Clinical characteristics and prognostic factors in elderly patients with COVID-19

Qin Cheng
Peking University Third Hospital  https://orcid.org/0000-0002-2107-7248

Yixuan Liao
Beijing Hospital

Yujing Lin
Peking University Third Hospital

Liyuan Tao
Peking University Third Hospital

He Wang
Beijing Hospital

Mohan Li
Beijing Hospital

Qinggang Ge
Peking University Third Hospital

Yanming Li
Beijing Hospital

Ning Shen (✉️ shenning1972@126.com)

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Abstract

**Background:** The COVID-19 pandemic poses tremendous threats to the world. Elderly patients are among the high-risk population, and apt to experience worse outcomes.

**Methods:** Elderly patients (age ≥ 60 years old) were enrolled from January 28 to February 29, 2020, in Tongji Hospital, one of designated COVID-19 medical centers in Wuhan, China.

A retrospective study was performed to describe clinical characteristics, laboratory findings, chest imaging, treatment, and outcomes of elderly COVID-19 patients. COX regression was used to analyze predictors for 28-day mortality. Linear regression models were constructed to analyze factors associated with length of hospital stay (LOS).

**RESULT:** A total of 186 elderly patients (aged 70.4 ± 7.1 years, 95 males (51.6%)) were enrolled, 120 patients (64.5%) were severe or critical type, and mortality rate was 16.1% (30/186). Of 156 survived patients, 150 were discharged. Fever (83.3%), cough (80.6%) and dyspnea (68.3%) were the most frequent symptoms. Common comorbidities included hypertension (48.9%) and diabetes (32.8%). Ground-glass opacities (97.3%) and peripheral distribution (59.1%) were the most predominant patterns on chest imaging. Patients in non-survival group had a higher smoking rate, more symptoms of dyspnea, lab results indicative of poorer health, and needed more medications or supportive treatment. Age (HR 1.128, 95% CI 1.066-1.194), lymphocyte count (HR 0.261, 95% CI 0.073-0.930), LDH (HR 1.003, 95% CI 1.002-1.005), procalcitonin (HR 1.061, 95% CI 1.002-1.125), and qSOFA (HR 3.162, 95% CI 1.646-6.072) were predictors of independently associated with 28-day mortality. CURB-65 plus LDH on admission were strong predictors of death by ROC analysis (AUROC=0.891). Among surviving patients, consolidation on CTs (β=8.611), elevated ferritin level (β=0.004) and neutrophil count (β=0.806) were associated with increased LOS.

**Conclusion:** High incidence of comorbidities and mortality were observed in elderly patients. Decreased lymphocyte, older age, higher qSOFA score, procalcitonin and LDH levels were associated with 28-day mortality independent factors associated with death, and CURB-65 plus LDH could bewere a strong predictive model of deathfatal outcome. Consolidation on CTs, elevated ferritin and neutrophil level correlated with increased LOS. Further prospective studies should be performed to test our findings and for explore potential treatments.

**Background**

In December 2019, a previously unknown kind of pneumonia, emerged and outbroke in Wuhan, China. It was soon confirmed to be an acute respiratory infectious disease and named “novel coronavirus disease 2019 (COVID-19)” by World Health Organization (WHO). COVID-19 was highly contagious and had caused a global pandemic. According to data from WHO, by May 21, 2020, the disease had spread to 216 countries or regions, and nearly 5 million cases had been diagnosed worldwide, with more than 300,000 deaths.
The novel coronavirus is believed to have zoonotic origins and close genetic characteristics to those of the severe acute respiratory syndrome coronavirus (SARS-Cov). To facilitate research and communication, WHO and the International Committee on Taxonomy of Viruses adopted the official name SARS-CoV-2. The main manifestations of COVID-19 include fever and dry cough, some patients also experience dyspnea and hypoxemia. Severe cases may quickly progress to acute respiratory distress syndrome (ARDS), septic shock, multi-organ failure, and even death[1].

Elderly patients are among the high-risk group and are apt to experience worse outcomes. According to epidemiological data from China[2], most deaths occurred in patients over age 60 with underlying diseases, such as hypertension, cardiovascular disease, and diabetes. According to a few descriptive studies[3, 4], elderly patients tend to have more comorbidities compared with the younger group. There was a higher proportion of severe cases and complications like ARDS, cardiac injury, or acute kidney injury, which required close monitoring and treatment. A recent study from Wuhan[5] showed that comorbidities including cardiovascular disease, chronic obstructive pulmonary disease (COPD) were predictive of a fatal outcome.

This retrospective study aimed to describe the clinical and treatment courses of elderly COVID-19 patients and explore predictors associated with 28-day mortality and length of hospital stay (LOS).

Methods

Study design and participants

Tongji Hospital, one of the largest comprehensive medical centers in Wuhan, was designated as a specific hospital for COVID-19 patients, especially severe patients, during the outbreak. Isolation wards were managed by supporting medical teams from across China under coordination by the government, due to insufficient medical resources.

In this retrospective study, patients were recruited from six isolation wards of Tongji Hospital, which were managed by medical teams from Peking University Third Hospital, Beijing Hospital and their colleagues. From January 28, to February 29, 2020, all consecutive patients over age 60 and confirmed to have COVID-19 were enrolled. According to “the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)” by the National Health Commission of China[1], confirmed cases must have one of the following virologic or serological evidences: positive SARS-Cov-2 nucleic acid by real-time fluorescent RT-PCR or positive serum specific IgM and IgG antibodies of SARS-Cov-2. The severity of COVID-19 was classified according to the guidelines as follows: (1) mild type: clinical symptoms were mild without pneumonia, (2) moderate type: fever and other symptoms presented, with pneumonia on chest computed tomography (CT), (3) severe type: any of the following criteria was met: respiratory rate ≥ 30 per minute, oxygen saturation (SpO₂) ≤ 93% on room air at rest, arterial partial pressure of oxygen (PaO₂)/FiO₂ ratio ≤ 300mmHg, (4) critical type: any of the following conditions presented: respiratory
failure that required mechanical ventilation, septic shock or other organ failure that required ICU monitoring.

