Hypertension Exacerbates Severity and Outcomes of COVID-19 in Elderly Patients: A Retrospective Observational Study

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[Abstract] Objective: To evaluate the impact of hypertension on the clinical outcome of COVID-19 patients aged 60 years old and older. **Methods:** This single-center retrospective cohort study enrolled consecutive COVID-19 patients aged 60 years old and older, who were admitted to Liyuan Hospital from January 1, 2020 to April 25, 2020. All included patients were divided into two groups: hypertension and nonhypertension group. The baseline demographic characteristics, laboratory test results, chest computed tomography (CT) images and clinical outcomes were collected and analyzed. The prognostic value of hypertension was determined using binary logistic regression. **Results:** Among the 232 patients included in the analysis, 105 (45.3%) patients had comorbid hypertension. Compared to the nonhypertension group, patients in the hypertension group had higher neutrophil-to-lymphocyte ratios, red cell distribution widths, lactate dehydrogenase, high-sensitivity C-reactive protein, D-dimer and severity of lung lesion, and lower lymphocyte counts (all $P<0.05$). Furthermore, the hypertension group had a higher proportion of intensive care unit admissions [24 (22.9%) *vs.* 14 (11.0%), $P=0.02$) and deaths [16 (15.2%) *vs.* 3 (2.4%), $P<0.001$] and a significantly lower probability of survival ($P<0.001$) than the nonhypertension group. Hypertension (OR: 4.540, 95% CI: 1.203–17.129, $P=0.026$) was independently correlated with all-cause in-hospital death in elderly patients with COVID-19. **Conclusion:** The elderly COVID-19 patients with hypertension tend to have worse conditions at baseline than those without hypertension. Hypertension may be an independent prognostic factor of poor clinical outcome in elderly COVID-19 patients.

Key words: COVID-19; SARS-CoV-2; hypertension; prognosis; mortality; risk factor

The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread across the world[1]. By March 23, 2021, the COVID-19 pandemic resulted in over 123 million confirmed cases and 2.7 million deaths worldwide[2]. Although most patients with COVID-19 had mild or no symptoms, some patients had acute respiratory distress syndrome and multiple organ failure, and even died during hospitalization[3–6].

Regardless of whether people of all ages are generally susceptible to COVID-19, patients with advanced age tend to be more critically ill, and have higher mortality[3–5, 7, 8]. A report[4] on 72 314 COVID-19 patients by the Chinese Centre for Disease Control and Prevention revealed that the majority of deaths occurred in patients aged 60 years old and older. Similarly, in Italy, COVID-19 deaths were mainly observed in elderly patients[8]. In addition, as one of the

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most common comorbidities in COVID-19 patients, hypertension was considered to be associated with severe conditions, and a contributor to poor clinical outcome[9, 10]. The prevalence of hypertension in COVID-19 patients in previous studies[3, 7, 11, 12] ranged within 15.0%–31.2%, and this is even higher in non-survivors[5, 6].

Considering that hypertension is associated with higher risks of adverse outcomes in COVID-19, it is reasonable to speculate that elderly COVID-19 patients with hypertension may have more severe illness and worse prognosis, when compared to those without hypertension. However, few studies have focused on this frail group. Thus, the present study aimed to evaluate the impact of hypertension on elderly patients with SARS-CoV-2 infection by describing and comparing the clinical characteristics and outcome of elderly COVID-19 patients with or without hypertension.

1 MATERIALS AND METHODS

1.1 Study Population and Data Collection

The present study was approved by the ethics committee of Liyuan Hospital (Ethics code: [2020] IEC A011), and was conducted in accordance with the Declaration of Helsinki. All data used in the study were anonymized, and the informed consent was waived. The dataset analyzed in the present study is available from the corresponding author on reasonable request. In the present single-centre retrospective cohort study, a total of 481 consecutive COVID-19 patients, who were admitted to Wuhan Liyuan Hospital from January 1, 2020 to April 25, 2020, were enrolled. This hospital was one of the hospitals designated by the Chinese government to hospitalize COVID-19 patients during the pandemic. All included patients were diagnosed with COVID-19 according to the Diagnosis and Treatment of Novel Coronavirus Pneumonia guidelines (6th edition) issued by the National Health Commission of China, and confirmed by reverse transcription polymerase chain reaction (RT-PCR).

