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***Retrospective Study***

**High serum lactate dehydrogenase and dyspnea: Positive predictors for adverse event with critical COVID-19 patients in Yichang**

Lv XT *et al.* Positive predictors of critical COVID-19 patients

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**Abstract**

BACKGROUND

A series of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) break out in China, which constitutes a Public Health Emergency of International Concern. It was well known that COVID-19 patients may have increased serum lactate dehydrogenase (LDH) levels in early stage. The clinical changes of LDH may have predictive value in disease evolution and prognosis in critically ill COVID-19 patients.

AIM

To explore the serum LDH and clinical characteristics in patients with COVID-19 and its predictive value for prognosis.

METHODS

A retrospective study was performed to analyze the clinical data of forty-seven critical COVID-19 patients which were enrolled in the intensive care unit ward of the Third People's Hospital of Yichang City from January 27 to March 25, 2020 and divided into groups of survivors and non-survivors. The patients were diagnosed according to World Health Organization interim guidance and critical cases met any one of the following: respiratory failure and required mechanical ventilation, the occurrence of shock, and the combined failure of other organs that required intensive care unit monitoring and treatments, according to the diagnostic criteria of critical COVID-19. Clinical data including symptoms, detection of SARS-CoV-2, chest computed tomography images, changes of serum LDH in different clinical phases, and prognosis were collected. Statistical analysis was performed. Continuous variables were expressed as median (interquartile range) and compared by Mann-Whitney U test. Comparisons were made by Chi-square test for categorical variables. Survival data were analyzed by using Kaplan-Meier survival curves and log-rank tests.

RESULTS

According to Chest computed tomography images, we observed alveolitis and fibrosis stages in all the critical patients of our study. Most of non-survivors died in the fibrosis stage. Non-survivors had fewer days of hospitalization, shorter disease duration, shorter duration of alveolitis and fibrosis, and more patients with dyspnea symptoms at its onset (*P* = 0.05). Both first and lowest LDH values in alveolitis stage were more pronounced in non-survivors than those in survivors(449.0 U/L *vs* 288.0 U/L, *P* = 0.0243; 445.0 U/L *vs* 288.0 U/L, *P* = 0.0199, respectively), while the first, lowest and highest values of serum LDH in the non-survivors were all significantly increased compared to non-survivors in fibrosis phase (449.0 U/L *vs* 225.5 U/L, *P* = 0.0028; 432.0 U/L *vs* 191.0 U/L, *P* = 0.0007; 1303.0 U/L *vs* 263.5 U/L,*P* = 0.0001, respectively). The cut-off points of first LDH values in alveolitis and fibrosis phase for distinction of non-survivors from survivors were 397.0 U/L and 263.0 U/L respectively. In fibrosis stage, non-survivors had more days with high LDH than survivors (7.0 d *vs* 0.0 d, *P* = 0.0002). Importantly, patients with high LDH had a significantly shorter median survival days than patients with low LDH in alveolitis phase (22.0 d *vs* 36.5 d, *P* = 0.0002), while patients with high LDH also had a significantly shorter median survival days than patients with low LDH in fibrosis phase (27.5 d *vs* 40.0 d, *P* = 0.0008). Proportion of non-survivors with detectable SARS-CoV-2 until death in alveolitis stage was significantly increased than that in fibrosis stage (100% *vs* 35.7%, *P* = 0.0220).

CONCLUSION

High LDH and dyspnea symptom were positive predictors for adverse event in critical COVID-19. The rapid progressive fibrosis stage was more perilous than alveolitis stage, even if SARS-CoV-2 was undetectable.

**Key Words:**COVID-19; SARS-CoV-2; Lactate dehydrogenase; Pulmonary fibrosis; Dyspnea; Overall survival

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**Core Tip:** We explored the serum lactate dehydrogenase (LDH) and clinical characteristics in critical coronavirus disease 2019 (COVID-19) patients and its predictive value for prognosis. We retrospective evaluated 47 critical COVID-19 patients and divided them into non-survivors and survivors groups. Clinical data including symptoms, detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), chest computed tomography images, changes of serum LDH in different clinical phases, and prognosis was collected. In our study, high LDH was obviously positively correlated with worsening overall survival. High LDH and dyspnea symptom were positive predictors for adverse event in critical COVID-19 patients. The rapid progressive fibrosis stage may be more perilous than alveolitis stage, even if SARS-CoV-2 was undetectable.

