ORIGINAL ARTICLE

Epidemiologic Features, Radiological Findings and Clinical Outcomes of 19 Patients with COVID-19 in a Single Center in Beijing, China

Lan Song^{1#}, Zhenchen Zhu^{1,2#}, Ruijie Zhao¹, Pengchang Li³,
Duxue Tian¹, Tiekuan Du⁴, Yan Xu⁵, Qiwen Yang³,
Wei Cao⁶, Wei Song^{1*}, Zhengyu Jin^{1*}

¹Department of Radiology, ³Department of Laboratory Medicine, ⁴Department of Emergency, ⁵Department of Respiratory and Critical Care Medicine, ⁶Department of Infectious Disease, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China
²MD Program, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China

Key words: coronavirus; SARS-CoV-2; COVID-19; tomography, X-ray computed; follow-up

Objective To describe the epidemiologic, clinical, laboratory, and radiological characteristics and prognoses of COVID-19 confirmed patients in a single center in Beijing, China.

Methods The study retrospectively included 19 patients with nucleic acid-confirmed SARS-CoV-2 infection at our hospital from January 20 to March 5, 2020. The final follow-up date was March 14, 2020. The epidemiologic and clinical information was obtained through direct communication with the patients or their family members. Laboratory results retrieved from medical records and radiological images were analyzed both qualitatively by two senior chest radiologists as well as quantitatively *via* an artificial intelligence software.

Results We identified 5 family clusters (13/19, 68.4%) from the study cohort. All cases had good clinical prognoses and were either mild (3/19) or moderate (16/19) clinical types. Fever (15/19, 78.9%) and dry cough (11/19, 57.9%) were common symptoms. Two patients received negative results for more than three consecutive viral nucleic acid tests. The longest interval between an initial CT abnormal finding and a confirmed diagnosis

Received January 11, 2021. Published online May 31, 2021.

[#]These two authors contributed equally to this article.

*Corresponding authors Wei Song Tel: 86-13601069220, E-mail: cjr.songwei@vip.163.com; Zhengyu Jin Tel: 86-13601037675, E-mail: jinzy@pumch.cn

This study has received funding from the Beijing Municipal Science and Technology Planning Project (Grant No. Z211100003521009).

was 30 days. One patient's nucleic acid test turned positive on the follow-up examination after discharge. The presence of radiological abnormalities was non-specific for the diagnosis of COVID-19.

Conclusions COVID-19 patients with mild or no clinical symptoms are common in Beijing, China. Radiological abnormalities are mostly non-specific and massive CT examinations for COVID-19 screening should be avoided. Analyses of the contact histories of diagnosed cases in combination with clinical, radiological and laboratory findings are crucial for the early detection of COVID-19. Close monitoring after discharge is also recommended.

SINCE the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (also known as Coronavirus Disease 2019, i.e., COVID-19) in December 2019 in Wuhan, China,^[1-5] the disease has spread across the world causing more than 85 millions of infection-confirmed cases and more than 1.8 million deaths as of January 3, 2021.^[6] Compared with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), COVID-19 has a lower mortality rate, a more occult nature, and greater transmission capacity.^[7, 8] The number of confirmed cases has reached 990 in Beijing, China, and the city is likely to undergo a long-term coronavirus epidemic control due to the raising concerns over a second wave caused by imported cases.^[9]

Early detection of SARS-CoV-2 infection is key to efficiently controlling transmission, but it has encountered many challenges. An epidemiologic history and prodromes of fever and dry cough are highly indicative of SARS-CoV-2 infection.^[1] However, infections with other viruses, such as influenza A and influenza B, can cause similar clinical symptoms, which makes the clinical diagnosis of COVID-19 difficult, especially during the flu season. In addition, asymptomatic infections have also been reported.^[10-12] Pneumonia is a common manifestation of COVID-19.^[1, 13, 14] Common features include unilateral or bilateral ground-glass opacities (GGOs) and consolidations as the disease progresses. Nonspecific radiological findings ranging from normal appearance to diffuse changes have also been reported in mild or asymptomatic cases.^[11, 15] Laboratory detection with reverse transcription-polymerase chain reaction (RT-PCR) has been considered the gold standard to confirm SARS-CoV-2 infection, but concerns over the global shortage of test kits and the substantial false negativity rate are prominent.^[7] All these challenges have contributed to the rapid spread of the virus by undiagnosed carriers. Therefore, a complete review of patients' epidemiological information, auxiliary diagnostic test results and full clinical courses may be

helpful to facilitate the prompt diagnosis of COVID-19.

