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Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China

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ABSTRACT

Background: In December 2019, coronavirus disease 2019 (COVID-19) was first found in Wuhan, China and soon was reported all around the world.
Methods: All confirmed cases with COVID-19 in Wenzhou from January 19 to February 20, 2020, were collected and analyzed. Of the 116 patients with COVID-19, 27 were diagnosed as severe cases. Among severe cases, 9 were treated in ICU. The data of blood routine examination were analyzed and compared among common patients (as common group), severe patients admitted to intensive care unit (as severe ICU group) and severe patients not admitted to ICU (as severe non-ICU group). The blood routine examination results were dynamically observed in the above groups after admission.
Results: Patients with COVID-19 have lower counts of leucocytes, lymphocytes, eosinophils, platelets, and hemoglobin, but have higher neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR), which were compared with controls ($P < 0.001$). In severe ICU group, patients have the lowest count of lymphocytes, but the highest neutrophil count and NLR among the above three groups (all P values < 0.05); NLR and MLR indicators were combined for diagnostic efficacy analysis of severe COVID-19, and its area under the curve reached 0.925. The odds ratio of the delay in days to the start of the increase of eosinophil count for predicting the outcome of patients with severe COVID-19 was 2.291 after age adjusted.
Conclusions: Patients with COVID-19 have abnormal peripheral blood routine examination results. Dynamic surveillance of peripheral blood system especially eosinophils is helpful in the prediction of severe COVID-19 cases.

1. Introduction

Coronavirus disease 2019 (COVID-19) caused by β-coronavirus infection has been found all over the world since its first outbreak in Wuhan, Hubei Province in December 2019. As of 24th March, 320,268 cases have been reported worldwide, causing 16,435 deaths, and a total of 507 cases and one death were reported in Wenzhou, one of the worst affected areas in China outside Hubei Province. At present, COVID-19 lacks specific and effective drugs and vaccines. Mild and common patients have milder symptoms and good prognosis, but severe and critical patients are difficult to treat and have a high mortality rate. Therefore, it has great clinical significance to predict the progress of the disease. Previous studies have shown that the NLR, MLR, and PLR in blood routine parameters have certain clinical application value in predicting the progress of infectious diseases [1,2]. At the same time, Guan et al.'s analysis of clinical characteristics of 1099 patients with COVID-19 showed abnormal parameters of lymphocytes and platelets in peripheral blood of some patients [3]. So in order to further analyze the clinical application value of blood routine parameters in diagnosis and treatment of COVID-19, the changes of peripheral blood routine parameters of 116 patients with COVID-19 in Wenzhou were retrospectively tracked and analyzed, which are reported as follows.

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2. Methods

2.1. Study design and participants

2.1.1. Diagnostic criteria

All COVID-19 cases were confirmed by using real-time reverse-transcriptase polymerase-chain reaction (RT-PCR) assay to test nasal and pharyngeal swab specimens according to the WHO guidance. The common or severe cases of COVID-19 were diagnosed according to the Seventh Revised Version of the Novel Coronavirus Pneumonia Diagnosis and Treatment Interim Guidance [4].

1. Common cases:

Those who have fever, respiratory tract symptoms, and pneumonia on imaging.

2. Severe cases:

Those who have one of the following three clinical manifestations:

(1). shortness of breath with RR > 30 times/min;
(2). mean oxygen saturation ≤ 93% in resting state;
(3). partial pressure of arterial oxygen (PaO2)/oxygen Concentration (FiO2) ≤ 300 mmHg (1 mmHg = 0.133 kPa).

Or those whose pulmonary imaging shows that the lesions have progressed more than 50% within 24–48 h.

Severe patients were divided into two groups: those admitted to intensive care unit (ICU) were defined as severe ICU group, and those not admitted to ICU were defined as severe non-ICU group. The criteria for severe patients to be admitted to ICU are having one of the following conditions: (1) respiratory failure and requirement for mechanical ventilation; (2) shock; (3) combined other organ failure.

Patients with hematological diseases or blood transfusion during hospitalization were excluded. Various parameters of peripheral blood routines of patients with COVID-19 were recorded on day 3, day 5, day 7, day 10 and day 14 after admission, and their trends were analyzed. The control group was subjected to tests including clinical examination, computed tomography (CT) and RT-PCR for SARS-CoV-2, and results of all tests are negative. The study was approved by the Ethics Committee of Wenzhou Central Hospital (IRB ID: L2020-02-001X).