Data collection

Data were collected from electronic medical records by a trained team of physicians. The parameters consisted of demographic, clinical characteristics, comorbidities, laboratory tests, radiological findings, treatment, and outcome. Comorbidities were mainly determined by past medical history, but diabetes was also confirmed by hemoglobin A1c (HbA1c) ≥ 6.5%. Chronic respiratory diseases (CRD) were confirmed not only by history of chronic obstructive pulmonary disease (COPD), chronic bronchitis, bronchiectasis, and asthma, but also by existence of bilateral emphysema or bullae on chest CTs. Laboratory tests consisted of blood routine, biochemistry, coagulation, cardiac markers, infection-related indexes, and cytokines. Chest CTs were evaluated by two pulmonary specialists separately. The results were described as the number of lobes infiltrated, the distribution pattern (peripheral, random, or diffuse) and characteristics of pulmonary lesions (ground-glass opacities, consolidation, patchy shadow, and pleural effusion). CURB-65 (short for assessment of consciousness, serum urea nitrogen, respiratory rate, blood pressure, and age ≥ 65 years) and qSOFA (quick Sequential Organ Failure Assessment) were assessed on admission to quickly evaluate severity of disease. Activities of daily living (ADL) were assessed by Barthel Index score on admission for describing functional abilities[6]. Medications, such as antivirals, antibiotics, and corticosteroids, and advanced supportive procedures, such as mechanical ventilation, were recorded.

Outcome

Follow-up continued for the hospitalized patients until April 4, 2020. The primary measured outcome was survival or death after 28 days. The secondary outcome was LOS until discharge or endpoint of the study (a study flow diagram is shown in Supplement 1). According to the Chinese guidelines[1], patients could be discharged when symptoms improved significantly, with obvious absorption of infiltrates on chest imaging and negative results for at least two consecutive tests of SARS-CoV-2 nucleic acids.

Statistical analysis

Continuous variables were expressed as mean ± SD or median (IQR) with or without normal distribution. Categorical variables were reported as frequencies, and percentages. The independent sample T test or the Mann-Whitney Test were used for comparison between continuous data, and the chi-square test was used for comparison between categorical data. Univariate and multivariate Cox regression analysis, and ROC analysis were used to analyze risk factors of 28-day mortality. Spearman correlation test and multivariate linear regression were used to analyze factors associated with LOS. A two-sided p < 0.05 was considered statistically significant, and IBM SPSS Statistics (version 22.0) was used for all data analyses.

Results
Demographic data and clinical characteristics

186 elderly patients with confirmed COVID-19 were enrolled in the study, 64.5% were classified as severe or critical type on admission (shown in Table 1). The mean age was 70.4 ± 7.1 years old, and 95 patients (51.6%) were male. The mortality rate of patients over age 75 was much higher than that of patients aged 60-74 (28.9% vs 12.1%). Lower respiratory rates and higher S\textsubscript{p}O\textsubscript{2} levels were found among survivors, but peak temperatures were similar between the two groups. Fever (83.3%), cough (80.6%), dyspnea (68.3%) and fatigue (57.0%) were the most frequent symptoms among older adults, while dyspnea was the only symptom associated with death (93.3% vs 53.2%). Common comorbidities included hypertension (48.9%), diabetes (32.8%), chronic respiratory disease (19.4%), and coronary heart disease (16.7%). Non-survivors tended to have more comorbidities, without significant differences. More patients in non-survival group had a smoking history (30% vs 14.1%). ADL score in non-survival group was lower than survivors (58.8 ± 27.4 vs 78.6 ± 21.7). CURB-65 and qSOFA scores were higher in non-survivors.

Laboratory findings and chest imaging

On admission, lymphocytopenia (count <1.0 × 10\textsuperscript{9}/L) was found in 58.9% of patients. As shown in Table 2, significantly higher neutrophil count or lower lymphocyte levels were found among non-survivors. Concerning infection-related indexes, high-sensitivity C-reactive protein (hsCRP, 95.2 vs 28.3 mg/L), procalcitonin (PCT, 0.21 vs 0.05 ug/L), or ferritin (1514.1 vs 622.6 ug/L) and cytokines, such as IL-2R and IL-6, were significantly elevated in non-survivors. Lower levels of albumin (31.4 vs 33.0 g/L) and elevated levels of aspartate aminotransferase (AST, 44 vs 27 U/L), lactate dehydrogenase (LDH, 473 vs 275 U/L), and blood urea nitrogen (BUN, 8.0 vs 4.4 mmol/L) were observed in non-survival group. Coagulation abnormalities, such as prolonged prothrombin time (PT, 14.9 vs 14.1 s) and elevated D-dimer levels (2.72 vs 1.16 ug/ml), were more severe among non-survivors. Levels of cardiac markers, such as high-sensitivity Troponin I (hsTnI, 16.1 vs 5.3 pg/ml) and N-terminal pro-brain natriuretic peptide (NT-proBNP, 616 vs 224 pg/ml), were higher in non-survival group, but only slightly exceeded the normal range. All \( p \) values above were < 0.05.

Most elderly patients had bilateral and multi-lobular involvement, with the median affected lobes reaching to five. Ground-glass opacities were predominant lesions (97.3%, 181/186), while patchy shadows and consolidations were seen in 75.8% and 48.4% patients. Peripheral distribution was prevalent in both groups, diffuse distribution was more frequent among non-survivors (36.7% vs 22.4%, \( p = 0.098 \)). Pleural effusions were seen in 11.3% patients.

