft;

Jiuxin QU contributed to critical revision of the manuscript;

All authors reviewed and approved the final version.

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Figures

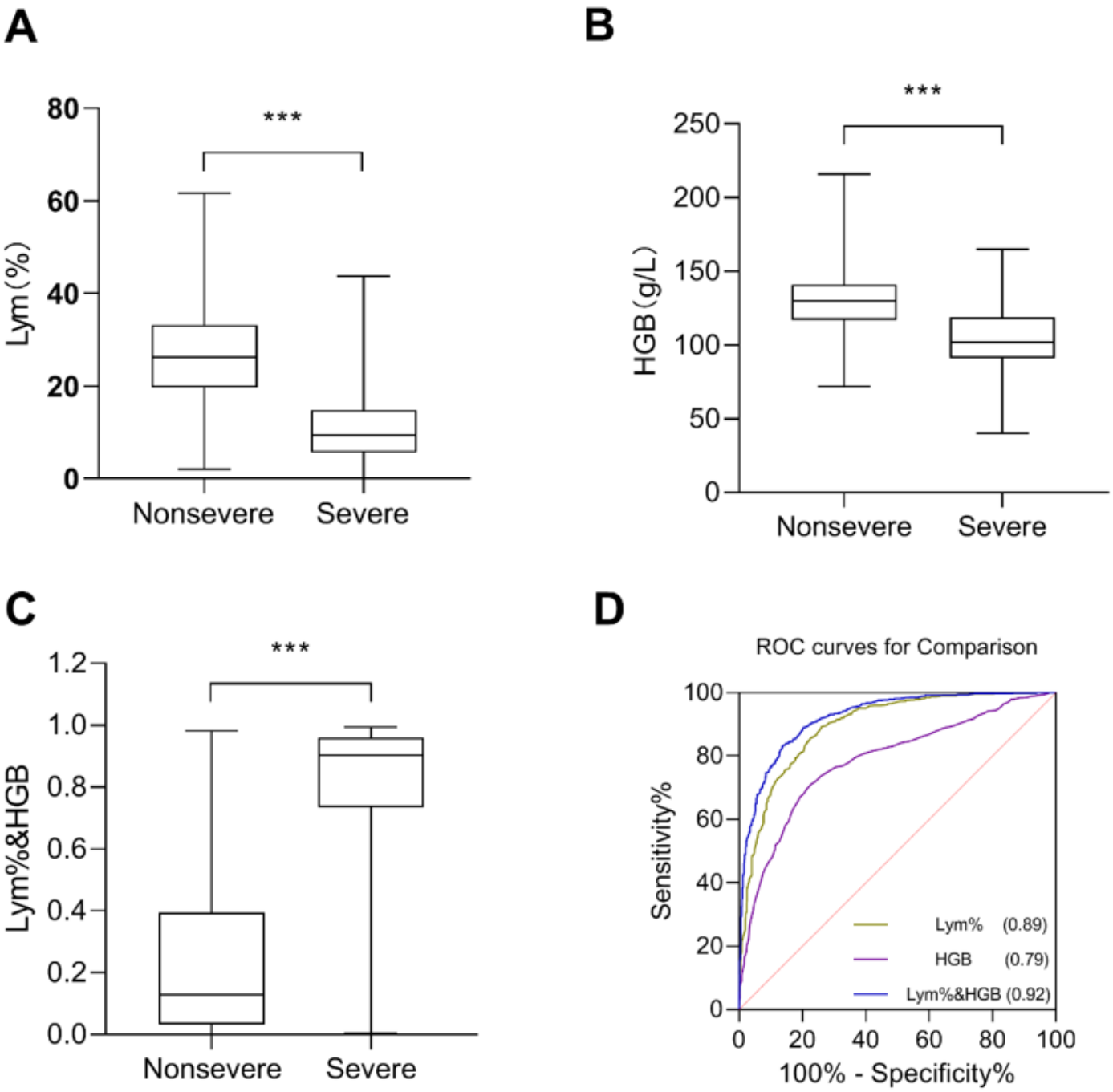

Figure 1

Box plots and ROC curves (Mann-Whitney U tests) for the severe and nonsevere groups; ***denotes p 0.001

