Respiration

Clinical Investigations

Respiration 2020;99:739–747
DOI: 10.1159/000508398

Received: March 27, 2020
Accepted: May 3, 2020
Published online: November 18, 2020

Factors Associated with a Positive Severe Acute Respiratory Syndrome Coronavirus 2 Testing in Suspected Cases Presenting with Pneumonia: A Retrospective Cohort Study in a Single Medical Center

Yupeng Li[a] Yu Shang[b] Yi Yang[a] Menghan Wang[a] Dongping Yu[a] Dongju Su[a] Lei Liu[c] Qin Wang[d] Xiaona Zhang[e] Juan Ren[a] Hong Chen[a]

[a]Department of Respiratory and Critical Care Medicine, The Second Affiliated Hospital of Harbin Medical University, Harbin, China; [b]Department of Respiration, Harbin City First Hospital, Harbin, China; [c]Department of Cadre's Ward, The Second Affiliated Hospital of Harbin Medical University, Harbin, China; [d]Department of Nephrology, The Second Affiliated Hospital of Harbin Medical University, Harbin, China; [e]Department of Endocrinology, The Second Affiliated Hospital of Harbin Medical University, Harbin, China

Keywords
Coronavirus disease 2019 · Positive SARS-CoV-2 testing · Negative SARS-CoV-2 testing · Pneumonia · Risk factors

Abstract

Background: Coronavirus disease 2019 (COVID-19) has become a global emerging infectious disease. ***Objectives:*** To analyze the initial clinical characteristics of COVID-19 suspected and confirmed patients on admission in order to find out which kinds may be more likely to get positive nucleic acid testing results, and to explore the risk factors associated with all-cause death. ***Methods:*** Medical records from 309 highly suspected cases with pneumonia were collected from February 13, 2020, to March 14, 2020, in a COVID-19-designated hospital of Wuhan. The majority of the clinical data were collected on the first day of hospital admission. ***Results:*** Of 309 patients with median age 64 years (interquartile ranges [IQR], 53–72 years), 111 patients (35.9%) were confirmed by nucleic acid testing (median age 64 years, IQR: 56–71 years; 48 males). Of those 111 patients, 13 (11.7%) patients died. In multivariate analysis, factors associated with positive testing included fatigue (odds ratios [OR] = 3.14; 95% confidence interval [CI]: 1.88–5.24, $p < 0.001$), cough (OR = 0.55; 95% CI: 0.32–0.95, $p = 0.032$), no less than 1 comorbidity (OR = 1.77; 95% CI: 1.06–2.98, $p = 0.030$), and severe pneumonia (OR = 2.67; 95% CI: 1.20–5.97, $p = 0.016$). Furthermore, age, dyspnea, noneffective antibiotic treatment, white blood cell, lymphocyte, platelets, and organ dysfunction (e.g., higher lactate dehydrogenase) were significantly associated with all-cause in-hospital death in patients with COVID-19. ***Conclusion:*** Patients with severe forms of this disease were more likely to get positive results. Age and organ dysfunction were associated with a greater risk of death.

Introduction

In December 2019, a new coronavirus was first reported in Wuhan, Hubei Province, China. The new coronavirus is a member of the Coronaviridae family, belonging

Drs. Yupeng Li and Yu Shang contributed equally to this article.

karger@karger.com
www.karger.com/res

Hong Chen
Respiratory and Critical Care Medicine
The Second Affiliated Hospital of Harbin Medical University
246 Xuefu Road, Harbin 150086 (China)
chenhong744563@aliyun.com

to the genus Betacoronavirus, subgenus Sarbecovirus [1], which was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease caused by it was named as coronavirus disease 2019 (COVID-19) [2]. As of September 27, 2020, over 32.7 million cases had been confirmed, and 991,0000 patients died in the world [3].

Some studies have shown that the common symptoms were fever, cough, myalgia, and fatigue in patients with COVID-19 [4, 5], and older age and chronic underlying conditions such as diabetes and cardiovascular disease were significantly associated with severe pneumonia and higher risk of death [4, 6]. Clinicians are facing challenges posed by the large number of admissions of suspected cases. The CT chest scan is the most common examination in the evaluation of COVID-19. Patients with confirmed COVID-19 pneumonia have typical imaging features: ground-glass opacities (GGO) or mixed GGO, consolidation and vascular enlargement in the peripheral areas or lower lobe of the lung [7]. However, during a period of year, pneumonia caused by other pathogens is widespread [8], for example, the common imaging feature of pneumonia caused by influenza virus such as influenza A (H1N1) virus was also GGO [9, 10]. Real-time RT-PCR (rRT-PCR) on respiratory tract specimens has been the gold standard for the etiological diagnosis of SARS-CoV-2 infection [11]. However, in the process of diagnosis for COVID-19, doctors often have to face false-negative testing results in highly suspected cases [12]. Thus, it is very hard for clinicians to distinguish in the outbreak, especially in Wuhan, the epicenter of the pandemic. There are limited data regarding the clinical features of suspected cases; however, most studies were outside of Wuhan, and not all patients had a history of exposure to confirmed cases of COVID-19 [13, 14]. In this study, we summarized and compared the initial clinical features between positive and negative SARS-CoV-2 testing by rRT-PCR in suspected cases with pneumonia to find out which kinds are more likely to get positive nucleic acid testing results. In addition, the assessment of risk factors for all-cause in-hospital death in confirmed cases was also essential.

