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Serum transgelin is a novel prognostic biomarker for COVID-19 patients

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Background: Transgelin is a central actin-binding protein of the calponin family and involved in the process of multiple pulmonary diseases. Nevertheless, the role of transgelin in Coronavirus disease 2019 (COVID-19) patients is confusing.

Methods: All 317 COVID-19 patients were recruited from two hospital. Peripheral blood was collected from the fasting patients at the onset and convalescent phases. Demographic data and clinical information were obtained. The expression of serum transgelin was estimated using ELISA.

Results: The expression of serum transgelin on admission was gradually elevated in parallel with the increased severity scores of COVID-19. After treatment, serum transgelin expression was reduced during the convalescent phase. Spearman correlative analyses found that serum transgelin expression was closely correlated to lots of clinical parameters. Besides, serum transgelin was positively associated with severity scores. Follow-up research found that serum higher transgelin on admission elevated the risks of mechanical ventilation, vasoactive agent utilization, ICU admission, death, and longer hospital stays during hospitalization through a prospective cohort study. Additionally, there were similarly predictive capacities for critical patients and death between serum transgelin on admission and severity scores among COVID-19 patients.

Conclusions: The expression of serum transgelin is positively with the severity and poorly prognostic outcomes among COVID-19 patients, indicating that transgelin is implicated in the pathological process of COVID-19. Transgelin can assist in the risk stratification and revealing the pathological mechanisms of COVID-19.

KEYWORDS

transgelin, cohort study, COVID-19, severity, prognosis

1 Background

Coronavirus disease 2019 (COVID-19) is an infectious disease evoked by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1, 2). It occurred at the end of 2019, and the first case was found and reported in Wuhan City of China (3). Due to the high transmissibility rate, COVID-19 has spread quickly to the entire world from China, and led to a pandemic (4). The former data revealed that an estimated 2% cases die for COVID-19, and there are 5~10% COVID-19 patients progressing to acute respiratory distress syndrome (ARDS) during the initial three years of the pandemic (5–7). A majority of COVID-19 patients finally develop into mild or moderate illness (8). Although the mortality rate is decreased because of the subsequent omicron variants, the frequency of the infected patients is elevated and incurs a relative rise of the dead cases (9). Due to the pandemic all over the world, COVID-19 has brought a severe and threatening challenge for medical system and global public health crisis.

Transgelin, also called SM22α, is a central actin-binding protein of the calponin family and in the cytoskeleton (10, 11). The previous investigation found that transgelin is widely and richly expressed in vascular smooth muscle cells. Transgelin expression is regarded as an earlier biomarker of smooth muscle differentiation (12). However, the latest researches hinted that transgelin exerts the important roles in tumor-suppressive and oncogenic functions in the different types of cancers. The expression of transgelin is reduced in bladder carcinoma and prostate cancer (13, 14). On the contrary, the levels of transgelin are elevated in colorectal cancer and ovarian cancer (15, 16). It is widely known that transgelin takes part in the process of pulmonary diseases. Elevated transgelin can promote the progression of lung cancer (17, 18). In addition, the expression of transgelin is elevated in the airway smooth muscle cells of rodent asthma models (19). Moreover, pulmonary transgelin is up-regulated in pulmonary epithelial cells of mice during bleomycin-evoked lung fibrosis and lung tissues from patients with idiopathic pulmonary fibrosis (20). However, the expression and change of transgelin are unclear in patients with COVID-19.

Up to now, there are no definite evidence and relative report about the role of transgelin in COVID-19 patients. As a consequence, COVID-19 patients were recruited and serum specimens were collected. The level of serum transgelin was measured. The relationships between serum transgelin with the severity and outcomes were analyzed through a perspective cohort study. The current research may provide an important clue about the application which was used as a biomarker to evaluate the severity and predict clinical outcomes, and guide the clinical therapeutics of COVID-19 cases.

2 Materials and methods

2.1 Study design and human participants

All patients admitted to Department of Respiratory and Critical Care Medicine, Second Affiliated Hospital of Anhui Medical University from December 2022 to May 2023 were enrolled. All cases must be confirmed with SARS-CoV-2 infection through reverse transcription-polymerase chain reaction in pharyngeal swab specimens. At last, 317 inpatients with COVID-19 were enrolled in this research. Clinical characteristics, demographic information, and blood specimens were obtained from all COVID-19 patients. The inclusion criteria were: (1) Age was more than 18 years; (2) All subjects were newly diagnosed and confirmed with SARS-CoV-2 by RT-PCR; 3 The onset time was shorter than 48 hours; (3) All subjects were volunteered to participate this research. The exclusion criteria were: (1) Pregnant women; (2) Patients were accompanied with malignant tumors, autoimmune diseases, and respiratory diseases; (3) Antibiotics and antiviral drugs were taken in one week before this admission. After admission, the severity was estimated by the scoring system, including SMART-COP, CURB-65, CURXO, COVID-GRAM, Pneumonia Severity Index (PSI), Coronavirus Clinical Characterization Consortium Mortality (4C)-Mortality, Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (DTPNCP), MuLBSTA, and A-DROP (21–27).

2.2 Enzyme-linked immunosorbent assay

Blood specimens were centrifuged. Human transgelin ELISA kits (CSB-E17844h) were purchased from Cusabio, Wuhan, China (https://www.cusabio.com/). Then, the expression of serum transgelin was detected in accordance with the published methods in detail (28, 29).