The workflow for the inclusion, exclusion and grouping of patients is presented in fig. 1. The medical records were examined to obtain the medical history, laboratory results, length of hospital stay for COVID-19, and comorbidity. Chest computed tomography (CT) images were extracted from picture archives and communication systems. The diagnosis of hypertension was based on the documented medical history of hypertension, with a systolic blood pressure of ≥140 mmHg or a diastolic blood pressure of ≥90 mmHg[13]. Among the 232 patients ultimately enrolled in the study, 105 patients who met the diagnostic criterion were assigned in the hypertension group, while the remaining 127 patients were assigned to the nonhypertension group.

1.2 Chest CT Parameters and Evaluation

Chest CT scans were performed on the 16-MDCT scanner uCT 510 (United Imaging, China) using the single inspiratory phase. The CT images were acquired using the following parameters: tube voltage, 120 kVp; tube current, 326 mA; reconstruction matrix size, 512×512; slice thickness, 1.5 mm.

In order to comprehensively quantify and evaluate the severity of the lung lesion on the chest CT scans, the scoring criteria developed by Huang *et al*[14] was applied, which takes into account the extent of involvement and CT manifestations [ground-glass opacity (GGO), crazy-paving pattern and consolidation] of lung lesions, in order to effectively achieve the semi-quantification of lesions. This scoring system initially scores according to the extent of the GGO involvement in each lobe (0 denotes no involvement, 1 denotes <5% involvement, 2 denotes 5%–25% involvement, 3 denotes 26%–49% involvement, 4 denotes 50%–75% involvement, and 5 denotes >75% involvement[14]). On this basis, if a crazy-paving pattern appears in a lung lobe, the score for that lobe was increased by 1, and if consolidation appears in a lung lobe (regardless of whether there was a crazy-paving pattern), the score for that lobe was increased by 2. This gives a score of 0–7 for each lobe, and a total score of 0–35 for

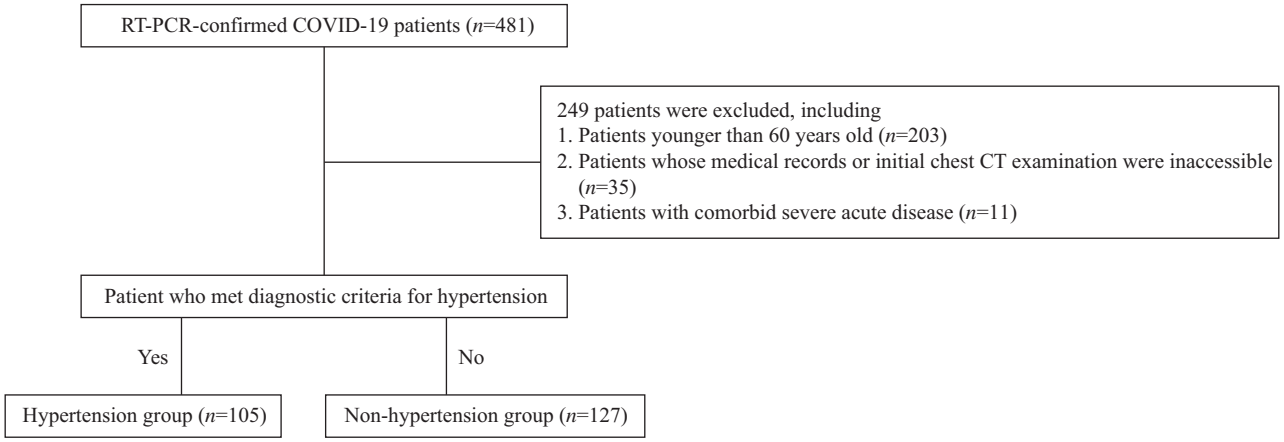

Fig. 1 Flowchart for patient inclusion, exclusion and grouping

the whole lung. The scoring of the chest CT scans was performed by two senior radiologists (X.X and H.Z, both have more than 10 years of experience in thoracic radiology). Disagreements were resolved by consensus. Fig. 2 presents two examples of chest CT images of COVID-19 patients.