Treatments and outcomes

As shown in Table 1, 172 (92.5%) patients received antiviral treatment, which included umifenovir, oseltamivir, lopinavir-ritonavir, and other medications. No significant differences were observed for antivirals between two groups. Significantly higher proportions of patients received antibiotics (100% vs 78.2%) and systemic corticosteroids (90% vs 31.4%) in non-survival group. More non-survival patients
required advanced supportive treatment, such as high-flow nasal cannula (36.7% vs 3.2%), non-invasive ventilation (73.3% vs 5.8%), or invasive mechanical ventilation (56.7% vs 0.6%).

The time from symptom onset to admission in non-survivors was shorter than survivors (13 vs 11 days, \( p = 0.039 \)). 30 (16.1%) patients died after 28-day follow-up. Three cases progressed from moderate to severe, while 26 cases progressed from severe to critical, indicating a deterioration rate of 24.8% (26/105) in the severe-type patients. Followed up to the endpoint, 150 patients were cured and discharged, while six patients stayed in hospital. One case was still intubated. The LOS was 30.0±13.1 days for survived patients and only 12.9 ± 7.0 days for non-survivors.

Prognostic factors of fatal outcomes in elderly patients

Univariate COX analysis was used to analyze risk factors associated with 28-day mortality. Older age (HR 1.083), decreased \( S_pO_2 \) (HR 0.947), or increased respiratory rate (HR 1.086) on admission and the symptom of dyspnea (HR 6.819) correlated with an increased likelihood of death. Comorbidities were not predictive of fatal outcomes, but the presence of smoking history was associated with death (HR 2.378). Decreased lymphocyte (HR 0.139) and elevated infection-related indexes, such as WBC, neutrophil, hsCRP, procalcitonin, ferritin, and cytokines, were predictive of death. As for other laboratory tests, decreased albumin, elevated LDH, BUN or D-Dimer, and prolonged PT were associated with an increased risk of death. CURB-65 (HR 3.525) and qSOFA (HR 4.262) were strong predictors of poor outcomes. All \( p \) values above were < 0.05, details were shown in Table 3.

In the multivariate COX regression, age (HR 1.128, 95% CI 1.066-1.194), lymphocyte count (HR 0.261, 0.073-0.930), LDH (HR 1.003, 1.002-1.005), procalcitonin (HR 1.061, 1.002-1.125), and qSOFA (HR 3.162, 1.646-6.072) were independent risk factors associated with 28-day mortality. According to ROC analysis, the cut-off value of PCT and qSOFA were 0.09 ug/ml and 0.5 scores, which having little clinical significance. The optimal cut-off of LDH, CURB-65 and lymphocyte count were 360.5U/L, 1 score and 0.665×10⁹/L, with the AUROC being 0.838, 0.775, 0.720, respectively. Combined indexes of CURB-65, LDH or lymphocyte count were used to obtain a more accurate prognostic value. CURB-65 combined with LDH (86.7% sensitivity, 78.9% specificity) was a stronger predictor of 28-day mortality than other markers (AUROC = 0.891), shown in Figure 1 and Supplement 2, 3.

Predictive factors for the LOS in elderly patients

150 patients (96.2%) were discharged at the endpoint of the study, and predictors associated with LOS were analyzed among the surviving 156 patients. Analysis by the Spearman correlation test, age, gender, main symptoms, and comorbidities had little correlation with LOS (\( p > 0.05 \)). On admission, severity classification of disease (\( r = 0.334 \)) and \( S_pO_2 \) (\( r = -0.296 \)) were associated with the LOS. LDH, hsCRP, neutrophil count and ferritin were positive correlated with the LOS (shown in Figure 2), while lymphocyte count was negative correlated. On chest imaging, more affected lobes (\( r = 0.270 \)), diffuse distribution (\( r = 0.205 \)) and existence of consolidation (\( r = 0.396 \)) increased the LOS. Use of antivirals or steroids, and
advanced supportive treatment was associated with an increased LOS, shown in Supplement 4. All \( p \) values above were < 0.05.

Parameters correlated with the LOS (\( r > 0.2 \) or \(-0.2, p < 0.05\)) were entered into backward stepwise linear regression analysis, which were shown in Supplement 4 and 5. Medications and supportive therapy were excluded because the model was of predictive purpose. In the multivariate linear regression, the existence of consolidation on CTs (\( \beta = 8.611 \)), elevated ferritin levels (\( \beta = 0.004 \)) and neutrophil count (\( \beta = 0.806 \)) were associated with an increased LOS.

**Discussion**

In this study, patients were enrolled consecutively from January 28th to February 29th, which was an intense period of the epidemic in Wuhan, and was relatively representative of the similar situations many countries now faced with. We found a high incidence of comorbidities and mortality, and a high proportion of severe/critical cases in the elderly COVID-19 patients. Compared with survivors, patients in the non-survival group had a higher smoking rate, more symptoms of dyspnea, lab results indicative of poorer health, higher CURB65 and qSOFA scores, and needed more medications or supportive treatment. Risk factors of 28-day mortality included increased age, qSOFA, LDH, and PCT, and a decreased lymphocyte count. CURB-65 combined with LDH was a stronger predictor of death. Consolidation on CT, higher ferritin and neutrophil count correlated with an increased LOS.