Methods

Study Population

This is a retrospective cohort study of 309 highly suspected cases with pneumonia from February 13, 2020, to March 14, 2020, hospitalized in Wuhan No. 1 Hospital, China. These patients were treated or managed by the Harbin Medical Team to aid Hubei province. Pneumonia was diagnosed according to CT or X-ray. All patients lived in Wuhan and had a history of exposure to confirmed cases of COVID-19. This study was reviewed and approved by the Medical Ethical Committee of the Second Affiliated Hospital of Harbin Medical University (KY2020-011).

Procedures

All suspected cases were admitted to the quarantined observing rooms. To identify SARS-CoV-2 infection, rRT-PCR was used for the testing of nasopharyngeal swab samples obtained from all patients on admission according to the recommendation by the National Institute for Viral Disease Control and Prevention (China) [15]. Second nucleic acid testing by rRT-PCR was applied to patients with negative initial results at least 1 day later. Patients discharged from this hospital when their condition significantly improved, and nucleic acid testing for SARS-CoV-2 antigens was negative. 111 patients with positive nucleic acid testing were diagnosed with COVID-19 according to the National Health Commission of the People's Republic of China interim guidance [16]. Serological assays (serum-specific IgG and IgM antibodies) were performed according to ELISA.

Data Collection

The epidemiology, clinical symptoms, comorbidities, and initial laboratory data from electronic medical records were extracted. Blood routine examination included white blood cells, lymphocytes, and platelets. Biochemical tests included aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, lactate dehydrogenase (LDH), and creatine kinase. C-reactive protein and D-dimer levels were also collected. The majority of the clinical data were collected on the first day of hospital admission unless indicated otherwise in this study. Two authors (Y.L. and Y.S.) extracted and interpreted the data independently, then in duplicate. The highest patient temperature was defined using the self-reported highest temperature prior to hospital admission, otherwise, highest temperature on admission. Fever and high fever were classified as 37.3°C or higher and 39°C or higher, respectively. Noneffective antibiotic treatment includes any of the following: (1) no declining temperature after 48–72 h antibiotic treatment and (2) no improvement in symptoms even worse after 48–72 h antibiotic treatment. Severe pneumonia includes any of the following: (1) respiratory distress and respiratory rate ≥30 breaths/min; (2) peripheral oxygen saturation (SpO_2) ≤93% at rest; and (3) partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ≤300 mm Hg (1 mm Hg = 0.133 kPa). Non-severe pneumonia does not meet the above criteria.

Outcomes

Two outcomes were evaluated: discharge and all-cause in-hospital death.

Statistical Analysis

SPSS Statistics 23 (IBM SPSS) was used for statistical analysis. Number/total number (percentage) was used to describe categorical variables, and number (median, interquartile ranges [IQR]) was used to describe the continuous variables. χ^2 test or Fisher's exact test was used for statistical testing when comparing proportions between 2 independent groups. The Mann-Whitney test was used for non-normal distributed continuous data, otherwise, independent group *t* tests. Furthermore, positive SARS-CoV-2 testing

Table 1. Demographic features between positive and negative COVID-19 testing by rRT-PCR in patients with suspected COVID-19 pneumonia

