Clinical and Biochemical Indexes from 2019-nCoV Infected Patients Linked to Viral Loads and Lung Injury

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Abstract

The novel coronavirus (2019-nCoV) emerged in Wuhan, Hubei Province, in December 2019 and rapidly spread to multiple regions in China and other countries. In this study, we report the epidemiological, clinical, biochemical, and imaging characteristics of early-stage 2019-nCoV-infected patients from Shenzhen, China, as well as potential biomarkers for predicting disease severity. All 12 patients with 2019-nCoV infection developed pneumonia, with half progressing to acute respiratory distress syndrome (ARDS). The most common laboratory abnormalities in biochemical indicators included hypoalbuminemia (albumin, ALB), decreased lymphocyte (lymphocytes, LYM) count, reduced percentages of lymphocytes and neutrophils (neutrophils, NEU), elevated C-reactive protein (CRP) and lactate dehydrogenase (LDH) levels, and decreased CD8 cell count. The 2019-nCoV viral titer detected in patients' respiratory tracts, particularly the lower respiratory tract, was positively correlated with lung disease severity. Levels of ALB, LYM, LYM(%), LDH, NEU(%), and CRP were highly correlated with acute lung injury severity. Age, viral titer, lung injury score, and blood biochemical indicators—including ALB, CRP, LDH, LYM(%), LYM, and NEU(%)—may serve as predictive indicators of disease severity. Furthermore, plasma angiotensin II levels were significantly elevated in 2019-nCoV-infected patients and linearly correlated with viral titer and lung injury severity. Our findings provide multiple potential diagnostic biomarkers and suggest that angiotensin II receptor blocker (ARB) drugs warrant further investigation as potential therapeutic agents for 2019-nCoV infection.

Full Text

Preamble

Clinical and Biochemical Indexes from 2019-nCoV Infected Patients Linked to Viral Loads and Lung Injury

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Abstract

The outbreak of 2019-nCoV infection began in December 2019 in Wuhan, Hubei province, and rapidly spread to multiple provinces in China as well as to other countries. Here we report the epidemiological, clinical, laboratory, and radiological characteristics, along with potential biomarkers for predicting disease severity, in 2019-nCoV-infected patients in Shenzhen, China. All 12 patients in our cohort developed pneumonia, and half of them progressed to acute respiratory distress syndrome (ARDS). The most common laboratory abnormalities were hypoalbuminemia (ALB), lymphopenia, decreased percentages of lymphocytes (LYM) and neutrophils (NEU), elevated C-reactive protein (CRP) and lactate dehydrogenase (LDH), and decreased CD8 count. Viral load of 2019-nCoV detected from patient respiratory tracts was positively associated with lung disease severity. ALB, LYM, LYM (%), LDH, NEU (%), and CRP were highly correlated with acute lung injury. Age, viral load, lung injury score, and

blood biochemistry indexes—including ALB, CRP, LDH, LYM (%), LYM, and NEU (%)—may serve as predictors of disease severity. Moreover, angiotensin II levels in plasma samples from 2019-nCoV infected patients were markedly elevated and linearly associated with viral load and lung injury. Our results suggest several potential diagnostic biomarkers and indicate that angiotensin receptor blocker (ARB) drugs may be candidates for repurposed treatment of 2019-nCoV infection.

Introduction

In December 2019, a cluster of pneumonia cases linked to the Wuhan seafood wholesale market was reported and found to be caused by the 2019 novel coronavirus (2019-nCoV), the seventh member of the coronavirus family known to infect humans (C. Huang et al. 2020; Li et al. 2020; Tan WJ 2020). Possible person-to-person transmission was identified when clusters of 2019-nCoV patients with Wuhan travel histories emerged in additional Chinese cities (Li et al. 2020; C. Huang et al. 2020). By February 2, 2020, 11,901 laboratory-confirmed cases and 259 deaths had been reported. All patients presented with novel coronavirus-infected pneumonia (NCIP). The novel coronavirus belongs to lineage B of the genus beta-coronavirus within the Coronaviridae family, which includes SARS-CoV and MERS-CoV (Zhu et al. 2020). A recent study reported that fever, cough, myalgia, and fatigue were common symptoms, while sputum production, headache, hemoptysis, and diarrhea were less frequent (C. Huang et al. 2020). All patients had pneumonia, and approximately half developed dyspnea. One-third of patients required ICU admission, and 15% died (C. Huang et al. 2020). Compared with the 10% fatality rate of SARS-CoV (Jiang et al. 2005) and 37% fatality rate of MERS-CoV (Niu et al. 2018), 2019-nCoV represents the third highly lethal virus in the coronavirus family.