Previous studies have mainly focused on the features of patients with confirmed SARS-CoV-2 infection.^[1, 2, 8, 11, 16] Little attention has been paid to the follow-up of recovered patients. Tian *et al.*^[11] reported the characteristics of 262 confirmed COVID-19 cases in Beijing, but they failed to give detailed descriptions of the patients' clinical courses, CT imaging findings, and prognoses. Here, we report the detailed epidemiological histories; clinical, laboratory and radiological findings, and clinical outcomes of 19 confirmed COVID-19 patients in Beijing, China. We aim to facilitate the early identification of suspected COVID-19 and to provide insight into the optimal management of the coronavirus outbreak.

PATIENTS AND METHODS

This retrospective study was approved by the Institutional Review Board of our hospital (S-K1127), and the requirement for informed consent for the clinical data collection was waived.

Patients

Our inclusion criteria were as follows: (1) patients who received positive results for two independent nucleic acid tests for SARS-CoV-2 conducted on specimens (nasopharyngeal swabs or other respiratory samples) using RT-PCR test kits in our hospital and (2) patients who underwent thin-section chest CT. Other causes of pneumonia, such as common bacterial and viral pathogens, were excluded. A total of 19 consecutive patients with SARS-CoV-2 infection from January 20 to March 5, 2020, in our hospital were included.

Collection of epidemiologic, clinical, laboratory, and clinical outcome data

Data from the electronic medical records of our hospital, including the clinical and laboratory test results, were summarized using a standardized data collection form. The researchers also directly communicated with

the patients or their families to obtain their epidemiological data and detailed clinical course information. Two researchers independently reviewed the data collection forms for accuracy. The final follow-up date was March 14, 2020. Nasopharyngeal swabs from all 19 patients were subjected to RT-PCR tests for the nucleic acid of SARS-CoV-2 two weeks after the patients were discharged. The clinical types of COVID-19 and the standard of discharge were determined according to the "Diagnosis and Treatment Protocol for COVID-19 (Trial Version 7)".^[17] The details of the criteria for the clinical classifications and discharge are listed in **Supplemental Digital Content 1**.

Image acquisition and interpretation

All patients underwent non-contrast thin-section CT scanning using multidetector CT scanners (Philips or Sinovision). The CT protocol was as follows: 120 kVp; automatic tube current (84 mA-250 mA); iterative reconstruction technique; slice thickness/interval, 1 mm or 1.25 mm; collimation, 0.625 mm; pitch, 0.984-1.2; matrix, 512×512; sharp reconstruction kernel; and breath-hold at full inspiration. CT images were obtained with the patients in the supine position from the apex to the lung base.

Two chest radiologists (LS and WS) with 15 and 30 years of experience in thoracic imaging (specialized in pulmonary infectious diseases), respectively, reviewed the CT images blindly and independently with consensus. The CT images were evaluated with both lung (width, 1200 HU; level, -600 HU) and mediastinal (width, 450 HU; level, 50 HU) window settings. The readers identified all separate pulmonary lesions on CT and analyzed the location, shape, and density of each. The details of the imaging interpretation are described in **Supplemental Digital Content 2**.

Quantitative measurements of lesions through CT images using artificial intelligence

Lung segmentation, lesion extraction, labeling, lesion volume calculation and CT attenuation measurements based on masks of opacities were performed using a dedicated artificial intelligence (AI) system with deep learning algorithm for characterizing pulmonary pneumonia (Beijing Deepwise & League of PhD Technology Co. Ltd., China).^[18] All lung segmentation, extracted opacity pieces and labeling were approved by an investigator (LS) with more than 15 years of experience in chest imaging. The AI algorithm achieved a dice of 0.97

in the HOUSE dataset (easy) and 0.89 in the LOLA dataset (hard), which proved its robustness. **Fig. 1** shows an example of pulmonary lobe and lesion segmentation. Based on these parameters, we calculated the lesion volume percentage in the whole lung.

Statistical analysis

All data were statistically analyzed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA). The data are expressed as the mean±standard deviation (*SD*) or as the median±interquartile range (P25, P75) for continuous variables.