2.3 Statistical analysis

Continuous variables were shown as mean or median. The categorical variables were represented as number (percentage). The difference of basic data was compared and evaluated by the Fisher test, one-way analysis of variance (ANOVA), or non-parametric test. The relationships between serum transgelin and clinical characteristics were estimated via Spearman correlation analyses. Additionally, the relationships between serum transgelin and severity scores were estimated by linear and logistic regression analyses. The correlations between serum transgelin and outcomes were assessed through logistic regression analyses and χ^2 test or Fisher exact probability. The predictive powers for critical cases and death were appraised through receiver operating characteristic (ROC) curve. The comparison of serum transgelin levels between onset and convalescent was assessed by paired Student's t-test. A $P<0.05$ was statistical significance.

3 Results

3.1 Basic information of COVID-19 patients

COVID-19 patients were divided into T1 group (the expression of serum transgelin was lower than 0.06 ng/mL), T2 group (the expression of serum transgelin was from 0.06 to 1.02 ng/mL), and T3 group (the expression of serum transgelin was higher than 1.02 ng/mL) in accordance with the tertitles of transgelin expression. Then, clinical and demographic characteristics were analyzed and compared. As represented in Table 1, the average age and the number of males

were highest in the T3 group. The comorbidities were analyzed. There was no difference of hypertension, diabetes mellitus, coronary heart diseases, chronic liver diseases, hepatitis B, and chronic kidney diseases among COVID-19 patients with different subgroups. However, the numbers of other chronic heart disease and cerebrovascular diseases in T3 group were more than T1 and T2 groups (Table 1). In addition, heart rate, the number of corticosteroids therapy, anticoagulant therapy, white blood cell (WBC), neutrophil, alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea nitrogen, D-Dimer, C-reactive protein (CRP), and procalcitonin (PCT) were gradually elevated in parallel with serum transgelin expression (Table 1). On the contrary, the levels of partial pressure of oxygen (PaO_2), fraction of inspiration O_2 (FiO_2), oxygen saturation (SpO2), and PaO2/FiO_2 were reduced with the increased serum transgelin (Table 1).

3.2 The expression of serum transgelin in COVID-19 patients with different severity

As shown in Figure 1A, the expression of serum transgelin was higher in 5~6 and 7~8 than those in 0~2 and 3~4 scores of SMART-COP. According to 4C-Mortality score, the level of serum transgelin was the highest in critical patients (Figure 1B). Moreover, in the basis of CURXO score, serum transgelin expression was obviously upregulated in the severe COVID-19 patients (Figure 1C). Based on A-DROP score, serum transgelin expression was the highest in critical COVID-19 cases (Figure 1D). In the light of DTPNCP, serum transgelin was increased in severe and critical cases (Figure 1E). In addition, we found that serum transgelin was the highest in the highest scores of MuLBSTA, PSI, CURB-65, and COVID-GRAM among COVID-19 patients (Figures 1F–I).

3.3 The change of serum transgelin in COVID-19 cases between onset and convalescent periods

The level of serum transgelin was compared at the onset and convalescent phases. As shown in Figure 2A, serum transgelin was dramatically lower in the convalescent period than those at the onset phase. Moreover, serum transgelin expression was further analyzed in the same subjects between onset and convalescent periods. Serum transgelin expression was substantially decreased in the same COVID-19 patients during the convalescent phase after treatment (Figure 2B).

3.4 The associations of serum transgelin with basic characteristics of COVID-19 cases

The correlations between serum transgelin and clinical parameters were evaluated. Spearman correlative analyses suggested serum transgelin was weakly and positively linked with WBC, neutrophil, urea nitrogen, and ALT (Figure 3). Furthermore, there were inverse relationships of serum transgelin with PaO_2, SpO_2, and PaO2/FiO_2 among COVID-19 patients. Besides, positive associations between serum transgelin with interleukin-6 (IL-6), CRP, D-Dimer, and lactate dehydrogenase (LDH) were observed among COVID-19 patients (Figure 3).

3.5 The associations of serum transgelin with severity of COVID-19 cases

In the univariate linear regression analysis, serum transgelin was positively associated with the scores of SMART-COP (β=0.566), CURB-65 (β=0.264), CURXO (β=0.077), COVID-GRAM (β=5.562), MuLBSTA (β=0.578), A-DROP (β=0.266), PSI (β=9.531), and 4C-Mortality (β=1.021) (Table 2). Moreover, univariate logistic regression analysis revealed that serum higher transgelin in T3 subgroup was strongly correlated with the elevated scores of SMART-COP (OR=7.073), CURB-65 (OR=3.042), COVID-GRAM (OR=3.274), MuLBSTA (OR=3.527), A-DROP (OR=4.485), PSI (OR=4.512), 4C-Mortality (OR=7.647), and DTPNCP (OR=4.048) (Table 2). In addition, confounding factors were eliminated, multivariate linear and logistic regression analyses also demonstrated that serum transgelin expression was positively related to the severity scores (Table 2).

3.6 The associations of serum transgelin with prognosis of COVID-19 cases

As shown in Table 3, the numbers of mechanical ventilation, the usage of vasoactive agent, ICU admission, death, and longer hospital stays were gradually elevated in parallel with serum transgelin expression. In addition, compared with the T1 subgroup, multivariate logistic regression analysis indicated that the risks of mechanical ventilation (OR=12.570), vasoactive agent usage (OR=20.992), ICU admission (OR=9.857), death (OR=12.635), and longer hospital stays (OR=2.673) were obviously ascended in T3 subgroup (Table 3).