Our study describes the clinical characteristics of 12 2019-nCoV-infected patients admitted to Shenzhen Third People' s Hospital, China. We recorded and examined clinical characteristics and blood biochemistry indexes, collected respiratory samples (throat swabs and bronchoalveolar lavage fluid [BALF]), and used real-time PCR to confirm 2019-nCoV infection. We identified potential biomarkers of disease severity, and our results should assist physicians in diagnosing and treating patients infected with 2019-nCoV.

Results

Patient Characteristics and Epidemiology

Twelve patients (4 females and 8 males) were admitted to Shenzhen Third People' s Hospital and confirmed as 2019-nCoV-infected by Guangdong CDC as of January 21, 2020. Seven patients were over 60 years old, and notably, one adolescent case (case 7, 10 years old) was identified. Except for case 5, who resided in Shenzhen, eleven cases (91.7%) had lived in or traveled to Wuhan city, and two family clusters were identified. Cases 1, 2, 6, and 7, members of

one family, stayed in a hotel approximately 2.5 miles from the Huanan seafood market for six days. On December 31, 2019, and January 1, 2020, they visited two local households for dinner. Cases 1, 2, and 6 developed fever on January 1, 2020, and case 6 also experienced diarrhea. On January 4, 2020, they returned to Shenzhen, where they lived with case 5, who subsequently developed fever, cough, and myalgia on January 8, 2020. Notably, none of the family members reported direct contact with seafood, live poultry, or other wild animals. Cases 10 and 11 were a couple living approximately 5.5 miles from the Huanan seafood market who developed fever and cough on January 4, 2020, and traveled to Shenzhen on January 13, 2020 [Figure 1: see original paper]. Based on the exposure histories of the 12 patients, the estimated incubation period ranged from 1 to 13 days.

Most cases developed influenza-like symptoms, with intervals between illness onset and admission ranging from 5 to 16 days . Six patients (50%) had underlying diseases, including chronic heart disease, renal disease, and diabetes. Pneumonia was the most common manifestation, followed by acute respiratory distress syndrome (ARDS), including two cases with severe ARDS. All patients received antiviral treatment (ribavirin and interferon), and six required mechanical ventilation, with cases 2, 4, and 10 receiving invasive mechanical ventilation. Corticosteroids and immunoglobulin were also administered to cases 2, 4, and 10 .

Laboratory and Radiological Findings

Complete blood counts and blood biochemistry were measured for each patient either on the date of hospital admission or at the earliest subsequent timepoint. The most common laboratory abnormalities included hypoalbuminemia, lymphopenia, decreased percentages of lymphocytes and neutrophils, elevated C-reactive protein (CRP) and lactate dehydrogenase (LDH), and decreased CD8 count . Chest computed tomography (CT) scans of all patients showed ground-glass opacity with surrounding shadowing and pleural effusion, particularly in the lower and peripheral lung regions [FIGURE:2; Figure S1 in Supporting Information]. During disease progression, the density of ground-glass opacity increased and the affected area expanded, diffusing centrally and eventually involving the entire lung [Figure 2: see original paper].

Case 4 developed fulminant myocarditis five days after illness onset. Biochemistry indexes associated with cardiac function—including creatine kinase (CK), myoglobin (MYO), cardiac troponin I (CtnI), brain natriuretic peptide (BNP), and CK myocardial band (CK-MB)—were significantly elevated in case 4 . Echocardiography showed a left ventricular ejection fraction (LVEF) of 32% and left ventricular diameter (LV) of 61 mm on January 15, 2020 (five days after illness onset) [Figure S2 in Supporting Information].