**INTRODUCTION**

The large-scale new corona virus disease pneumonia (coronavirus disease 2019, COVID-19) broke out in Wuhan City, China and the basic reproductive number was 2.68 (95%CI: 2.47-2.86)[1,2]. Millions of cases were reported worldwide, and the fatality rate was up to 7%[3]. The pathogen, officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was confirmed to relate to Middle East syndrome and severe acute respiratory syndrome (SARS)[3-6]. However, the prognosis of critically ill and severe patients is extremely poor. It was well known that some patients had increased lactate dehydrogenase (LDH) levels in the early stage of COVID-19[7]and predictors of poor outcome were increased age, comorbidities and high LDH in SARS in 2003[8]. Whether serum LDH can be used as a marker related to COVID-19 treatment response as well as SARS is inconclusive.

Computed tomography (CT) images and pathological findings of critical COVID-19 patients have characteristic manifestations in alveolitis and fibrosis stages. Chest CT images are characterized by multiple ground-glass opacity (GGO) and early infiltration in acute alveolitis stage. Furtherly, critical cases often subsequently progressed into fibrosis stage and showed consolidation, reticular pattern, and other fibrosis patterns in Chest CT[7,9-11]. Meanwhile, autopsy results with critical COVID-19 patients died in 14 d demonstrated typical pathological changes of acute respiratory distress syndrome such as desquamation of pneumocytes, hyaline membrane formation, interstitial monocytes and lymphocytes inflammatory infiltrates[12], while pathological findings of patients died in 17-19 d showed lighter exudation of alveolar fluid and cellulose, less hyaline membrane, obvious changes of proliferation of type II alveolar epithelial cells and alveolar fleshy change and interstitial fibrosis[13]. The pathological findings were in concord with CT images in different stages of COVID-19. Early recognition and isolation of critical COVID-19 patients in alveolitis and fibrosis stages is crucial in controlling this outbreak.

The aim of this study was to describe the clinical characteristics, as well as to explore the clinical changes of LDH in alveolitis and fibrosis stages according to the CT findings in critically ill COVID-19 patients of intensive care unit (ICU) ward and its predictive value for clinical prognosis.

**MATERIALS AND METHODS**

***Study design and participants***

A total of 47 patients were enrolled in the ICU ward of the Third People's Hospital of Yichang City (one of the highly impacted epidemic areas in China) from January 27 to March 25, 2020. The Third People's Hospital of Yichang is a teaching hospital affiliated to Sanxia University and is also an infectious disease specialist hospital responsible for the treatment of COVID-19 patients as assigned by the government. The patients were diagnosed according to World Health Organization interim guidance[14] and critical cases met any one of the following: respiratory failure and required mechanical ventilation, the occurrence of shock, and the combined failure of other organs that required ICU monitoring and treatments, according to the diagnostic criteria of critical COVID-19[7]. The protocols for the study and informed consents were approved by the ethics committee of First Affiliated Hospital of Fujian Medical University [Approval No. (2020) 153]. All the discharged survivors were in accordance with twice negative nucleic acid tests of throat swab samples[7].

***Cases collection***

General information included the gender, age, days of hospitalization, disease duration, duration of viral shedding, days from illness onset to hospital admission, duration of alveolitis and fibrosis phases, the complications of chronic obstructive pulmonary disease, hypertension, coronary heart disease, cerebrovascular disease, diabetes, renal dysfunction, malignant tumors and other underlying diseases, the numbers of complications, the initial symptoms such as fever, cough, dyspnea, fatigue and so on. Chest CT images were used to make a distinction between the alveolitis and fibrosis phases.

***Laboratory inspection***

The serum concentrations of LDH were detected by the detection Kit (No. A0701) ordered from Sichuan Chengdu New Health City Biological Co., Ltd. (China), according to the manufacturer’s instruction. The recommended reference range for the normal population is (109-245) U/L. Throat swab samples of the patients were collected and fluorescent polymerase chain reaction was used to detect the coronavirus ribonucleic acid of SARS-CoV-2 by using the new coronavirus 2019-nCov nucleic acid detection kit (No. DA0930-DA0932) provided by Sun Yat-sen University Daan Gene Co., Ltd. (China). Patients with positive results from the ribonucleic acid detection were identified as confirmed cases.