RESULTS

Epidemiologic features

Of the 19 patients, 7 (36.8%) were residents of Wuhan. Four patients (21.1%) reported travel histories to Wuhan within 14 days before the illness onset. Six patients (31.6%) had close contact histories with confirmed COVID-19 patients. Two patients (10.5%) had recent travel histories to destinations other than

Figure 1. Examples of pulmonary lobe segmentation and lesion segmentation. Chest CT images of 40-year-old male (case 17) diagnosed with COVID-19. Right: Original axial unenhanced CT images; Left: Pulmonary lobes and lesion segmentation (corresponding output with deep learning algorithm shows the multifocal subpleurally distributed GGOs in left lower lobe). GGO: ground glass opacity.

Wuhan. During the diagnostic procedure, 16 patients (84.2%) had positive viral nucleic acid results in their first RT-PCR tests, 1 (5.3%) had a positive result in the second test, and 2 (10.5%) had more than three nu-

cleic acid tests before positive results were obtained. Detailed information regarding the exposures, dates of illness onset and clinical courses is shown in **Fig. 2** and **Fig. 3**.

Figure 2. Time course of symptoms, hospital admission, and discharge of patients infected with SARS-CoV-2. The epidemiological and clinical characteristics of the 19 patients with COVID-19. The cases were successively listed according to the date of diagnosis. Date of diagnosis was defined as the origin point; the contact history was reviewed; abnormal blood test and CT image upon admission were listed; and symptom and nucleic acid test were recorded during hospitalization.

Figure 3. Epidemic map of 19 COVID-19 patients. Dotted lines indicate close contact between cases. Dates refer to the dates of symptom onset (for 3 asymptomatic patients: case 10 refers to the date arriving in Beijing; case 11 and case 19 refer to the date contacting with case 10).

There were 5 family clusters including 13 patients in this case series (**Fig. 3**).

Cluster 1&2: Case 4 & case 5, case 8 & case 9 were spouses and residents of Wuhan, respectively, and both the former cluster had close contact histories with the Huanan Seafood Market of Wuhan.

Cluster 3: Cluster 3 was a family with four members, including a husband (case 18), a wife (case 10), a daughter (case 19) and a 7-year-old grandson (case 11). Case 10, 11 and 18 resided in Wuhan and came to Beijing on January 22, 2020 to visit case 19. Case 10 was confirmed to have COVID-19 by both CT and RT-PCR tests on February 5, 2020. Case 18 had presented a low-grade fever (37.6°C) and exhibited abnormal chest CT findings, but the nucleic acid test was negative. He was not confirmed until the sixth test on February 11, 2020. Case 11 was asymptomatic and was diagnosed with COVID-19 on February 6, 2020, immediately after his first negative nucleic acid test result one day earlier, but his chest CT scans appeared normal. Case 19 had abnormal chest CT findings but a negative nucleic acid test result on February 6, 2020. A total of six nucleic acid tests were performed with negative results during her quarantine and hospitalization from February 6 to February 20, 2020. She quarantined for two weeks after discharge and then received a positive nucleic acid test for SARS-CoV-2 on her seventh test. In this case, the interval between the initial abnormal CT finding and the positive nucleic acid test result for SARS-CoV-2 was 30 days.

Cluster 4: Case 12 and case 13 were spouses. Case 13 was a nurse who had recent contact history with Wuhan residents.

Cluster 5: This family cluster consisted of a mother (case 15), a father (case 17) and a son (7 years old, case 16). They were diagnosed with COVID-19 together on February 11, 2020. They had dinner with case 15's relatives (an elder male cousin and an uncle-in-law) for 4-5 hours on January 27, 2020. The asymptomatic elder male cousin of case 15 had abnormal chest CT findings that resembled those of viral pneumonia on February 11, 2020, but the nucleic acid tests and serum IgM and IgG antibodies for SARS-CoV-2 were negative for multiple times from February 11 to March 11, 2020 in Shanxi province, China. He had dinner with his colleague (confirmed COVID-19 on January 29, 2020 in Shanghai) on January 17, 2020 and then attended his company's annual meeting on January 21-22 in Shanghai, after which 11 colleagues

were diagnosed with COVID-19 within 14 days. Case 15's uncle-in-law was diagnosed with COVID-19 on February 10, 2020 in Shanxi Province. Case 16 only had a low fever for 4 days and normal chest CT scans for 3 times during the disease course.

Baseline clinical and laboratory findings

The baseline demographic information, clinical characteristics and laboratory results of the 19 patients are summarized in **Fig. 2** and **Table 1**.