3.7 The predictive powers for critical cases and death in COVID-19 patients

The predictive powers for critical cases were assessed by ROC. As shown in Figure 4A, the predictive powers for critical cases were as shown below: serum transgelin: 0.769; CURB-65: 0.751; A-DROP: 0.839; SMART-COP: 0.904; MuLBSTA: 0.769; PSI: 0.758; COVID-GRAM: 0.747; 4C-Mortality: 0.798; CURXO: 0.833; DTPNCP: 0.823; IL-6: 0.699; CRP: 0.690. Serum transgelin had a cutoff value of 0.95 ng/mL to discriminate the critical patients. The sensitivity and specificity were 90.2% and 83.5, respectively. Moreover, the predive capacities for death were analyzed. As shown in Figure 4B, the power capacities for death were as follows: serum transgelin: 0.879; CURB-65: 0.942; A-DROP: 0.921; SMART-COP: 0.930; MuLBSTA: 0.707; PSI: 0.874;

TABLE 1 Demographic characteristics and clinical information at baseline.

Characteristic	Tertile of serum transgelin (ng/mL)			*P*
	T1 (≤0.60)	T2 (0.60~1.02)	T3 (≥1.02)	
N	106	105	106	
Age, years	67.7±16.0	68.9±14.0	73.7±13.2	**0.006**
Male, n (%)	57 (53.8)	53 (50.5)	74 (69.8)	**0.010**
BMI	24.3±4.7	24.7±4.4	24.7±3.93	0.722
Smoker, n (%)	15 (14.2)	11 (10.5)	17 (16.0)	0.517
Systolic pressure (mmHg)	132.2±21.2	137.7±19.2	133.4±21.6	0.127
Diastolic pressure (mmHg)	77.2±11.7	81.2±11.3	79.0±13.8	0.059
Hypertension, n (%)	51 (48.1)	49 (46.7)	53 (50.0)	0.889
Diabetes mellitus, n (%)	22 (20.8)	20 (19.0)	30 (28.3)	0.232
Coronary heart diseases, n (%)	23 (21.7)	19 (18.1)	19 (17.9)	0.742
Other chronic heart disease, n (%)	5 (4.7)	8 (7.6)	18 (17.0)	**0.009**
Cerebrovascular diseases, n (%)	26 (24.6)	14 (13.3)	28 (26.4)	**0.040**
Chronic liver diseases, n (%)	4 (3.8)	4 (3.8)	3 (2.8)	1.000
Hepatitis B, n (%)	3 (2.8)	3 (2.9)	2 (1.9)	1.000
Chronic kidney diseases, n (%)	9 (8.5)	9 (8.6)	9 (8.5)	1.000
Heart rate (Breath/minute)	90.2±10.6	87.4±16.3	93.5±10.5	**0.042**
Respiratory rate (Breath/minute)	20.8±9.3	20.4±4.0	22.2±8.6	0.205
Temperature (°C)	36.7±1.0	36.8±0.8	36.6±0.6	0.475
PaO_2 (mm Hg)	88.3 (73.0, 103.3)	86.1 (68.2, 104.0)	73.1 (59.8, 91.9)	**0.001**
FiO_2 (%)	29.9±4.2	30.3±4.6	35.3±3.5	**<0.001**
SpO_2 (%)	95.8±2.7	94.3±5.1	91.1±6.7	**<0.001**
$PaO2/FiO_2$ (%)	307.1 (260.7, 355.2)	296.6 (230.5, 354.5)	237.4 (162.5, 312.6)	**<0.001**
Corticosteroids therapy, n (%)	80 (75.5)	82 (78.1)	95 (89.6)	**0.016**
Antibiotics therapy, n (%)	101 (95.3)	99 (94.3)	104 (98.1)	0.363
Antiviral therapy, n (%)	37 (34.9)	47 (44.8)	54 (50.9)	0.061
Anticoagulant therapy, n (%)	40 (37.7)	63 (60.0)	76 (71.7)	**<0.001**
WBC (10^9/L)	6.6 (5.1, 8.5)	7.2 (5.1, 9.7)	8.6 (5.5, 12.0)	**0.005**
Neutrophil (10^9/L)	4.6 (3.5, 6.5)	5.4 (3.6, 7.8)	6.6 (3.7, 9.6)	**0.002**
Lymphocyte (10^9/L)	1.1 (0.6, 1.4)	1.0 (0.7, 1.5)	0.8 (0.5, 1.5)	0.241
Monocyte (10^9/L)	0.5 (0.4, 0.6)	0.5 (0.3, 0.6)	0.5 (0.3, 0.7)	0.763
ALT (U/L)	22.0 (15.0, 38.5)	22.0 (18.0, 36.7)	29.0 (19.0, 48.5)	**0.011**
AST (U/L)	26.0 (20.0, 37.0)	26.0 (19.8, 37.0)	32.0 (20.0, 49.0)	**0.026**
Uric acid (μmol/L)	267.0 (195.8, 351.6)	244.2 (201.7, 312.1)	230.9 (178.8, 293.0)	0.244
Urea nitrogen (mmol/L)	6.3 (4.7, 8.1)	6.2 (4.7, 8.0)	7.1 (5.4, 10.6)	**0.012**
Creatinine (μmol/L)	65.5 (56.3, 85.0)	66.0 (53.6, 83.1)	67.5 (56.0, 83.0)	0.944
CK (U/L)	56.0 (36.0, 79.0)	47.0 (28.5, 73.0)	55.0 (35.0, 112.5)	0.087
CK-MB (U/L)	12.5 (7.0, 18.0)	12.0 (7.0, 17.0)	14.0 (7.0, 24.0)	0.142
Myoglobin (ng/mL)	51.3 (34.1, 73.0)	94.4 (27.9, 240.1)	81.2 (40.2, 296.1)	0.108