Viral Load Correlations

We used Spearman correlation coefficients to analyze relationships between 2019-nCoV cycle threshold (Ct) values (which are inversely proportional to viral load) and clinical disease severity scores, including APACHE II, PaO /FiO ratios, and Murray scores [FIGURE:3A, Figure S3, and Table S1 in Supporting Information]. Viral load was highly correlated with both the ARDS index (PaO /FiO ratio) and lung injury Murray score, but not with the MODS score APACHE II [FIGURE:3A; Figure S3 in Supporting Information]. This finding aligns with our clinical observation that half of infected patients developed ARDS and all had pneumonia, indicating that lung failure is the primary dysfunction caused by 2019-nCoV infection. Using Spearman analysis, we further correlated Ct values (viral load) with biochemical and clinical indexes, finding that levels of infectious disease indicators (ALB) and immunological cell percentages (LYM and NEU) were significantly correlated with viral load [Figure 3B: see original paper].

Biomarkers of Lung Injury

Among eight distinguished blood biochemistry indexes in 2019-nCoV-infected patients—specifically ALB, creatinine (CRE), LYM, LYM (%), NEU (%), LDH, CRP, and CD8—we found that ALB, LYM, LYM (%), NEU (%), LDH, and CRP were highly linked to the lung injury Murray score [Figure 4: see original paper]. Previous studies reported that hypoalbuminemia is a potent, dose-dependent predictor of poor outcome (Vincent et al. 2003), suggesting that albumin therapy might be a potential remedy for NCIP.

Predictors of Disease Severity

We statistically analyzed associations between clinical and biochemical characteristics and disease severity, as defined by the second edition of medical guidelines for 2019-nCoV infection from the National Health Commission of the People' s Republic of China. We calculated area under the curve (AUC) values from receiver operating characteristic (ROC) curves. The AUC for age was 1.0, indicating that age could fully predict disease severity in 2019-nCoV-infected patients [Figure 5: see original paper]. The youngest "severe" patient in our Shenzhen cohort was 56 years old. Viral load (measured inversely as Ct value), lung injury Murray score, and PaO /FiO ratio may also predict disease severity [Figure 5: see original paper]. Among biochemical indexes, the AUCs for infection and tissue damage indicators were 1.0 for ALB, 0.938 for CRP, and 0.844 for LDH, suggesting these may be potential predictors. The AUCs for lymphocyte count and percentages of lymphocytes and neutrophils were 1.0, 0.844, and 0.812, respectively, indicating they may also predict disease severity.

Angiotensin II Levels

A recent study analyzing the 2019-nCoV genome sequence predicted that the novel coronavirus shares the ACE2 receptor with SARS-CoV (Xintian Xu 2020), which is a critical enzyme in the renin-angiotensin system (RAS) (F. Huang et al. 2014; Zou et al. 2014). RAS plays important roles in maintaining blood pressure homeostasis (Forrester et al. 2018) and salt/fluid balance (Lin et al. 2017). ACE and ACE2 have opposing roles in RAS: ACE generates angiotensin II, whereas ACE2 negatively regulates the system by decreasing angiotensin II (Crackower et al. 2002). Abnormal increases in angiotensin II are primarily associated with hypertension and heart failure (Packer and McMurray 2017) but can also cause lung and renal dysfunctions (Frohlich et al. 2016; Kuba et al. 2005; Zou et al. 2014; Damman et al. 2018; Imai et al. 2005; Rai et al. 2017; Torres et al. 2014).

We measured plasma angiotensin II levels in 2019-nCoV-infected patients and healthy individuals, finding significantly higher levels in infected patients [Figure 6A: see original paper]. Moreover, angiotensin II levels in 2019-nCoV patients were strongly associated with viral load and lung injury [FIGURE:6B and 6C], suggesting that 2019-nCoV causes RAS imbalance. This implies that ACE inhibitors and ARBs, which balance RAS, could be repurposed for treating 2019-nCoV-infected patients.