According to a nationwide epidemiological data of whole population, 18.5% of confirmed COVID-19 patients in China were classified as severe/critical type, with a crude fatality rate of 2.3%. The fatality rate increased with age[2]. Patients in Hubei have poorer prognosis compared with those outside Hubei (severe event rate was 23.0% vs 11.1%, and mortality rate was 7.3% vs 0.3%).[7] In this study, among elderly COVID-19 patients, 64.5% were classified as severe or critical type, and the mortality rate was 16.1%, which is higher than previous studies. This is not only owing to the characteristics of elderly patients, but also to the fact that Tongji hospital was designated as the center for severe COVID-19 patients in Wuhan. Common symptoms of COVID-19 in elderly patients included fever, cough, dyspnea and fatigue, which were consistent with those of other viral pneumonias. The symptom of dyspnea with an increased respiratory rate and a decreased \( S_pO_2 \) level were significantly prevalent in non-survival group, indicating a poor prognosis. 75.3% patients had at least one comorbidity, which is a higher rate than that of COVID-19 patients overall[7–10]. 32.8% of patients were diagnosed with diabetes in this study, which is higher than that in previous data[3, 5]. Most studies acquired diabetes information from the past medical history, which may underestimate of its actual prevalence in COVID-19 patients. The ADL scores in non-survival group were lower with mean value less than 60, indicating that these patients could not fulfill daily activities and relied highly on caregivers. It has been reported that time from symptom onset to hospitalization was an independent risk factor for prognosis[7]. In this study, the time from illness onset to admission in non-survival group was slightly shorter than that of the survival group. So increase in mortality due to delayed diagnosis and treatment was not considered. The time before admission was longer than that in other large studies[7], but was similar with local research reports in
Wuhan[5], which can be attributed to the severe epidemic situation and relatively limited medical resources during this period.

Previous studies have found that patients with COVID-19 were often associated with decreased lymphocyte count and increased inflammatory indicators [8, 11]. In COVID-19 patients with severe and fatal diseases, biomarkers of inflammation, cardiac and muscle injury, liver function, kidney function and coagulation function were significantly elevated, and IL-6, IL-10, and ferritin were strong predictors for severe disease[12]. In this study, decreased lymphocyte and elevated inflammatory indicators (WBC, neutrophil, hsCRP, ferritin, PCT, IL-2R, and IL-6) occurred more often among non-survivors, while changes in other lab parameters, such as hypoalbuminemia, myocardial injury (hsTnI, NT-proBNP, LDH), liver injury (AST, LDH), acute kidney injury (BUN, creatinine) and coagulopathy (PT, D-Dimer), indicated increased likelihood of multi-organ dysfunction or failure in non-survival group. Increased inflammatory parameters indicated a hyperinflammatory state, which was susceptible to systemic inflammatory syndrome (SIRS) or sepsis. LDH, ferritin, IL-2R, and IL-6 were all significantly elevated in non-survival group, indicating the presence of cytokine storm syndrome[13].

Li et al. reported [14] that incidences of consolidation, crazy-paving patterns, and bronchial wall thickening in severe/critical patients were significantly higher than those in the moderate patients. Another study showed that the median CT score of the mortality group was higher compared with that of the survival group, with higher frequencies of consolidation and air bronchogram[15]. In this study, chest imaging of elderly patients was multi-lobular and mainly peripherally distributed, and lesions were characterized by GGO, patchy shadows, and consolidation. Pleural effusion was relatively uncommon.

In this study, 92.5% of patients received antiviral drugs, with no significant difference between survival and death groups. A higher proportion of patients received antibiotics, systemic corticosteroids, and advanced supportive procedures in non-survival group. This may be due to poor therapeutic response, the critical conditions of these patients, and subsequent bacterial infections. Death occurred 12.9 ± 7.0 days after admission, with a longer survival period than that of similar studies from an earlier period[5], which might be related to the active use of respiratory support and medications. Elderly patients tended to complain less about discomforts or hypoxemia and waited a longer time before hospitalization. Timely and active treatment were important among those patients.

At present, few studies have discussed the prognosis of elderly COVID-19 patients. This study found that increased age, LDH, PCT levels, and qSOFA scores and reduced lymphocyte were predictors of death. Even among the older adults, age was still a risk factor of death. Mortality rate was higher in older patients (≥ 75 years) than those aged 60 to 74. LDH exists in the heart, liver, skeletal muscle, and red blood cells, and increased LDH level indicates damage of these tissue or cells. On other hand, LDH is also an inflammatory biomarker and, combined with other factors like ferritin, may be strong discriminators for severe COVID-19 or ARDS[12, 13]. PCT was usually regarded as an indicator of bacterial infection. Viral pneumonia patients had poorer outcomes (death, ventilation, ICU admission, LOS and costs) with bacteria co-infection[16]. qSOFA only requires a few parameters and vital signs, which makes it easy to
operate in isolation wards. From the analysis of a single-center study, the prognostic performance of qSOFA for in-hospital mortality and ICU admission was similar with those of CURB-65 and PSI (pneumonia severity index) in community-acquired pneumonia (CAP)[17]. Based on autopsies, immune systems of COVID-19 patients were damaged, with the spleen and lymph nodes shrinking, lymphocyte decreasing, and necrosis occurring remarkably[1]. Studies have shown that the reduced in COVID-19 were mainly T lymphocyte[18] and speculated that coronavirus acts directly on ACE2 receptors of lymphocyte to cause damage[19], or through virus-mediated lymphocyte apoptosis by activating inflammatory responses, similar with SARS[20]. Immune system was weakened in patients with severe lymphocytopenia, they were apt to suffer secondary infection and poor prognosis[21]. The optimal cut-off value of PCT or qSOFA had little clinical significance by ROC analysis, making neither of these two indexes ideal indicators of death. The areas under the ROC for LDH, CURB-65 and lymphocyte count were all higher than 0.7, and LDH was the highest of the single factor index in predicting death. CURB-65 was another useful assessment in predicting 30-day mortality of CAP, it contained five parameters and was easy to operate. But its predictive value in viral pneumonia were relatively low[16]. CURB-65 plus LDH might be a strong predictive index of 28-day mortality in elderly COVID-19 patients, with 86.7% sensitivity and 78.9% specificity.