(Continued)

TABLE 1 Continued

Characteristic	Tertile of serum transgelin (ng/mL)			*P*
	T1 (≤0.60)	T2 (0.60~1.02)	T3 (≥1.02)	
N	106	105	106	
D-Dimer (ng/mL)	0.6 (0.4, 1.1)	0.5 (0.3, 1.6)	1.0 (0.4, 3.0)	**0.003**
CRP (mg/L)	20.1 (5.2, 47.8)	23.6 (5.5, 70.8)	29.0 (10.8, 98.9)	**0.046**
IL-6 (pg/mL)	19.0 (5.9, 53.9)	16.4 (5.5, 41.7)	33.3 (8.0, 77.9)	0.128
PCT (ng/mL)	0.05 (0.03, 0.2)	0.05 (0.03, 0.09)	0.07 (0.03, 0.4)	**0.031**
LDH (U/L)	234.0 (184.0, 281.0)	234.0 (192.5, 298.0)	252.0 (183.8, 399.5)	0.066

Bold values indicate statistical significance. BMI, body mass index; PaO_2, partial pressure of oxygen; FiO_2, fraction of inspiration O_2; SpO_2, oxygen saturation; WBC, white blood cell; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CK-MB, creatine kinase isoenzyme; CRP, C-reactive protein; IL-6, interleukin-6; PCT, procalcitonin; LDH, lactate dehydrogenase.

COVID-GRAM: 0.912; 4C-Mortality: 0.970; CURXO: 0.808; DTPNCP: 0.855; IL-6: 0.721; CRP: 0.778. The cutoff concentration of transgelin was 1.12 ng/mL. The sensitivity was 94.4% and the specificity was 77.1%.

4 Discussion

In the current investigation, serum transgelin was detected for the first time among COVID-19 patients. The data indicated that the expression of serum transgelin was ascended in line with COVID-19 severity scores. And, the expression of serum transgelin was obviously decreased in the convalescent phase after treatment. Moreover, the level of serum transgelin was strongly related to many clinical characteristics. Furthermore, serum transgelin expression on admission had a positive relationship respectively with severity scores and poorly prognostic outcomes during hospitalization. To a certain extent, the expression of serum transgelin on admission can indicate the disease condition and predict the prognosis ahead. This study found a potential role of transgelin in COVID-19 patients.

Transgelin is predominantly localized in the cytoskeleton and used as an earlier biomarker of smooth muscle differentiation (11, 12). Aberrant expression of transgelin has been depicted to be linked with many tumors related diseases (13–16). Interestingly, transgelin expression disorder is associated with a serious of pulmonary diseases. The previous investigations have elucidated that transgelin takes parts in the process of lung cancer, asthma, and lung fibrosis (17–20). In the present study, serum transgelin expression on admission was increased in parallel with COVID-19 severity scores. After treatment, serum transgelin was reduced during the convalescent phase. Correlative analyses found that serum transgelin expression was strongly related to the levels of many clinical parameters in COVID-19 patients. Further, regression analyses revealed that serum transgelin expression was positively related to the severity scores. Collectively, all of these outcomes indicated that serum transgelin expression on admission can indicate the severity of COVID-19.

Mounting evidences suggested that the expression of transgelin is associated with the prognosis of many tumors diseases. Pulmonary transgelin increase is related to tumor progression in lung adenocarcinoma (30). Additionally, transgelin overexpression leads to a poor prognosis in metastatic renal cell carcinoma (31). Moreover, transgelin is an adverse prognostic factor of tumor growth and migration in colorectal cancer patients (15). Therefore, we wanted to know the relationships of serum transgelin level with the prognostic outcomes of COVID-19 cases. In the present study, the numbers of mechanical ventilation, vasoactive agent usage, ICU admission, death, and longer hospital stays were increased with the elevated transgelin expression during hospitalization. Further analyses demonstrated that serum transgelin expression on admission was positively related to the adversely prognostic risks in COVID-19 patients. The previous study has revealed that inflammation is implicated in the process of COVID-19 (32). In addition, the predictive powers of different parameters for critical cases and death were compared among COVID-19 patients. The results revealed that the predictive capacities of serum transgelin for critical cases and death were similar with COVID-19 severity scores, and obviously higher compared with IL-6 and CRP. Overall, follow-up research provided new evidence that transgelin elevation on admission increases the risk of poor prognosis in COVID-19 cases during hospitalization.