Demographic features	All patients (n = 309)	Positive group (n = 111, 35.9%)	Negative group (n = 198, 64.1%)	p value[a]
Age, median (IQR), years	64 (53–72)	64 (56–71)	63 (52–72)	0.671
0–20	1/309 (0.3)	1/111 (0.9)	0/198	
21–40	31/309 (10.0)	7/111 (6.3)	24/198 (12.1)	0.398
41–60	96/309 (31.1)	34/111 (30.6)	62/198 (31.3)	
61–80	147/309 (47.6)	55/111 (49.6)	92/198 (46.5)	
81–100	34/309 (11.0)	14/111 (12.6)	20/198 (10.1)	
Gender				
Male	149/309 (48.2)	48/111 (43.2)	101/198 (51.0)	0.190
Female	160/309 (51.8)	63/111 (56.8)	97/198 (49.0)	
Epidemiological investigation				
Contact with people with cough recently	309/309 (100)	111/111 (100)	198/198 (100)	
Exposure to confirmed cases of COVID-19	309/309 (100)	111/111 (100)	198/198 (100)	
Clinical symptoms				
Cough	229/309 (74.1)	74/111 (66.7)	155/198 (78.3)	0.025
Productive cough	67/309 (21.7)	28/111 (25.2)	39/198 (19.7)	0.258
Fever	210/309 (68.0)	74/111 (66.7)	136/198 (68.7)	0.715
Dyspnea	63/309 (20.4)	25/111 (22.5)	38/198 (19.2)	0.486
Fatigue	173/309 (53.6)	81/111 (73.0)	92/198 (46.5)	<0.001
Highest patient temperature, °C				
≥39 (high fever)	55/210 (26.2)	23/74 (31.1)	32/136 (23.5)	0.234
<39	155/210 (73.8)	51/74 (68.9)	104/136 (76.5)	
Comorbidities				
Any	153/309 (49.5)	64/111 (57.7)	89/198 (44.9)	0.032
>1 comorbidity	52/309 (16.8)	20/111 (18.0)	32/198 (16.2)	0.676
COPD	9/309 (2.9)	5/111 (4.5)	4/198 (2.0)	0.291
Hypertension	108/309 (35.0)	44/111 (39.6)	64/198 (32.3)	0.196
Diabetes	52/309 (16.8)	22/111 (19.8)	29/198 (14.6)	0.240
Cardiovascular disease	30/309 (9.7)	12/111 (10.8)	18/198 (9.1)	0.624
Cancer	10/309 (3.2)	5/111 (4.5)	5/198 (2.5)	0.340
Other chronic history	17/309 (5.5)	6/111 (5.4)	11/198 (5.6)	0.956
Items of severe pneumonia				
SpO_2 ≤93%	28/309 (9.1)	16/111 (14.4)	12/198 (6.1)	0.014
Respiratory rate ≥30/min	6/309 (1.9)	4/111 (3.6)	2/198 (1.0)	0.193
PaO_2/FiO_2 ≤300 mm Hg	9/309 (2.9)	7/111 (6.3)	2/198 (1.0)	0.012
Severe pneumonia	28/309 (9.1)	16/111 (14.4)	12/198 (6.1)	0.014
Noneffective antibiotic treatment	42/278 (15.1)	19/102 (18.6)	23/176 (13.1)	0.212
Serum-specific IgG and IgM antibodies testing	96/309 (31.1)	27/111 (24.3)	69/198 (34.8)	
Positive IgM antibody	56/96 (58.3)	16/27 (59.3)	40/69 (58.0)	
Positive IgG antibody	89/96 (92.7)	25/27 (92.6)	64/69 (93.0)	
Double-positive antibodies	56/96 (58.3)	16/27 (59.3)	40/69 (58.0)	
Prognosis				
All-cause in-hospital death	281/309 (90.9)	13/111 (11.7)	15/198 (7.6)	0.224
Discharge	28/309 (9.1)	98/111 (88.3)	183/198 (92.4)	

Values are presented as median (IQR) or n/N (%). COVID-19, coronavirus disease 2019; rRT-PCR, real-time rRT-PCR; COPD, chronic obstructive pulmonary disease; SpO_2, peripheral oxygen saturation; IQR, interquartile range; PaO_2, partial pressure of oxygen; FiO_2, fraction of inspired oxygen. [a] Mann-Whitney test was used for continuous variables. χ^2 test or Fisher's exact test was used for categorical variables.

Table 2. Initial laboratory indices of patients with suspected COVID-19 pneumonia

Tests in study population	Reference values	Positive group (n = 111)	Negative group (n = 198)	p value[a]
C-reactive protein >5 mg/L	0–5	58/101 (57.4)	81/168 (48.2)	0.143
Hematologic				
White blood cells, $\times 10^9$/L	3.5–9.5	83 (6.11, 4.93–8.03)	56 (6.02, 4.9–7.1)	0.574
$>9.5 \times 10^9$/L		13/83 (15.7)	4/56 (7.1)	0.188
$\leq 9.5 \times 10^9$/L		70/83 (84.3)	52/56 (7.1)	
Lymphocytes, $\times 10^9$/L	1.1–3.2	85 (1.35, 0.84–1.91)	56 (1.49, 1.02–1.48)	0.418
$<1.1 \times 10^9$/L		28/85 (32.9)	17/56 (30.4)	0.747
$\geq 1.1 \times 10^9$/L		57/85 (67.1)	39/56 (69.6)	
Platelets, $\times 10^9$/L	125–350	84 (230.5, 184–286.75)	56 (221.5, 187.5–286)	0.482
$<125 \times 10^9$/L		8/84 (9.5)	4/56 (7.1)	0.763
$\geq 125 \times 10^9$/L		76/84 (90.5)	52/56 (92.9)	
Biochemical				
AST, U/L	13–35	84 (23, 19.25–34)	56 (25, 17.5–36.75)	0.992
>35 U/L		20/84 (23.8)	14/56 (25.0)	0.872
≤35 U/L		64/84 (76.2)	42/56 (75.0)	
ALT, U/L	7–45	83 (24, 15–40)	55 (23, 13–23)	0.954
Albumin, g/L	40–55	85 (32.5, 28.45–38.1)	56 (33, 29.83–36.08)	0.471
Glucose, mmol/L	3.9–6.1	30 (5.05, 4.6–6.9)	19 (5.6, 5–6.7)	0.196
LDH, U/L	114–250	67 (218, 179–300)	45 (201, 175–277)	0.393
Creatine kinase, U/L	0–171	66 (51, 42–100)	45 (51, 33.5–70)	0.183