2.2. Statistical analysis

SPSS19.01 statistical software was used for processing data. The hematological cell count data are expressed as 10^9/L The data of non-normal distribution was represented by the median (quartile value). Mann-Whitney *U* test was used to compare the mean between the two groups. Proportions for categorical variables were compared using the $\chi 2$ test. Binary logistic regression analysis was used to combine NLR and MLR. Receiver operation characteristic curve (ROC curve) was used to analyze the efficiency of diagnosing patients' disease stage. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Blood routine parameters in patients with COVID-19 on admission

Table 1 presents the parameters of blood routine in patients with COVID-19 and controls. Among 116 patients who underwent blood routine examinations on admission, most of them have abnormalities in peripheral blood system. There were many differences in the parameters of blood routine between patient group and control group. Patients with COVID-19 had lower leucocyte count (4.60 vs 5.95 × 10^9/L; $P < 0.001$), lower lymphocyte count (1.00 vs 2.10 × 10^9/L; $P < 0.001$), lower eosinophil count (0.02 vs 0.10 × 10^9/L; $P < 0.001$), lower hemoglobin concentration (132.5 vs 146.5 g/L; $P < 0.001$), lower platelet count (180.5 vs 240.0 × 10^9/L; $P < 0.001$), higher NLR (2.91 vs 1.58; $P < 0.001$), higher MLR (0.37 vs 0.19; $P < 0.001$) and higher PLR (169.0 vs 113.0; $P < 0.001$). There were no significant differences in age, gender ratio, neutrophil count and monocyte count between patient group and control group.

Table 1
Blood routine parameters of patients with COVID-19 on admission.

	Median (IQR)		
	All patients (n = 116)	Controls (n = 100)	*P* value
Age, Median(IQR),Range, years	50.0 (41.0–57.0), 20–93	48.5(37.3–59.8), 21–90	0.397
Sex			0.739
Male(%)	60 (51.7%)	53 (53.0%)	
Female(%)	56 (48.3%)	47 (47.0%)	
Blood routine			
Leucocytes(×10^9 per L)	4.60 (3.76–6.40)	5.95 (5.13–6.88)	< 0.001
Neutrophils(×10^9 per L)	3.10 (2.33–4.30)	3.20 (2.70–3.88)	0.456
Lymphocytes(×10^9 per L)	1.00 (0.72–1.40)	2.10 (1.80–2.40)	< 0.001
Monocyte(×10^9 per L)	0.39 (0.29–0.49)	0.40 (0.34–0.47)	0.372
Eosinophil(×10^9 per L)	0.02 (0.01–0.05)	0.10 (0.06–0.16)	< 0.001
Hemoglobin(g/L)	132.5 (122.3–145.8)	146.5 (135.0–156.0)	< 0.001
Platelet(×10^9 per L)	180.5 (145.5–229)	240.0 (202.8–274.8)	< 0.001
MLR	0.37 (0.27–0.56)	0.19 (0.17–0.23)	< 0.001
NLR	2.91 (1.87–4.83)	1.58 (1.34–1.98)	< 0.001
PLR	169.0 (123.5–245.6)	113.0 (95.1–138.2)	< 0.001

Data are median (IQR), n (%), or n/N, where N is the total number of patients with available data. P values comparing patients and controls are from $\chi 2$, or Mann-Whitney *U* test. COVID-19 = coronavirus disease 2019. NLR: Neutrophils-to-lymphocytes ratio; MLR: Monocyte-to- lymphocytes ratio; PLR: Platelet-to-lymphocytes ratio.

3.2. Blood routine parameters of common group and severe group on admission

Table 2 presents the parameters of blood routine in common group and severe group. A total of 89 common patients and 27 severe patients underwent blood routine examinations on admission. There were many differences in the parameters of blood routine between common group and severe group. Severe cases had higher leucocyte count (7.44 vs 4.40 × 10^9/L; $P < 0.001$), higher neutrophil count (6.07 vs 2.90 × 10^9/L; $P < 0.001$), higher MLR (0.71 vs 0.32; $P < 0.001$), higher NLR (8.71 vs 2.41; $P < 0.001$), higher PLR (246.0 vs 160.7; $P < 0.001$), lower lymphocyte count (0.63 vs 1.20 × 10^9/L; $P < 0.001$), lower eosinophil count (0.01 vs 0.03 × 10^9/L; $P < 0.001$), and lower hemoglobin concentration (124.0 vs 134.0 g/L; $P = 0.013$). There were no significant differences in gender ratio, monocyte count and platelet count between severe group and common group. Compared with common patients, severe patients were significantly older (median age, 62.0 years [IQR, 53.0–71.0] vs 47.0 years [37.0–54.5]; $P < 0.001$).