1.3 Statistical Analysis

Continuous variables were presented in median and interquartile range (IQR). Categorical variables were presented in number and percentage. The Kolmogorov-Smirnov test was used to determine the normality. Chi-square test or Fisher exact test was used for categorical variables, and independent sample Student's *t*-test or Mann-Whitney test was used for continuous variables, as appropriate. The prognostic value of hypertension was determined using binary logistic regression. Variables with significant between-group differences at baseline were included in the univariate analysis, and these were selected as candidates for the multivariate analysis when $P<0.1$. The results were presented in odds ratio (OR) with 95% confidence interval (CI). The two-sided *P*-value of <0.05 was recognized as statistically significant. The statistical analyses were performed using SPSS software version 26 (IBM, USA).

2 RESULTS

2.1 Demographics and Basic Clinical Characteristics

The demographics and baseline clinical characteristics on hospital admission of patients are presented in table 1. The median age of the 232 elderly COVID-19 patients included in the present cohort was 69 (IQR, 64–78) years old, and 110 (47.4%) patients were male. There were no statistically significant differences in age ($P=0.89$) and gender ($P=0.84$) between the two groups. The most common symptoms at onset of the disease were fever (200 [86.2%]), cough (164 [7.7%]) and fatigue (96 [41.4%]). The median time interval from the onset of symptoms to hospital admission was seven (IQR, 3–13) days. The most common underlying comorbidities other than hypertension was diabetes (65 [28.0%]), followed by cardiovascular disease [26 (11.2%)], cerebrovascular disease [12 (5.2%)], chronic pulmonary disease [12 (5.2%)], chronic kidney disease [7 (3.0%)], chronic liver disease [4 (1.7%)] and malignancy [3 (1.3%)]. A total of 53 (22.8%) patients were current smokers.

The median hypertension duration of 105 patients in the hypertension group was nine (IQR, 6–14) years. Compared to the nonhypertension group, the hypertension group had significantly higher systolic pressure, diastolic pressure, pulse pressure and mean arterial pressure (all $P<0.001$). In addition, patients with hypertension had a higher prevalence of cerebrovascular disease [9 (8.6%) *vs.* 3 (2.4%), $P=0.034$].

2.2 Laboratory Findings

The laboratory test results collected on hospital admission for all patients in the hypertension group and nonhypertension group are presented in table 2. Overall, the hypertensive group had the worse laboratory test results. Compared to patients without hypertension, patients in the hypertension group had lower lymphocyte count (LC) [1.25 (IQR, 0.80–1.68) *vs.* 1.40 (IQR, 0.99–1.82), $P=0.031$], and higher neutrophil-to-