Our study included 11 (57.9%) men and 8 (42.1%) women, with mean age 42 ± 18 (range: 7-68) years. Three cases were mild, and sixteen were moderate clinical types. Common symptoms were fever (15/19, 78.9%) and cough (11/19, 57.9%). Fifteen patients (78.9%) presented with no fever or a low-grade fever (maximum temperature $\leq 38^\circ\text{C}$). Four of the 19 (21.1%) patients had comorbidities. Six of the 19 (31.6%) patients were smokers. Except for case 14 (mild elevation of white blood cell count), the other 18 (94.7%) patients had normal or lower-than-average total white blood cell counts. Three (15.8%) patients had leukopenia and lymphopenia, respectively, and an elevated C-reactive protein level was observed in 11 of the 19 (57.9%) patients.

Clinical outcomes

There were no deaths in our study as of March 14, 2020. The mean duration of hospitalization was 20 ± 5 (11-25) days. The time interval between symptom onset and recovery ranged from 12 to 32 days. The follow-up nucleic acid test was positive in one patient (5.3%, case 11) after discharge, and his mother (case 19) was finally diagnosed on the same day (March 5, 2020). These two cases had been living together the entire time. They were readmitted to the hospital, and their conditions were stable without progression as monitored through chest CT scans. The remaining 17 patients were discharged with good prognoses.

Baseline chest CT findings and follow-up data

The median time interval between symptom onset and CT examination in 17 symptomatic patients was (4.0 ± 4.0) (2.5, 6.0) days. Illustrations of the CT imaging findings are displayed in **Table 2** and **Table 3**. Quantitative CT parameters measured with AI are shown in **Table 4**. Three (15.8%) patients had normal CT scans (Case 11, 13, & 16) at diagnosis. Fifteen patients (78.9%) had mixed GGO with consolidations.

Table 1. Summary of clinical features and laboratory results of patients infected with SARS-CoV-2 at initial presentation ($n=19$)

Items	Results
Age [mean $\pm$ SD (range), yrs]	42 $\pm$ 18 (7–68)
Male [No. (%)]	11 (57.9)
Any comorbidity [No. (%)] ^a	4 (21.1)
Signs and symptoms on presentation [No. (%)]	
Fever	15 (78.9)
Dry cough	11 (57.9)
Chill	6 (31.6)
Fatigue	4 (21.1)
Sore throat	3 (15.8)
Myalgia	3 (15.8)
Rhinorrhea	3 (15.8)
Shortness of breath	2 (10.5)
Diarrhea	2 (10.5)
Expectoration	1 (5.3)
Headache	1 (5.3)
Asymptomatic and afebrile	2 (10.5)
Vital signs at presentation [median (range)]	
Temperature (°C)	38 (37.3, 38.0)
Pulse oximeter O ₂ saturation (%)	98 (97, 99)
Baseline investigations [median (range)]	
White blood cells [$\times 10^9$ /L, mean $\pm$ SD (range), normal range (3.5–9.5)]	5.0 $\pm$ 1.6 (3.2–10.3)
Hemoglobin [g/L, mean $\pm$ SD (range), normal range (120–160)]	143.2 $\pm$ 21.2 (98–196)
Platelets [$\times 10^9$ /L, mean $\pm$ SD (range), normal range (100–350)]	212 $\pm$ 60 (122–336)
Neutrophils [$\times 10^9$ /L, normal range (2.0–7.5)]	3.0 (2.0–3.3)
Lymphocytes [$\times 10^9$ /L, normal range (0.8–4.0)]	1.5 (0.3–3.3)
C-reactive protein [No. (%) above normal range, normal range (0.0–8.0) mg/L]	11 (57.9)
Procalcitonin [No. (%) above normal range, normal range <0.5 ng/ml, $n=15$]	1 (6.7)
LDH [No. (%) above normal range, normal range (0–250) U/L, $n=9$]	1 (11.1)
Creatine kinase [No. (%) above normal range, normal range (24–195) U/L]	3 (15.8)
Cardiac troponin I [No. (%) above normal range, normal range (0–0.04) μ g/L, $n=13$]	1 (7.7)
NT-proBNP [No. (%) of negative results, normal range (0–125) g/ml, $n=12$]	12 (100)
CK-MB [No. (%) of negative results, normal range (0–3.6) μ g/L, $n=13$]	13 (100)
Abnormal chest CT [No. (%)]	16 (84.2)
Duration of symptoms [d, median (P25, P75), $n=17$]	12 (10, 13.5)
Days of hospitalization [d, mean $\pm$ SD (range)]	20 $\pm$ 5 (11–25)

^aEmphysema ($n=3$), obsolete tuberculosis ($n=1$), hypertension ($n=1$), mild renal insufficiency ($n=1$), coronary artery disease ($n=1$); Some patients have several comorbidities.