Values are presented as n (median, IQR) or n/N (%). In negative group, the initial laboratory indices of most patients were absent because our team went to support another hospital. COVID-19, coronavirus disease 2019; IQR, interquartile range; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase. [a] χ^2 test or Fisher's exact test was used for categorical variables. Mann-Whitney test was used for non-normal distributed continuous data, otherwise, independent group t tests.

and all-cause in-hospital mortality were reviewed using univariate and multivariate logistic regression analyses presenting with odds ratios (ORs) and 95% confidence interval (CI). Bilateral test (test level $\alpha = 0.05$) was used, and $p < 0.05$ was considered statistically significant.

Results

Study Samples

From February 13, 2020, to March 14, 2020, the final study cohort consisted of 309 patients with suspected COVID-19 pneumonia (149 males and 160 females). The median age was 64 years (IQR: 53–72 years), and patients aged over 60 years accounted for 58.6% (Table 1). All patients contacted with confirmed cases of COVID-19 recently; however, history of cluster was unclear in most patients. Of those 309 patients, 281 cases discharged from this hospital and the remaining 28 cases died. Serological assays (serum-specific IgG and IgM antibodies) according to ELISA were applied to 96 patients. Both serum-specific IgM and IgG antibodies were positive not only in 40 patients with negative SARS-CoV-2 testing but also in 16 patients with positive SARS-CoV-2 testing. Of those 309 patients, 111 (35.9%) patients had positive testing results and were referred to as "positive group" and the remaining 198 (64.1%) patients were referred to as "negative group."

Clinical Features

Demographic characteristics between the positive group and the negative group are described in Table 1. Age or different age groups, gender, and all-cause in-hospital death between the 2 groups did not show any statistically significant differences. Compared with patients in the negative group, more patients presented with fatigue (81 [73.0] vs. 92 [46.5%], $p < 0.001$) and no less than 1 underlying condition (64 [57.7] vs. 89 [44.9%], $p = 0.032$) in the positive group. Patients in the positive group were less likely to present with cough (74 [66.7] vs. 155 [78.3%], $p = 0.025$) compared with those in the negative group. In addition, compared with negative patients, positive pa-

Table 3. Factors associated with positive nucleic acid testing in patients with suspected COVID-19 pneumonia

Clinical characteristics	Univariate analysis OR (95% CI)	*p* value[a]	Multivariate analysis OR (95% CI)	*p* value[a]
Initial symptoms				
Cough	0.56 (0.33–0.93)	0.026	0.55 (0.32–0.95)	0.032
Fatigue	3.11 (1.88–5.15)	<0.001	3.14 (1.88–5.24)	<0.001
Comorbidities				
Any	1.67 (1.04–2.67)	0.033	1.77 (1.06–2.98)	0.030
Severe pneumonia	2.61 (1.19–5.74)	0.017	2.67 (1.20–5.97)	0.016

COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval. [a] Logistic regression analysis.

tients were more likely to have PaO_2/FiO_2 ≤300 mm Hg (7 [6.3] vs. 2 [1.0%], $p = 0.012$) and SpO_2 ≤93% (16 [14.4] vs. 9 [5.5%], $p = 0.014$) on admission. Therefore, patients in the positive group had severe symptoms compared with those in the negative group (16 [14.4] vs. 12 [6.1%], $p = 0.014$) on admission. Initial laboratory indices between the 2 groups did not show any statistically significant differences (Table 2).

Factors Associated with a Positive SARS-CoV-2 Testing

As summarized in Table 3, univariate analysis showed that fatigue (OR = 3.11; 95% CI: 1.88–5.15, $p < 0.001$), cough (OR = 0.56; 95% CI: 0.33–0.93, $p = 0.026$), no less than 1 underlying condition (OR = 1.67; 95% CI: 1.04–2.67, $p = 0.033$), and severe pneumonia (OR = 2.61; 95% CI: 1.19–5.74, $p = 0.017$) were significantly associated with positive SARS-CoV-2 testing in patients with suspected COVID-19 pneumonia. Multivariate analysis showed that fatigue (OR = 3.14; 95% CI: 1.88–5.24, $p < 0.001$), cough (OR = 0.55; 95% CI: 0.32–0.95, $p = 0.032$), no less than 1 underlying condition (OR = 1.77; 95% CI: 1.06–2.98, $p = 0.030$), and severe pneumonia (OR = 2.67; 95% CI: 1.20–5.97, $p = 0.016$) were independent factors for positive SARS-CoV-2 testing.