3.3. Blood routine parameters of severe non-ICU group and severe ICU group on admission

Table 3 presents the parameters of blood routine in severe non-ICU group and severe ICU group. A total of 18 severe non-ICU patients and 9 severe ICU patients underwent blood routine examinations on admission. There were many differences in the parameters of blood routine between severe non-ICU group and severe ICU group. Severe ICU cases had higher neutrophil count (7.03 vs 4.50 × 10^9/L; $P = 0.037$), higher NLR (14.44 vs 5.47; $P = 0.010$) and lower lymphocyte count (0.45 vs 0.70 × 10^9/L; $P = 0.045$). There were no significant differences in gender ratio, leucocyte count, monocyte count, eosinophil count,

Table 2
Blood routine parameters of common group and severe group on admission.

	Median (IQR)		
	Common (n = 89)	Severe (n = 27)	*P* value
Age, Median(IQR),Range, years	47.0 (37.0–54.5), 20–84	62.0 (53.0–71.0), 40–93	< 0.001
Sex			0.076
Male(%)	42 (47.2%)	18 (66.7%)	
Female(%)	47 (52.8%)	9 (33.3%)	
Blood routine			
Leucocytes($\times 10^9$ per L)	4.40 (3.65–5.70)	7.44 (4.20–8.68)	< 0.001
Neutrophils($\times 10^9$ per L)	2.90 (2.15–3.80)	6.07 (3.10–7.60)	< 0.001
Lymphocytes($\times 10^9$ per L)	1.20 (0.90–1.50)	0.63 (0.45–0.86)	< 0.001
Monocyte($\times 10^9$ per L)	0.38 (0.29–0.48)	0.42 (0.31–0.76)	0.150
Eosinophil($\times 10^9$ per L)	0.03 (0.01–0.05)	0.01 (0.00–0.02)	< 0.001
Hemoglobin(g/L)	134.0 (126.0–146.5)	124.0 (112–140)	0.013
Platelet($\times 10^9$ per L)	184.0 (153.0–230.5)	161.0 (123–204)	0.065
MLR	0.32 (0.24–0.43)	0.71 (0.48–1.18)	< 0.001
NLR	2.41(1.73–3.47)	8.71(3.77–14.44)	< 0.001
PLR	160.7(116.7–207.5)	246.0(167.9–456.7)	< 0.001

Data are median (IQR), n (%), or n/N, where N is the total number of patients with available data. P values comparing common cases and severe cases are from $\chi 2$, or Mann-Whitney *U* test. COVID-19 = coronavirus disease 2019. NLR: Neutrophils-to-lymphocytes ratio; MLR: Monocyte-to- lymphocytes ratio; PLR: Platelet-to-lymphocytes ratio.

platelet count, hemoglobin concentration, MLR and PLR between severe group and common group. Compared with severe non-ICU patients, severe-ICU patients were significantly older [median age, 71.0 years (IQR, 60.5–80.5) vs 57.0 years (47.5–67.8); P = 0.008].

3.4. Analysis of the efficiency of peripheral blood routine parameters in the diagnosis of severe COVID-19 on admission

The severe group was set as the positive group, and the common group was set as the negative group. The ROC curve was established to analyze the efficacy of various parameters of blood routine in the diagnosis of severe COVID-19 on admission.

Table 4 presents the value of blood routine parameters in the diagnosis of severe COVID-19 on admission. The area under the curve (AUC) of NLR is 0.888 [95%CI (0.812–0.963); P < 0.001]; the AUC of MLR is 0.862 [95%CI (0.778–0.947); P < 0.001]; the AUC of Lymphocytes is 0.856 [95%CI (0.777–0.936); P < 0.001]; the AUC of eosinophils is 0.763 [95%CI (0.641–0.886); P < 0.001]; the AUC of Neutrophils is 0.774 [95%CI (0.653–0.896); P < 0.001]; the AUC of PLR is 0.746 [95%CI (0.637–0.854); P < 0.001]; the AUC of leucocytes is 0.709 [95%CI (0.574–0.844); P < 0.001]; NLR and MLR indicators were combined for diagnostic efficacy analysis of severe COVID-19, and its AUC reached 0.925 [95%CI (0.867–0.983); P < 0.001]. Compared to the AUCs of NLR, MLR and Lymphocytes, the AUC of NLR + MLR was not significantly different (the all P values > 0.05). Compared to the AUCs of eosinophil and PLR, the AUC of NLR + MLR was significantly different (the all P values < 0.05) (see Fig 1).

