

ORIGINAL ARTICLE

Elevated Lactate, D-dimer, and IL-6 Associated with Elderly Community-Acquired SARS-CoV-2 Pneumonia Severity

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SUMMARY

Background: Uncontrolled systemic inflammatory responses significantly contribute to the pathogenesis of severe community-acquired pneumonia (CAP) following SARS-CoV-2 infection (CASP). Elderly populations, being particularly vulnerable to respiratory infections, demonstrate both increased susceptibility to SARS-CoV-2 infection and greater disease severity. This study aimed to identify readily available routine hematological biomarkers that could serve as independent risk factors for predicting severe CASP (sCASP) in elderly patients.

Methods: A retrospective study was conducted to analyze 77 elderly people with CASP. According to the severity of the disease, the elderly people were divided into a non-sCASP group and a sCASP group, and the routine comprehensive laboratory examinations were compared.

Results: A total of 77 elderly patients with CASP were enrolled in this study, comprising 35 cases in the non-sCASP group and 42 cases in the sCASP group. Significant differences were observed in admission laboratory parameters, including routine blood counts, coagulation profiles, liver and kidney function tests, inflammatory markers, and composite laboratory-derived indices, between non-sCASP and sCASP cases infected with SARS-CoV-2 Omicron subvariants BA.5.2 and BF.7 ($p < 0.05$). Multivariate logistic regression and receiver operating characteristic (ROC) curve analyses identified lactate > 1.95 mmol/L, D-dimer > 0.85 mg/L, and IL-6 > 33.5 pg/mL as the most probable independent risk factors for sCASP in elderly patients. Notably, the combined diagnostic model (lactate-D-dimer-IL-6) demonstrated superior predictive performance for disease severity (AUC = 0.981; 95% CI: 0.954 - 1) compared to any single biomarker alone.

Conclusions: Elevated admission lactate, D-dimer, and IL-6 can be used as independent risk factors for the evaluation of CASP severity in elderly people, and the joint detection might be a better choice. This is imperative for guiding the development of effective interventions to alleviate severe patients' symptoms and burden.

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Supplementary Data

Table S1. Analysis of demographic and laboratory hematological parameters between sCASP group and non-sCASP group.