Risk Factors Associated with All-Cause In-Hospital Death

Of the 111 patients with COVID-19 pneumonia, 13 cases died during the hospitalization period. Age, dyspnea, cough, noneffective antibiotic treatment, white blood cells, lymphocytes, platelets, AST, albumin, creatine kinase, and LDH were significantly different between the 2 groups ($p < 0.05$; Table 4). The higher level of D-dimer was demonstrated obviously in dead patients (8.47 [IQR: 0.83–19.8] vs. 0.82 [IQR: 0.28–3.97] mg/L) compared with that in discharged patients; however, such difference was not statistically significant ($p = 0.072$), likely owing to the small samples. Univariate analysis showed that age, dyspnea, cough, noneffective antibiotic treatment, white blood cells >9.5 × 10^9/L, lymphocytes <1.1 × 10^9/L, platelets <125 × 10^9, AST >35 U/L, albumin <35 U/L, LDH >250 U/L, and creatine kinase were significantly associated with death ($p < 0.05$; Table 5). In multivariable logistic regression, we found that age (OR = 1.12; 95% CI: 1.002–1.24, $p = 0.046$), dyspnea (OR = 52.36; 95% CI: 4.73–579.74, $p = 0.001$), noneffective antibiotic treatment (OR = 8.02; 95% CI: 1.15–55.74, $p = 0.035$), white blood cells >9.5 × 10^9/L (OR = 9.26; 95% CI: 1.68–50.79, $p = 0.010$), lymphocytes <1.1 × 10^9/L (OR = 9.30; 95% CI: 1.46–59.38, $p = 0.018$), platelets <125 × 10^9 (OR = 12.61; 95% CI: 1.90–83.58, $p = 0.009$), AST >35 U/L (OR = 14.92; 95% CI: 2.44–91.25, $p = 0.003$), and LDH >250 U/L (OR = 16.84; 95% CI: 1.70–166.46, $p = 0.016$) were significantly associated with death.

Discussion

This study described the clinical characteristics of highly suspected cases with pneumonia. As of March 14, 2020, of 309 patients included in this study, 111 (35.9%) patients had positive SARS-CoV-2 testing. Common symptoms were cough, fever, fatigue, dyspnea, and productive cough on admission. Hypertension was the most common underlying condition. These results were basically consistent with a study with 116 suspected cases in Anhui province, China [13]. However, not all patients were exposed to confirmed cases and diagnosed with pneumonia, besides they were

Table 4. Comparison of clinical features between discharged and dead patients with COVID-19 pneumonia

Clinical features	Discharge (n = 98, 88.3%)	All-cause death (n = 13, 11.7%)	p value[a]
Age, median (IQR), years	63 (52–69)	79 (71–85)	<0.001
Gender			
Male	41/98 (41.8)	7/13 (53.8)	0.412
Female	57/98 (58.2)	6/13 (46.2)	
Clinical symptoms			
Cough	69/98 (70.4)	5/13 (38.5)	0.030
Productive cough	26/98 (26.5)	2/13 (15.4)	0.511
Fever	67/98 (68.4)	7/13 (53.8)	0.322
Dyspnea	13/98 (13.3)	12/13 (92.3)	<0.001
Fatigue	70/98 (71.4)	11/13 (84.6)	0.314
Highest patient temperature, °C			
≥39 (high fever)	17/67 (25.4)	3/7 (42.9)	0.379
<39	50/67 (74.6)	4/7 (57.1)	
Underlying conditions			
Any	55/98 (56.1)	9/13 (69.2)	0.552
>1 comorbidity	16/98 (16.3)	4/13 (30.8)	0.247
COPD	4/98 (4.1)	1/13 (7.7)	
Hypertension	38/98 (38.8)	6/13 (46.2)	0.609
Diabetes	19/98 (19.4)	4/13 (30.8)	0.464
Cardiovascular disease	10/98 (10.2)	2/13 (15.4)	0.631
Cancer	5/98 (5.1)	0 (0)	
Other chronic history	1/98 (1.0)	5/13 (38.5)	<0.001
Noneffective antibiotic treatment	11/90 (12.2)	8/12 (66.7)	<0.001
C-reactive protein >5 mg/L	49/88 (55.7)	9/13 (69.2)	0.549
D-dimer, mg/L	8 (0.82, 0.28–3.97)	7 (8.47, 0.83–19.8)	0.072
Hematologic			
White blood cells, $\times10^9$/L	72 (5.92, 4.75–7.27)	13 (11.3, 6.6–15.1)	0.002
>9.5 $\times$ 10^9/L	6/72 (8.3)	7/13 (53.8)	<0.001
≤9.5 $\times$ 10^9/L	66/72 (91.7)	6/13 (46.2)	
Lymphocytes, $\times10^9$/L	72 (1.43, 1.10–1.83)	13 (0.66, 0.47–0.84)	<0.001
<1.1 $\times10^9$/L	17/72 (23.6)	11/13 (84.6)	<0.001
≥1.1 $\times10^9$/L	55/72 (76.4)	2/13 (15.4)	
Platelets, $\times10^9$/L	72 (238.5, 193.8–289.3)	12 (145.5, 89.0–223.8)	0.001
<125 $\times10^9$/L	3/72 (4.2)	5/12 (41.7)	0.001
≥125 $\times10^9$/L	69/72 (95.8)	7/12 (58.3)	
Biochemical			
AST, U/L	72 (22.0, 18.3–29.0)	12 (48.0, 28.8–63.3)	<0.001
>35 U/L	12/72 (16.7)	8/12 (66.7)	0.001
≤35 U/L	60/72 (83.3)	4/12 (33.3)	
ALT, U/L	72 (23.0, 15.3–39.5)	11 (35, 12–49)	0.541
Albumin, g/L	72 (34.9, 28.7–38.8)	13 (29.4, 26.4–32.0)	<0.001
≤35 g/L	36/72 (50.0)	12/13 (92.3)	0.005
>35 g/L	36/72 (50.0)	1/13 (7.7)	
LDH, U/L	58 (208.0, 175.5–258.8)	9 (721.0, 404.5–890.0)	<0.001
>250 U/L	16/58 (27.6)	8/9 (88.9)	0.001
≤250 U/L	42/58 (72.4)	1/9 (11.1)	
Creatine kinase, U/L	58 (50.0, 39.8–86.3)	8 (107.0, 57.0–409.3)	0.014
>171 U/L	2/58 (3.4)	2/8 (25.0)	0.069
≤171 U/L	56/58 (96.6)	6/8 (75.0)	