In this study, consolidation of chest CTs, increased ferritin level and neutrophil count were predictors of the LOS. As mentioned above, consolidation on CTs, ferritin, and neutrophil were all associated with severity of diseases[12–14]. Severe patients usually needed more advanced treatment and longer recovery times, which were the main reasons for prolonged hospital stay. On the other hand, consolidation indicated filling of airspace on CTs, which was related to hypoxemia and sometimes required treatment with steroids. Patients with elevated ferritin or neutrophil might have uncontrolled underlying inflammation, which should better be monitored in hospital.

**Limitations**

There were several limitations of the study. First, data might be incomplete due to its retrospective design. Second, it was a single-center study, and Tongji hospital was a designated center mainly for severe COVID-19 patients in Wuhan. Selected bias would be inevitable. Third, this study only studied baseline data and did not conduct further dynamic analysis along with disease change.

**Conclusion**

High incidence of comorbidities and high mortality rates were seen in elderly COVID-19 patients. Decreased lymphocyte, increased age, qSOFA score, PCT and LDH levels were associated with 28-day mortality, and CURB-65 plus LDH were strong predictive of death. Existence of consolidation on CTs, and elevated ferritin level and neutrophil count on admission correlated with increased LOS. Further prospective, well-controlled studies should be performed to find optimal treatments.

**Abbreviations**
LOS: Length of hospital stay.

BMI: body mass index, RR: respiratory rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, SpO₂: pulse oxygen saturation, CRD: chronic respiratory diseases, CHD: coronary heart disease, ADL: ability score in daily life.

CURB-65: short for assessment of consciousness, serum urea nitrogen, respiratory rate, blood pressure, and age 65 or older, qSOFA: quick Sequential Organ Failure Assessment.

HFNC: High-flow nasal cannula oxygen, NIV: Non-invasive ventilation, IMV: Invasive mechanical ventilation.

WBC: count of white blood cell, ALT: alanine aminotransferase, AST: aspartate aminotransferase, TBil: total bilirubin, LDH: lactate dehydrogenase, BUN, blood urea nitrogen, hsCRP, high sensitivity C-reactive protein, IL-2R: interleukin-2 receptor, IL-6: interleukin-6, hsTNI: high sensitivity Troponin I, NT-proBNP: N-terminal pro brain natriuretic peptide, PT: prothrombin time, APTT: Activated partial thromboplastin time, IL-2R: interleukin-2 receptor, IL-6: interleukin-6.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Peking University Third Hospital (IRB00006761-M2020060), and written informed consent was waived because of its retrospective design.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used for the current study are available from the corresponding authors upon reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions
NS and YmL contributed to the conception and design of the study. QC contributed to the design of the study, data acquisition, analysis, and interpretation of the results. YxL contributed to the design of the study, analysis, and interpretation. YjL contributed to the design of the study, data acquisition, and interpretation. LT contributed to statistical analysis of the study. HW and ML contributed to data acquisition and analysis. QG contributed to the design of the study. All authors read and approved the final manuscript.

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References

1. National Health Commission of P.R.China. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7). Mar 4 2020.

2. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145–51.

3. Lian J, Jin X, Hao S, Cai H, Zhang S, Zheng L, et al. Analysis of Epidemiological and Clinical features in older patients with Corona Virus Disease 2019 (COVID-19) out of Wuhan. Clin Infect Dis. 2020.

4. Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. J Infect. 2020.

5. Wang L, He W, Yu X, Hu D, Bao M, Liu H, et al. Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up. J Infect. 2020.

6. Granger CV, Albrecht GL, Hamilton BB. Outcome of comprehensive medical rehabilitation: measurement by PULSES profile and the Barthel Index. Arch Phys Med Rehabil. 1979;60(4):145–54.

7. Liang WH, Guan WJ, Li CC, Li YM, Liang HR, Zhao Y, et al. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China. Eur Respir J. 2020.

8. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.

9. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507–13.

10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497–506.
11. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020.

12. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020.

13. Henderson LA, Canna SW, Schulert GS, Volpi S, Lee PY, Kernan KF, et al. On the alert for cytokine storm: Immunopathology in COVID-19. Arthritis Rheumatol. 2020.

14. Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, et al. The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia. Invest Radiol. 2020.

15. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PLoS One. 2020;15(3):e0230548.

16. Guo L, Wei D, Zhang X, Wu Y, Li Q, Zhou M, et al. Clinical Features Predicting Mortality Risk in Patients With Viral Pneumonia: The MuLBSTA Score. Front Microbiol. 2019;10:2752.

17. Tokioka F, Okamoto H, Yamazaki A, Itou A, Ishida T. The prognostic performance of qSOFA for community-acquired pneumonia. J Intensive Care. 2018;6:46.

18. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020.

19. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci. 2020;12(1):8.

20. He L, Ding Y, Zhang Q, Che X, He Y, Shen H, et al. Expression of elevated levels of pro-inflammatory cytokines in SARS-CoV-infected ACE2 + cells in SARS patients: relation to the acute lung injury and pathogenesis of SARS. J Pathol. 2006;210(3):288–97.

21. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther. 2020;5:33.