***Statistical analysis***

Statistical analysis was performed using the Statistic Package for Social Science 18.0 software package (Statistic Package for Social Science Inc., Chicago, IL, United States). Continuous variables were expressed as median (interquartile range) and compared by Mann-Whitney U test. Comparisons were made by Chi-square test for categorical variables. Survival data were analyzed by using Kaplan-Meier survival curves and log-rank test. For all tests, *P* < 0.05 was considered to be statistically significant.

**RESULTS**

***Clinical characteristics of patients with critical COVID-19***

Forty-seven COVID-19 patients were divided into non-survivors (*n* = 17) and survivors (*n* = 30) groups. The baseline characteristics of the patients with critical COVID-19 were summarized in Table 1. Non-survivors had fewer days of hospitalization, shorter disease duration and more dyspnea symptoms than the survivors (*P* = 0.01). There was no significant difference between two groups in the age (*P* = 0.595), gender (*P* = 0.330), days from illness onset to hospital admission (*P* = 0.689), duration of viral shedding (*P* = 0.118), complications as well as the number of complications (*P* = 0.139).

According to Chest CT images, we observed alveolitis and fibrosis stages in all the critical patients of our study. Chest CT images of the alveolitis showed that patients with critical COVID-19 had bilateral lung involvement, mainly with peripheral and diffused distribution and focal GGO. As it progressed into fibrosis stage, Chest CT showed consolidation and pulmonary interstitial fibrosis changes such as air bronchogram sign, bronchiectasis and reticular pattern. Some non-survivors showed more consolidation lesions than the survivors (Figure 1). According to the imaging findings, we found that the duration of inflammation and fibrosis was shorter in non-survivors than survivors (*P* = 0.020 and 0.016).

***High serum LDH levels were positively related to poor prognosis of patients with critical COVID-19***

Our results (Figure 2) showed that both first and lowest LDH values in alveolitis stage were more pronounced in non-survivors than those in survivors (449.0 U/L *vs* 288.0 U/L, *P* = 0.0243; 445.0 U/L *vs* 288.0 U/L, *P* = 0.0199, respectively). And there was no difference found at the highest value of serum LDH between non-survivors and survivors in this stage (499.0 U/L *vs* 349.0 U/L, *P* = 0.1360). The cutoff point of the first serum LDH concentration in the alveolitis stage for differentiating non-survivors from survivors was 397.0 U/L, according to receiver operating characteristic curve analysis. The ratio of days with high LDH (more than 397.0 U/L) to disease duration in the non-survivors was markedly higher compared to survivors (0.14 *vs* 0.00, *P* = 0.0284), though the days with high LDH was not statistically significant between these two groups in the alveolitis stage.

In fibrosis phase, the first, lowest and highest values of serum LDH in the non-survivors were all significantly increased compared to non-survivors (449.0 U/L *vs* 225.5 U/L, *P* = 0.0028; 432.0 U/L *vs* 191.0 U/L, *P* = 0.0007; 1303.0 U/L *vs* 263.5 U/L,*P* = 0.0001, respectively). And the cutoff value of serum LDH for differentiating non-survivors from survivors was 263.0 U/L. Non-survivors had more days with LDH above 263.0 U/L than survivors (7.0 *vs* 0.0 d, *P* = 0.0002) in fibrosis phase. Moreover, the ratio of days with high LDH to disease duration in the non-survivors was higher than that in the survivors (0.31 *vs* 0.00, *P* = 0.0001). Our results revealed that serum LDH was increased in non-survivors, and the elevated levels of serum LDH were positively related to the adverse event in acute alveolitis and fibrosis phrases.

***High serum LDH was correlated with worsening overall survival in patients with critical COVID-19***

Kaplan-Meier analysis and log-rank test showed that patients with high LDH (≥ 397.0 U/L) had a significantly shorter median survival days compared to low LDH (< 397.0 U/L) in alveolitis phase (22.0 d *vs* 36.5 d, *P* = 0.0002) (Figure 3A). Meanwhile, patients with high LDH (≥ 263.0 U/L) also had a significantly shorter median survival days compared to low LDH (< 263.0 U/L) in fibrosis phase (27.5 d *vs* 40.0 d, *P* = 0.0008) (Figure 3B).