Discussion

We report 12 laboratory-confirmed 2019-nCoV infections at Shenzhen Third People' s Hospital, Shenzhen, China. All patients had lived in or traveled to Wuhan from late December 2019 to early January 2020, except case 5 who remained in Shenzhen. Two family clusters were identified, with case 5 representing secondary infection within a family cluster including cases 1, 2, 6, and 7, providing evidence of possible person-to-person transmission. Cases 1, 2, 6, and 7 were likely simultaneously infected in Wuhan, possibly by a super-spreader in their hotel or relatives' home, as five relatives in Wuhan developed similar symptoms (Chan et al. 2020). Since case 5 developed symptoms four days after family members returned from Wuhan, the incubation period might be as short as 1-4 days, while most other patients had incubation periods of 7-13 days [Figure 1: see original paper]. Two of the 12 patients had no documented fever, including case 7 who was clinically evaluated when accompanying family members to the hospital . The risk of viral spread from non-febrile patients underscores the importance of establishing epidemiological history during clinical evaluation.

Respiratory tract samples, including throat swabs and BALF, were collected from 10 patients. Comparative testing revealed inconsistent results between throat swabs and BALF collected simultaneously from cases 1, 3, and 4 [TABLE:S1], with BALF positive and throat swabs negative, indicating that BALF may be a more reliable specimen for 2019-nCoV detection. Notably, BALF from case 8 tested negative while throat swabs were positive; this patient was

discharged after one week. Further studies are needed to determine whether disease pathogenesis relates to viral location within the respiratory tract.

Viral load was crucial in determining disease severity, showing strong correlation with lung injury Murray score [Figure 3A: see original paper]. Notably, case 4 had very high viral load when fulminant myocarditis occurred [TABLE:2 and FIGURE:3], and this high viral load persisted for one week, suggesting that early detection of high viral load may predict high risk of fulminant myocarditis.

Our study identifies several potential predictors of disease severity. ALB and LYM counts were negatively correlated with Murray scores, while CRP and LDH levels were positively correlated with Murray scores in 2019-nCoV patients [Figure 4: see original paper]. The Murray score was originally developed to assess acute lung injury severity in ARDS, with higher scores indicating greater severity. These findings align with previous studies showing that hypoalbuminemia, lymphopenia, and CRP 4 mg/dL predicted pneumonia progression to respiratory failure in MERS-CoV patients, and that elevated lactate dehydrogenase was associated with severe SARS-CoV infection at hospital admission (Ko et al. 2016; Liu et al. 2004; Leem et al. 2018). Therefore, the combination of hypoalbuminemia, lymphopenia, and high CRP and LDH concentrations in 2019-nCoV patients at admission may predict more severe acute lung injury.

We discovered markedly elevated angiotensin II levels in plasma from 2019-nCoV-infected patients. Our previous mouse studies demonstrated that SARS-CoV could bind its receptor ACE2, downregulating its expression and increasing angiotensin II levels, which signals through angiotensin II receptor 1 to induce acute lung injury (F. Huang et al. 2014; Imai et al. 2005; Zou et al. 2014). We also reported that avian influenza A virus H5N1 caused acute lung injury through RAS dysregulation, and that markedly elevated angiotensin II levels in H7N9-infected patients were associated with disease severity and outcomes (Guo et al. 2015). Additionally, a retrospective cohort study of hospitalized pneumonia patients in Texas, USA, reported that prior and inpatient use of ACE inhibitors and ARBs was associated with decreased mortality (Mortensen et al. 2012).

Our previous studies demonstrated that ARB drugs, particularly losartan, effectively ameliorated acute lung injury induced by SARS-CoV and H5N1 influenza A virus in mice (Kuba et al. 2005; Yan et al. 2015). These data suggest that ARB drugs may be useful for treating ICU patients infected with 2019-nCoV.

The number of laboratory-confirmed patients is rapidly increasing. We hope this report of 12 cases in Shenzhen provides useful information for preparing for potential NCIP pandemics.