Due to serum transgelin was only a single indicator, this meant that it was easily to detect and less time spent in the clinical practice. Not only that, the assessed efficiency of serum transglin was not less than COVID-19 severity scores and was a little higher than those in commonly inflammatory cytokines, such as IL-6 and CRP. Therefore, serum transgelin level may be used to estimate the illness state and predict the prognosis for COVID-19 patients. And it can help to make clinical decision. The current study has demonstrated that the higher serum transgelin on admission was, the higher risk of poor prognosis during hospitalization was. These results indicated that the COVID-19 patients whose the levels of serum transgelin on admission were higher than the cut-off concentrations were more likely to develop critical cases or die during hospitalization. Consequently, when the clinicians met

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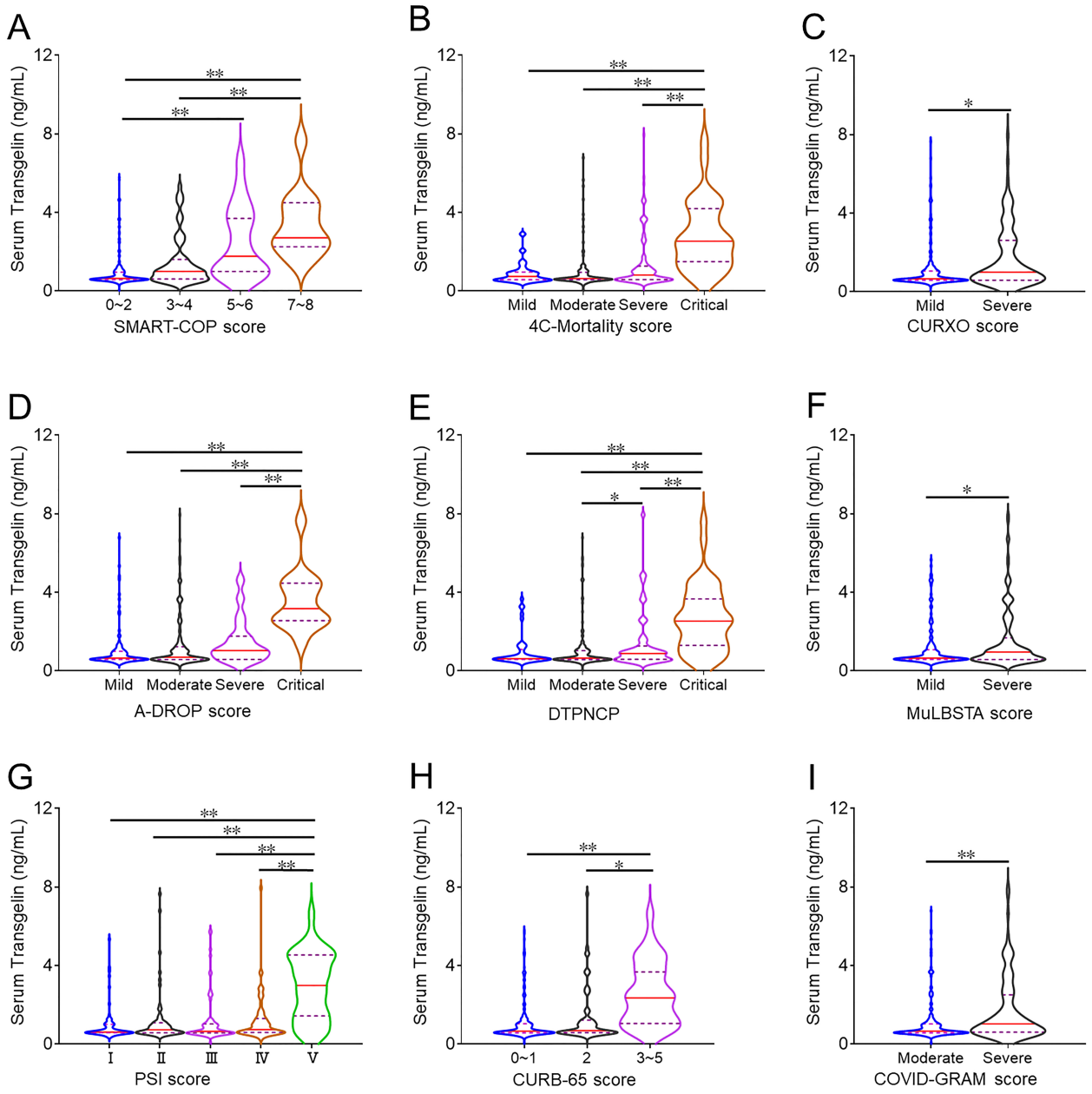

FIGURE 1
The expression of serum transgelin in COVID-19 patients with different severity scores. The expression of serum transgelin was measured using ELISA. The difference of serum transgelin was compared in COVID-19 patients with different severity scores. **(A)** SMART-COP score. **(B)** 4C-Mortality score. **(C)** CURXO score. **(D)** A-DROP score. **(E)** DTPNCP score. **(F)** MuLBSTA score. **(G)** PSI score. **(H)** CURB-65 score. **(I)** COVID-GRAM score. *$P<0.05$, **$P<0.01$.

COVID-19 patients with highly serum transgelin, we should pay more attention to these cases and avoided the disease progression and death during hospitalization. Therefore, we could consider to initiate institute early therapeutic interventions, including respiratory support, the usage of vasoactive agent, and ICU admission, to improve the evolution or even stop the progression from moderate to severe forms, and to reduce the risk of death. Although this study has hinted that serum transgelin expression may be regarded as a biomarker for monitoring the severity and prognosis among CVOID-19 patients. However, this research was only an observational and epidemiological investigation. The specific role of transgelin in the progression of COVID-19 was not explored in this research. Transgelin knockout should be executed, and the effect of transgelin knockout on the process was needed to conduct in mice model of COVID-19. Only intervention experiment can better reveal the role and significance of transgelin in COVID-19.

