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ORIGINAL RESEARCH

Association Between Artificial Intelligence Based Chest Computed Tomography and Clinical/ Laboratory Characteristics with Severity and Mortality in COVID-19 Hospitalized Patients

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Background: Some patients with COVID-19 rapidly develop respiratory failure or mortality, underscoring the necessity for early identification of those prone to severe illness. Numerous studies focus on clinical and lab traits, but only few attend to chest computed tomography. The current study seeks to numerically quantify pulmonary lesions using early-phase CT scans calculated through artificial intelligence algorithms in conjunction with clinical and laboratory helps clinicians to early identify the development of severe illness and death in a group of COVID-19 patients.

Methods: From December 15, 2022, to January 30, 2023, 191 confirmed COVID-19 patients admitted to Xinhua Hospital Affiliated with Shanghai Jiao Tong University School of Medicine were consecutively enrolled. All patients underwent chest CT scans and serum tests within 48 hours prior to admission. Variables significantly linked to critical illness or mortality in univariate analysis were subjected to multivariate logistic regression models post collinearity assessment. Adjusted odds ratio, 95% confidence intervals, sensitivity, specificity, Youden index, receiver-operator-characteristics (ROC) curves, and area under the curve (AUC) were computed for predicting severity and in-hospital mortality.

Results: Multivariate logistic analysis revealed that myoglobin (OR = 1.003, 95% CI 1.001–1.005), APACHE II score (OR = 1.387, 95% CI 1.216–1.583), and the infected CT region percentage (OR = 113.897, 95% CI 4.939–2626.496) independently correlated with in-hospital COVID-19 mortality. Prealbumin stood as an independent safeguarding factor (OR = 0.965, 95% CI 0.947–0.984). Neutrophil counts (OR = 1.529, 95% CI 1.131–2.068), urea nitrogen (OR = 1.587, 95% CI 1.222–2.062), SOFA score(OR = 3.333, 95% CI 1.476–7.522), qSOFA score(OR = 15.197, 95% CI 3.281–70.384), PSI score(OR = 1.053, 95% CI 1.018–1.090), and the infected CT region percentage (OR = 548.221, 95% CI 2.615–114,953.586) independently linked to COVID-19 patient severity.

Keywords: COVID-19, chest CT, artificial intelligence, mortality, severity

Introduction

Coronavirus disease 19 (COVID-19), caused by the Severe Acute Respiratory Coronavirus-2 (SARS-CoV-2), has emerged as a global pandemic and the most significant public health crisis of the 21st century.[1] As of March 1, 2023, the global count surpasses 700 million confirmed COVID-19 cases with over 7 million reported deaths.[2] China experienced a minor peak in COVID-19 transmission in December 2022 due to adjustments in epidemic prevention policies.

Existing research reveals that the occurrence of severe COVID-19 cases among all patients is approximately 15%.[3] The mortality rate in severe cases varies from 8.0% to 61.5%, notably higher among elderly patients.[4,5] Early medical

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intervention is crucial in reducing the mortality rate among severe cases. Thus, timely and accurate identification of risk factors predicting severity and high mortality risk is imperative.

Several risk factors contributing to severe COVID-19 and increased morbidity have been identified, including advanced age, male gender, pre-existing health conditions, and racial/ethnic disparities.[6] A systematic review of 61 cohort studies comprising 31,089 hospitalized COVID-19 patients demonstrated elevated mortality risks linked to underlying chronic kidney disease, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, hypertension, malignancy, diabetes, and immunodeficiency.[7] A study including 3322 COVID-19 cases in Stockholm revealed a higher mortality risk in patients with heart failure, ischemic heart disease, obesity, type II diabetes, and kidney failure.[8] Previous observational studies, however, were constrained by limited sample sizes, potential biases, and a focus on specific risk factors,[9,10] often lacking comprehensive CT imaging features and quantification(use values instead of descriptions to reflect the situation of pulmonary infection).

This study combines clinical and laboratory traits with CT-based pneumonia lesion features, calculated through artificial intelligence algorithms, to find the association between them with the mortality and severity among COVID-19 adult patients.To achieve the target of early identification and early intervention.In addition,We innovatively combined with severity of illness scores including CURB-65, SOFA, QSOFA, APACHE II, and PSI which is different from the the existing works and it can improve the accuracy of prediction. We wish to apply the achievements to other types pneumonia not only COVID-19 in the future.

Methods

Study Design and Population

In this retrospective case-control study, all consecutive adult patients confirmed SARS-CoV-2 infection admitted to Xinhua Hospital Affiliated with Shanghai Jiao Tong University School of Medicine between December 15, 2022, and January 30, 2023, were enrolled. The diagnosis of COVID-19 adhered to the World Health Organization (WHO) interim guidance and the 10th version of the National Health Commission of China's guidelines for diagnosis and treatment of novel coronavirus pneumonia.[11] Patients meeting the diagnostic criteria, having positive COVID-19 nucleic acid or antigen tests along with or without clinical symptoms and CT-identified pneumonia lesions, were included. The following exclusion criteria were applied: (a) age <18 years, (b) prior treatment at Xinhua Hospital, (c) incomplete clinical data.

A total of 366 adult patients suspected of having COVID-19 were admitted to Xinhua Hospital between December 15, 2022, and January 30, 2023. Among them, 69 patients had no recorded positive nucleic acid test or antigen test results in the electronic medical record system. Additionally, 72 patients had received treatment at other hospitals before their visit to Xinhua Hospital, 2 patients did not undergo complete CT scans, and 32 patients had incomplete clinical data. Ultimately, a total of 191 patients with COVID-19 were included in the subsequent analysis. The patient enrollment process is illustrated in Supplementary Figure 1.