Methods

Patients

Twelve patients with pneumonia of unknown cause were admitted to Shenzhen Third People' s Hospital between January 11 and January 20, 2020, and confirmed as 2019-nCoV-infected by Guangdong CDC. Patient ages ranged from 10 to 72 years. According to guidelines from the National Health Commission of the People' s Republic of China, 3 patients were in critical condition and 5 were classified as severe. BALF and throat swab samples were collected to detect viral titers. Blood samples from 2019-nCoV-infected patients and healthy hospital staff were collected for plasma angiotensin II measurement. The study was approved by the Ethics Committee of Shenzhen Third People' s Hospital (SZTHEC2016001), and verbal informed consent was obtained from all patients or family members.

Data Collection and Clinical Analysis

Clinical information, including complete blood counts, blood biochemistry, chest radiographs, and CT scans, was collected at the earliest possible time-points after hospitalization.

Quantitative Reverse Transcription PCR

Throat swabs and BALF were collected at various time-points after hospitalization. Viral RNAs were extracted using the QIAamp RNA Viral Kit (Qiagen, Heiden, Germany), and quantitative reverse transcription PCR (qRT-PCR) was performed using primers and probes targeting the ORF1ab and N genes of 2019-nCoV (http://ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.html) with a commercial detection kit (GeneoDX Co., Ltd., Shanghai, China). Specimens were considered positive if Ct 38.0, negative if undetermined. Specimens with Ct $>$ 38 were repeated; those with consistent results between 38 and 40 were considered positive, while those with undetectable repeat Ct were considered negative.

Quantification of Hypoxia and Lung Injury

Quantification was performed as previously described (Bi et al. 2019; Yang et al. 2019). Partial pressure of oxygen (PaO) in arterial blood was measured using an ABL90 blood gas analyzer (Radiometer). Fraction of inspired oxygen (FiO) was calculated as: FiO = (21 + oxygen flow [L/min] $\times$ 4)/100. The PaO /FiO ratio (mmHg) was calculated by dividing PaO by FiO . A PaO /FiO ratio 100 mmHg was considered severe ARDS.

Plasma Angiotensin II Measurement

Plasma samples from 12 2019-nCoV-infected patients were separated in a BSL-3 laboratory. Angiotensin II concentrations were measured by ELISA (Cloud-

Clone, TX, USA) following manufacturer instructions.

Statistical Analysis

The Mann-Whitney U test compared continuous variables between two groups. Spearman rank correlation coefficient assessed linear relationships between continuous variables. Receiver operating characteristic (ROC) curves with area under curve (AUC) estimation were used for predictive analysis. $P < 0.05$ was considered statistically significant. Analyses were performed using SPSS 16.0 for Windows (SPSS, Inc.).

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Author Contributions

L. Liu, C. Jiang, and Y. Liu conceived the project and guided the study. Y. Yang, F. Wang, J. Yuan, Z. Wang, Jingxiu Li, Jianming Li, C. Feng, Z. Zhang, L. Wang, L. Peng, and L. Chen collected clinical samples. Y. Yang and C. Zhang, supervised by C. Zhou, performed experiments. F. Huang analyzed biostatistical data with assistance from C. Zhang, Y. Qin, and D. Zhao. S. Tan, L. Yin, and J. Xu provided critical assistance. C. Jiang, Y. Liu, Y. Yang, C. Zhang, F. Huang, and Y. Qin wrote the manuscript, which all authors revised and approved.

Compliance and Ethics

The authors declare no conflict of interest.

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Figure Legends

Figure 1. Timeline of events in human cases with 2019-nCoV. Patients are ordered chronologically by hospital admission date. Various disease course milestones are indicated with different graphics. Patients within families are marked in red and blue, respectively.

Figure 2. Computed tomographic (CT) scans and chest radiographs of case 2. (A) CT scans and (B) chest radiographs taken on indicated dates are shown. d.a.o: days after illness onset.