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; LDH: lactate dehydrogenase; NT-proBNP: N-terminal B-type natriuretic peptide; CK-MB: creatine kinase-MB.

Twelve (63.2%) patients had involvements of three or more lobes, and four (21.1%) patients had involvements of one or two lobes. Bilateral [13 (68.4%) patients] and peripheral [14 (73.7%) patients] patterns

were predominant. Three (15.8%) patients had small amounts of pleural effusion or pericardial effusion. No mediastinal lymphadenopathy or tree-in-bud signs were found in any patient.

Common CT findings included vascular dilation [16 (84.2%) patients, **Fig. 4A, 4D**], air bronchogram

Table 2. Baseline CT imaging findings in 262 lesions of 19 patients with COVID-19

CT imaging findings	No. of patients (%)	No. of lesions (%)
<i>n</i>	19	262
Distribution		
Peripheral distribution	14 (73.7)	223 (85.1)
Both peripheral and central distribution	2 (10.5)	39 (14.9)
Peri-bronchial distribution	14 (73.7)	170 (64.9)
Anterior predominant	1 (5.3)	65 (24.8)
Posterior predominant	15 (78.9)	197 (75.2)
Upper lobe distribution	14 (73.7)	80 (30.5)
Middle lobe distribution	9 (47.4)	31 (11.8)
Lower lobe distribution	14 (73.7)	151 (57.6)
Patterns of the lesion		
Pure ground glass opacities	15 (78.9)	87 (33.2)
Ground glass opacities with consolidation	15 (78.9)	147 (56.1)
Consolidation	7 (36.8)	28 (10.7)
Other signs surrounding the lesion		
Halo-sign	8 (42.1)	69 (26.3)
Reversed halo-sign	3 (15.8)	18 (6.9)
Other signs in the lesion		
Interlobular septal thickening	10 (52.6)	102 (38.9)
Crazy paving pattern	7 (36.8)	30 (11.5)
Air bronchogram sign	15 (78.9)	89 (34.0)
Architectural deformation	6 (31.6)	36 (13.7)
Bronchus distortion	6 (31.6)	38 (14.5)
Bronchial wall thickening	13 (68.4)	76 (29.0)
Vascular dilation sign	16 (84.2)	105 (40.1)
Vacuole sign	7 (36.8)	38 (14.5)

Table 3. Lobe of lesion distribution of the pulmonary involvement in each lobe in 19 patients of COVID-19

Lobe of lesion distribution	No. (%) of 19 patients	Percentage of total 57 involved lobes (%)
Left upper lobe	11 (57.9)	11 (19.3)
Left lower lobe	14 (73.7)	14 (24.6)
Right upper lobe	11 (57.9)	11 (19.3)
Right middle lobe	9 (47.4)	9 (15.8)
Right lower lobe	12 (63.2)	12 (21.1)

sign [15 (78.9%) patients], vacuole signs [7 (36.8%) patients, **Fig. 4B and 4C**] and crazy-paving signs [7 (36.8%) patients, **Fig. 5A, 5B and 6B**]. Multiple discrete round consolidations (**Fig. 4D, 5C**) or GGOs (**Fig. 6A, 6B**) occurred in a subset of patients which often associated with halo signs. In total, 262 pulmonary lesions were identified in 16 patients, including 182 (69.5%) patchy lesions (**Fig. 4A**), 36 (13.7%) confluent lesions (**Fig. 5A and 5B**), 40 (15.3%) nodular lesions (**Fig. 6A**), and 4 (1.5%) segmental lesions (**Fig. 7A, 7B and 7C**). An interesting finding was that patients with family clustering had similar CT imaging findings (**Fig. 4A-C, Fig. 5 and Fig. 6**). It is noteworthy that the lung lesions of COVID-19 could be localized and distributed along the lung segments in some patients (**Fig. 7**). During follow-up, the CT findings of the two 7-year-old boys were normal throughout their course of illness, and so was case 13 (a 36-year-old female). Among the other 16 patients, the lesions of 6 (37.5%) patients were directly absorbed in the follow-up examination, whereas those of the rest 10 (62.5%) patients exhibited an initial progression (increased extent or density) and then a gradual absorption (**Fig. 8**).