Subsequently, patients were divided into four groups based on disease severity (mild or severe) and survival status (survival or non-survival). The severe COVID-19 group encompassed patients meeting at least one of the following criteria: (a) Shortness of breath, breathing rate ≥ 30/min, (b) Resting arterial oxygen saturation (SaO2) ≤ 93%, (c) Ratio of partial pressure of arterial oxygen (PaO2) to fraction of inspired oxygen (FiO2) ≤ 300 mmHg, (d) Manifestation of shock or multiple organ dysfunction.[11]

Data Collection

The research team from the Department of Emergency at Xinhua Hospital Affiliated with Shanghai Jiao Tong University School of Medicine conducted an analysis of patients' medical records. Patient characteristics, treatment details, and outcomes data were extracted using electronic medical record-based data collection forms. Trained physicians meticulously reviewed the gathered data.

Key patient characteristics,Comorbidities,Laboratory parameters,Symptoms and Severity of illness scores, Data on medications and respiratory support methods and Complications were collected.

Chest CT Image and AI Data Collection

CT scans were conducted using Brilliance iCT (256-slice) and SOMATOM Definition (64-slice) machines. Patient CT images were imported into AI software in DICOM format, developed by Shanghai United Imaging (UI) Intelligence Co., Ltd. This software autonomously outlined regions of interest (ROIs). In instances where precise ROIs were not established, a radiologist with 6 years of experience manually corrected them. Subsequently, the UI_AI software automatically generated AI-based parameters, encompassing whole-lung volume, infected region volume, and the corresponding percentage (infected region volume to whole-lung volume). Three quantitative characteristics were computed through CT value thresholding within pneumonia lesions, denoting the percentages of lesion volume within ranges of −750 to −301 Hounsfield units (HU), −300 to −49 HU, and ≥50 HU. These AI-derived CT attributes corresponded to the percentages of ground glass opacity volume (PGV), consolidation volume (PCV), and atelectasis volume (PAV).[12] The calculations were performed using the following equation:

Infected Region Percentages Corresponding to CT Values = Infected Region Volume Corresponding to CT Values / Whole-Lung Volume

Details of UI_AI analysis were explicitly shown in Supplementary Figure 2.

Data Analysis

All data underwent analysis and processing using SPSS 27.0 software. Initial assessment involved the K–S test to evaluate if measurement data adhered to normal distribution. Normally distributed measurement data were expressed as mean ± standard deviation. Independent sample *t*-tests were utilized for intergroup comparisons in such cases. For non-normally distributed measurement data, median (quartile) values were employed, and the independent sample rank sum test was used for intergroup comparisons. Count data were presented as case numbers and proportions, with statistical analysis carried out using the Chi-squared test. Variables significantly linked to critical illness or mortality in univariate analysis were subjected to multivariate logistic regression models post collinearity assessment. Adjusted odds ratio, 95% confidence intervals, sensitivity, specificity,Youden index and ROC curves and AUC were computed for predicting severity and in-hospital mortality.Statistical significance was defined as $P < 0.05$.

Results

Presenting Characteristics

The study included 191 hospitalized patients diagnosed with COVID-19, of which 81 had severe cases and 110 were non-severe. Among these, 148 patients survived while 43 succumbed during hospitalization. Comparative analysis revealed that deceased patients were significantly older (median age: 81 years [IQR: 73–87] vs 73 years [IQR: 65–82]; $P < 0.001$) compared to survivors. Similar trends were observed in severe vs non-severe groups (median age: 80 years [IQR: 73–86] vs 71 years [IQR: 62–80]; $P < 0.001$). The severe group exhibited higher rates of comorbidities, including cerebrovascular disease (19 [23.46%] vs 8 [7.27%]) and diabetes (38 [46.91%] vs 32 [29.09%]). Deceased patients were more likely to have chronic kidney disease (CKD) compared to survivors (8 [18.6%] vs 8 [5.4%]). Notably higher proportions of patients in the severe group and non-survivors experienced panting (breathing rate ≥ 30/min), tachycardia (heart rate ≥ 125/min), and consciousness changes ($P < 0.05$).

Complications, including sepsis, shock, acute respiratory distress syndrome (ARDS), cardiac injury, acute myocardial infarction, acute kidney injury, acute heart failure, and co-infections, were more prevalent in the severe and non-surviving groups ($P < 0.05$). All patients who experienced shock during hospitalization eventually died. Detailed results are outlined in Table 1.

Laboratory Parameters

Comparison of laboratory parameters across the four patient cohorts is provided in Table 2. Higher levels of WBC, neutrophil count, CRP, PCT, CD64, urea nitrogen, Cr, and coagulation indicators including PT, INR, TT, D-dimer, ATA, cardiac markers such as MYO, TNI, and NT-proBNP, along with cytokines including TNF-α, IL-6, IL-8, IL-10, and IL-1β, as well as glucose, pH, and Lac, were identified in severe and non-survival cases ($P < 0.05$). Conversely, lower levels