***Proportion of non-survivors with detectable SARS-CoV-2 until death in the stages of alveolitis and fibrosis***

All the non-survivors died in the alveolitis stage had a detectable SARS-CoV-2 until death, but only some patients (35.7%) died in the fibrosis stage had detectable SARS-CoV-2 results. Proportion of non-survivors with detectable SARS-CoV-2 until death in alveolitis stage was significantly increased than that in fibrosis stage (*P* = 0.0220) (Figure 4).

**DISCUSSION**

Our results showed that fewer days of hospitalization, shorter course of disease, shorter duration of alveolitis and fibrosis, and more dyspnea symptoms at its onset were positively associated with the adverse event of critical COVID-19. In addition, the first and lowest values of LDH in alveolitis and fibrosis phase, the highest LDH value in fibrosis phase of non-survivors were higher than those in the survivors, together with more days with high LDH (≥ 263.0 U/L) in fibrosis phase and the higher ratio of days with high LDH levels (≥ 397.0 U/L) in alveolitis phase and (≥ 263.0 U/L in fibrosis phase, respectively) to disease duration. The elevated levels of first LDH in the acute alveolitis and fibrosis phrase were obviously correlated with worsening overall survival. The rapid progressive fibrosis stage may be more perilous than alveolitis stage, even if the SARS-CoV-2 was undetectable.

It was reported that older age was correlated with unfavorable outcomes in COVID-19, SARS and Middle East syndrome[15-18]. Previous study confirmed that SARS-CoV-infected aged macaques developed an exacerbated innate host response with an increased expression of genes associated with inflammation[18]. The current study showed there was no significant difference between non-survivors and survivors in the age of patients in Yichang, and the median age of survivors with critical COVID-19 was older than survivors in COVID-19 patients in Wuhan (67.0 years *vs* 52.0 years)[15]. These results supported the older age may be a predictor of death with critical COVID-19. Also there was no significant difference between the two groups in gender as well as median days of illness onset to hospital admission, as those in COVID-19 patients in Wuhan[15].

The median days of illness onset to hospital admission (5.0 d) were similar in survivors and non-survivors, yet those in Wuhan were 11.0 d. The concern about COVID-19 in Wuhan city helped patients receiving earlier recognition and treatment in Yichang. Otherwise, our results indicated that shorter course of disease, shorter duration of alveolitis and fibrosis were associated with death consequences in Yichang, which suggested non-survivors had more rapid progression, no matter in what stages.

Based on Chest CT appearance, critical patients had diffused GGO at alveolitis stage, and massive consolidation lesions at fibrosis phase. Less GGO and consolidation lesions could be found in survivors than non-survivors. Obviously, most non-survivors in our study mostly died in the fibrosis phase (14/17), and few died in the stage of alveolitis (3/17). It was reported the virus was continuously detectable until death in all non-survivors[15]. Our study demonstrated that alveolitis stage was significantly associated with detectable SARS-CoV-2 in non-survivors and only 35.7% non-survivors with detectable SARS-CoV-2 until death in fibrosis phase. The replicated SARS-CoV injured alveolar epithelial cells, leading to alveolitis and fibrotic lesions[19]. Combined with shorter duration of fibrosis stage in non-survivors, the rapid progressive fibrosis stage may be more perilous than alveolitis stage, even if the SARS-CoV-2 was undetectable. As accumulating evidence suggested that a subgroup of patients with severe COVID-19 might had a cytokine storm syndrome[20], it was hard for those died in alveolitis stage to eradicate virus, and duration of viral shedding for them may be longer.