**Tables**

Table 1. Demographic and clinical characteristics of elderly COVID-19 patients
|                                | Total (n=186) | Survivors (n=156) | Non-Survivors (n=30) | P value |
|--------------------------------|--------------|------------------|----------------------|--------|
| **Age, years old**            |              |                  |                      |        |
| 60-74 yrs. n (%)              | 70.4±7.1     | 69.8±6.4         | 73.9±9.4             | 0.028* |
| ≥75 yrs.                      | 141(75.8)    | 124(79.5)        | 17(56.7)             | 0.008* |
| **Gender, Male, n (%)**       |              |                  |                      |        |
|                               | 96(51.6)     | 76(48.7)         | 20(66.7)             | 0.072  |
| **BMI, kg/m²**                | 23.5(22.0, 25.3) | 23.4(21.8, 25.2) | 23.8(23.0, 25.8)     | 0.292  |
| **Vital signs on admission**  |              |                  |                      |        |
| Heart rate, per minute        | 92±16        | 91±16            | 97±18                | 0.056  |
| SBP, mmHg                     | 136±20       | 137±19           | 132±26               | 0.362  |
| DBP, mmHg                     | 81±13        | 82±12            | 81±17                | 0.734  |
| RR, per minute                | 21(20, 24)   | 20(20, 23)       | 25(21, 30)           | <0.001*|
| **SpO₂, %**                   | 94(90, 97)   | 95(92, 98)       | 82(76, 91)           | <0.001*|
| **Peak temperature, °C**      | 38.5±0.7     | 38.5±0.7         | 38.6±0.7             | 0.923  |
| **Symptoms, n (%)**           |              |                  |                      |        |
| Fever                         | 155(83.3)    | 128(82.1)        | 27(90.0)             | 0.422  |
| Cough                         | 150(80.6)    | 123(78.8)        | 27(90.0)             | 0.244  |
| Dyspnea                       | 127(68.3)    | 99(53.2)         | 28(93.3)             | 0.003* |
| Fatigue                       | 106(57.0)    | 89(57.1)         | 17(56.7)             | 0.969  |
| Poor appetite                  | 87(46.8)     | 71(45.5)         | 16(53.3)             | 0.432  |
| Expectoration                 | 103(55.4)    | 83(53.2)         | 20(66.7)             | 0.247  |
| **Diarrhea**                  | 73(39.2)     | 61(39.1)         | 12(40.0)             | 0.927  |
| Myalgia                       | 71(38.2)     | 61(39.1)         | 10(33.3)             | 0.551  |
| Nausea or vomiting            | 54(29.0)     | 45(38.8)         | 9(30.0)              | 0.899  |
| Headache                      | 44(23.7)     | 38(24.4)         | 6(20.0)              | 0.607  |
| **Comorbidities, n (%)**      |              |                  |                      |        |
| **Hypertension**              | 91(48.9)     | 75(48.1)         | 16(53.3)             | 0.598  |
| **Diabetes mellitus**         | 61(32.8)     | 48(30.8)         | 13(43.3)             | 0.179  |
| **CRD**                       | 36(19.4)     | 29(18.6)         | 7(23.3)              | 0.547  |
| **CHD**                       | 31(16.7)     | 26(16.7)         | 5(16.7)              | 1.000  |
| **Smoking history**           | 31(16.7)     | 22(14.1)         | 9(30.0)              | 0.032* |
| **Severity of disease, n (%)**|              |                  |                      |        |
| **Moderate**                  | 66(35.5)     | 66(42.3)         | 0(0)                 | <0.001*|
| **Severe**                    | 105(56.4)    | 85(54.5)         | 20(66.7)             |        |
| **Critical**                  | 15(8.1)      | 5(3.2)           | 10(33.3)             |        |
| **ADL score**                 | 75.4±23.8    | 78.6±21.7        | 58.8±27.4            | 0.001* |
| **CURB-65**                   | 1.20±0.83    | 1.04±0.70        | 2.03±0.93            | <0.001*|
| **qSOFA**                     | 0.52±0.58    | 0.43±0.53        | 1.00±0.59            | <0.001*|
| **Treatments, n (%)**         |              |                  |                      |        |
| **Medications**               |              |                  |                      |        |
| Antiviral treatment           | 172(92.5)    | 142(91.0)        | 30(100)              | 0.180  |
| Umifenovir                    | 135(72.6)    | 111(71.2)        | 24(80)               | 0.320  |
| Oseltamivir                   | 77(41.4)     | 69(44.2)         | 8(26.8)              | 0.074  |
| Lopinavir-Ritonavir           | 41(22.0)     | 37(23.7)         | 4(13.3)              | 0.310  |
| Antibiotics                   | 152(81.7)    | 122(78.2)        | 30(100)              | 0.010* |
| Corticosteroids               | 76(40.9)     | 49(31.4)         | 27(90)               | <0.001*|
| **Supportive treatment,**     |              |                  |                      |        |
| HFNC                          | 16(8.6)      | 5(3.2)           | 11(36.7)             | <0.001*|
| NIV                           | 31(16.7)     | 9(5.8)           | 22(73.3)             | <0.001*|
| IMV                           | 18(9.7)      | 1(0.6)           | 17(56.7)             | <0.001*|
| **Time from illness onset to admission,** | 12(9.16) | 13(9.16) | 11(7.13,3) | 0.039* |
|                          | 27.3±13.8 | 30.0±13.1 | 12.9±7.0 | <0.001* |
|--------------------------|-----------|-----------|----------|---------|
| **LOS, days**            |           |           |          |         |
| **Time from illness onset to death or discharge, days** | 40.6±14.6 | 43.8±13.2 | 23.9±9.5 | <0.001* |

* p<0.05. BMI: body mass index, RR: respiratory rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, SpO₂: pulse oxygen saturation, CRD: chronic respiratory diseases, CHD: coronary heart disease, ADL: ability score in daily life, CURB-65: short for assessment of consciousness, serum urea nitrogen, respiratory rate, blood pressure, and age 65 or older, qSOFA: quick Sequential Organ Failure Assessment. HFNC: High-flow nasal cannula oxygen, NIV: Non-invasive ventilation, IMV: Invasive mechanical ventilation, LOS: Length of hospital stay.