Assessing the relationships of serum transgelin expression with severity and outcomes are beneficial to illuminate the role of transgelin in COVID-19 patients. However, there were some

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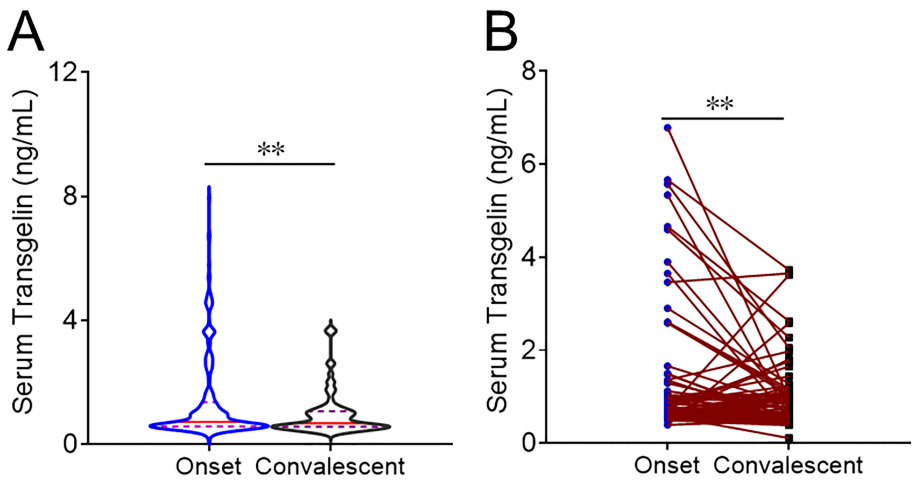

FIGURE 2
The expression of serum transgelin in COVID-19 patients between onset and convalescent periods. The expression of serum transgelin was detected and compared in COVID-19 cases with different periods. **(A)** The expression of serum transgelin was analyzed in COVID-19 cases at the onset and convalescent phases. **(B)** The expression of serum transgelin was analyzed in the same COVID-19 cases between onset and convalescent periods. ***P*<0.01.

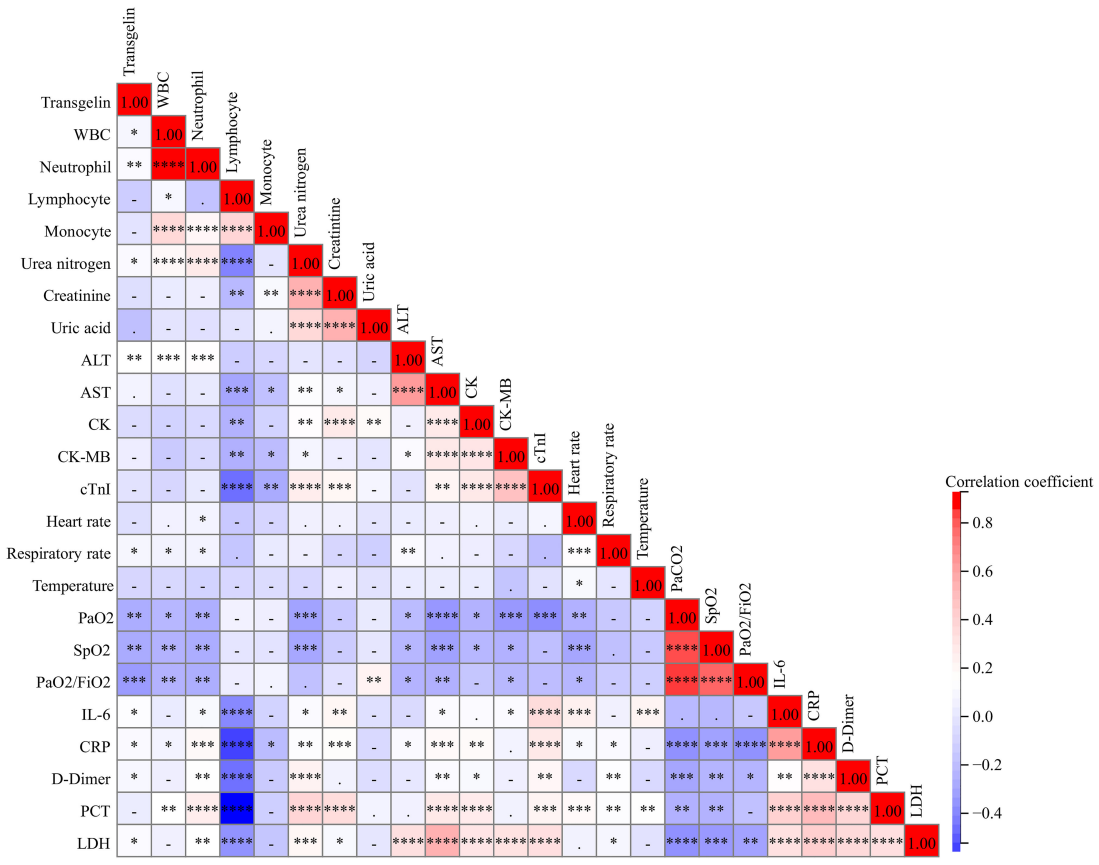

FIGURE 3
The relationships of serum transgelin with clinical characteristics in COVID-19 patients. The relationships between serum transgelin and clinical characteristics were evaluated among COVID-19 patients by Spearman correlation coefficient or Pearson rank correlation analyses. All characteristics consisted of WBC, neutrophil, lymphocyte, monocyte, urea nitrogen, creatinine, uric acid, ALT, AST, CK, CK-MB, cTnI, heart rate, respiratory rate, temperature, PaO2, SpO2, PaO2/FiO2, IL-6, CRP, D-Dimer, PCT, and LDH. **P*<0.05, ***P*<0.01, ****P*<0.001, *****P*<0.0001.