In addition, dyspnea symptom at its onset was associated with fatal outcome of COVID-19 in our study. Dyspnea was also an independent clinical factor for H1N1 pneumonia[21]. There are many possible causes for dyspnea. One hand, pathological findings in COVID-19 patients showed pulmonary edema and hyaline membrane formation associated formation[12]. Aquaporin 5 (AQP5) and AQP1, located in the endothelial cells and secretory cells of terminal bronchiole and the alveolar type I cells, play an important role in water clearance in lungs. It was reported that porcine reproductive and respiratory syndrome virus infection usually caused pulmonary inflammation and edema in the infected lungs[13]. The expression of AQPs and Na, K-adenosine triphosphatase may be downregulated, causing lung edema with apoptosis of alveolar epithelial cells in porcine reproductive and respiratory syndrome virus infection. The replicated SARS-CoV may have alveolitis and fibrotic changes, leading to acute lung injury that may develop into life-threatening acute respiratory distress syndrome[18,19]. On the other hand, a substantial portion of SARS patients had evidence of respiratory muscle weakness leading to air trapping, whereas inspiratory muscle weakness may lead to atelectasis, at least 40% of patients suffered from acute respiratory failure requiring supplemental oxygen[22]. Respiratory muscle weakness may be one cause for dyspnea.

LDH has been reported to be a useful inflammatory biomarker of community acquired pneumonia, Mycoplasma pneumoniae pneumonia, and complicated pneumonia[23-25]. Our findings indicated that COVID-19 was associated with high levels of LDH, and elevated serum LDH could be used as the severity and poor prognosis indicators for patients with critical COVID-19 in different stages. Moreover, the best threshold of LDH level for predicting COVID-19 in alveolitis and fibrosis phase were 397.0 U/L and 263.0 U/L, respectively. Among non-survivors, the first and lowest values of LDH in alveolitis and fibrosis phase, the highest LDH value in fibrosis phase were higher than those in the survivors, together with more days with high LDH (≥ 263.0 U/L) in fibrosis phase and the higher ratio of days with high LDH levels (≥ 397.0 U/L in alveolitis phase and ≥ 263.0 U/L in fibrosis phase, respectively) to disease duration. Laboratory results showed that increase of LDH (28.3%) were more common in patients with COVID-19[3]. The level of LDH in severe patients was significantly higher than those of the mild patients in Wuhan[15,26].

Possible sources of serum elevated LDH levels during infection may be the immunologic changes after SARS-COV-2 infection of the upper and lower respiratory tract to develop early acute respiratory inflammatory response with consequent release of pro-inflammatory cytokines, including interleukin-1β, followed by inflammasome activation and production of active mature interleukin -1β which is a mediator of lung inflammation and fibrosis[27]. High levels of serum LDH were also reported to be associated with the severe form of H1N1 influenza and serum LDH level above 500 U/L were significantly more common in patients with pneumonia[21,28]. Lung parenchymal cells and/or local inflammatory cells may be potential sources of elevated LDH in serum[29,30] and elevated serum values of LDH indirectly indicate lung tissue damage[31,32]. Therefore, the best threshold of LDH level for predicting COVID-19 in acute alveolitis phase was higher than that in fibrosis phase. The first, lowest and highest values of LDH in alveolitis and fibrosis phase, together with more days with high LDH and the higher ratio of days with high LDH levels, were important for predicting the severity of critical COVID-19. As critical COVID-19 in ICU ward often combined with bacterial infection, LDH can convert pyruvate to lactate and might be the key enzyme for pneumococcal pyruvate metabolism and thus pneumococcal survival in blood[33].

**CONCLUSION**

High serum LDH and dyspnea symptom in the early stages of infection could be expected to predict the severity and the poor prognosis for patients with critical COVID-19. The non-survivors developed rapidly in both alveolitis stage and fibrosis stage, and the progressive fibrosis stage may be more perilous than alveolitis stage, even if SARS-CoV-2 was undetectable.

**ARTICLE HIGHLIGHTS**

***Research background***

Millions of new corona virus disease pneumonia (coronavirus disease 2019, COVID-19) cases were reported worldwide. Moreover, the prognosis of critically ill and severe COVID-19 patients is extremely poor.

***Research motivation***

COVID-19 patients may have an increased serum lactate dehydrogenase (LDH) levels in early stage. The clinical changes of LDH may have predictive value in disease evolution and prognosis in critically ill COVID-19 patients.

***Research objectives***

To describe the clinical characteristics and explore the clinical changes of LDH in alveolitis and fibrosis stages according to the computed tomography findings in critically ill COVID-19 patients and its predictive value for clinical prognosis.

***Research methods***

We analyze the clinical data of forty-seven critical COVID-19 patients which were enrolled in the intensive care unit ward of the Third People's Hospital of Yichang City and divided into groups of non-survivors and survivors. Clinical data including symptoms, detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), chest computed tomography images, changes of serum LDH in different clinical phases, and prognosis was collected.