Values are presented as n (median, IQR) or n/N (%). COVID-19, coronavirus disease 2019; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; IQR, interquartile range. [a] χ^2 test or Fisher's exact test was used for categorical variables. Mann-Whitney test was used for non-normal distributed continuous data, otherwise, independent group t tests.

Table 5. Risk factors associated with all-cause in-hospital death in patients with COVID-19 pneumonia

Clinical characteristics	Univariate analysis OR (95% CI)	*p* value[a]	Multivariate analysis OR (95% CI)	*p* value[a]
Age	1.13 (1.06–1.21)	<0.001	1.12 (1.002–1.24)	0.046
Initial symptoms				
Cough	0.26 (0.08–0.87)	0.029		
Dyspnea	78.5 (9.4–654.9)	<0.001	52.36 (4.73–579.74)	0.001
Noneffective antibiotic treatment	12.66 (3.51–45.58)	<0.001	8.02 (1.15–55.74)	0.035
Hematologic				
White blood cells, $\times 10^9$/L	1.29 (1.10–1.51)	0.002		
$>9.5 \times 10^9$/L	12.83 (3.25–50.70)	<0.001	9.26 (1.68–50.89)	0.010
Lymphocytes, $\times 10^9$/L	0.03 (0.003–0.199)	<0.001		
$<1.1 \times 10^9$/L	17.79 (3.59–88.30)	<0.001	9.30 (1.46–59.38)	0.018
Platelets, $\times 10^9$/L	0.98 (0.97–0.99)	0.003		
$<125 \times 10^9$/L	16.43 (3.22–83.76)	0.001	12.61 (1.90–83.58)	0.009
Biochemical				
AST, U/L	1.04 (1.01–1.07)	0.006		
>35 U/L	10.0 (2.59–38.61)	0.001	14.92 (2.44–91.25)	0.003
Albumin, g/L	0.87 (0.77–0.97)	0.016		
≤35 g/L	12.0 (1.48–97.18)	0.020	7.16 (0.79–64.64)	0.079
LDH, U/L	1.007 (1.003–1.011)	0.001		
>250 U/L	21.0 (2.43–181.57)	0.006	16.84 (1.70–166.46)	0.016
Creatine kinase, U/L	1.004 (1.0–1.007)	0.040	1.002 (0.998–1.006)	0.257

COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase. [a] Logistic regression analysis.

younger than our patients, and no patient died (that study showed 9.1% mortality) [13]. In addition, it was estimated that the risk for death in Wuhan may reach 12%, whereas it was ≈1% in other, more mildly affected areas of China [17]. Therefore, the demographic features of patients with suspected COVID-19 pneumonia in Wuhan (the previous epicenter of the pandemic) were relatively severe. Especially, we should pay more attention to the suspected cases in Europe (the new epicenter of the pandemic) [3].