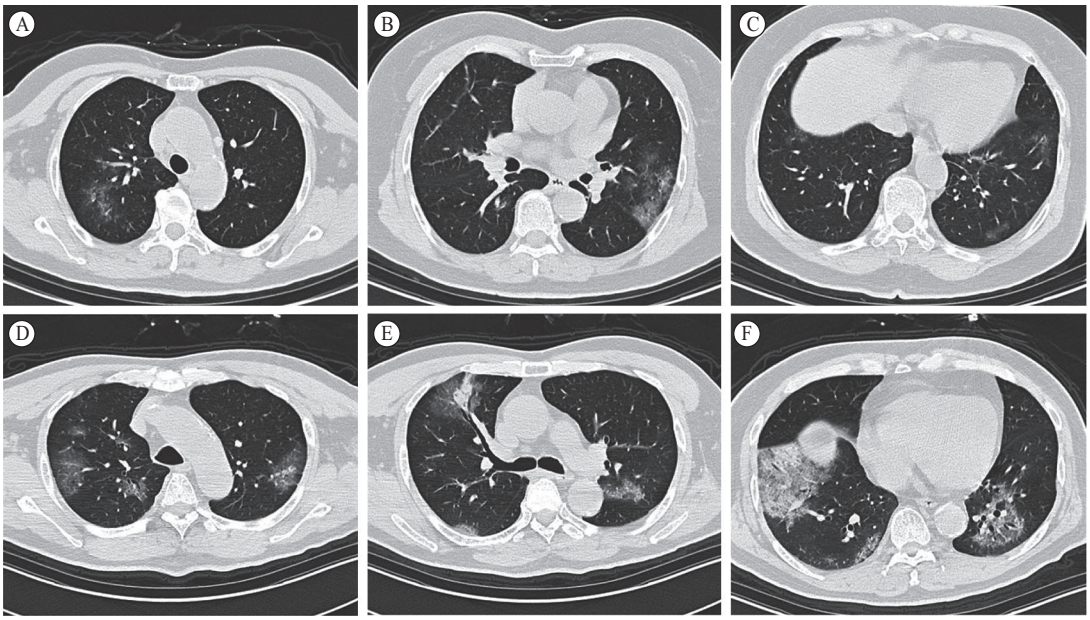

Fig. 2 Chest CT image of COVID-19 patients
A–C: Chest CT scan of a 76-year-old non-hypertensive woman, showing multiple patchy ground glass opacity with a total score of 9; D–F: Chest CT scan of a 61-year-old man with hypertension, showing multiple patchy ground glass opacity, crazy-paving pattern and consolidation in both lungs, with a total score of 16

Table 1 Demographics and basic clinical characteristics

	All patients (*n*=232)	Patients with hypertension (*n*=105)	Patients without hypertension (*n*=127)	*P*-value
Age, years	69 (64–78)	69 (65–78)	70 (64–78)	0.887
Gender				
Male	110 (47.4)	49 (46.7)	61 (48.0)	0.836
Female	122 (52.6)	56 (53.3)	66 (52.0)	–
Blood pressure, mmHg				
Systolic pressure	132 (122–140)	140 (132–150)	125 (119–132)	<0.001
Diastolic pressure	76 (70–84)	83 (77–90)	71 (68–77)	<0.001
Pulse pressure	54 (49–61)	58 (50–68)	51 (48–57)	<0.001
Mean arterial pressure	94 (88–102)	103 (96–109)	89 (86–94)	<0.001
Hypertension duration, years	–	9 (6–14)	–	–
Heart rate, beats/min	76 (67–84)	75 (64–85)	76 (68–81)	0.415
Respiratory rate, rate/min	20 (18–22)	20 (18–22)	20 (19–21)	0.458
Length of onset of symptom to hospitalization, days	7 (3–13)	7 (4–12)	7 (3–14)	0.408
Length of hospital stay, days	14 (10–20)	14 (9–18)	15 (10–22)	0.060
Current smoker	53 (22.8)	26 (24.8)	27 (21.3)	0.527
Signs and symptoms				
Fever	200 (86.2)	88 (83.8)	112 (88.0)	0.336
Cough	164 (70.7)	78 (61.2)	86 (65.3)	0.274
Fatigue	96 (41.4)	49 (38.6)	47 (37.0)	0.137
Myalgia	45 (19.4)	23 (18.1)	22 (17.3)	0.380
Dyspnea	32 (13.8)	13 (10.2)	19 (15.0)	0.571
Chest tightness	32 (13.8)	17 (13.4)	15 (11.8)	0.336
Chest pain	13 (5.6)	4 (3.1)	9 (7.1)	0.280
Headache	11 (4.7)	6 (4.7)	5 (3.9)	0.746
Dizziness	6 (2.6)	4 (3.1)	2 (1.6)	0.514
Comorbidities other than hypertension				
Diabetes	65 (28.0)	31 (29.5)	34 (26.8)	0.642
Cardiovascular disease	26 (11.2)	16 (15.2)	10 (7.9)	0.077
Cerebrovascular disease	12 (5.2)	9 (8.6)	3 (2.4)	0.034
Chronic pulmonary disease	12 (5.2)	7 (6.7)	5 (3.9)	0.350
Chronic kidney disease	7 (3.0)	3 (2.9)	4 (3.1)	1.000
Chronic liver disease	4 (1.7)	2 (1.9)	2 (1.6)	1.000
Malignancy	3 (1.3)	1 (1.0)	2 (1.6)	1.000
ICU admission	38 (16.3)	24 (22.9)	14 (11.0)	0.015
Death	19 (8.2)	16 (15.2)	3 (2.4)	<0.001

Variables are presented as *n* (%) or median (interquartile range).