***Research results***

Most of non-survivors died in the fibrosis stage. Non-survivors had fewer days of hospitalization, shorter disease duration, shorter duration of alveolitis and fibrosis, and more patients with dyspnea symptoms at its onset. Both first and lowest LDH values in alveolitis and fibrosis stage were more pronounced in non-survivors than those in survivors. Importantly, patients with high LDH had a significantly shorter median survival days in alveolitis and fibrosis phase.

***Research conclusions***

High serum LDH and dyspnea symptom in the early stages of infection were positive predictors for the severity and the poor prognosis of critical COVID-19. The rapid progressive fibrosis stage was more perilous than alveolitis stage, even if SARS-CoV-2 was undetectable.

***Research perspectives***

The immunologic mechanism of serum elevated LDH during SARS-COV-2 infection need to investigate furtherly.

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**Footnotes**

**Institutional review board statement:** This study was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Fujian Medical University [ (No. (2020) 153)].

**Informed consent statement:** Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient gave their informed verbal consent prior to study inclusion.

**Conflict-of-interest statement:** We have no financial relationships to disclose.

**Data sharing statement:** No additional data are available.

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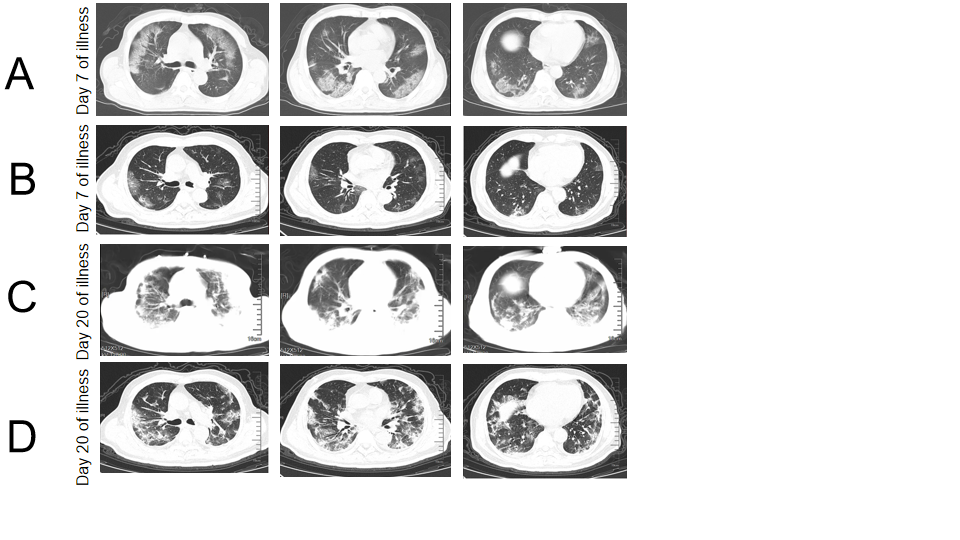
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Grade D (Fair): 0