Figure 3. Ct values of virus are highly correlated with clinical and laboratory manifestations in 2019-nCoV-infected patients. Ct values are highly correlated with (A) PaO /FiO ratio, Murray score and (B) CRP, ALB, LYM (%), LYM, NEU in 2019-nCoV-infected patients. Ct values were available for 10 patients. PaO /FiO ratio, Murray score, ALB, LYM (%), LYM, NEU, CRP, and LDH were detected in 12 patients. Spearman rank correlation coefficients (r) and P values are provided in each graph.

Figure 4. Murray scores are highly correlated with laboratory manifestations in 2019-nCoV-infected patients. (A) Murray scores are highly correlated with ALB, LYM, LDH, LYM (%), NEU (%), and CRP. Murray scores, ALB, LYM, LDH, LYM (%), NEU (%), and CRP were detected in 12 patients. Spearman rank correlation coefficients (r) and P values are provided in each graph.

Figure 5. Receiver operating characteristic (ROC) curves of clinical and biochemical indicators in 2019-nCoV-infected patients. (A) ROC curves for age, Murray score, Ct value, and PaO /FiO ratio, and (B) ROC curves for ALB, LYM, CRP, LYM (%), LDH, and NEU (%) were calculated between 4 mild and 8 severe 2019-nCoV-infected patients. Detailed information is shown in Table 1 and Table 2.

Figure 6. Plasma angiotensin II levels are increased in 2019-nCoV-infected patients and correlated with viral Ct value and PaO /FiO ratio. (A) Box plot of angiotensin II levels in plasma from healthy controls (n=8) and 2019-nCoV-infected patients (n=12). ***P<0.001 (Mann-Whitney U test). Correlation analysis between plasma angiotensin II levels and (B) viral Ct value or (C) PaO /FiO ratio. Viral titers were available for 10 patients. PaO /FiO ratios were detected in 12 patients. Spearman rank correlation coefficients (r) and P values are provided in each graph.

Figure S1. Computed tomographic (CT) scans of human cases with 2019-nCoV. CT scans of cases 1 and 3-12 taken on indicated dates are shown.

Figure S2. Assessment of myocardial function in case 4. (A-B) Echocardiogram results. (C) Left ventricular ejection fraction (LVEF) and left ventricular diameter (LV) on indicated dates.

Figure S3. Correlation between APACHE II scores and viral Ct values in 2019-nCoV-infected patients. Viral titers were available for 10 patients. APACHE

II scores were detected in 12 patients. Spearman rank correlation coefficient (r) and P value are provided.

Tables and Figures

Figure 1. Potential travel exposure timeline

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Stayed in hotel X
Visited local household
Potential local exposure
Mechanical ventilation
Symptoms onset
Admitted to our hospital
Discharged from hospital

Dec 26   Dec 31   Jan 05   Jan 10   Jan 15   Jan 20
Pneumonia confirmed by investigation

Incubation Period (days)
Case 01 65 year-old woman
Case 02 66 year-old man
Case 03 62 year-old man
Case 04 63 year-old man
Case 05 63 year-old woman
Case 06 36 year-old man
Case 07 10 year-old man
Case 08 35 year-old man
Case 09 51 year-old man
Case 10 65 year-old woman
Case 11 72 year-old man
Case 12 56 year-old woman

Dec 26   Dec 31   Jan 05   Jan 10   Jan 15   Jan 20
1-5      1-6      1-10     9-13     1-4      1-3
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Table 1. Epidemiological and clinical features of human subjects hospitalized with 2019-nCoV infection

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Onset to admission (days)	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Initial symptoms							
Fever	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Cough	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Headache	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Myalgia	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Chill	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Nausea or vomiting	[data]	[data]	[data]	[data]	[data]	[data]	[data]

Diarrhea	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Underlying diseases							
Chronic heart disease	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Chronic lung disease	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Chronic renal disease	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Chronic liver disease	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Diabetes	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Hypertension	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Cancer	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Bacterial co-infections	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Complications							
Pneumonia	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Severe ARDS	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Respiratory failure	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Hepatic insufficiency	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Renal insufficiency	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Cardiac failure	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Shock	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Treatment							
Antiviral agents	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Corticosteroid	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Mechanical ventilation	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Invasive mechanical ventilation	[data]	[data]	[data]	[data]	[data]	[data]	[data]
Immunoglobulin	[data]	[data]	[data]	[data]	[data]	[data]	[data]

