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Original Article

Clinical characteristics of patients with confirmed and suspected COVID-19

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Abstract: Objective: To compare the differences between two groups of patients with confirmed and suspected COVID-19. Methods: We retrospectively collected and analyzed the data of confirmed and suspected patients, including demographic, epidemic, laboratory, clinical, radiologic, and treatment data, at the fever clinic and isolation ward of our hospital from December 1, 2019 to December 30, 2019. Results: The study included 73 patients with confirmed or suspected COVID-19. The median age was 43.6 years old, and 41 patients (56.2%) were male. Patients in the suspected group (SG) (n=47) were significantly older than those in the confirmed group (CG) (n=26). Among 73 patients, 18 (24.6%) had comorbidities. Most laboratory test results in this study were normal, except for total lymphocyte counts and C-reactive protein levels. Patients in the CG had fewer lymphocyte count abnormalities than those of the SG. More patients in the CG (13 cases, 50%) displayed involvement of three or more lobes than those in the SG (8 cases, 17%). More patients in the SG (36 cases, 76.6%) displayed involvement of 1-2 lobes than those in the CG (12 cases, 46.2%). In the CG, computed tomography (CT) lung lesions were mainly distributed in the left lower lung lobe (65.4%) and left upper lung lobe (80.8%). Conclusion: The reference standard for detecting COVID-19 is still RT-PCR. However, characteristic chest CT results and a history of close contact strongly suggest COVID-19 infection.

Keywords: COVID-19, novel coronavirus pneumonia, RT-PCR, pneumonia

Introduction

In December 2019, a cluster of pneumonia cases emerged in Wuhan City in Hubei Province, China [1, 2]. This disease is officially known as coronavirus disease 2019 (COVID-19) and is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [3-5]. Novel coronavirus pneumonia (NCP) has rapidly spread across the world, and the number of patients with NCP has exceeded the total number of patients with severe acute respiratory syndrome (SARS) in 2003 [6, 7]. The number of confirmed and suspected NCP cases continues to increase. Thus, early diagnosis, early isolation, and early treatment are particularly important for patients with NCP [8-10].

The nucleic acid of the novel coronavirus was detected by reverse transcription-polymerase chain reaction (RT-PCR), and samples were taken from nasopharynx swabs [11, 12]. Theoretically, the sensitivity of this method is very high; therefore, it has a high positivity rate [13]. However, testing in clinical practice is affected by several factors such as the severity of the patient's condition, different stages of disease development, sampling methods, and testing conditions in laboratories [14, 15]. In some studies, patients tested negative for SARS-CoV-2 infection three times by RT-qPCR three weeks before the acquisition of bronchoalveolar lavage fluid (BALF) samples; however, results of RT-qPCR and next-generation sequencing of BALF samples were positive for SARS-CoV-2 [16-18]. As a result, it remains difficult to distinguish patients with suspected and confirmed COVID-19 efficiently.

As more data on SARS-CoV-2 and COVID-19 are madeavailable, it is likely that there will be a deficiency of diagnostic methods for detecting viral nucleic acids [19, 20]. In addition to nucleic acid detection, it is necessary to conduct a

detailed investigation of epidemiological history, observe imaging manifestations of the lung, and make comprehensive judgments to improve diagnostic accuracy.

Materials and methods

Ethical approval

This series of cases was approved by the Ethics Committee of the University of Hong Kong-Shenzhen Hospital (No. 2020020).

Study design and participants

All patients met the diagnostic or suspected diagnostic criteria mentioned in the interpretation of the "Guidelines for the Diagnosis and Treatment of Novel Coronavirus (2019-nCoV) Infection by the National Health Commission (Trial Version 6, 2019)".

Cases included in the confirmed group (CG) (n=26) were with positive results of pathogenic evidence either by the real-time fluorescent RT-PCR detection of the novel coronavirus nucleic acid or by virus gene sequencing, which was highly homologous to the known novel coronavirus.

Cases included in the suspected group (SG) met any one of the following criteria in their epidemiological history and conformed to any two of the following manifestations in their clinical manifestations: fever or respiratory symptoms, typical imaging features, or normal or reduced count for leukocytes and lymphocytes in the early stage of the disease. In the absence of significant epidemiological history, individuals must have presented with three of the aforementioned clinical manifestations.