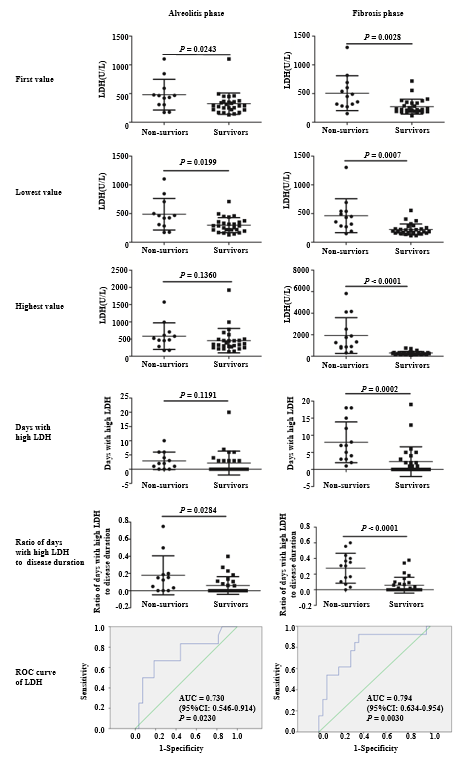
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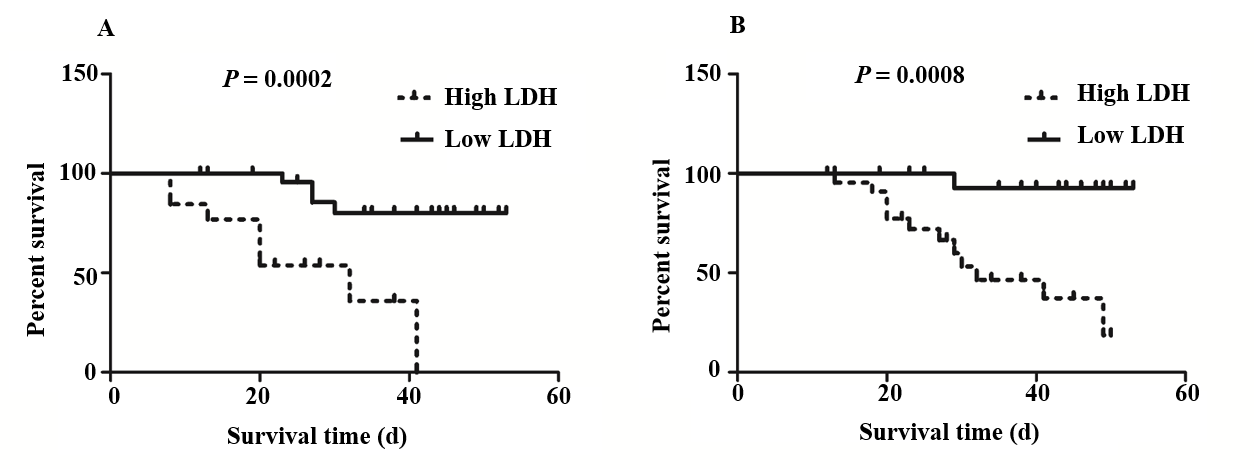
**Figure Legends**



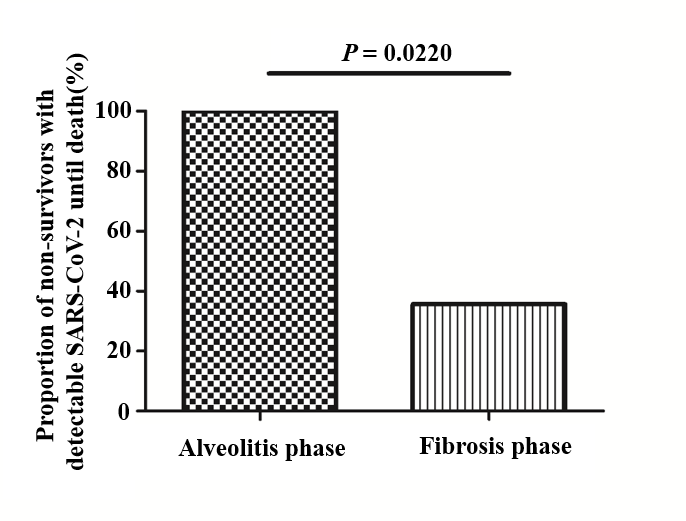
**Figure 1 Chest computed tomography of critical coronavirus disease 2019 patients with different severity.** A: Chest computed tomography (CT) of a 71-year-old man (non-survivor, case 1) showed multifocal and bilateral ground-glass opacity (GGO) in alveolitis stage (Day 7 of illness); B: Chest CT of a 73-year-old male patient (survivor, case 2) exhibited slight GGO in alveolitis stage (Day 7 of illness); C: Classified into fibrosis stage (Day 20 of illness) and Chest CT (case 1) showed bilateral massive shadows of high density and GGO, accompanied by air bronchogram sign and reticular pattern in fibrosis stage; and D: Chest CT (case 2) showed that bilateral and multifocal lesions were observed with a combination of mixed GGO, reticular pattern, bronchiectasis and few consolidation (Day 20 of illness).



**Figure 2 The relationship between serum lactate dehydrogenase levels and the prognosis of patients with critical coronavirus disease 2019.** The first, lowest and highest values of serum lactate dehydrogenase (LDH), together with the days with high LDH (≥ 397.0 U/L in alveolitis phase and ≥ 263.0 U/L in fibrosis phase according to the receiver operating characteristic curve analysis, respectively) and the ratio of the days with high LDH to disease duration were analyzed by Mann-Whitney U test between non-survivors and survivors in their alveolitis phase and fibrosis phase. *P* < 0.05 was considered statistically significant. LDH: lactate dehydrogenase.