Note: Severe ARDS defined as PaO /FiO < 100 mmHg

Table 2. Clinical characteristics and laboratory results of subjects hospitalized with 2019-nCoV infection

Parameter	Normal range	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case
PaO /FiO	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[data
WBC (×10 /L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
LYM (%)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
LYM (×10 /L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
NEU (%)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
NEU (×10 /L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
PLT (×10 /L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
AST (U/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
ALT (U/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
TB (mol/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
ALB (g/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CRE (mol/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
BUN (mmol/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CK (U/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
MYO (ng/mL)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CtnI (g/mL)	<0.22	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat

BNP (pmol/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CK-MB (ng/mL)	<0.22	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
LDH (U/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CRP (mg/L)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
PCT (ng/mL)	<0.020	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CD4 (count/ l)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CD8 (count/ l)	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat
CD4/CD8	[range]	[data]	[data]	[data]	[data]	[data]	[data]	[data]	[dat

Note: NA = Not available

Table S1. Ct values of different sample types from the same case determined by qRT-PCR

Sample collection date (d.a.o)		Ct Values	
		Throat swab	BALF
Case 1	[date]	[value]	[value]
Case 3	[date]	[value]	[value]
Case 4	[date]	[value]	[value]
... (additional rows)			

U: Undetected
d.a.o: Days after illness onset
BALF: Bronchoalveolar Lavage Fluid

Figure 2. CT scans and chest radiographs

8 d.a.o 13 d.a.o 16 d.a.o
[Image representations showing progression]

Figure 3. Correlation plots

2019-nCoV Ct value vs PaO /FiO ratio: r = -0.765, P = 0.01
2019-nCoV Ct value vs Murray score: r = 0.815, P = 0.004
2019-nCoV Ct value vs ALB: r = 0.717, P = 0.01
2019-nCoV Ct value vs LYM (%): r = 0.717, P = 0.01
2019-nCoV Ct value vs LYM: r = -0.584, P = 0.038
2019-nCoV Ct value vs NEU (%): r = -0.529, P = 0.05

Figure 4. Murray score correlations

Murray score vs ALB: r = 0.775, P = 0.003
Murray score vs LYM: r = 0.590, P = 0.044
Murray score vs LDH: r = -0.959, P < 0.001
Murray score vs LYM (%): r = -0.919, P < 0.001
Murray score vs NEU (%): r = -0.686, P = 0.01
Murray score vs CRP: r = 0.664, P = 0.018

Figure 5. ROC curves

Age: AUC = 1.000 (Mild vs Severe)

```
Murray score: AUC = 0.984 (Mild vs Severe)
Ct value:     AUC = 0.976 (Mild vs Severe)
PaO /FiO :    AUC = 0.938 (Mild vs Severe)

ALB:          AUC = 1.000 (Mild vs Severe)
LYM:          AUC = 1.000 (Mild vs Severe)
CRP:          AUC = 0.938 (Mild vs Severe)
LYM (%):      AUC = 0.844 (Mild vs Severe)
LDH:          AUC = 0.844 (Mild vs Severe)
NEU (%):      AUC = 0.812 (Mild vs Severe)
```

Figure 6. Angiotensin II analysis

```
Box plot: Healthy vs 2019-nCoV patients (***P < 0.001)

Angiotensin II vs Ct value:      r = -0.669, P = 0.035
Angiotensin II vs PaO /FiO :     r = -0.545, P = 0.06
```

Figure S1. Additional CT scans

```
Case 1   10 d.a.o
Case 3   12 d.a.o
Case 4   13 d.a.o
...
```

Figure S2. Myocardial function assessment

```
Ejection Fraction and Diameter changes over time
```

Figure S3. APACHE II correlation

```
APACHE II vs Ct value:  r = -0.503, P = 0.08
```

Note: Figure translations are in progress. See original paper for figures.