lymphocyte ratio (NLR) [3.19 (IQR, 2.01–6.41) *vs.* 2.58 (IQR, 1.71–4.14), *P*=0.009), red cell distribution width (RDW) [12.5 (IQR, 11.9–13.1) *vs.* 12.0 (IQR, 11.7–12.6), *P*=0.002), lactate dehydrogenase (LDH) [224.0 (IQR, 168.5–265.2) *vs.* 186.4 (158.9–228.0), *P*<0.001], high-sensitivity C-reactive protein (hs-CRP) [4.5 (IQR, 2.8–6.4) *vs.* 3.7 (IQR, 1.2–6.2), *P*=0.026], and D-dimer [0.47 (IQR, 0.28–1.50) *vs.* 0.43 (IQR, 0.27–0.63), *P*=0.041] (table 2).

2.3 Chest CT Features and Scores

The chest CT features, including the extent and distribution of lesion involvement and predominant radiologic pattern, and scores for each lobe and the whole lung, are presented in table 3. The lung involvement, location and predominant CT pattern of pulmonary lesions were comparable between the hypertension and non-hypertension groups. The majority [212 (91.4%)] of patients had bilateral involvement lesions. More than half [132 (56.9%)] of the patients had peripheral lung lesions, followed by 86 (37.1%) patients with lesions located both in the central and peripheral areas of lungs. The most frequent lesion pattern was GGO [133 (57.3%)]. The other predominant CT patterns consisted of crazy-paving pattern [32 (13.8%)] and consolidation [25 (1.8%)]. A total of 42 (18.1%) patients had mixed pattern lesions.

As shown in table 3, the median chest CT scores for the right middle lobe [2 (IQR, 1–3) *vs.* 1 (IQR, 1–2), *P*=0.037], right lung [7 (IQR, 4–10) *vs.* 5 (IQR, 2–9), *P*=0.024], left upper lobe [2 (IQR, 1–4) *vs.* 1 (IQR, 1–2), *P*=0.001], left lung [5 (IQR, 3–8) *vs.* 4 (IQR, 2–6), *P*=0.008], and whole lung [11 (IQR, 7–18) *vs.* 9 (IQR, 5–14), *P*=0.009] were higher in the hypertension group than in the nonhypertension group (table 3).

2.4 Clinical Outcomes

The median length of hospital stay of the 232 elderly COVID-19 patients was 14 (IQR, 10–20) days. During hospitalization, a total of 38 (16.3%) patients