Data collection

Medical records of patients from December 1, 2019 to December 30, 2019 were analyzed by the research team of the University of Hong Kong-Shenzhen Hospital. Data on patients' epidemiological, clinical, laboratory, and radiologic characteristics, as well as treatment regimens and outcomes, were obtained using data collection forms from electronic medical records. The data were reviewed by a team of physicians. The information recorded included demographic data, medical history, contact history, symptoms, signs, laboratory findings (including complete blood count, coagulation profile, and serum biochemical test), chest computed tomography (CT), and treatment measures.

Statistical analysis

Continuous variables were presented as mean, median, and interquartile range (IQR) values. Mean values for continuous variables were compared between the two groups using independent group t-tests when data were normally distributed; otherwise, the Mann-Whitney U test was used. Data with non-normal distributions from repeated measures were compared using a generalized linear mixed model. Categorical variables were presented as percentages and were compared using a χ^2 test or Fisher's exact test between the CG and SG. All statistical analyses were performed using SPSS 23.0. *P* values <0.05 suggested a significant difference.

Results

Presenting characteristics and vital signs

The study population included 73 patients with confirmed or suspected NCP. Among them, one patient in the SG was transferred to the CG after three positive RT-PCR test results. The median age was 43.6 years old (IQR, 33.5-54; range, 10-76 years old), and 41 patients (56.2%) were men. Patients in the SG (n=47) were significantly older (median age, 50 years old; IQR, 35.5-64.25 years old) than those in the CG (n=26) (median age, 40.1 years old; IQR, 33-46 years old) (*P*<0.001). Among 73 patients, 18 (24.6%) had comorbidities, including 11 cases of hypertension (31.2%), three of diabetes (4.1%), one of malignancy (1.3%), one of HIV (1.3%), one of chronic liver disease (1.3%), and one of bronchiectasis (1.3%).

Twenty-two patients (30.1%) came from or traveled to Hubei Province. Patients in the CG and SG had similar contact histories with patients with COVID-19. However, most patients in the SG (28, 59.6%) reported that they did not have contact with confirmed COVID-19 cases.

The most common symptoms at the onset of illness were cough (49 cases, 67.1%), fever (45 cases, 61.7%), sputum (22 cases, 30.1%), sore

Table 1. Patient characteristics

Characteristic		All patients (N=73)	Confirmed group (N=26)	Suspected group (N=47)	*P*-value
Age, median (IQR), years		43.6 (33.5-54)	50 (35.5-64.25)	40.1 (33-46)	0.011
Sex	Female	32 (43.8%)	12 (46.2%)	20 (42.6%)	0.767
	Male	41 (56.2%)	14 (53.8%)	27 (57.4%)	
Exposure					
Contact with COVID-19 patients		20 (27.4%)	10 (38.5%)	10 (21.3%)	0.015
No exposure		31 (42.5%)	3 (11.5%)	28 (59.6%)	0.007
From Hubei (traveler or resident)		22 (30.1%)	13 (50%)	9 (19.1%)	0.006
Comorbidity					
Diabetes		3 (4.1%)	2 (7.7%)	1 (2.1%)	0.287
Hypertension		11 (15.1%)	8 (30.8%)	3 (6.4%)	0.013
Malignancy		1 (1.4%)	0 (0%)	1 (2.1%)	0.644
Chronic liver disease		1 (1.4%)	0 (0%)	1 (2.1%)	0.644
HIV		1 (1.4%)	0 (0%)	1 (2.1%)	0.644
Bronchiectasis		1 (1.4%)	0 (0%)	1 (2.1%)	0.644
Onset of symptom to hospital, median (IQR)		6 (3-8)	5.5 (3-7)	7 (3.5-8)	0.764
Family		1 (5 persons)	1 (5 persons)	0	
Signs and symptoms					
Fever		45 (61.7%)	20 (76.9%)	25 (53.2%)	0.88
Cough		49 (67.1%)	13 (50%)	36 (76.6%)	0.021
Sputum		22 (30.1%)	5 (19.2%)	17 (36.2%)	0.131
Hemoptysis		1 (1.4%)	0 (0%)	1 (2.1%)	0.454
Sore throat		13 (17.8%)	4 (15.4%)	9 (19.1%)	0.297
Diarrhea		6 (8.2%)	5 (19.2%)	1 (2.1%)	0.011
Chest discomfort		3 (4.1%)	2 (7.7%)	1 (2.1%)	0.251
Fatigue		11 (15.1%)	7 (26.9%)	4 (8.5%)	0.038
Dyspnea		4 (5.4%)	3 (11.5%)	1 (2.1%)	0.091
Heart rate, median (IQR), bpm		88.75 (78-99)	92.3 (81.7-105.5)	86.7 (75-98)	0.112
Respiratory rate, median (IQR)		19 (18-20)	18.9 (18-20)	19.4 (19-20)	0.054
Systolic pressure, median (IQR), mmHg		123.5 (113-130)	127.5 (111.5-140.75)	121.4 (113-127)	0.147
Saturations, median (IQR)		96.8% (70%-100%)	96.9% (92%-100%)	96.6% (70%-99%)	0.723