3.5. Analysis of changes in peripheral blood routine parameters of patients with COVID-19 from different groups at different time points after admission

There were 51 cases of 116 patients with COVID-19 who received the routine blood tests on admission and on day 3, 5, 7, 10 and 14, including 24 cases in the common group and 27 cases in the severe group. According to whether the patients in the severe group were admitted to the ICU or not during the course of the disease, they were divided into 9 cases in the severe ICU group and 18 cases in the severe non-ICU group. The time is used as the abscissa, and the median values of the blood routine parameters of each group are plotted as the ordinate. The leucocyte and neutrophil counts in the severe ICU group were higher than those in the common group and the severe non-ICU group

Table 3
Blood routine parameters of severe non-ICU group and severe ICU group on admission.

	Median (IQR)		
	Severe non-ICU(n = 18)	Severe ICU(n = 9)	*P* value
Age, Median(IQR),Range, years	57.0 (47.5–67.8), 40–76	71.0 (60.5–80.5), 53–93	0.008
Sex			1.0
Male(%)	12 (66.7%)	6 (66.7%)	
Female(%)	6 (33.3%)	3 (33.3%)	
Blood routine			
Leucocytes($\times 10^9$ per L)	5.63 (3.78–8.05)	8.68 (5.82–12.09)	0.064
Neutrophils($\times 10^9$ per L)	4.50 (2.88–6.51)	7.03(4.59–11.30)	0.037
Lymphocytes($\times 10^9$ per L)	0.70 (0.50–0.88)	0.45 (0.30–0.69)	0.045
Monocyte($\times 10^9$ per L)	0.50 (0.30–0.83)	0.41 (0.25–0.51)	0.198
Eosinophil($\times 10^9$ per L)	0.01 (0.00–0.02)	0.00 (0.00–0.07)	0.661
Hemoglobin(g/L)	134.5 (114.8–144.0)	112.0 (106.0–130.5)	0.054
Platelet($\times 10^9$ per L)	169.5(117.3–255.3)	137.0 (122.5–182.5)	0.456
MLR	0.70 (0.48–1.21)	0.71 (0.40–1.35)	0.979
NLR	5.47(3.36–10.44)	14.44 (6.89–27.00)	0.010
PLR	250.1 (156.5–331.4)	235.4(185.1–573.9)	0.355

Data are median (IQR), n (%), or n/N, where N is the total number of patients with available data. P values comparing severe non-ICU cases and severe ICU cases are from $\chi 2$, or Mann-Whitney *U* test. COVID-19 = coronavirus disease 2019. NLR: Neutrophils-to-lymphocytes ratio; MLR: Monocyte-to- lymphocytes ratio; PLR: Platelet-to-lymphocytes ratio.

Table 4
The value of blood routine parameters in diagnosis of severe COVID-19 on admission.

Blood routine parameters	AUC (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	*P* value
Leucocytes > 7.1 ($\times 10^9$ per L)	0.709 (0.574–0.844)	55.56 (35.3–74.5)	93.26 85.9–97.5)	71.4 (47.8–88.7)	87.4 (78.9–93.3)	< 0.003
Neutrophils > 5.7 ($\times 10^9$ per L)	0.774 (0.653–0.896)	51.85 (31.9–71.3)	98.88 (93.9–100.0)	93.3 (68.1–99.8)	87.1 (79.0–93.0)	< 0.001
Lymphocytes ≤ 0.86 ($\times 10^9$ per L)	0.856 (0.777–0.936)	81.48 (61.9–93.7)	76.40 (66.2–84.8)	51.2 (35.5–66.7)	93.2 (84.7–97.7)	< 0.001
Eosinophils ≤ 0 ($\times 10^9$ per L)	0.763 (0.641–0.886)	48.15 (28.7–68.1)	98.88 (93.9–100.0)	92.9 (66.1–99.8)	86.3 (78.0–92.3)	< 0.001
MLR > 0.43	0.862 (0.778–0.947)	85.19 (28.7–68.1)	76.40 (66.2–84.8)	52.3 (36.7–67.5)	94.4 (86.4–68.5)	< 0.001
NLR > 4.5	0.888 (0.812–0.963)	74.07 53.7–88.9)	89.89 81.7–95.3)	69.0 (48.8–85.0)	92.0 (84.1–96.7)	< 0.001
PLR > 226.67	0.746 (0.637–0.854)	59.26 38.8–77.6)	80.90 71.2–88.5)	48.5 (30.8–66.5)	86.7 (77.5–93.2)	< 0.001
MLR + NLR > 0.1214	0.925 (0.867–0.983)	96.30 81.0–99.9)	76.40 66.2–84.8)	55.3 (40.1–69.8)	98.6 (92.2–100)	< 0.001