Table 2 Laboratory findings

Variables	Normal range	All patients (*n*=232)	Patients with hypertension (*n*=105)	Patients without hypertension (*n*=127)	*P*-value
WBC ($\times10^9$/L)	3.50–9.50	5.77 (4.45–7.62)	6.13 (4.52–8.49)	5.40 (4.38–7.22)	0.075
NC ($\times10^9$/L)	1.80–6.30	3.88 (2.76–5.36)	4.34 (2.77–5.78)	3.70 (2.76–4.80)	0.093
LC ($\times10^9$/L)	1.10–3.20	1.32 (0.93–1.77)	1.25 (0.80–1.68)	1.40 (0.99–1.82)	0.031
MC ($\times10^9$/L)	0.10–0.60	0.36 (0.25–0.48)	0.34 (0.24–0.49)	0.37 (0.26–0.48)	0.678
PC ($\times10^9$/L)	125–350	182 (140–217)	183 (135–233)	181 (140–212)	0.836
Hemoglobin (g/L)	115–150	138 (125–153)	137 (122–153)	139 (127–154)	0.327
NLR		2.77 (1.83–4.67)	3.19 (2.01–6.41)	2.58 (1.71–4.14)	0.009
LMR		133.24 (94.53–191.71)	138.52 (98.61–218.83)	125.20 (91.22–168.70)	0.078
PLR		3.91 (2.50–5.30)	3.32 (2.30–5.03)	4.09 (2.68–5.35)	0.096
RDW (%)	0–14.9	12.2 (11.7–12.8)	12.5 (11.9–13.1)	12.0 (11.7–12.6)	0.002
PDW (fl)	9.0–17.0	16.3 (16.0–16.6)	16.4 (16.1–16.7)	16.3 (16.0–16.5)	0.084
ALT (U/L)	7.0–40.0	19.3 (12.6–31.4)	18.1 (12.9–29.8)	20.9 (12.2–34.6)	0.477
AST (U/L)	13.0–35.0	25.5 (18.8–35.8)	25.0 (18.9–37.9)	25.8 (18.6–35.8)	0.923
Albumin (g/L)	40.0–55.0	38.6 (35.2–42.8)	37.6 (35.1–42.3)	39.2 (35.6–43.3)	0.325
Creatinine (μmol/L)	47.0–73.0	62.3 (52.5–74.3)	63.1 (50.3–85.2)	61.5 (53.2–70.6)	0.181
GFR (mL/min/1.73 m^2)		95.3 (83.2–110.0)	94.3 (76.2–109.3)	95.8 (84.1–112.3)	0.394
Potassium (mmol/L)	3.50–5.30	3.90 (3.61–4.15)	3.86 (3.55–4.18)	3.90 (3.65–4.14)	0.320
Sodium (mmol/L)	137.0–147.0	139.2 (136.6–140.8)	138.6 (135.9–140.6)	139.5 (137.5–140.9)	0.106
Calcium (mmol/L)	2.11–2.52	2.11 (1.98–2.20)	2.09 (1.94–2.22)	2.12 (2.02–2.20)	0.223
LDH (U/L)	120.0–250.0	198.9 (163.6–247.3)	224.0 (168.5–265.2)	186.4 (158.9–228.0)	<0.001
HbA1c (%)	3.8–5.8	5.2 (4.5–6.4)	5.3 (4.7–6.5)	5.0 (4.3–6.4)	0.078
Myoglobin (ng/mL)	0–58.0	40.3 (30.0–74.6)	41.6 (29.6–102.2)	40.3 (30.6–69.8)	0.629
CK-MB (ng/mL)	0–3.61	2.01 (1.19–3.53)	2.03 (1.19–3.58)	1.98 (1.17–3.34)	0.867
BNP (pg/mL)	0–125	76 (36–169)	80 (37–202)	73 (34–146)	0.304
hs-CRP (mg/L)	0–6.0	4.1 (1.7–6.3)	4.5 (2.8–6.4)	3.7 (1.2–6.2)	0.026
ESR (mm/h)	0–20	30 (18–72)	31 (19–72)	28 (17–70)	0.650
PCT (ng/mL)	0–0.25	0.04 (0.02–0.19)	0.04 (0.02–0.20)	0.04 (0.02–0.18)	0.968
D-dimer (mg/L)	0–0.55	0.44 (0.27–0.91)	0.47 (0.28–1.50)	0.43 (0.27–0.63)	0.041
INR	0.94–1.30	0.96 (0.92–1.01)	0.98 (0.93–1.02)	0.96 (0.91–1.01)	0.102

Variables are presented as median (interquartile range). WBC: white blood cell count; NC: neutrophil count; LC: lymphocyte count; MC: monocyte count; PC: platelet count; NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; PLR: platelet-to-lymphocyte ratio; RDW: red cell distribution width; PDW: platelet distribution width; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GFR: glomerular filtration rate; LDH: lactate dehydrogenase; HbA1c: hemoglobin A1c; CK-MB: creatine kinase MB isoenzyme; BNP: brain natriuretic peptide; hs-CRP: high-sensitivity C-reactive protein; ESR: erythrocyte sedimentation rate; PCT: procalcitonin; INR: international normalized ratio