TABLE 2 Associations between serum transgelin and severity in COVID-19 patients.

Models	Variables	Estimated changes by continues transgelin (ng/mL)	Estimated changes (95% CI) by tertiles of transgelin (ng/mL)			*P* trend
			T1 (≤0.60)	T2 (0.60~1.02)	T3 (≥1.02)	
	N	317	106	105	106	
Unadjusted						
	SMART-COP	**0.566 (0.434, 0.699)**	1.0 (Ref)	1.391 (0.560, 3.454)	**7.073 (3.223, 15.523)**	**<0.001**
	CURB-65	**0.264 (0.183, 0.346)**	1.0 (Ref)	1.388 (0.773, 2.629)	**3.042 (1.659, 5.575)**	**0.021**
	CURXO (Severe)	**0.077 (0.039, 0.115)**	1.0 (Ref)	0.964 (0.521, 1.783)	**2.487 (1.398, 4.425)**	0.051
	COVID-GRAM	**5.562 (1.346, 9.778)**	1.0 (Ref)	1.339 (0.651, 2.756)	**3.274 (1.688, 6.349)**	**0.011**
	MuLBSTA	**0.578 (0.234, 0.922)**	1.0 (Ref)	1.788 (0.843, 3.794)	**3.527 (1.738, 7.156)**	**0.001**
	A-DROP	**0.266 (0.181, 0.352)**	1.0 (Ref)	1.452 (0.686, 3.075)	**4.485 (2.266, 8.880)**	**0.001**
	PSI	**9.531 (6.237, 12.825)**	1.0 (Ref)	1.101 (0.490, 2.470)	**4.512 (2.241, 9.084)**	**0.021**
	4C Mortality	**1.021 (0.712, 1.331)**	1.0 (Ref)	2.121 (0.935, 4.811)	**7.647 (3.592, 16.281)**	**0.033**
	DTPNCP	0.229 (0.162, 0.296)	1.0 (Ref)	1.401 (0.733, 2.678)	**4.048 (2.198, 7.455)**	**<0.001**
Adjusted						
	SMART-COP	**0.489 (0.356, 0.622)**	1.0 (Ref)	1.416 (0.544, 3.688)	**5.664 (2.464, 13.017)**	**<0.001**
	CURB-65	**0.178 (0.106, 0.249)**	1.0 (Ref)	1.815 (0.865, 3.808)	**2.663 (1.320, 5.372)**	**0.006**
	CURXO (Severe)	**0.048 (0.011, 0.085)**	1.0 (Ref)	0.979 (0.495, 1.936)	**1.980 (1.042, 3.763)**	0.063
	COVID-GRAM	3.033 (-0.806, 6.873)	1.0 (Ref)	1.789 (0.799, 4.005)	**3.134 (1.485, 6.612)**	**0.002**
	MuLBSTA	**0.373 (0.048, 0.698)**	1.0 (Ref)	2.177 (0.971, 4.883)	**3.189 (1.487, 6.840)**	**0.002**
	A-DROP	**0.176 (0.102, 0.251)**	1.0 (Ref)	2.059 (0.844, 5.022)	**4.301 (1.914, 9.666)**	**0.002**
	PSI	**6.633 (3.634, 9.632)**	1.0 (Ref)	1.308 (0.527, 3.245)	**4.161 (1.873, 9.246)**	**0.013**
	4C Mortality	**0.543 (0.343, 0.744)**	1.0 (Ref)	**3.215 (1.173, 8.810)**	**8.889 (3.500, 22.573)**	**<0.001**
	DTPNCP	0.198 (0.130, 0.266)	1.0 (Ref)	1.509 (0.762, 2.989)	**3.600 (1.885, 6.875)**	**0.021**

Models were adjusted for age, sex, hypertension, diabetes mellitus, coronary heart diseases, other chronic heart disease, cerebrovascular diseases, chronic liver diseases, hepatitis B, and chronic kidney diseases. Bold values indicate statistical significance.

TABLE 3 Associations between serum transgelin and prognostic outcomes in COVID-19 patients.