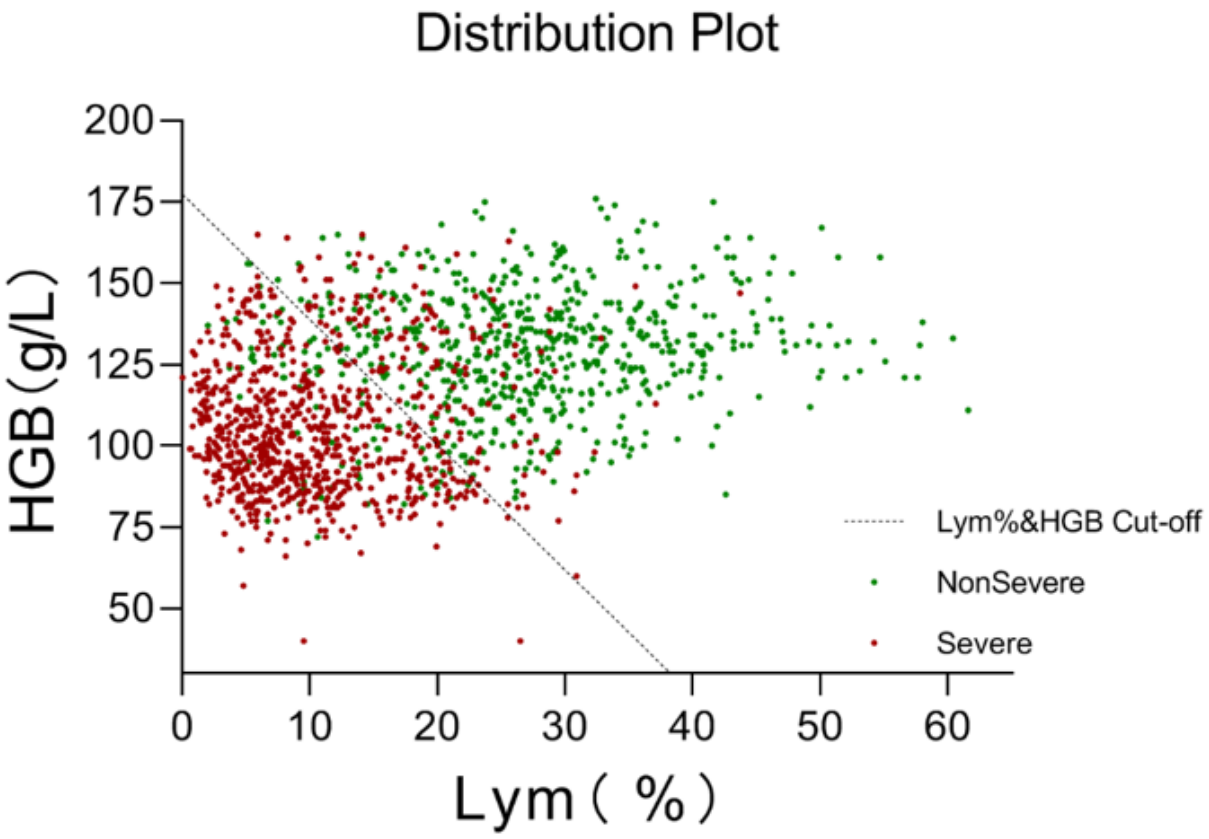

Figure 2

Two-dimensional scatter diagram of Lym% and HGB

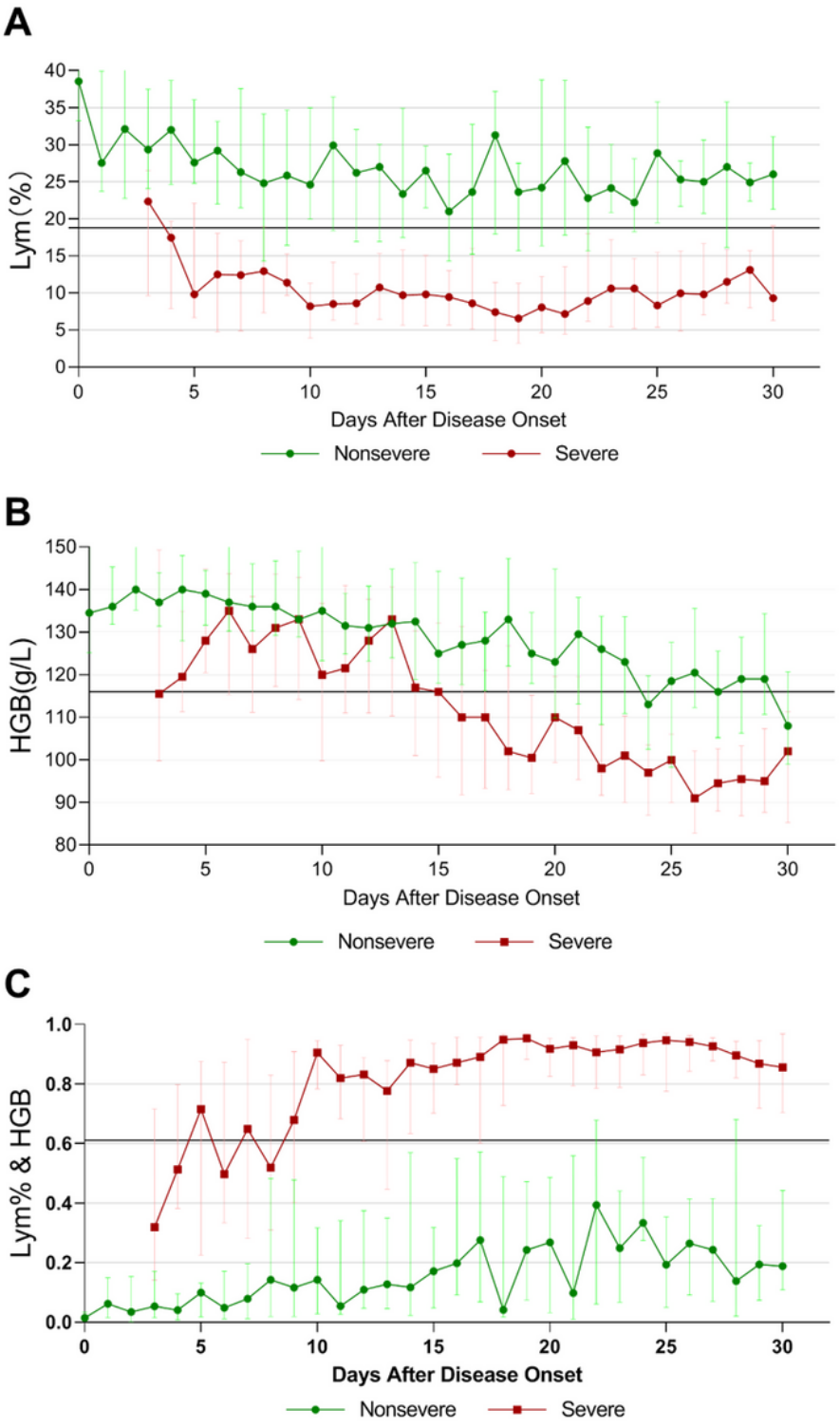

Figure 3

Dynamic profiles of the three parameters in patients with severe and nonsevere COVID-19. The black solid line represents the optimal cutoff level determined by ROC analysis.