Table 3 Chest CT findings and scores

	All patients (*n*=232)	Patients with hypertension (*n*=105)	Patients without hypertension (*n*=127)	*P*-value
Lung involvement, *n* (%)				
Unilateral	20 (8.6)	9 (8.6)	11 (8.7)	0.981
Bilateral	212 (91.4)	96 (91.4)	116 (91.3)	–
Location, *n* (%)				
Central	14 (6.0)	5 (4.8)	9 (7.1)	0.459
Peripheral	132 (56.9)	63 (60)	69 (54.3)	0.385
Both central and peripheral	86 (37.1)	37 (35.2)	49 (38.6)	0.600
Predominant CT pattern, *n* (%)				
Ground glass opacity	133 (57.3)	55 (52.4)	78 (61.4)	0.166
Crazy-paving pattern	32 (13.8)	14 (13.3)	18 (14.2)	0.853
Consolidation	25 (10.8)	13 (12.4)	12 (9.4)	0.473
Mixed pattern	42 (18.1)	23 (21.9)	19 (15)	0.172
Chest CT score				
Right upper lobe	2 (1–3)	2 (1–4)	2 (1–2)	0.170
Right middle lobe	1 (1–3)	2 (1–3)	1 (1–2)	0.037
Right lower lobe	3 (1–5)	3 (1–5)	2 (1–4)	0.205
Right lung	6 (3–9)	7 (4–10)	5 (3–8)	0.024
Left upper lobe	1 (1–3)	2 (1–4)	1 (1–2)	0.001
Left lower lobe	3 (1–5)	3 (1–5)	3 (1–5)	0.258
Left lung	4 (2–7)	5 (3–8)	4 (2–6)	0.008
Whole lung	10 (6–15)	11 (7–18)	9 (5–14)	0.009

Variables are presented as *n* (%) or median (interquartile range).

were admitted to the intensive care unit (ICU), and 19 (8.2%) patients died from COVID-19. Compared to the nonhypertension group, the hypertension group had a higher proportion of ICU admission [24 (22.9%) *vs.* 14 (11.0%), *P*=0.015] and a higher mortality [16 (15.2%) *vs.* 3 (2.4%), *P*<0.001] (table 1).

As shown in table 4, hypertension (OR: 4.540, 95% CI: 1.203–17.129, *P*=0.026), D-dimer (OR: 3.957, 95% CI: 1.181–13.261, *P*=0.026) and the CT score (OR: 3.327, 95% CI: 1.142–9.690, *P*=0.028) were the only variables associated with in-hospital death in elderly COVID-19 patients in the binary logistic regression.

3 DISCUSSION

The present study demonstrated the adverse effect of hypertension on elderly COVID-19 patients by comparing the clinical data, laboratory findings, chest CT features and clinical outcomes between elderly patients with SARS-CoV-2 infection with and without hypertension. Compared to elderly COVID-19 patients without hypertension, patients with hypertension had the worse baseline laboratory test results and more severe lesions on the chest CT on hospital admission. In addition, patients with comorbid hypertension had a higher risk of ICU admission and in-hospital death, when compared to those without hypertension. Hence, hypertension is independently associated with in-hospital death in elderly patients with COVID-19.

Previous researches[15–20] have documented that comorbid hypertension can exacerbate COVID-19 in all age patients, and the present study further evaluated its impact on elderly patients. Hypertension had a more pronounced effect on in-hospital death in the present study, when compared to previous studies that focused on patients of all ages[17, 18, 21]. The investigators considered that this might be attributed to the older age of the present cohort. This suggests that older adults with COVID-19 are more vulnerable to be negatively affected by comorbid hypertension, when compared to younger individuals. This age-related susceptibility to poor outcome in COVID-19 patients may be mediated by the more extensive cellular senescence in the elderly, which is associated with the decline in immune, respiratory and vascular function[22]. This leads to poor adaptation and difficulty in maintaining homeostasis in the elderly in the face of SARS-CoV-2 infection. Unfortunately, the present results suggest that the comorbid hypertension further exacerbates this problem.

The prevalence of hypertension (45.3%) was higher in the present study, when compared to that in the previous studies[3, 7, 11, 12], which is reasonable, given that a nationwide survey[13] revealed that the prevalence of hypertension in a Chinese population aged ≥55 years old ranged approximately within 42.4%–46.9%. The mechanisms underlying the interconnections between comorbid hypertension and more severe COVID-19 remain to be elucidated.