AUC: area under the curve; CI: confidence intervals PPV: positive predictive value; NPV: negative predictive value; NLR: Neutrophils-to-lymphocytes ratio; MLR: Monocyte-to- lymphocytes ratio; PLR: Platelet-to- lymphocytes ratio; MLR + NLR: the integration parameters of MLR and NLR; COVID-19 = coronavirus disease 2019.

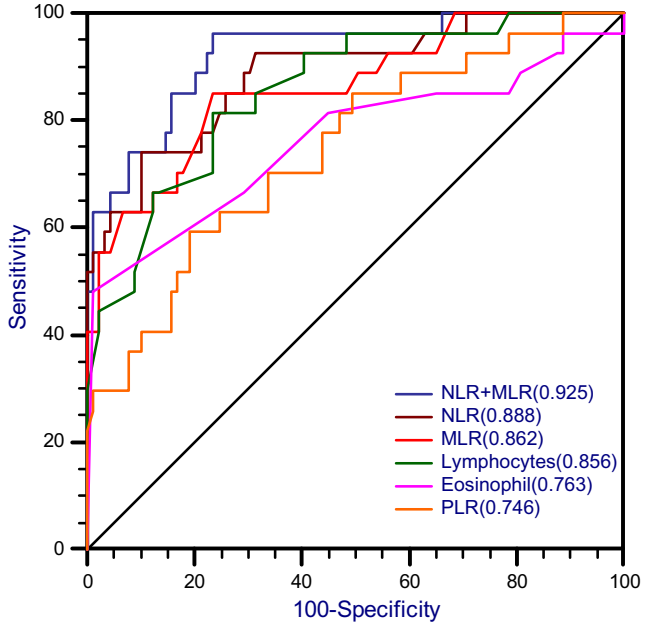

Fig. 1. The ROC curves of various parameters of blood routine in the diagnosis of severe COVID-19 on admission. NLR: Neutrophils-to-lymphocytes ratio; MLR: Monocyte-to- lymphocytes ratio; PLR: Platelet-to-lymphocytes ratio; MLR + NLR: the integration parameters of MLR and NLR; COVID-19 = coronavirus disease 2019.

on admission, and remained at a high level; these parameters in common and severe non-ICU groups showed a slight increasing trend during hospitalization (Fig. 2A and B). Lymphocyte count in the severe ICU group remained low, while this parameter in the severe non-ICU group showed a progressive rise, reaching the level of this parameter in common group on the fourteenth day (Fig. 2C). Monocyte count in the severe ICU group was lower than that in the severe non-ICU group; the two groups showed different trends: the former decreased in number and remained low, while the latter like the common group showed an upward trend during hospitalization (Fig. 2D). The number of eosinophils in the three groups decreased significantly on admission and showed an upward trend with the course of the disease; this number in the severe ICU group remained longer at low detection levels than those in the severe non-ICU group and the common group (Fig. 2E). There was a downward trend of hemoglobin concentration in the three groups, with the most obvious in the severe ICU group (Fig. 2F). Platelet count in the common group and the severe non-ICU group showed an upward trend, and that in the severe ICU group remained low (Fig. 2G). The MLR in the common group was significantly lower than that in other two groups on admission, and it showed a downward trend after a slight increase in the initial treatment; the MLR in the severe non-ICU group and the severe ICU group showed a slight decline (Fig. 2H). The NLR in the severe ICU group was significantly higher than that in the other two groups, and remained at a high level; the NLR in the severe non-ICU group was higher than that in the common group on admission and showed a gradual downward trend, which was consistent with that in the common group at the later stage; the NLR in common group was lower and kept a stable trend (Fig. 2I). The PLR in the severe ICU group decreased rapidly after reaching its peak on the seventh day, and that in the other two groups showed a general downward trend (Fig. 2J).