Notes: Data are presented as median (IQR), n (%), or n/N (%), where N is the total number of patients with available data. *P*-values comparing the confirmed and suspected groups are obtained using the χ^2 test, Fisher's exact test, or Mann-Whitney U test. IQR, interquartile range; HIV, human immunodeficiency virus.

throat (13 cases, 17.8%), fatigue (11 cases, 15.1%), diarrhea (six cases, 8.2%), and dyspnea (four cases, 5.4%). Patients in the CG were more likely to report diarrhea and fatigue than those in the SG. Heart rate, respiratory rate, mean systolic pressure, and saturation were not significantly different between patients in the CG and SG (**Table 1**).

Laboratory values and chest CT findings

Most laboratory results observed in this study were normal, except for total lymphocyte counts and C-reactive protein (CRP) levels. Patients in the CG had fewer lymphocyte count abnormalities (lymphocyte count $\times 10^9$/L; median, 1.45; IQR, 1.09-1.17) than those in the SG (median, 1.94; IQR, 1.37-2.40) (P=0.004) (**Table 2**). The most common chest CT manifestation in all patients was bilateral areas of multiple lobules and subsegmental consolidation (34 patients, 46.6%) (P=0.663) (**Figure 1**). The second most common chest CT manifestation showed a mix of ground-glass opacity and consolidation (25 patients, 34.2%) (*P*=0.641) (**Figure 2**). There was no difference between the CG and SG with respect to the appearance of CT lung lesions. However, in the case of lung involvement, more patients in the CG displayed involvement of three or more lobes (13

Table 2. Laboratory values of the patients

Characteristic	All patients (N=73) Median (IQR)	Confirmed group (N=26)	Suspected group (N=47)	*P*-value
White blood cell count, $\times 10^9$/L	6.95 (5.27-8.27)	5.97 (4.39-6.95)	7.5 (5.76-8.93)	0.012
<4	4 (5.5%)	2 (7.7%)	2 (4.3%)	0.613
4-10	61 (83.6%)	22 (84.6%)	39 (83.0%)	1.002
>10	8 (11%)	2 (7.7%)	6 (7.7%)	0.730
Neutrophil count, $\times 10^9$/L	4.45 (3.2-5.29)	4.06 (2.92-4.99)	4.65 (3.42-5.54)	0.211
Lymphocyte count, $\times 10^9$/L	1.76 (1.27-2.27)	1.45 (1.09-1.17)	1.94 (1.37-2.40)	0.004
<1	9 (12.3%)	6 (23.1%)	3 (6.4%)	
≥1	64 (87.7%)	20 (76.9%)	44 (93.6%)	0.047
Monocyte count, $\times 10^9$/L	0.48 (0.32-0.59)	0.46 (0.30-0.625)	0.48 (0.32-0.57)	0.691
Hemoglobin, g/L	143 (133-158)	145 (133-156.7)	141.9 (133-159)	0.50
Platelet count, $\times 10^9$/L	221 (174.5-256.5)	183 (157-209)	242 (192-282)	0.012
Prothrombin time, s	13.2 (12.6-13.7)	12.7 (12.3-13.0)	13.3 (12.8-13.85)	0.531
Activated partial thromboplastin time, s	38.9 (35.4-41.8)	38.5 (35.4-41.7)	38.9 (35.4-41.9)	0.76
FIB, mg/L	4.48 (2.89-5.17)	5.33 (3.55-5.54)	4.2 (2.65-5.07)	0.170
Creatine kinase, U/L	55 (51-109)	93.5 (48.7-110)	87.5 (51-109)	0.718
Lactate dehydrogenase, U/L	166 (149-195.2)	191 (169.7-221.5)	154 (139-186.7)	0.058
Albumin, g/L	43.3 (41.1-45.4)	43.09 (36.2-51.7)	43.5 (42.1-45.3)	0.692
Alanine aminotransferase, U/L	24 (14.2-28)	24.9 (15.6-34.2)	23.7 (11.7-27.1)	0.359
Aspartate aminotransferase, U/L	23.1 (16.35-28.05)	28.4 (19.7-32.9)	21 (15.2-25.7)	0.006
Total bilirubin, mmol/L	9.5 (5.9-11.5)	8.33 (5.9-9.2)	10 (5.9-12.0)	0.256
Blood urea nitrogen, mmol/L	4.28 (3.2-5.1)	4.3 (3.4-5.2)	4.26 (3.2-5.1)	0.891
Creatinine, μmol/L	72.4 (60.5-85)	74.6 (59-87)	71.5 (61-85)	0.511
C-reactive protein, mg/L	21 (0.09-116)	26 (0.17-84.37)	18.8 (0.09-116)	0.031
Procalcitonin, ng/mL	7 (9.6%)	2 (7.7%)	5 (10.6%)	0.100
≥lg/a				