Table 1 Baseline Characteristics of Patients Infected with 2019-nCoV

	Non-Severe(n=110)	Severe(n=81)	*P* value[a]	Survival(n=148)	Non-Survival(n=43)	*P* value[b]
Age(IQR)	71.00(62.00,80.00)	80.00(73.00,86.00)	<0.001	73.00(65.00,82.00)	81.00(73.00,87.00)	<0.001
Male	62(56.36)	51(62.96)	0.359	83(56.08)	30(69.77)	0.108
BMI(IQR)	24.64(22.51,26.28)	24.67(22.69,25.61)	0.949	24.67(22.68,26.12)	24.67(21.48,25.51)	0.579
Comorbidity						
Chronic heart failure	8(7.27)	12(14.81)	0.092	12(8.11)	8(18.60)	0.090
Coronary heart disease	21(19.09)	19(23.46)	0.464	30(20.27)	10(23.26)	0.672
COPD	8(7.27)	2(2.47)	0.141	8(5.41)	2(4.65)	1.000
CKD	7(43.80)	9(56.30)	0.242	8(5.40)	8(18.60)	0.015
Cerebrovascular disease	8(7.27)	19(23.46)	0.002	18(12.16)	9(20.93)	0.146
Diabetes	32(29.09)	38(46.91)	0.012	49(33.11)	21(48.84)	0.060
Hypertension	64(58.18)	61(75.31)	0.064	93(62.84)	32(74.42)	0.160
Lung cancer	5(4.55)	1(1.23)	0.381	5(3.38)	1(2.33)	1.000
Cancer besides lung	11(10.00)	10(12.35)	0.609	16(10.81)	5(11.63)	1.000
Immunodeficiency disease	5(4.55)	2(2.47)	0.715	6(4.05)	1(2.33)	0.944
Symptoms						
Cough	103(93.64)	76(93.83)	0.957	140(94.59)	39(90.70)	0.569
Expectoration	99(90.00)	69(85.19)	0.312	131(88.51)	37(86.05)	0.662
RR≥24/min	16(14.55)	51(62.96)	<0.001	35(23.65)	32(74.42)	<0.001
HR≥125/min	4(3.64)	11(13.58)	0.012	5(3.38)	10(23.26)	<0.001
T>37.3°C	101(91.82)	72(88.89)	0.493	134(90.54)	39(90.70)	1.000
Consciousness change	2(1.82)	20(24.69)	<0.001	9(6.08)	13(30.23)	<0.001
Feeble	44(40.00)	26(32.10)	0.263	57(38.51)	13(30.23)	0.321
Complications						
Sepsis	28(25.45)	80(98.77)	<0.001	43(29.05)	43(100)	<0.001
Shock	0(0.00)	15(18.52)	<0.001	0(0.00)	15(34.88)	<0.001
ARDS	0(0.00)	28(34.57)	<0.001	2(1.35)	26(60.47)	<0.001
Cardiac injury	3(2.73)	37(45.68)	<0.001	9(6.08)	31(72.09)	<0.001
Acute myocardial infarction	0(0.00)	7(8.64)	0.006	2(1.35)	5(11.63)	0.007
Acute cerebral stroke	0(0.00)	1(1.23)	0.243	0(0.00)	1(2.33)	0.225
Acute heart failure	7(6.36)	31(38.27)	<0.001	12(8.11)	26(60.47)	<0.001
AKI	4(3.64)	19(23.46)	<0.001	8(5.41)	15(43.88)	<0.001
Co-infection	0(0.00)	34(41.98)	<0.001	3(2.03)	31(72.09)	<0.001
Onset of symptom to admission(IQR)	8.00(6.00,11.00)	6.00(3.00,10.00)	<0.001	7.00(5.00,10.00)	6.00(3.00,10.00)	0.171

Notes: *P* values[a] indicate differences between non-severe and severe patients. *P* values[b] indicate differences between survival and non-survival patients. *P* <0.05 was considered statistically significant.

Abbreviations: COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; RR, respiratory rate; HR, heart rate.

of lymphocyte count, including CD3+, CD4+, and CD8+ T-cell counts, prealbumin, albumin, fibrinogen degradation products, and parameters like PO2, PCO2, HCO3-, and PO2/FIO2, were significantly evident in severe and non-survival cases ($P < 0.05$). Furthermore, RDW was significantly higher in severe cases compared to non-severe cases ($P < 0.001$), while no statistical differences were observed between the other two groups ($P > 0.05$). Platelet count was lower in both severe and non-survival cohorts.

CT Features

Noteworthy distinctions were observed in the entire infected volume and the percentages of the infected region between severe and non-severe patients ($P < 0.01$). Similar results were noticed between survival and non-survival cases ($P < 0.01$). However, no statistically significant differences were discerned regarding PGV, PCV, and PAV across the four groups. The study also calculated the infected region percentages for each lobe and found that pneumonia lesions were