The cellular entry of SARS-CoV-2 depends on its recognition of angiotensin-converting enzyme 2 (ACE2), and leads to the activation of T cell proliferation and differentiation into Th1 cells[23], which secretes proinflammatory cytokines and eventually triggers immune hyperresponsiveness, and this is referred to as a "cytokine storm"[24]. There is substantial evidence that human circulating T cells are activated in hypertension, and inflammation has been considered to have a significant role in the promotion and maintenance of hypertension[25, 26]. Overactivated circulating T cells in pre-existing hypertension may amplify the cytokine storm of COVID-19, and thereby exacerbate the condition. The present study revealed that elderly patients with hypertension had significantly higher NLRs, indicating their overall inflammatory status[27]. In addition, the levels of LDH, hs-CRP and D-dimer were higher in the hypertension group, which usually increase after the onset of inflammation, cell damage, or tissue injury, and this may be associated with the more serious tissue damage led by the cytokine storm magnified by hypertension.

Another possible explanation for the correlation between severe COVID-19 and hypertension is that the end-organ damage from chronic hypertension may have led to some degree of immune dysfunction in the elderly[26, 28, 29]. Similar to previous findings[16, 17], the

Table 4 Binary logistic regression analysis

Variables	Univariate analysis		Multivariate Analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
LC <1.1×10^9/L	1.395 (0.537–3.620)	0.494		
NLR	1.797 (0.681–4.740)	0.236		
RDW	0.822 (0.318–2.124)	0.685		
LDH >250 U/L	4.148 (1.590–10.820)	0.004	1.707 (0.582–5.005)	0.330
hs-CRP >6.0 mg/L	1.559 (0.585–4.153)	0.374		
D-dimer >0.55 mg/L	6.361 (2.040–19.838)	0.001	3.957 (1.181–13.261)	0.026
CT score	5.308 (1.986–14.187)	0.001	3.327 (1.142–9.690)	0.028
Hypertension	7.431 (2.102–26.27)	0.002	4.540 (1.203–17.129)	0.026
Cerebrovascular disease	2.160 (0.442–10.550)	0.341		

LC: lymphocyte count; NLR: neutrophil-to-lymphocyte ratio; RDW: red cell distribution width; LDH: lactate dehydrogenase; HbA1c: hemoglobin A1c

LC of patients in the hypertension group in the present study was significantly lower, when compared to that in the nonhypertension group, suggesting that immune cell depletion and immune system dysregulation were more severe in the elderly in the hypertension group. In addition, the higher chest CT score in the hypertension group denotes the further involvement of lung infection. This also indirectly supports the notion that hypertensive elderly patients are more likely to develop immune dysfunction.

Notably, higher levels of baseline RDW were observed in the hypertension group, which has rarely been mentioned in previous studies. RDW is reflective of the inflammation, and is regarded as a robust predictor of mortality in critically ill patients[30]. Recent studies have revealed that RDW is a predictive factor for severity in COVID-19 patients[31, 32]. This corroborates with the worse baseline condition of elderly COVID-19 patients with hypertension in the present study.

Since elderly hypertensive patients suffering from COVID-19 may be more severely ill at baseline and more likely to have a worse prognosis, when compared to younger individuals, such patients may require more intense clinical care. Ran *et al*[33] reported that poor blood control during hospitalization is associated with higher risks of adverse outcomes for COVID-19. Thus, maintaining normal and stable blood pressure during hospitalization may contribute to a favourable prognosis in elderly COVID-19 patients with comorbid hypertension. The early initiation of clinical intervention in the initial stages of the disease may be also helpful to improve the prognosis and shorten the time to disease resolution[14].

There were some limitations worth noting in the present study. First, the present study had a single-centre design, and the present cohort had a relatively small sample size and low mortality, especially those in the nonhypertension group, in which there were only three cases of death. Hence, it is important to note that the sample size was small, and that the evidence presented in the present study may have been underpowered. Multicentre studies with a larger sample size are worth implementing to validate the present conclusion. Second, the collected medication history of patients was insufficient, and the hypertensive patients were not sub-classified according to whether they used angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, in order to explore the impact on elderly hypertensive COVID-19 patients.

In conclusion, the present retrospective observational study revealed that elderly COVID-19 patients with hypertension are prone to having more severe illness at baseline and a worse clinical outcome during hospitalization, when compared to those without hypertension. Hypertension may be regarded as one of the risk factors for mortality among elderly COVID-19 patients. This alerts the healthcare system that this frail population needs more medical attention.

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Conflict of Interest Statement

The authors declare that they have no conflicts of interest to this work.

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