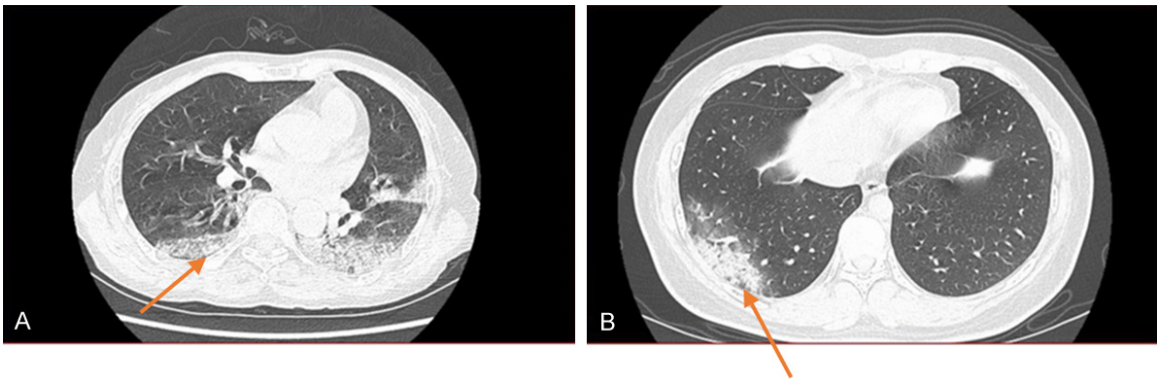

Figure 1. Computed tomography (CT) images of patients in the confirmed and suspected groups who presented with consolidation (arrow). A: A CT image of a 65-year-old woman in the confirmed group showing consolidation in multiple lung lobes. B: A 37-year-old woman in the suspected group showing consolidation in the right lower lung.

patients, 50%) than those in the SG (eight cases, 17%) (P<0.05). More patients in the SG displayed involvement of 1-2 lobes (36 cases, 76.6%) than those in the CG (12 cases, 46.2%) (P<0.05). In the CG, CT lesions were mainly distributed in the left lower lobe (65.4%) and left upper lobe (80.8%) (**Table 3**). The CT of an SG patient who was transferred to the CG after