Variables	Serum transgelin (ng/mL)			*P*trend
	T1 (≤0.60)	T2 (0.60~1.02)	T3 (≥1.02)	
N	106	105	106	
Mechanical ventilation				
N, (%)	1 (0.9)	2 (1.9)	17 (16.0)	**<0.001**
Unadjusted RR (95% CI)	Ref (1.0)	2.039 (0.182, 22.832)	**20.056 (2.617, 153.699)**	**0.002**
Adjusted RR (95% CI)	Ref (1.0)	2.107 (0.163, 27.170)	**12.570 (1.326, 119.185)**	**0.036**
Vasoactive agent				
N, (%)	1 (0.9)	6 (5.7)	13 (12.3)	**0.002**
Unadjusted RR (95% CI)	Ref (1.0)	6.364 (0.753, 53.803)	**14.677 (1.884, 114.356)**	**0.001**
Adjusted RR (95% CI)	Ref (1.0)	**16.693 (1.118, 249.158)**	**20.992 (1.409, 312.760)**	**0.015**

(Continued)

TABLE 3 Continued

Variables	Serum transgelin (ng/mL)			*P*trend
	T1 (≤0.60)	T2 (0.60~1.02)	T3 (≥1.02)	
N	106	105	106	
ICU admission				
N, (%)	2 (1.9)	4 (3.8)	20 (18.9)	**<0.001**
Unadjusted RR (95% CI)	Ref (1.0)	2.059 (0.369, 11.493)	**12.093 (2.749, 53.196)**	**0.004**
Adjusted RR (95% CI)	Ref (1.0)	2.296 (0.331, 15.943)	**9.857 (1.623, 59.860)**	**0.020**
Death				
N, (%)	2	2 (1.0)	19 (20.8)	**<0.001**
Unadjusted RR (95% CI)	Ref (1.0)	1.827 (0.965, 10.365)	**14.977 (6.573, 137.693)**	**<0.001**
Adjusted RR (95% CI)	Ref (1.0)	1.365 (0.876, 9.857)	**12.635 (5.362, 88.528)**	**0.021**
Longer hospital stays				
N, (%)	10 (9.4)	18 (17.1)	33 (31.1)	**0.001**
Unadjusted RR (95% CI)	Ref (1.0)	1.966 (0.861, 4.489)	**4.354 (2.014, 9.413)**	**0.001**
Adjusted RR (95% CI)	Ref (1.0)	1.680 (0.694, 4.065)	**2.673 (1.149, 6.221)**	0.056

RR, Relative risk.
Models were adjusted for age, sex, hypertension, diabetes mellitus, coronary heart diseases, other chronic heart disease, cerebrovascular diseases, chronic liver diseases, hepatitis B, chronic kidney diseases, treatments of corticosteroids, antibiotics, antiviral, and anticoagulant. Bold values indicate statistical significance.

flaws in this epidemiological study. First, this was a relative sample size, a larger sample size was needed to further confirm the above results. Second, this was just epidemiological research, the mechanism of transgelin elevation can't be explored in COVID-19 cases. More *in vitro* and vivo experiments should be conducted in the following study. Third, transgelin was only measured in serum samples, the expression of transgelin wasn't detected in both lung specimens and alveolar lavage fluid.

5 Conclusion

To sum up, this study primarily found that serum transgelin expression on admission was positively related to the severity and poor prognosis in COVID-19 cases. The evidences above revealed that transgelin may involve in the progression of COVID-19, supporting its probable usefulness as a serum biomarker for estimating illness state and prognosis of COVID-19 patients. The

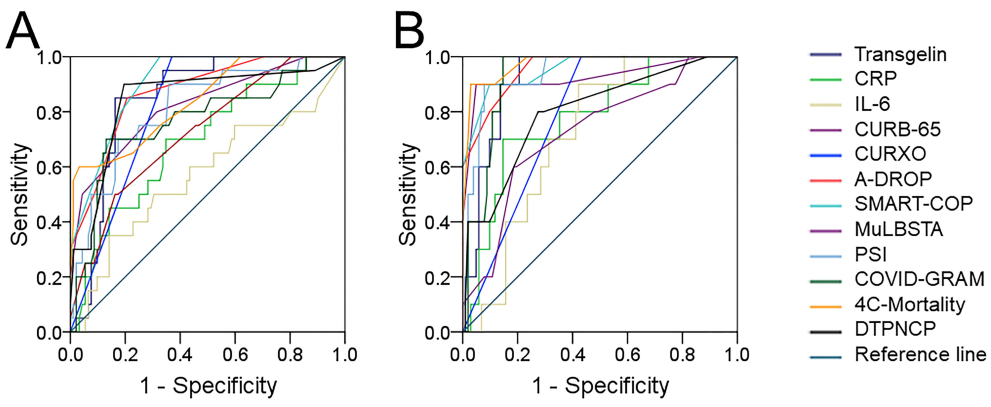

FIGURE 4
The predictive capacities for critical cases and death among COVID-19 patients. The predictive capacities for critical cases and death were assessed via ROC curve. **(A)** The predictive capacity for critical cases between serum transgelin and COVID-19 severity scores. **(B)** The predictive capacity for death between serum transgelin and COVID-19 severity scores.

development and utilization of transgelin may assist in managing COVID-19 cases on the basis of disease extent.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was supported by the Ethics Committee of Second Affiliated Hospital of Anhui Medical University (YJ-YX2021-147). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s), and minor (s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

LF: Conceptualization, Funding acquisition, Resources, Writing – original draft, Writing – review & editing. LG: Conceptualization, Investigation, Methodology, Writing – original draft. YL: Conceptualization, Investigation, Methodology, Data curation, Writing – original draft. Q-YH: Conceptualization, Investigation, Methodology, Data curation, Writing – original draft. YW: Conceptualization, Investigation, Methodology, Data curation, Writing – original draft. Y-LJ: Conceptualization, Funding acquisition, Investigation, Methodology, Data curation, Writing – original draft. JY: Conceptualization, Investigation, Methodology, Data curation, Writing – original draft. HZ: Conceptualization, Funding acquisition, Investigation, Resources, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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