Table 2 Laboratory Findings of Patients Infected with 2019-nCoV

	Non-Severe (n=110)	Severe(n=81)	*P* value[a]	Survival(n=148)	Non-Survival (n=43)	*P* value[b]
WBC×10^9 /L	5.72(4.20,7.68)	8.06(5.22,11.66)	<0.001	6.11(4.33,8.28)	8.06(5.22,12.59)	0.003
Neutrophils	4.15(2.95,5.79)	6.68(4.45,9.97)	<0.001	4.56(2.99,6.57)	6.54(4.49,10.03)	0.001
Lymphocyte	0.86(0.61,1.32)	0.61(0.42,0.93)	<0.001	0.83(0.55,1.23)	0.58(0.37,0.79)	0.001
NLR	7.50(4.80,12.48)	5.40(3.15,8.70)	0.002	6.85(4.10,11.58)	5.90(3.30,10.90)	0.226
Monocyte	0.51(0.30,0.70)	0.53(0.29,0.80)	0.566	0.53(0.30,0.70)	0.42(0.22,0.87)	0.623
Haemoglobin	125.00 (117.75,136.25)	122.00 (111.00,135.50)	0.244	124.00 (114.25,135.00)	124.00 (107.00,143.00)	0.867
RDW	12.85(12.30,13.63)	13.40(12.80,14.75)	<0.001	13.00(12.50,13.80)	13.20(12.60,14.50)	0.089
Platelet count	185.50 (147.50,237.00)	174.00 (133.50,246.50)	0.282	186.50 (146.00,248.50)	163.00 (115.00,194.00)	0.008
PDW	16.34(15.55,16.78)	16.43(13.15,17.32)	0.363	16.32(14.53,16.84)	16.50(13.70,17.35)	0.185
CRP	27.00(10.00,52.00)	93.00(35.50,144.00)	<0.001	32.50(12.00,75.00)	93.00(36.00,141.00)	<0.001
Prealbumin	134.00 (120.00,160.25)	134.00 (105.00,134.00)	0.003	134.00 (125.50,159.75)	134.00 (84.00,134.00)	<0.001
Albumin	36.80(33.58,39.43)	34.40(31.10,36.60)	<0.001	36.10(33.25,39.08)	33.60(30.70,35.90)	<0.001
Urea nitrogen	6.00(4.00,7.41)	8.00(5.50,11.00)	<0.002	6.00(4.97,8.00)	9.00(6.00,13.00)	<0.001
Serum creatinine	65.00(52.00,86.45)	83.50(64.75,114.95)	<0.003	68.00(54.10,91.88)	92.30(62.70,141.60)	0.002
PT	11.50(11.00,12.23)	12.10(11.40,13.10)	<0.004	11.60(11.10,12.30)	12.30(11.70,13.30)	<0.001
INR	1.00(0.96,1.07)	1.05(0.99,1.14)	<0.005	1.02(0.97,1.07)	1.07(1.02,1.15)	<0.001
APTT	29.95(27.38,32.48)	30.00(28.00,32.60)	0.540	30.00(27.70,32.60)	30.00(27.90,32.60)	0.834
FIB	4.13±0.87	4.26±0.97	0.255	4.20±0.85	4.13±1.11	0.797
TT	13.35(12.58,14.23)	13.90(12.70,14.75)	0.037	13.40(12.60,14.28)	14.00(13.20,15.70)	0.007
D-dimer	0.66(0.46,1.06)	1.36(0.87,4.31)	<0.001	0.77(0.52,1.18)	1.77(1.11,7.06)	<0.001
Fibrinogen degradation products	81.45±16.54	73.07±16.26	<0.001	78.00(69.00,89.00)	73.00(60.00,86.00)	0.042
ATA	2.54(1.71,3.60)	5.00(3.27,7.70)	<0.001	2.86(2.00,4.43)	5.22(3.71,17.16)	<0.001
PCT	0.05(0.04,0.09)	0.22(0.08,0.91)	<0.001	0.07(0.04,0.12)	0.25(0.08,0.70)	<0.001
MYO	45.20(27.18,63.50)	83.30(56.35,239.50)	<0.001	57.20(28.68,78.75)	124.40 (56.40,337.40)	<0.001
TNI	0.01(0.00,0.01)	0.03(0.01,0.07)	<0.001	0.01(0.00,0.02)	0.04(0.02,0.11)	<0.001
NT-proBNP	222.54 (77.80,399.56)	610.62 (294.75,1441.56)	<0.001	329.87 (109.77,491.39)	939.73 (301.41,3244.14)	<0.001
CD64	1.44(0.58,2.16)	2.16(1.23,2.47)	<0.001	2.02(0.61,2.16)	2.16(1.16,3.35)	<0.001
CD4/CD8ratio	1.81(1.31,2.50)	2.11(1.27,2.91)	0.093	1.82(1.25,2.41)	2.11(1.92,3.20)	0.007
CD3	583.84 (457.89,823.57)	397.30 (247.06,507.49)	<0.001	537.20 (407.07,800.24)	315.89 (215.56,507.49)	<0.001
CD4	346.17 (243.18,523.60)	227.71 (161.10,289.02)	<0.001	294.61 (227.94,503.72)	205.74 (144.71,289.02)	<0.001
CD8	191.83 (161.92,284.81)	159.64 (78.66,173.47)	<0.001	178.03 (150.73,280.99)	105.58 (47.20,173.47)	<0.001
IL-8	22.75(14.40,27.08)	29.20(23.90,49.80)	<0.001	23.90(15.53,29.55)	45.00(24.35,68.40)	<0.001
IL-1β	4.00(4.00,5.54)	6.53(4.00,13.55)	<0.001	4.00(4.00,6.64)	7.75(4.00,18.80)	<0.001
IL-6	6.95(2.81,12.80)	10.90(7.34,35.70)	<0.001	8.33(3.22,13.00)	19.70(9.45,47.40)	<0.001
IL-10	4.00(4.00,4.26)	4.00(4.00,10.70)	0.004	4.00(4.00,5.11)	6.20(4.00,13.40)	<0.001
TNF-α	12.40(9.74,15.43)	15.20(13.35,21.20)	<0.001	13.05(10.40,15.73)	17.00(13.35,22.70)	<0.001
IL-2R	822.00 (633.75,999.25)	1016.00 (873.75,1433.00)	<0.001	886.50 (658.50,1035.50)	1149.00 (900.50,1681.00)	<0.001
Ph	7.43(7.41,7.45)	7.45(7.42,7.47)	0.017	7.43(7.41,7.46)	7.45(7.42,7.47)	0.042
lac	1.50(1.10,1.60)	1.68(1.40,2.24)	<0.001	1.50(1.20,1.70)	1.80(1.37,2.38)	0.002
Po2	103.39±33.20	66.06±30.82	<0.001	82.44(66.43,115.80)	62.80(50.37,76.54)	<0.001

(*Continued*)

Table 2 (Continued).

	Non-Severe (n=110)	Severe(n=81)	*P* value[a]	Survival(n=148)	Non-Survival (n=43)	*P* value[b]
pco2	35.76±5.72	32.78±6.28	<0.001	35.39(32.23,39.18)	31.00(26.88,36.38)	<0.001
HCO3-	23.20(20.95,25.35)	21.50(18.95,23.90)	0.001	22.83±3.28	20.72±4.64	0.002
PO2/FIO2	303.50 (258.00,396.50)	171.00 (141.35,208.00)	<0.001	280.35 (218.00,381.00)	171.00 (138.00,253.00)	<0.001
GLU	7.35(5.98,9.66)	9.20(7.55,13.57)	<0.001	7.67(6.30,10.08)	10.33(7.70,15.04)	<0.001

Notes: [a]*P* values indicate differences between non-severe and severe patients. [b]*P* values indicate differences between survival and non-survival patients. *P* <0.05 was considered statistically significant.