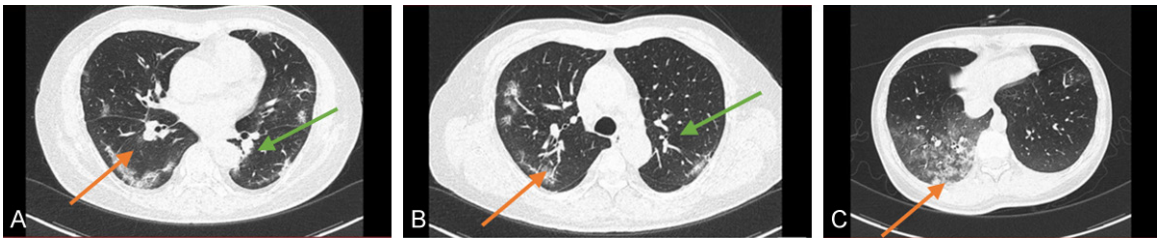

Figure 2. Computed tomography (CT) images of patients in the confirmed and suspected groups who presented with a mixture of ground glass and consolidation. A and B: A 65-year-old woman in the confirmed group whose CT images show a mixture of ground glass and consolidation in the peripheries, which is the typical appearance for patients with confirmed coronavirus disease 2019. C: A 37-year-old woman in the suspected group whose CT findings show a mixture of ground glass and consolidation that is mainly limited to the right lower lung.

Table 3. Chest computed tomography findings of the patients

Lobar involvement	All patients (N=73) Median (IQR)	Confirmed group (N=26)	Suspected group (N=47)	*P*-value
Involving bilateral lungs	34 (46.5%)	16 (61.5%)	18 (38.3%)	0.057
Limited left lung	19 (26%)	7 (26.9%)	12 (25.5%)	0.897
Limited right lung	16 (21.9%)	2 (7.7%)	14 (29.8%)	0.029
RUL	27 (37%)	11 (42.3%)	16 (34%)	0.484
RML	19 (26%)	9 (34.6%)	10 (31.3%)	0.214
RLL	37 (50.7%)	17 (65.4%)	20 (42.6%)	0.062
LUL	27 (37.0%)	17 (65.4%)	10 (21.3%)	0.000
LLL	44 (60.3%)	21 (80.8%)	23 (48.9%)	0.008
Peripheral	49 (67.1%)	24 (92.3%)	25 (53.2%)	0.001
The number of involved lobes				
3-5	21 (28.8%)	13 (50%)	8 (17%)	0.003
1-2	48 (65.5%)	12 (46.2%)	36 (76.6%)	0.009
CT lung lesion appearances				
Ground-glass opacification	14 (19.2%)	7 (26.9%)	7 (14.9%)	0.211
Consolidation	34 (46.6%)	13 (50%)	21 (44.7%)	0.663
Mix of ground glass and consolidation	25 (34.2%)	8 (30.8%)	17 (36.2%)	0.641
Cavitation	1 (1.4%)	0 (0%)	1 (2.1%)	0.454
Pleural effusion	4 (5.5%)	4 (15.4%)	0 (0%)	0.014
Enlarged mediastinal or hilar lymph nodes	4 (5.5%)	3 (11.5%)	1 (2.1%)	0.126
CT (normal)	4 (5.5%)	1 (3.8%)	3 (6.4%)	0.648

Notes: CT, computed tomography; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

three positive RT-PCR test results displayed typical multiple ground-glass shadows (**Figure 3**).

Treatments and clinical outcomes

In the CG, 26 patients (35.6%) were transferred to a SARS-designated hospital. In the SG, 47 patients (58.9%) were admitted to isolation wards and were discharged only when two RT-PCR tests for SARS-CoV-2 antigens taken at an interval of 24 hours were negative and when their symptoms disappeared. This occurred on February 25. Therefore, treatment data were only available for the SG. Among patients in the SG, 28 (59.6%) were administered empirical antibiotic treatment (6 mg/kg, three times, Shanghai Ongli HSBC Pharmaceutical Co., Ltd.), and three patients received oseltamivir treatment (**Table 4**). Based on CT findings 32