This study found that fever (74 patients, 66.7%), cough (74 patients, 66.7%), fatigue (81 patients, 73.0%), and dyspnea (25 patients, 22.5%) were common symptoms, and hypertension (44, 39.6%), diabetes (22, 19.8%), and cardiovascular disease (12, 10.8%) were common underlying conditions. This study also showed that majority of patients had normal or low white blood cell counts (84.3%). These clinical characteristics were basically consistent with previous studies [4–6, 18]. However, our study showed that median age (64 years old) was higher than that in the 3 studies (49, 51, and 56 years, respectively) [4–6]. In addition, our data differ from the recent report that showed SARS-CoV-2 infection was more likely to affect females [6]. Whether the differences are due to regional differences, which requires further multicenter research. Internationally, health authorities and governments are warning older age is the strongest risk factor associated with death in patients with COVID-19. The mortality data from the Oxford COVID-19 Evidence Service showed that the mortality was 3.6% for patients aged 60–69 years, 8.0% for those aged 70–79 years, and 14.8% for those aged over 80 years [19]. Dyspnea, viral hyperinflammation (e.g., elevated white blood cells), dysregulation of immune responses (e.g., decreased lymphocyte), and organ dysfunction (e.g., elevated LDH) were significantly associated with the development of death in patients with COVID-19 [4, 6, 20, 21], which was consistent with results of this study. Furthermore, this study suggested that antibiotic treatment was more noneffective in dead patients compared with discharged patients.

We reported here a comparative analysis between 111 patients with laboratory-confirmed COVID-19 and 198 patients with negative COVID-19 testing by rRT-PCR. Patients in the positive group were more likely to present with fatigue and less likely to present with cough com-

pared with those in the negative group. A study found patients with COVID-19 pneumonia presented remarkably with more abnormal laboratory tests including AST, alanine aminotransferase, LDH, γ-glutamyl transpeptidase (γ-GT), and α-hydroxybutyrate dehydrogenase(α-HBDH) compared to those with other pneumonia [22]. However, the differences are hard to distinguish, because the symptoms (e.g., fever, cough, or sore throat) and laboratory indices due to SARS-CoV-2 infection are similar to those of influenza [23], and the outbreak occurred during seasons when influenza, respiratory syncytial viruses, and other respiratory viruses are highly prevalent. Therefore, early identification of infected patients is very important for clinicians. In this study, patients in the positive group showed higher proportion of severe pneumonia and no less than 1 comorbidity on admission compared with those in the negative group, which may be meaningful differentiating items. According to multivariate analysis, suspected cases presenting with severe pneumonia were 2.67 times likely to have positive SARS-CoV-2 testing compared with those without. Suspected cases presenting with comorbidity were 1.77 times likely to have positive SARS-CoV-2 testing compared with those without. We should pay more attention to these patients, and pathogenic detection is necessary as soon as possible.

PCR on respiratory tract specimens has been the gold standard for the etiological diagnosis of SARS-CoV-2 infection; however, the diagnostic accuracy of this technique is affected by many factors such as inadequate procedures for specimen (e.g., swab) collection, handling, transport, and storage, and presence of interfering substances [11]. In 19 suspected cases, the authors found the positive ratio of nucleic acid detection for SARS-CoV-2 was only 47.4% according to the comparison among 3 different samples (oropharyngeal swab, blood, and urine) and 3 different fluorescent RT-PCR kits, which suggested that it is possible that the really infected patients have been missed by using nucleic acid detection only [14]. Another study found that the positive detection rate according to a single rRT-PCR test is low and combined humoral response (serum-specific IgG and IgM) to SARS-CoV-2 can significantly increase positive detection rate [24]. Serological assays are useful methods for the diagnosis among viral diseases, and their effectiveness has been proved in the confirmatory diagnosis of Middle East respiratory syndrome [25], whereas they have not been developed for COVID-19 [26]. On March 3, 2020, the diagnostic criterion of serum-specific antibodies (IgG and IgM) for COVID-19 was added into the seventh version of the National Health Commission of the People's Republic of China interim guidance [27]. Therefore, precise diagnosis of COVID-19 seemed very difficult by relying on nucleic acid detection alone. This study showed that 40 patients had double-positive serum-specific IgM and IgG antibodies, and 15 (7.6%) patients died in the negative group likely owing to the false-negative result by nucleic acid testing. We recommend that serum-specific antibody testing or gene sequencing should be applied to highly suspected cases with negative SARS-CoV-2 testing to decrease the misdiagnosed rate.

There are several limitations in this study. First, it is a retrospective, single-center study rather than a prospective study or a multicenter study. Second, there are inherent limitations in the selection of research methods; the research sample size is relatively small, the representative meaning is limited. Third, the majority of medical records were collected on admission, which could not represent the whole process of hospitalization. Fourth, only rough clinical characteristics were compared, and more detailed information were not compared, so the conclusions of this study were limited. Fifth, the study did not distinguish pneumonia caused by which pathogens except caused by COVID-19.