Abbreviations: Lac, lactic acid; PO2, arterial partial pressure of oxygen; PCO2, arterial carbon dioxide pressure; HCO3-, bicarbonate; PO2/FIO2, oxygen index; WBC, white blood cell count; RDW, red blood cell distribution width; PWD, platelet distribution width; Cr, serum creatinine; CRP, C-reactive protein; PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; FIB, fibrinogen; TT, thrombin time; ATA, antithrombin activity; PCT, procalcitonin; MYO, myoglobin; TNI, troponin-I; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Table 3 CT Images of Patients Infected with 2019-nCoV

	Non-Severe (n=110)	Severe(n=81)	*P* value[a]	Survival (n=148)	Non-Survival (n=43)	*P* value[b]
The whole infected volume	217.10 (106.28,424.70)	718.60 (306.70,1076.85)	<0.001	246.40 (117.05,587.70)	863.70 (486.70,1252.30)	<0.001
The infected region percentages	0.06(0.03,0.12)	0.23(0.10,0.41)	<0.001	0.07(0.03,0.19)	0.23(0.17,0.47)	<0.001
PGV	0.06(0.03,0.15)	0.05(0.02,0.17)	0.587	0.05(0.03,0.15)	0.06(0.03,0.18)	0.573
PCV	0.02(0.01,0.07)	0.01(0.00,0.06)	0.454	0.02(0.00,0.06)	0.03(0.01,0.07)	0.494
PAV	0.00(0.00,0.00)	0.00(0.00,0.00)	0.362	0.00(0.00,0.00)	0.00(0.00,0.00)	0.783
Left upper lobe infected region percentages	0.01(0.00,0.03)	0.01(0.00,0.04)	0.674	0.01(0.00,0.03)	0.01(0.00,0.06)	0.263
Left lower lobe infected region percentages	0.02(0.01,0.05)	0.02(0.01,0.06)	0.874	0.02(0.01,0.06)	0.03(0.01,0.06)	0.687
Right upper lobe infected region percentages	0.02(0.00,0.05)	0.01(0.00,0.05)	0.655	0.01(0.00,0.05)	0.01(0.00,0.06)	0.803
Right middle lobe infected region percentages	0.01(0.00,0.02)	0.00(0.00,0.02)	0.079	0.01(0.00,0.02)	0.00(0.00,0.02)	0.576
Right inferior lobe infected region percentages	0.04(0.02,0.08)	0.04(0.01,0.07)	0.463	0.04(0.01,0.08)	0.05(0.01,0.07)	0.913

Notes: [a]*P* values indicate differences between non-severe and severe patients. [b]*P* values indicate differences between survival and non-survival patients. *P* <0.05 was considered statistically significant.

Abbreviations: PGV, percentages of ground glass opacity volume; PCV, percentages of consolidation volume; PAV, percentages of atelectasis volume.

predominantly situated in the lower lobes of both lungs. GGO emerged as the most prevalent CT feature. Further details are provided in Table 3.

Severity of Illness Scores

All severity of illness scores, including CURB-65, SOFA, QSOFA, APACHE II, and PSI, demonstrated notably higher values in severe and non-survival cases ($P < 0.01$). Further information can be found in Supplementary Table 1.

Main Interventions

A higher proportion of severe and non-survival cases received respiratory support, such as high-flow nasal canula-(HFNC), noninvasive ventilation(NIV), and mechanical ventilation(MV), in accordance with individual clinical conditions ($P < 0.01$). Detailed insights can be found in Supplementary Table 2.

Risk Factors for Severity

The multivariate logistic analysis identified several independent high-risk factors associated with the severity of COVID-19 patients(Supplementary Table 3). These include neutrophils (OR = 1.529, 95% CI 1.131–2.068), urea nitrogen (OR = 1.587, 95% CI 1.222–2.062), SOFA score (OR = 3.333, 95% CI 1.476–7.522), QSOFA score (OR = 15.197, 95% CI 3.281–70.384), and PSI (OR = 1.053, 95% CI 1.018–1.090), along with the percentages of the infected region corresponding to CT values (OR = 548.221, 95% CI 2.615–114,953.586).

The ROC curves derived from the combination of clinical and laboratory characteristics with CT quantification are depicted in Figure 1. Notably, neutrophils exhibited an AUC of 0.712 (95% CI 0.635–0.788, sensitivity 58%, specificity 78.9%), while urea nitrogen demonstrated an AUC of 0.690 (95% CI 0.613–0.767, sensitivity 48.1%, specificity 87.2%). The SOFA score presented an AUC of 0.861 (95% CI 0.809–0.913, sensitivity 60.5%, specificity 93.6%), and QSOFA score displayed an AUC of 0.867 (95% CI 0.811–0.923, sensitivity 85.2%, specificity 85.3%). Additionally, PSI had an AUC of 0.883 (95% CI 0.836–0.930, sensitivity 82.7%, specificity 82.6%). The percentages of the infected region corresponding to CT values achieved an AUC of 0.808 (95% CI 0.742–0.874, sensitivity 70.4%, specificity 81.7%). Importantly, the combined prediction model demonstrated a high AUC of 0.985 (95% CI 0.974–0.997, sensitivity 95.1%, specificity 92.7%).Detailed insights can be found in Supplementary Table 4.

Risk Factors for in-Hospital Mortality

The multivariate logistic analysis identified several independent high-risk factors associated with in-hospital mortality in COVID-19 patients(Supplementary Table 5). These factors include MYO (OR = 1.003, 95% CI 1.001–1.005), APACHE II score (OR = 1.387, 95% CI 1.216–1.583), and the percentages of the infected region corresponding to CT values (OR = 113.897, 95% CI 4.939–2626.496). Conversely, prealbumin was determined to be an independent protective factor (OR = 0.965, 95% CI 0.947–0.984).

The ROC curves resulting from the combination of clinical and laboratory characteristics with CT quantification is revealed in Figure 2. Prealbumin yielded an AUC of 0.292 (95% CI 0.206–0.378, sensitivity 7.0%, specificity 61.5%). MYO exhibited an AUC of 0.747 (95% CI 0.660–0.834, sensitivity 51.2%, specificity 87.8%). APACHE II achieved an AUC of 0.869 (95% CI 0.812–0.926, sensitivity 81.4%, specificity 80.4%). The percentages of the infected region corresponding to CT values showed an AUC of 0.790 (95% CI: 0.711–0.869, sensitivity 81.4%, specificity 71.6%).