Feature	sCASP (n = 42)	non-sCASP (n = 35)	p-value
Age (years), median (range)	83 (75, 88)	73 (62, 85)	p < 0.05
Gender; male:female	29:13	14:21	p < 0.05
Complete blood count			
WBC (x 10 ⁹ /L)	8.43 (5.43, 10.33)	6.15 (3.79, 8.06)	p < 0.05
NEUT (x 10 ⁹ /L)	7.15 (4.35, 9.45)	4.20 (2.66, 6.65)	p < 0.05
LY (x 10 ⁹ /L)	0.69 (0.48, 0.96)	0.85 (0.54, 1.37)	p > 0.05
MY (x 10 ⁹ /L)	0.32 (0.20, 0.52)	0.30 (0.20, 0.56)	p > 0.05
Eos (x 10 ⁹ /L)	0.03 (0.01, 0.07)	0.03 (0.01, 0.06)	p > 0.05
Baso (x 10 ⁹ /L)	0.01 (0.01, 0.03)	0.01 (0.01, 0.02)	p > 0.05
PLT (x 10 ⁹ /L)	183.50 (140.50, 240.75)	185.00 (152.00, 269.00)	p > 0.05
Coagulation function			
PT (second)	12.10 (11.40, 12.70)	11.50 (10.60, 12.00)	p < 0.05
APTT (second)	30.50 (27.85, 35.68)	26.90 (24.80, 29.70)	p < 0.05
TT (second)	18.25 (17.68, 19.53)	18.00 (17.10, 18.50)	p > 0.05
FIB (g/L)	4.88 (3.77, 6.16)	4.28 (3.53, 5.30)	p > 0.05
D-dimer (mg/L)	1.56 (0.87, 4.94)	0.61 (0.36, 1.28)	p < 0.01
Biochemical parameters			
ALT (U/L)	22.35 (12.18, 34.30)	19.00 (13.20, 30.60)	p > 0.05
AST (U/L)	41.15 (22.93, 54.73)	22.90 (17.20, 31.10)	p < 0.05
TP (g/L)	61.95 ± 7.86	63.58 ± 8.11	p > 0.05
ALB (g/L)	30.55 (26.95, 33.78)	35.70 (31.90, 39.70)	p < 0.01
GGT (U/L)	37.35 (20.73, 62.03)	23.00 (18.00, 42.00)	p > 0.05
LDH (U/L)	330.82 (246.02, 453.70)	250.00 (212.40, 339.00)	p < 0.05
BUN (mol/L)	9.20 (5.66, 12.34)	4.71 (3.22, 6.77)	p < 0.01
Creatinine (μmol/L)	96.67 (58.80, 142.03)	64.10 (52.80, 80.90)	p < 0.05
Uric acid (μmol/L)	334.28 (216.38, 492.51)	265.00 (182.20, 312.00)	p < 0.05
CK (U/L)	129.96 (58.88, 282.43)	96.40 (64.18, 177.00)	p > 0.05
CKMB (U/L)	12.84 (9.44, 19.29)	11.20 (7.80, 14.94)	p > 0.05
Lactate (mmol/L)	1.70 (1.40, 2.50)	1.20 (0.70, 1.50)	p < 0.001
Electrolyte			
K (mmol/L)	4.02 (3.52, 4.51)	3.89 (3.51, 4.27)	p > 0.05
Na (mmol/L)	137.25 (133.89, 139.24)	137.39 (133.26, 140.40)	p > 0.05
Cl (mmol/L)	103.62 (99.87, 107.12)	102.12 (99.00, 105.42)	p > 0.05
Trace elements			
Ca (mmol/L)	1.09 (1.04, 1.96)	2.08 (1.94, 2.23)	p < 0.01
Fe (μmol/L)	15.92 (9.27, 23.95)	11.90 (5.78, 15.99)	p < 0.05
Mg (mmol/L)	0.79 ± 0.13	0.89 ± 0.14	p < 0.05
P (mmol/L)	0.89 (0.66, 1.17)	1.04 (0.93, 1.21)	p < 0.05
Inflammatory factors			
CRP (mg/L)	77.38 (36.26, 108.44)	24.60 (6.02, 46.00)	p < 0.01
PCT (ng/mL)	0.29 (0.15, 0.54)	0.13 (0.10, 0.24)	p < 0.05
IL-6 (pg/mL)	49.35 (26.75, 89.00)	29.00 (7.70, 45.00)	p < 0.05

WBC white blood cell, NEUT neutrophil, LY lymphocyte, MY monocyte, Eos eosinophil, Baso basophil, PLT platelet, PT prothrombin time, APTT activated partial thromboplastin time, TT thrombin time, FIB fibrinogen, ALT alanine transaminase, AST aspartate aminotransferase, TP total protein, ALB albumin, GGT gamma-glutamyl transferase, LDH lactate dehydrogenase, BUN blood urea nitrogen, CK creatine kinase, CKMB creatine kinase isoenzyme-MB, K potassium, Na sodium, Cl chloride, Ca calcium, Fe iron, Mg magnesium, P phosphorus, CRP C reactive protein, PCT procalcitonin, IL-6 interleukin-6.

Table S2. Analysis of laboratory composite derived indexes between sCASP group and non-sCASP group.