Table 2. Laboratory finding and chest imaging of elderly COVID-19 patients
|                          | Total (n=186) | Survivors (n=156) | Non-Survivors (n=30) | P value |
|--------------------------|--------------|-------------------|----------------------|---------|
| **Blood routine**        |              |                   |                      |         |
| WBC, 10^9/L              | 5.8(4.6, 7.9)| 5.6(4.5, 7.1)     | 9.3(5.4, 12.1)       | <0.001* |
| Neutrophil count, 10^9/L | 4.3(3.2, 6.2)| 4.0(3.1, 5.4)     | 8.0(4.2, 10.6)       | <0.001* |
| Lymphocyte count, 10^9/L | 0.93±0.44    | 0.99±0.44         | 0.66±0.36            | <0.001* |
| Platelet count, 10^9/L   | 227±92       | 232±89            | 201±107              | 0.053   |
| **Hemoglobin, g/L**      | 124(114, 136)| 122(114, 133)     | 137(119, 147)        | 0.004*  |
| **Biochemical results**  |              |                   |                      |         |
| ALT, U/L                 | 23(15, 40)   | 24(14, 39)        | 23(19, 46)           | 0.183   |
| AST, U/L                 | 29(20, 42)   | 27(19, 40)        | 44(36, 63)           | <0.001* |
| Albumin, g/L             | 32.5(30.1, 35.5)| 33.0(30.3, 36.0)| 31.4(28.3, 33.8)     | 0.005*  |
| TBil, umol/L             | 10.0(7.4, 14.1)| 9.9(7.3, 14.2)   | 10.8(8.1, 14.7)      | 0.490   |
| LDH, U/L                 | 286(234, 394)| 275(227, 342)     | 473(365, 628)        | <0.001* |
| BUN, mmol/L              | 4.6(3.4, 6.5)| 4.4(3.4, 5.8)     | 8.0(5.5, 11.1)       | <0.001* |
| Creatinine, umol/L       | 70(58, 87)   | 69(58, 84)        | 84(67, 104)          | 0.003*  |
| **Infection-related indexes** |              |                   |                      |         |
| hsCRP, mg/L              | 38.8(8.8, 82.4)| 28.3(6.9, 67.2)| 95.2(50.9, 170.3)    | <0.001* |
| Procalcitonin, ug/L      | 0.06(0.03, 0.14)| 0.05(0.03, 0.09)| 0.21(0.10, 0.74)     | <0.001* |
| Ferritin, ug/L           | 680.4(418.7, 1278.3)| 622.6(362.8, 1146.0)| 1514.1(874.3, 2113.8)| <0.001* |
| IL-2R, U/ml              | 740.0(468.0, 1171.5)| 676.0(443.0, 1036.5)| 1189.5(843.0, 1534.5)| <0.001* |
| IL-6, pg/ml              | 17.3(5.8, 46.1)| 15.3(4.5, 39.2)   | 64.1(16.7, 125.5)    | <0.001* |
| Cardiac markers          |              |                   |                      |         |
| hsTNI, pg/ml             | 6.0(3.6, 14.1)| 5.3(3.12, 9.9)    | 16.1(6.4, 75.2)      | <0.001* |
| NT-proBNP, pg/ml         | 251(126, 588)| 224(112, 428)     | 616(227, 1513)       | <0.001* |
| **Coagulation factors**  |              |                   |                      |         |
| PT, seconds              | 14.1(13.6, 14.8)| 14.1(13.5, 14.6)| 14.9(14.2, 15.8)     | <0.001* |
| APTT, seconds            | 40.9±6.0     | 40.7±5.9          | 41.9±6.9             | 0.324   |
| Fibrinogen, g/L          | 5.24±1.45    | 5.19±1.37         | 5.50±1.79            | 0.274   |
| D-dimer, ug/ml           | 1.32(0.66, 2.62)| 1.16(0.61, 2.05)| 2.72(1.69, 16.58)    | <0.001* |
| **Chest imaging, n (%)** |              |                   |                      |         |
| Number of affected lobes | 5(5, 5)      | 5(5, 5)           | 5(5, 5)              | 0.181   |
| Distribution of infiltrate |            |                   |                      |         |
| Peripheral               | 110(59.1)    | 93(59.6)          | 17(56.7)             | 0.763   |
| Random                   | 30(16.1)     | 28(17.9)          | 2(6.7)               | 0.205   |
| Diffuse                  | 46(24.7)     | 35(22.4)          | 11(36.7)             | 0.098   |
| Ground-glass opacity     | 181(97.3)    | 151(96.8)         | 30(100)              | 0.706   |
| Consolidation            | 90(48.4)     | 74(47.4)          | 16(53.3)             | 0.554   |
| Patchy shadow            | 141(75.8)    | 121(77.6)         | 20(66.7)             | 0.202   |
| Pleural effusion         | 21(11.3)     | 19(12.2)          | 2(6.7)               | 0.576   |

*p<0.05. WBC: count of white blood cell, ALT: alanine aminotransferase, AST: aspartate aminotransferase, TBil: total bilirubin, LDH: lactate dehydrogenase, BUN, blood urea nitrogen, hsCRP, high sensitivity C-reactive protein, IL-2R:
interleukin-2 receptor, IL-6: interleukin-6, hsTNI: high sensitivity Troponin I, NT-proBNP: N-terminal pro brain natriuretic peptide, PT: prothrombin time, APTT: Activated partial thromboplastin time.