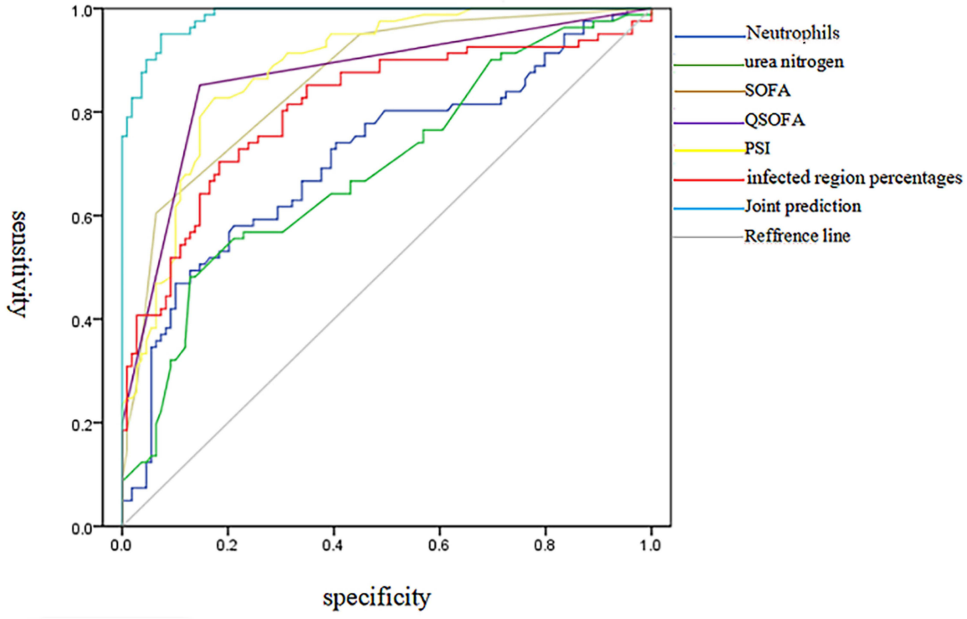

Figure 1 ROC Curve of Independent Influencing Factors Associated with Severity of COVID-19 Patients.

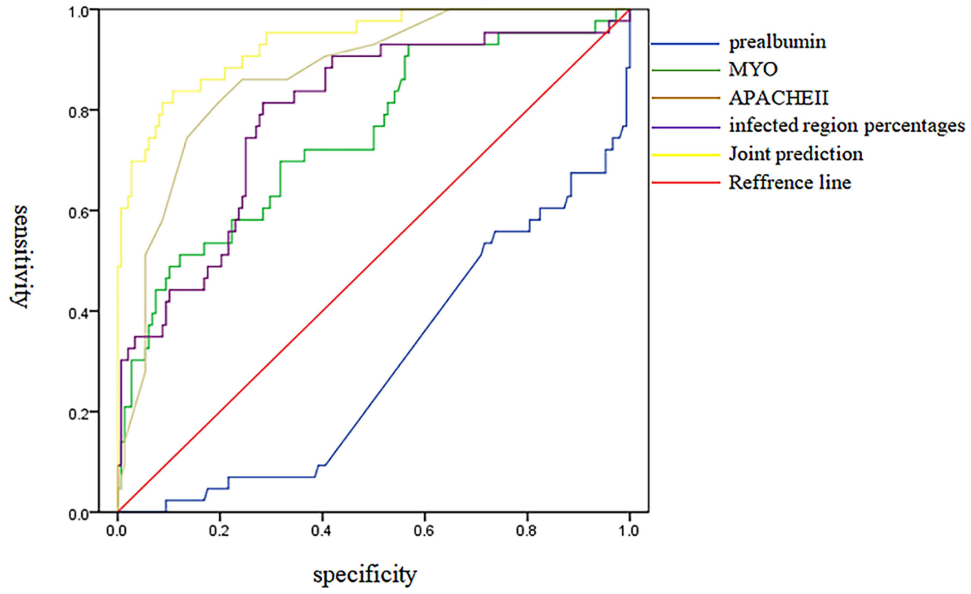

Figure 2 ROC Curve of Independent Influencing Factors Associated with Mortality of COVID-19 Patients.

Ultimately, the combined prediction model achieved an AUC of 0.935 (95% CI 0.894–0.976, sensitivity 83.7%, specificity 89.2%).Detailed insights can be found in Supplementary Table 6.

Discussion

In this retrospective study conducted at a single center, including 191 inpatient encounters with COVID-19, our findings underscore the significance of quantified CT imaging features, particularly the percentages of infected region corresponding to CT values, in predicting both the severity and in-hospital mortality associated with the disease. Notably, these predictive outcomes surpass the predictive utility of conventional clinical and laboratory indicators. Evaluating the extent of infection and the infected region's proportion within CT scans through quantitative methodologies has long posed a challenge for healthcare practitioners. Our study effectively demonstrates that the proportion of infected region bears a strong correlation with the severity and in-hospital mortality of COVID-19 patients. Furthermore, we employed artificial intelligence algorithms to quantify CT features of pneumonia lesions. This innovation enables a more precise assessment of disease severity and adverse prognosis in COVID-19 patients, thereby offering the potential to curtail hospital stays and reduce mortality rates.

The common CT findings in COVID-19 are bilateral and predominantly peripheral ground glass opacities.[13] Earlier research demonstrated that CT abnormalities showed peripheral and lower zone distribution with involvement on both sides. Pleural effusion was infrequent.[14,15] Our study reached a similar conclusion, finding that pneumonia lesions were mainly situated in the lower lobes of both lungs, and GGO were the most frequent CT feature. Another study indicated that changes in CT features between day 0 and day 4 had the highest accuracy in predicting severe illness. It proposed that dynamic trends in CT manifestation changes hold significant value in predicting unfavorable outcomes in COVID-19.[16] Unfortunately, due to the retrospective nature of this study, there were variations in the time patients reviewed CT scans, preventing us from analyzing CT feature changes to predict outcomes.