**Figure 3 Association between the first value of serum lactate dehydrogenase and survival days of patients with critical** **coronavirus disease 2019.** Kaplan-Meier analysis and log-rank test were performed to analyze the association between the first values of serum lactate dehydrogenase (LDH) and the survival days of patients with critical coronavirus disease 2019. A: Patients with high LDH (≥ 397.0 U/L) had a significantly shorter survival days compared to low LDH (< 397.0 U/L) in alveolitis phase; B: Patients with high LDH (≥ 263.0 U/L) also had a significantly shorter survival days compared to low LDH (< 263.0 U/L) in fibrosis phase. LDH: lactate dehydrogenase.



**Figure 4 Proportion of non-survivors with detectable severe acute respiratory syndrome coronavirus 2 until death in alveolitis and fibrosis phase.** All the non-survivors (100.0%) who died in the alveolitis stage had a persistent positive test of severe acute respiratory syndrome coronavirus 2 until death. And only 5 patients (35.7%) who died in the pulmonary fibrosis stage had positive results in virus nucleic acid tests. SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

**Table 1 Clinical characteristics of patients with critical coronavirus disease 2019**

|  |  |  |  |
| --- | --- | --- | --- |
| **Clinical features** | **Groups** | | ***P* value** |
| **Non-survivors (*n* = 17)** | **Survivors (*n* = 30)** |
| Age (yr) | 69.0 (63.5-78.0) | 67.0 (55.5-77.0) | 0.595 |
| Male (%) | 11 (64.7) | 15 (50.0) | 0.33 |
| Days of hospitalization (d) | 14.0 (8.0-24.5) | 33.0 (16.8-38.3) | 0.0015 |
| Disease duration (d)1 | 23.0 (15.5-29.5) | 38.0 (24.5-45.3) | 0.0055 |
| Duration of viral shedding (d) | 8.0 (6.0-18.0) | 11.0 (8.8-20.5) | 0.118 |
| Days from illness onset to hospital admission (d) | 5.0 (2.0-10.0) | 5.0 (3.75-7.25) | 0.689 |
| Duration of alveolitis phase (d) | 12.0 (8.0-17.5) | 17.0 (13.8-21.0) | 0.020a |
| Duration of fibrosis phase (d) | 10.0 (5.5-15.5) | 19.0 (10.0-26.0) | 0.016a |
| Complication of COPD (%) | 3 (17.6) | 3 (10.0) | 0.764 |
| Complication of hypertension (%) | 10 (58.8) | 11 (36.7) | 0.142 |
| Complication of coronary heart disease (%) | 7 (41.2) | 6 (20.0) | 0.222 |
| Complication of cerebrovascular disease (%) | 3 (17.6) | 7 (23.3) | 0.931 |
| Complication of diabetes (%) | 5 (29.4) | 7 (23.3) | 0.912 |
| Complication of renal dysfunction (%) | 2 (11.8) | 5 (16.7) | 0.978 |
| Complication of malignant tumors (%) | 2 (11.8) | 3 (10.0) | 1.000 |
| Complication of others (%)2 | 7 (41.2) | 6 (20.0) | 0.222 |
| Number of complications | 2.0 (1.5-3.5) | 1.5 (0.0-3.0) | 0.139 |
| Fever (%) (temperature ≥ 37.3℃) | 13 (76.5) | 26 (86.7) | 0.624 |
| Cough (%) | 7 (41.2) | 20 (66.7) | 0.089 |
| Dyspnea (%) | 9 (52.9) | 4 (13.3) | 0.010a |
| Fatigue (%) | 5 (29.4) | 4 (13.3) | 0.337 |
| Other symptoms (%)3 | 5 (29.4) | 4 (13.3) | 0.337 |

1Time from illness onset to death or discharge, days; 2Thyroid dysfunction, prostatic hyperplasia, schizophrenia; 3Arthralgia, sputum, dizziness, nausea, chest pain, diarrhea; a*P* < 0.05; b*P* < 0.01. COPD: Chronic obstructive pulmonary disease.