3.6. Prediction of the outcome of the patients with severe COVID-19 by using the binary logistic regression model

We found that the delay in days to the start of the increase of lymphocytes count and eosinophils count in patients with COVID-19 may be related to the outcome of this disease (Fig. 2). The analysis of the prognosis of the severe COVID-19 group was based on the number of days required for the blood routine parameters to recover to the level on admission. By binary regression analysis, we found the odds ratio (OR) of eosinophil is 1.827[95%CI (1.174–2.844); P = 0.008], with age-adjusted OR being 2.291[95%CI (1.104–4.753); P = 0.026]; the OR of lymphocytes is 1.311[95%CI (1.056–1.626); P = 0.014], with age-adjusted OR being 1.281[95%CI (1.013–1.620); P = 0.038] (Table 5).

4. Discussion

COVID-19 is a systemic multiple organ damage disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with the lung as the main target organ. It can cause severe lung injury and acute respiratory distress syndrome (ARDS) in severe cases which may lead to death [3].The virus binds to the ACE2 receptor and enters the alveolar epithelial cells [5], which induces the cells to release inflammatory factors and activate the abundant macrophages in the alveolar tissue; then macrophages releases the inducing factors and chemokines, which recruit a large number of mononuclear immune cells to aggregate and infiltrate the lung tissue; these further immune activation leads to a storm of inflammation and tissue damage [6]. Xu