Feature	sCASP (n = 42)	non-sCASP (n = 35)	p-value
NLR	9.98 (5.89, 17.06)	4.76 (2.15, 12.09)	p < 0.05
PLR	302.68 (175.30, 467.92)	238.20 (154.01, 330.65)	p > 0.05
PMR	639.36 (331.11, 1,047.81)	621.05 (284.72, 1,077.27)	p > 0.05
MLR	0.49 (0.31, 0.66)	0.33 (0.16, 0.76)	p > 0.05
AISI	700.66 (271.16, 1,315.40)	358.23 (101.41, 776.26)	p > 0.05
SII	1,931.72 (1,067.09, 3,969.13)	1,204.39 (488.34, 2,143.82)	p < 0.05
SIRI	3.29 (1.56, 4.89)	1.95 (0.55, 4.45)	p < 0.05
NPAR	0.03 (0.02, 0.03)	0.02 (0.02, 0.03)	p < 0.01
UAR	10.98 (7.26, 15.37)	6.93 (5.26, 9.37)	p < 0.05
CLR	110.19 (60.28, 186.66)	24.34 (4.87, 80.47)	p < 0.01
CPR	220.82 (94.49, 485.86)	144.41 (15.60, 246.00)	p > 0.05

NLR absolute neutrophil count-to-absolute lymphocyte count ratio, PLR platelet count-to-absolute lymphocyte count ratio, PMR platelet count-to-absolute monocyte count ratio, MLR absolute monocyte count-to-absolute lymphocyte count ratio, AISI aggregate index of systemic inflammation (AISI = absolute neutrophil count x platelet count x absolute monocyte count/absolute lymphocyte count), SII systemic immune inflammation index (SII = platelet count x absolute neutrophil count/absolute lymphocyte count), SIRI systemic inflammation response index (SIRI = absolute neutrophil count x absolute monocyte count/absolute lymphocyte count), NPAR neutrophil percentage-to-albumin ratio, UAR uric acid-to-albumin ratio, CLR C-reactive protein-to-absolute lymphocyte count ratio, CPR C-reactive protein-to-procalcitonin ratio.

Table S3. Univariate logistic regression analysis of variables associated with sCASP.

Variables	p-value	OR	95% CI	
			Lower limit	Upper limit
Age	0.003	1.08	1.027	1.135
Gender	0.012	3.346	1.306	8.574
WBC	0.038	1.167	1.008	1.35
NEUT	0.015	1.205	1.036	1.401
PT	0.298	1.23	0.833	1.818
APTT	0.06	1.081	0.997	1.173
D-dimer	0.004	1.567	1.153	2.132
AST	0.392	1.007	0.991	1.024
ALB	0.001	0.832	0.748	0.925
LDH	0.011	1.005	1.001	1.01
BUN	0.001	1.272	1.097	1.474
Creatinine	0.01	1.018	1.004	1.031
Uric acid	0.008	1.005	1.001	1.009
Lactate	< 0.001	12.449	3.713	41.744
Ca	< 0.001	0.013	0.001	0.107
Fe	0.011	1.079	1.017	1.145
Mg	0.002	0.003	0	0.129
P	0.012	0.092	0.014	0.595
CRP	0.001	1.023	1.01	1.037
PCT	0.259	1.859	0.633	5.46
IL-6	0.002	1.026	1.01	1.043
NLR	0.023	1.083	1.011	1.16
SII	0.03	1	1	1.001
SIRI	0.176	1.09	0.962	1.234
NPAR	< 0.001	4.142	1.872	9.165
UAR	0.002	1.233	1.083	1.404
CLR	0.015	1.008	1.002	1.014

OR odds ratio, CI confidence interval, WBC white blood cell, NEUT neutrophil, PT prothrombin time, APTT activated partial thromboplastin time, AST aspartate aminotransferase, ALB albumin, LDH lactate dehydrogenase, BUN blood urea nitrogen, Ca calcium, Fe iron, Mg magnesium, P phosphorus, CRP C reactive protein, PCT procalcitonin, IL-6 interleukin-6, NLR absolute neutrophil count-to-absolute lymphocyte count ratio, SII systemic immune inflammation index (SII = platelet count x absolute neutrophil count/absolute lymphocyte count), SIRI systemic inflammation response index (SIRI = absolute neutrophil count x absolute monocyte count/absolute lymphocyte count), NPAR neutrophil percentage-to-albumin ratio, UAR uric acid-to-albumin ratio, CLR C-reactive protein-to-absolute lymphocyte count ratio.