Table 3. Univariate and multivariate COX analysis of factors associated with 28-day mortality

|                               | Univariate COX analysis | Multivariate COX analysis Δ |
|-------------------------------|-------------------------|----------------------------|
|                               | HR 95%CI P value        | HR 95%CI P value           |
| Age                           | 1.083 1.032-1.136 0.001* | 1.128 1.066-1.194 <0.001*  |
| Gender                        | 0.514 0.241-1.099 0.086 |                           |
| S_{\text{P}}O_{2}, \%         | 0.947 0.932-0.963 <0.001* |                           |
| Respiratory rate              | 1.086 1.040-1.134 <0.001* |                           |
| Initial Symptom               |                         |                            |
| Fever                         | 1.861 0.565-6.137 0.307 |                           |
| Cough                         | 2.114 0.641-6.968 0.219 |                           |
| Dyspnea                       | 6.819 1.624-28.625 0.009* |                           |
| Comorbidities                 |                         |                            |
| Hypertension                  | 1.274 0.622-2.612 0.508 |                           |
| Diabetes                      | 1.7 0.825-3.503 0.15   |                           |
| CRD                           | 1.273 0.546-2.968 0.576 |                           |
| CHD                           | 1.04 0.398-2.718 0.936 |                           |
| Smoking history               | 2.378 1.087-5.203 0.030* |                           |
| Blood routine                 |                         |                            |
| WBC, 10^9/L                   | 1.142 1.075-1.214 <0.001* |                           |
| Neutrophil, 10^9/L            | 1.144 1.079-1.212 <0.001* |                           |
| Lymphocyte, 10^9/L            | 0.139 0.045-0.427 0.001* 0.261 0.073-0.930 0.038* |                           |
| Platelet count, 10^9/L        | 0.996 0.992-1.001 0.094 |                           |
| Hemoglobin, g/L               | 1.013 0.993-1.032 0.2   |                           |
| Biochemical                   |                         |                            |
| ALT, U/L                      | 1.002 0.994-1.011 0.569 |                           |
| AST, U/L                      | 1.003 0.999-1.007 0.113 |                           |
| Albumin, g/L                  | 0.885 0.808-0.970 0.009* |                           |
| LDH, U/L                      | 1.003 1.002-1.004 <0.001* 1.003 1.002-1.005 <0.001* |                           |
| BUN, mmol/L                   | 1.132 1.081-1.186 <0.001* |                           |
| Cr, umol/L                    | 1.003 0.999-1.007 0.143 |                           |
| Coagulation factors           |                         |                            |
| PT, s                         | 1.659 1.348-2.041 <0.001* |                           |
| APTT, s                       | 1.022 0.964-1.083 0.46  |                           |
| FIB, g/L                      | 1.122 0.868-1.451 0.379 |                           |
| D-dimer, ug/ml                | 1.085 1.041-1.130 <0.001* |                           |
| Cardiac marker                |                         |                            |
| hsTNI, pg/ml                  | 1.001 1.000-1.001 0.075 |                           |
| NT-proBNP, pg/ml              | 1 1.000-1.000 0.906 |                           |
| Infection-related indexes     |                         |                            |
| hsCRP, mg/L                   | 1.01 1.006-1.014 <0.001* |                           |
| Procalcitonin, ug/L           | 1.079 1.033-1.127 0.001* 1.061 1.002-1.125 0.044* |                           |
| Ferritin, ug/L                | 1.001 1.000-1.001 <0.001* |                           |
| IL-2R, U/ml                   | 1 1.000-1.001 0.009* |                           |
| IL-6, pg/ml                   | 1.004 1.002-1.006 <0.001* |                           |
| CURB-65                       | 3.525 2.343-5.305 <0.001* |                           |
| qSOFA                         | 4.262 2.364-7.685 <0.001* 3.162 1.646-6.072 0.001* |                           |
* $p<0.05$. $S_pO_2$: pulse oxygen saturation, CRD: chronic respiratory diseases, CHD: coronary heart disease, WBC: white blood cell, ALT: alanine aminotransferase, AST: aspartate aminotransferase, LDH: lactate dehydrogenase, BUN, blood urea nitrogen, hsTNI: high sensitivity Troponin I, NT-proBNP: N-terminal pro brain natriuretic peptide, PT: prothrombin time, APTT: Activated partial thromboplastin time, hsCRP, high sensitivity C-reactive protein, IL-2R: interleukin-2 receptor, IL-6: interleukin-6, qSOFA: quick Sequential Organ Failure Assessment, CURB-65: short for assessment of consciousness, serum urea nitrogen, respiratory rate, blood pressure, and age 65 or older.

$\Delta$: The following numerical or categorical indexes (16 parameters, all of which were $p<0.05$) were selected for a backward stepwise multivariate COX regression analysis: age, $S_pO_2$, symptom of dyspnea, smoking history, qSOFA, WBC and lymphocyte count, and other hematological biomarkers, like albumin, LDH, BUN, D-Dimer, hsCRP, PCT, Ferritin, IL-2R, and IL-6.

**Figures**
Figure 1

ROC curve of 28-day mortality LDH: lactate dehydrogenase, Lym: lymphocyte count, CURB65: short for assessment of consciousness, serum urea nitrogen, respiratory rate, blood pressure, and age 65 or older. AUC of LDH, CURB65, lymphocyte count, CURB65 + LDH, and CURB65 + lymphocyte count were 0.838, 0.775, 0.720, 0.891 and 0.821, respectively.
Figure 2

Scatter diagrams, LOS correlated with other indexes. LOS: length of hospital stay. LDH (A. r=0.340, p<0.001), hsCRP (B. r=0.301, p<0.001), neutrophil count (C. r=0.285, p<0.001), and ferritin (D. r=-0.296, p<0.001) were positive correlated with the LOS.

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