In conclusion, with the outbreak of COVID-19 in the world, the study of the clinical characteristics of suspected cases, and the comparison of the data between positive and negative nucleic acid testing results can help clinicians better to understand this disease. Patients with severe forms of this disease are more likely to get the positive results on admission, but we also need to guard against false-negative results. In patients with COVID-19, age, dyspnea, noneffective antibiotic treatment, white blood cells, lymphocytes, platelets, AST, albumin, and LDH were significantly associated with all-cause in-hospital death.

Acknowledgement

We thank Wuhan No. 1 Hospital for providing the medical records.

Statement of Ethics

This study was reviewed and approved by the Medical Ethical Committee of the Second Affiliated Hospital of Harbin Medical University (KY2020-011).

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

Funding Sources

The authors did not receive any funding.

Author Contributions

D.S., L.L., Q.W., and X.Z. performed data collection. Y.Y., D.Y., and M.W. performed data analysis and edited the manuscript. J.R. performed data analysis. Y.L. and Y.S. prepared the first manuscript draft, validated data collection, refined the research idea, performed data analysis, and edited the manuscript. H.C. developed the research idea, refined the research idea, validated data collection, and edited the manuscript. H.C. is the guarantor of the manuscript.

References

1 Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020 Mar;579(7798):265–9.
2 World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it.
3 World Health Organization. Coronavirus disease 2019 (COVID-19) situation report: Weekly Epidemiological and Operational updates. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.
4 Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020 Jul 1;180(7):934–43.
5 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.
6 Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061–69.
7 Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: a multicenter study. AJR Am J Roentgenol. 2020 Mar 3;214(5):1072–77.
8 Viasus D, Marinescu C, Villoslada A, Cordero E, Gálvez-Acebal J, Fariñas MC, et al. Community-acquired pneumonia during the first post-pandemic influenza season: a prospective, multicentre cohort study. J Infect. 2013 Sep;67(3):185–93.
9 Laqmani A, Adam G, Regier M. Pulmonary manifestation of novel swine-origin influenza A (H1N1) virus (S-OIV) infection in immunocompromised patients: initial findings with multidetector computed tomography. Med Princ Pract. 2012;21(6):548–53.
10 Chandler TM, Leipsic J, Nicolaou S, Quiney B, Romney M, Müller NL, et al. Confirmed swine-origin influenza A(H1N1) viral pneumonia: computed tomographic findings in the immunocompetent and the immunocompromised. J Comput Assist Tomogr. 2011 Sep–Oct;35(5):602–7.
11 Lippi G, Simundic AM, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clin Chem Lab Med. 2020 Mar 16;58(7):1070–6.
12 Guo L, Ren L, Yang S, Xiao M, Chang D, Yang F, et al.
13 Zhu W, Xie K, Lu H, Xu L, Zhou S, Fang S. Initial clinical features of suspected coronavirus disease 2019 in two emergency departments outside of Hubei, China. J Med Virol. 2020 Mar 13.
14 Xie C, Jiang L, Huang G, Pu H, Gong B, Lin H, et al. Comparison of different samples for 2019 novel coronavirus detection by nucleic acid amplification tests. Int J Infect Dis. 2020 Apr;93:264–7.
15 National Institute for Viral Disease Control and Prevention (China). Specific primers and probes for detection 2019 novel coronavirus. http: //ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.html.
16 National Health Commission of the People's Republic of China.
17 Mizumoto K, Chowell G. Estimating risk for death from 2019 novel coronavirus disease, China, January-February 2020. Emerg Infect Dis. 2020 Jun;26(6):1251–6.
18 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 Feb 15;395(10223):507–13.
19 Oxford COVID-19 Evidence Service. Global COVID-19 Case Fatality Rates. https://www.phc.ox.ac.uk/covid-19/evidence-service/reviews/global-covid-19-case-fatality-rates.
20 Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. J Med Virol. 2020 Apr 3.
21 Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis. 2020 Jul 28;71(15):762–8.
22 Zhao D, Yao F, Wang L, Zheng L, Gao Y, Ye J, et al. A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias. Clin Infect Dis. 2020 Jul 28;71(15):756–61.
23 Dharmapalan D. Influenza. Indian J Pediatr. 2020 Oct;87(10):828–32.
24 Guo L, Ren L, Yang S, Xiao M, Chang YF, et al. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). Clin Infect Dis. 2020 Jul 28;71(15):778–85.
25 Okba NMA, Widjaja I, Li W, GeurtsvanKessel CH, Farag E, Al-Hajri M, et al. Serologic detection of Middle East respiratory syndrome coronavirus functional antibodies. Emerg Infect Dis. 2020 May 17;26(5):1024–7.
26 Pang J, Wang MX, Ang IYH, Tan SHX, Lewis RF, Chen JI, et al. Potential rapid diagnostics, vaccine and therapeutics for 2019 novel coronavirus (2019-nCoV): a systematic review. J Clin Med. 2020 Feb 26;9(3):623.
27 National Health Commission of the People's Republic of China.