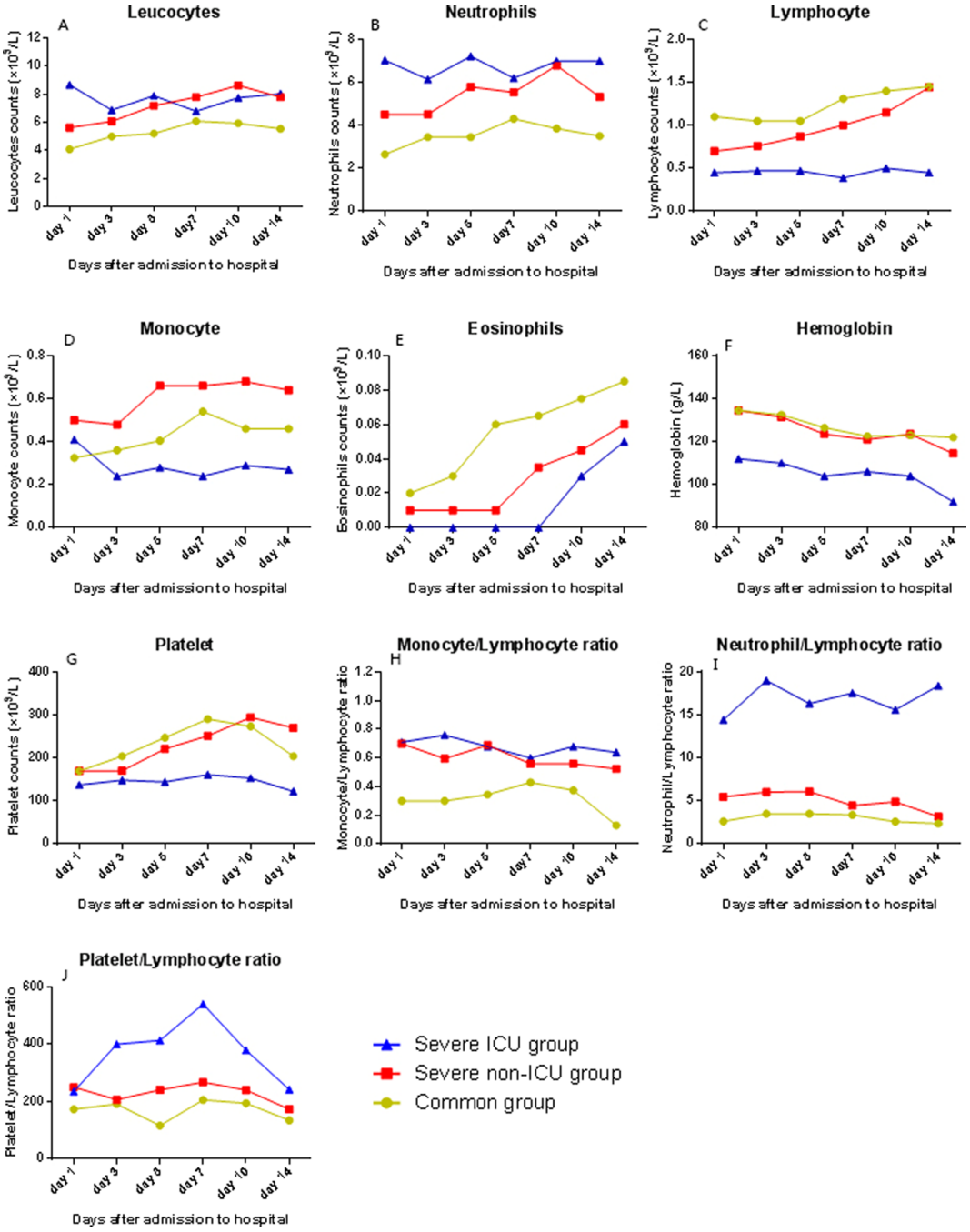

Fig. 2. Changes in peripheral blood routine parameters in three groups of COVID-19 after admission to hospital. The time is used as the abscissa, and the median values of the blood routine parameters of each group are plotted as the ordinate. Severe ICU group: severe patients admitted to intensive care unit (ICU); Severe non-ICU group: severe patients not admitted to intensive care unit (ICU); Common group: Common cases; COVID-19 = coronavirus disease 2019.

Table 5
Association between the delay in days to the start of the increase of parameters and the outcome of severe COVID-19.

	Unadjusted ORs		Adjusted ORs	
	OR(95%CI)	*P* value	OR*(95%CI)	*P* value
Lymphocyte	1.311(1.056–1.626)	0.014	1.281(1.013–1.620)	0.038
Eosinophil	1.827(1.174–2.844)	0.008	2.291 (1.104–4.753)	0.026

* Adjusted: age; OR: Odds ratio; COVID-19 = coronavirus disease 2019.

et al. also reported that the pathological anatomy results of death cases with COVID-19 showed that inflammatory infiltration of mononuclear cells, mainly lymphocytes, was dominant in the interstitial lung [7]. The above studies indicate that the significant decrease in the number of lymphocytes in patients with COVID-19 may be related to the redistribution and the increased consumption of lymphocytes and defective hematopoiesis [8]. Li et al. found that some death cases of COVID-19 have superimposed bacterial pneumonia [9]. Bacterial infection leads to significant increased leucocyte count and neutrophil count. Some patients with COVID-19 have abnormal blood coagulation

function: prothrombin time is prolonged and D-dimer is elevated [10]; thrombosis leads to increased platelet consumption and decreased platelet number. In addition, SARS-CoV-2 has been reported to causes damage to the ACE2-receptor-rich kidney tissue [11] and increase of inflammatory factors, which can cause reduced erythrogenesis and increased destruction of RBC, leading to anemia. The above pathophysiological changes of COVID-19 are consistent with those shown in Table 1. The parameters of peripheral blood cells in patients with COVID-19 were significantly abnormal. Among them, the decrease in the number of lymphocytes was the most obvious. Hemoglobin and platelets were also significantly lower than those in the healthy control group. Peripheral blood combined parameters including NLR, MLR and PLR of patients increased significantly. This shows that monitoring the changes in blood routine parameters has important clinical significance.

Studies have shown that the progression and prognosis of COVID-19 are related to the body's immune status and excessive inflammatory response [7]. In this study, by comparing and analyzing the peripheral blood routine parameters of common group and severe group, it was found that the absolute value of lymphocytes in severe group was significantly lower than that of common group, while the count of inflammatory neutrophils of severe group was significantly higher than that of common group. These changes showed the degree of inflammation in the body was further intensified, triggering an inflammatory storm and leading to increased tissue and cell damage [12]. Low lymphocyte level and impaired immune cell function lead to the dysfunction of immune system, which makes patients with severe COVID-19 might be more sensitive to bacterial infection [13]. The blood cell parameter NLR reflects this situation, so we speculate that the NLR has certain value in judging the severity of COVID-19. In order to further understand the value of various parameters of peripheral blood routine in COVID-19, this study performed a diagnostic analysis of various parameters of common and severe COVID-19. The results showed that NLR, MLR, lymphocyte absolute value and PLR all had high diagnostic value. The area under ROC curve of NLR was the largest, followed by the AUC of MLR. NLR and MLR indicators were combined for diagnostic efficacy analysis of severe COVID-19, and it was found that the area under the curve reached 0.925, with higher sensitivity and specificity. As the disease progresses, some severe patients with COVID-19 need to be treated in the ICU. In this study, the severe patients were divided into two groups according to whether they were transferred to ICU or not, and the parameters of blood routine were compared between the two groups when they were admitted to the hospital. The results showed that the absolute value of lymphocytes in the severe ICU group was significantly lower, while the count of neutrophils in the severe ICU group were significantly higher, which is consistent with the results of Qin et al. [14]. The blood routine combination parameter NLR was more significant than the other two combination parameters MLR and PLR. NLR is a widely used biomarker for assessing the severity of bacterial infection [15]. Bacterial infections maybe play an important role in the outcome of COVID-19. Therefore, it may be necessary to enhance the immunity of patients and improve anti-bacterial treatment, especially for severe and critical patients with COVID-19.