Elevated respiratory and heart rates were notable clinical characteristics of hypoxia and ARDS, which were major causes of death in severe COVID-19 patients. A prior study demonstrated that a respiratory rate of ≥ 24/min and a heart rate of ≥ 125/min were risk factors for death in univariate analysis, but their significance was lost in multivariate regression analysis. Our study yielded the same outcome. Given their ease of measurement, physicians need to utilize these vital signs to identify potentially severe patients.

Moreover, alterations in consciousness were a crucial clinical indicator reflecting disease severity. The overwhelming majority of patients encountered consciousness changes due to severe hypoxia, presenting as drowsiness, sluggish

responses, and even comatose states. Studies have unveiled the detrimental impact of viral infections on neurological functions, potentially leading to severe neurological impairments. Notably, coronaviruses, especially severe acute respiratory syndrome SARS-CoV-2, exhibit neurotropic properties and may induce neurological disorders. The current understanding is that coronaviruses, coupled with host immune responses, could transform these infections into persistent states contributing to neurological diseases. Early identification of neurological symptoms such as headaches, altered consciousness, and abnormal sensations, along with effective management of infection-related neurological complications, is pivotal in enhancing the prognosis of critically ill patients.[17]

Numerous studies have evidenced a higher prevalence of comorbidities among severe COVID-19 patients, encompassing cardiovascular diseases, hypertension, diabetes, COPD, malignancy, cerebrovascular diseases, and chronic kidney disease.[1,4,18,19] Based on data from 79,394 Chinese COVID-19 patients, the mortality rate for individuals aged >59 years was 0.6 to 5.1 times greater than those aged 30–59 years after symptom onset.[5] A meta-analysis revealed an elevated risk of severe disease, intensive care requirement, and mortality in COVID-19 patients aged >70 years.[20] Our findings substantiated that older patients with preexisting comorbidities, particularly those requiring respiratory support, faced notably reduced survival rates. Patients with chronic kidney disease exhibited a markedly diminished survival rate. However, age and chronic kidney disease did not emerge as independent factors associated with mortality in the multivariable analysis.

COVID-19's impact extends beyond pneumonia, affecting organs such as the heart, liver, kidneys, blood system, and immune system. Patients often succumb to multiple organ failure (MOF), shock, ARDS, heart failure, arrhythmias, or renal failure.[21] Our study also unveiled a striking observation: nearly all critically ill patients (98.77%) experienced sepsis. Among patients who encountered shock (100%), fatality was inevitable Furthermore, 72.09% of patients suffered co-infections involving multi-resistant bacteria such as Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and others.

In a retrospective study conducted at a single center involving 13,781 COVID-19 inpatient cases, it was established that co-infections with bacteria had a profound impact, increasing the likelihood of in-hospital mortality, ICU admission, and the need for mechanical ventilation. These findings underscore the significance of bacteria in the mortality associated with SARS-CoV-2.[22] An important question persists about how best to manage high-risk presentations of COVID-19 and potentially other respiratory viruses.

Despite targeted antimicrobial therapy being a key part of managing critically ill patients, a multi-omic study in 2022 comparing broncho-alveolar lavage samples from cases of influenza virus and COVID-19 co-infections indicated that beginning antimicrobial treatment during COVID-19 co-infection did not change lung inflammation. Notably, nearly all patients in the co-infected group and all patients in suspected co-infection groups received prompt antimicrobial treatment. These results imply that using antimicrobials alone may not be sufficient to prevent progression to severe disease and worse clinical outcomes in cases of COVID-19 bacterial co-infections.[23] Despite this, our study found that almost all patients received antibiotics. Clinicians might be concerned about co-infection with other pathogens. Nevertheless, for some mild cases, it is still worth considering whether this approach offers any benefits.

Severe COVID-19 infection is characterized by hyperinflammatory syndrome, cytokine storms, sepsis, and multiple organ dysfunction syndrome (MODS). Our study demonstrated significant associations between several laboratory factors and the severity and mortality of COVID-19. These laboratory parameters include: 1. changes in blood cell counts, such as increased leukocyte and neutrophil counts, neutrophil-to-lymphocyte ratio, RDW, and decreased lymphocyte counts; 2. increased levels of biochemical parameters like CRP, PCT, blood urea nitrogen, creatinine, MYO, TNI, and NT-proBNP; 3. changes in coagulation indicators like decreased platelet counts and fibrinogen degradation products, and increased D-dimer, PT, INR, TT, and ATA. Furthermore, severe COVID-19 patients showed lymphocytopenia, evidenced by low CD3+, CD4+, and CD8+ T-cell counts. This could result from direct viral cytopathic effects, cytokine effects including TNF-α, IL-6, and IL-10, and immune cell redistribution into lungs and lymphoid organs. Decreases in CD4+ and CD8+ T cells might also be due to lymphocyte consumption during the infection. Coagulation factors significantly correlate with disease severity or fatality. A high incidence of thromboembolic events was observed in deceased COVID-19 patients, possibly due to COVID-19-triggered coagulation disorders. Moreover, prolonged PT could relate to anticoagulants, coagulation factor deficiency, and fibrinolysis. In summary, monitoring the

mentioned laboratory changes will aid clinicians in enhancing treatment plans, preventing disease progression, and reducing the risk of COVID-19-related death.[24,25]

Nutrition was initially considered a protective factor against COVID-19. Assessing serum prealbumin levels stands as a highly valuable and effective strategy for predicting disease progression in critically ill patients, as well as those affected by chronic disorders and malnutrition. Reliable evidence has been published, indicating decreased serum prealbumin values in patients with COVID-19. The progressive decline of serum prealbumin values in COVID-19 is indicative of worsened clinical status.[26] Our study reinforced this by showing that serum prealbumin independently predicts poor outcomes in COVID-19.