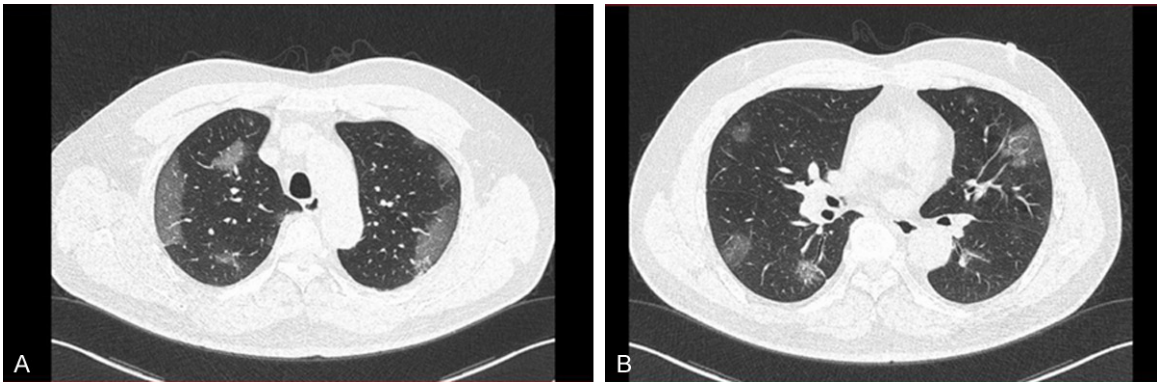

Figure 3. Computed tomography images of a patient in the suspected group who was transferred to the confirmed group after three positive results for reverse transcription-polymerase chain reaction tests. A and B: Typical multiple ground-glass shadows.

Table 4. Treatments administered to patients in the suspected group

Treatment	Suspected group (N=47)
Augmentin	4 (8.5%)
Doxycycline	10 (21.3%)
Doxycycline + Augmentin	8 (17%)
Cephalosporins	2 (4.2%)
Cephalosporins + Doxycycline	2 (4.2%)
Levofloxacin	2 (4.2%)
No Antibiotic	16 (34%)
Oseltamivir	3 (6.4%)

patients had lesions that were absorbed more obviously than before, three patients were still normal as before, and 10 patients were the same as before with no progression. Two patients did not undergo a review by CT.

Discussion

To determine the presence of helpful features for distinguishing between different entities, we described the clinical course and findings of a cohort of 26 confirmed and 47 suspected NCP patients and compared the clinical presentation of NCP with that of other respiratory illnesses.

In our series, 10 CG patients were diagnosed based on contact history; one patient had symptom onset in the family, thus suggesting the possibility of human-to-human transmission. This family case has been elaborated by Yuan et al. [21]. In the current study, CG patients (median, 50 years old; IQR, 35.5-64.25 years old) were older than SG patients (median, 40.1 years old; IQR, 33-46 years old) ($P<0.05$). Twenty (76.9%) patients in the CG presented to the hospital because of fever, whereas 36 (76.6%) patients in the SG presented to the hospital because of cough. A small group of patients had symptoms of diarrhea and sore throat in the CG. These findings are similar to the results of other studies [22-24].

Abnormal results for laboratory data on patient characteristics indicated that patients in the CG had higher aspartate aminotransferase and CRP levels and lower leukocyte and lymphocyte counts than those in the SG, which is same with previous findings [25]. These abnormalities are similar to those previously observed in patients with Middle East respiratory syndrome coronavirus and SARS coronavirus infections [26, 27]. Most of the patients in our study had mild degree of disease; therefore, the number of abnormalities observed was fewer, and these cases could be different from those in Wuhan. Imaging has been at the forefront of investigations that focus on patients with suspected or confirmed to have NCP [28, 29]. In our study, CT presentations of NCP in the CG displayed ground-glass opacities and consolidation under the pleura, and these findings were similar to those presented in a previous study [30]. Although there was no difference in the appearance of CT lung lesions between the CG and SG, we observed that 3-4 lobes were more involved in chest CT lesions among patients in the CG (13 cases in the CG [50%] compared with eight cases in the SG [17%]; $P<0.05$). In

contrast, 1-2 lobes were involved in the SG (12 cases in the CG [46.2%] compared with 36 cases in the SG [76.6%]; $P<0.05$). Although these descriptions are consistent with previous reports, special attention should be paid to patients with typical CT findings.

As for the treatment and outcome of patients in the SG, most patients used antibiotics or did not receive any treatment. However, most of the reviewed CT images indicated that lesions were absorbed within five to seven days. These patients were likely to have common pneumonia or mild NCP. In the event that hospitals did not have isolation wards, such patients could be isolated at home.

This study had some limitations. First, the sample size of the study population was small since there were only 26 confirmed patients. Second, given that the patients in the CG were transferred to SARS-designated hospitals, no data were available on their subsequent treatment regimen and clinical outcome. Therefore, it was not possible to compare the differences between the two groups in this regard.

RT-PCR testing could only be used as reference for COVID-19 detection. However, characteristic chest CT features and a close contact history strongly suggest COVID-19.

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Disclosure of conflict of interest

None.

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