The Seventh Revised Version of the Novel Coronavirus Pneumonia Diagnosis and Treatment Interim Guidance pointed out that the progressive decline of lymphocytes can be used as an early warning indicator for severe and critical clinical conditions. In order to understand the role of various parameters of peripheral blood cells in the early clinical typing, this study tracked and analyzed these parameters on admission, day 3, day 5, day 7, day 10 and day 14 in the common group, the severe non-ICU group and the severe ICU group, and drew a curve with the median value. The results showed that the absolute values of lymphocytes and monocytes in the severe ICU group remained low, which may be related to the fact that patients in the severe ICU group were prone to sepsis, resulting in a low immune response state [16], unable to make a normal immune response to infection and a low number of immune cells [17]. And those of the common and severe non-ICU groups showed a progressive rise. The NLR parameters were always running at a high level and were significantly higher than the other two groups. The patient were constantly in a state of excessive inflammation, and the inflammatory storm is closely related to the severity of the disease [6], indicating that NLR can better reflect the progress of the disease course. The severe non-ICU group showed a progressive decline as the condition improved. The PLR in the severe ICU group fluctuated greatly, reaching a peak on the 7th day after admission, which is consistent with the report by Qu using PLR as a monitoring indicator of disease progression [18].This study also found that the hemoglobin of all three groups showed a downward trend, especially in the severe ICU group. This indicates that this novel coronavirus may affect the red blood cell system. Normally, in the acute phase of the lung infection caused by virus, eosinophils accumulate in infected tissues to resist virus infection, resulting in a decrease in eosinophils in peripheral blood [19]. This study found that this phenomenon also exists in COVID-19. The eosinophils significantly decreased in all three groups on admission. The time for eosinophil to increase in common group and severe non-ICU group was earlier than that in severe ICU group. In the severe ICU group, eosinophil gradually increased after the seventh day of admission. We also found that patients who have delay to the start of increase of eosinophil counts were at increased risk of severe outcome of COVID-19 after age adjustment (odds ratio, 2.291). Persistent low eosinophils counts might be an ominous sign [20]. The above results suggest that the lower count and delay in increasing of eosinophils may be the signs of poor outcome of COVID-19. It can be seen that the dynamic observation of blood routine parameters has important clinical value for judging the disease progression and early warning of clinical type changes.

There were some limitations in our study. First, it was a retrospective study and the sample is small. Second, the lack of clinical data is one of the deficiencies of this study, so we can't rule out the influence of stress response and treatment (e.g, hormones) on blood routine parameters. Further research is needed to overcome these limitations. Nevertheless, our results provided moderate and important illumination for this topic.

In summary, COVID-19 will cause abnormalities of the parameters of peripheral blood routine. The decrease in lymphocytes and the increase in NLR ratio are the most obvious abnormalities, which are related to the severity of the disease and clinical classification. The lower count and delay in increasing of eosinophils can also be the signs of poor outcome of COVID-19. Thus, dynamic monitoring of the parameters of peripheral blood routine has important reference value for judging the progression and prognosis of COVID-19.

CRediT authorship contribution statement

Suyu Sun: Supervision, Validation, Writing - original draft. **Xuejiao Cai:** Methodology, Resources, Visualization. **Huaguo Wang:** Software, Visualization. **Guiqing He:** Investigation, Resources. **Yin Lin:** Data curation. **Bibi Lu:** Data curation. **Chaoyue Chen:** Project administration. **Yong Pan:** Formal analysis, Writing - review & editing. **Xingzhong Hu:** Conceptualization, Funding acquisition, Writing - original draft, Writing - review & editing.

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