Utilizing existing disease severity scores would greatly aid risk stratification and resource allocation during the COVID-19 pandemic. A single-center retrospective study from Wuhan Jin Yin-tan Hospital enrolled all hospitalized COVID-19 pneumonia patients. The AUC for CURB-65, PSI, and qSOFA in predicting in-hospital death were 0.85, 0.85, and 0.73, respectively.[27] Conversely, some studies questioned the suitability of qSOFA for identifying critically ill COVID-19 patients, citing that ventilated patients did not display distinct qSOFA values compared to those without ventilator support. It's important to note that this study only included 52 critically ill ICU patients with confirmed SARS-CoV-2 infection.[28] In our view, qSOFA, composed of mental status, respiratory rate, and blood pressure, has been proposed as a swift screening tool for infected patients. Each variable, according to univariate analysis in our study, can predict poor outcomes in COVID-19 patients. qSOFA's effectiveness has been verified across various sepsis patients. Its primary advantage lies in its simplicity and ease of obtaining variables, enabling rapid assessment of disease severity.

Our study had a relatively low proportion of critically ill patients requiring mechanical ventilation. This does not necessarily mean these patients lacked indications for mechanical ventilation. Traditional Chinese beliefs sometimes prioritize pain relief, leading to cases where patients may need ventilation but their families disagree.

Limitations

This study possesses several limitations. Firstly, its retrospective nature introduces potential biases in patient selection. Secondly, the sample size is relatively modest, necessitating further validation in a larger group. Furthermore, our study did not include a comprehensive array of disease severity scores, as the performance of A-DROP, CRB-65, SMART-COP, and NEWS2 remained unexplored. Lastly, due to incomplete information during medical record compilation, we omitted patients' vaccination status—a crucial factor for assessing disease severity based on vaccination history. Enhancements will be incorporated in subsequent research endeavors.

Conclusion

Comparative analysis revealed that deceased patients were significantly older compared to survivors. Similar trends were observed in severe vs non-severe groups. Complications were more prevalent in the severe and non-surviving groups. RDW was significantly higher in severe cases compared to non-severe cases.The entire infected volume and the percentages of the infected region quantified by using early-phase CT scans based artificial intelligence algorithms were apparently different between severe and non-severe patients.Similar results were noticed between survival and non-survival cases.All severity of illness scores demonstrated notably higher values in severe and non-survival cases.

Neutrophils, urea nitrogen, SOFA, QSOFA, PSI, and the percentages of infected lung regions based on CT values were independent high-risk factors for COVID-19 severity. MYO, APACHE II, and the infected region percentages were independent high-risk factors for in-hospital mortality. Prealbumin emerged as an independent protective factor.

Comparative analysis revealed that deceased patients were significantly older compared to survivors. The severe group exhibited higher rates of comorbidities, including cerebrovascular disease. Deceased patients were more likely to have CKD compared to survivors.

Abbreviations

ROC, receiver-operator-characteristics; AUC, area under the curve; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; qSOFA, quick Sequential Organ Failure Assessment; PSI, Pneumonia Severity Index; SARS-CoV-2, Coronavirus-2; COVID-19, Coronavirus disease 19; WHO, World Health

Organization; SaO2, arterial oxygen saturation; PaO2, partial pressure of arterial oxygen; FiO2, fraction of inspired oxygen; ROI, regions of interest; UI, United Imaging; HU, Hounsfield units; GGO, ground glass opacity; PGV, percentages of ground glass opacity volume; PCV, percentages of consolidation volume; PAV, percentages of atelectasis volume; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; RR, respiratory rate; HR, heart rate; Lac, lactic acid; PO2, arterial partial pressure of oxygen; PCO2, arterial carbon dioxide pressure; HCO3-, bicarbonate; PO2/FIO2, oxygen index; WBC, white blood cell count; RDW, red blood cell distribution width; PDW, platelet distribution width; Cr, serum creatinine; CRP, C-reactive protein; PT, prothrombin time; INR, PT-international normalized ratio; APTT, activated partial thromboplastin time; FIB, fibrinogen; TT, thrombin time; ATA, antithrombin activity; PCT, procalcitonin; MYO, myoglobin; TNI, troponin-I; NT-proBNP, N-terminal pro-B-type natriuretic peptide; HFNC, high-flow nasal canula; NIV, noninvasive ventilation; MV, mechanical ventilation; RRT, renal replacement therapy; ECMO, Extra-corporeal Membrane Oxygenation; MOF, multiple organ failure; MODS, multiple organ dysfunction syndrome.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval Statement

Jiawei Ye, Yingying Huang et al have submitted this research proposal entitled Association between artificial intelligence based chest computed tomography and clinical/laboratory characteristics with severity and mortality in COVID-19 hospitalized patients. The research subjects in this study were patients with COVID-19 who were admitted to Xinhua Hospital from December 15, 2022, to January 30, 2023. Based on clinical information of case data, image data, from patients in division of emergency,respiratory medicine and SICU, we proposed to retrospectively analyze 191 patients who were confirmed COVID-19. By analyzing the Chest computed tomography,clinical and laboratory characteristics we seek a method for early clinical prediction of high-risk patients. The case data used in this study were fully desensitized at the time of extraction to strictly protect patients' private information. The investigator has applied to the ethics committee for exemption from informed consent.As the study does not cause harm to the human body, and it dose not involve sensitive personal information or commercial interests, the exemption from informed consent has been approved. The ethics committee evaluated the design, implementation process, and protection of the rights and interests of the subjects. The researchers strictly followed the "Declaration of Helsinki", "International Ethical Guidelines for Research Involving Human Health" and other medical ethics standards, and fully respected the subjects' rights to know and privacy, and effectively protected the subjects' rights and well-being.This study was approved by the Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no potential conflicts of interest.

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