DISCUSSION

This descriptive study comprehensively examined the epidemiologic, clinical, and radiological features and prognoses of nineteen COVID-19 patients in a single center in Beijing. All patients had good prognoses. Most of the cases were clustered onset, had subtle symptoms especially in children, and various CT manifestations. Two patients were not confirmed COVID-19 until more than three nucleic acid tests. One patient had a positive nucleic acid test result during the follow-up after discharge. Abnormal lung CT findings can be present in asymptomatic patients.

Our findings support that fever and cough are the most common symptoms, which are frequently observed in previous studies of different clinical settings.^[1, 5, 14, 16, 19] In our study, the oxygen saturation of all patients was at least 95% at presentation, much higher than that of more severe patients who require oxygen supplementation.^[1, 2, 14] The blood test results in our study were nonspecific but we noticed that pediatric blood tests were more likely to be normal than adult blood tests.

In areas of endemic disease, chest CT findings are of great significance to evaluate COVID-19.^[20]

Table 4. Baseline quantitative CT parameters in the initial CT-positive 16 patients with COVID-19 and 5 family clusters (including 13 patients) [mean±SD (range)]

Clusters	<i>n</i>	No. of lesions (<i>n</i>)	Total lesion (volume, ml)	Mean CT value (HU)	Pneumonia volume/ total lung volume (%)
CT positive patients	16	13.8±17.8 (1–53)	216.7±292.5 (2.7–944.7)	–357.2±166.9 (–583.3––135.4)	6.4±10.6 (0.1–40)
Family cluster 1	2	9.0±1.4 (8–10)	320.9±335.5 (83.7–558.1)	–534.6±43.8 (–565.6––506.6)	7.1±5.9 (2.9–11.2)
Family cluster 2	2	19.5±13.4 (10–29)	116.6±145.7 (13.6–219.6)	–394.6±166.9 (–470.7––318.4)	4.3±5.8 (0.2–8.4)
Family cluster 3	4	6.5±4.7 (0–10)	452.7±457.5 (0–944.7)	–275.0±173.8 (–475.3––164.5)	15.5±18.0 (0–40)
Family cluster 4	2	2.0±2.8 (0–4)	3.8±5.4 (0–7.6)	–466.4±68.7 (–515.0––417.8)	0.1±0.1 (0–0.2)
Family cluster 5	3	8.0±8.5 (0–17)	13.4±16.7 (0–32.1)	–238.2±127.6 (–328.4––148.0)	0.3±0.3 (0–0.6)

Figure 4. Thin-slice CT images in three patients with COVID-19. A. 60-year-old woman (case 4). CT image obtained on day 3 after onset of symptoms shows subpleural patchy GGO in the lingual segment of the left upper lobe, with vascular dilation (arrow). B. The same patient on the same day. CT shows subpleural patchy consolidation with scattered vacuole signs (arrow) and bronchial wall thickening (arrowhead) in the dorsal segment of the right lower lobe. C. 68-year-old man (case 5, husband of case 4). CT image obtained on day 19 after onset of symptoms shows multiple patchy GGOs with predominant peri-bronchial distribution and multiple vacuole signs (arrow) in the left upper lobe. D. 31-year-old woman (case 6). CT image obtained on day 4 after onset of symptoms shows subpleural wedge-shaped consolidation with vascular dilation (arrowhead) and fuzzy margin in the right lower lobe.

Close follow-up CT scans are necessary to determine the change of lesions. The deep learning model, by automatically calculating lesion volume and precisely locating lesions on CT images from the baseline and the follow-up examinations, can facilitate the observation of changes in lesions during the course of dis-

Figure 5. Thin-slice CT images in three patients of a family with COVID-19. A. 61-year-old woman (case 10). CT image obtained on day 15 after the date on which she arrived in Beijing shows diffuse subpleural and peri-bronchial confluent GGOs and fibrous cords in both lungs with architecture deformation (arrow) and crazy paving sign (box). B. 64-year-old man (case 18, husband of case 10). CT image obtained on day 15 after the date on which he arrived in Beijing shows diffuse subpleural confluent GGOs and mixed GGOs with consolidations accompanied by crazy paving sign and traction bronchiectasis in both lungs (box). C. Asymptomatic and afebrile 37-year-old woman (case 19, daughter of case 10 and case 18). Her nucleic acid test results of SARS-CoV-2 were negative for 6 times. The seventh nucleic acid test result was positive after 30 days from her first test. CT image obtained on day 14 after contacting with case 10 shows a subpleural patchy consolidations with halo sign (box) in the right lower lobe.

ease. Such technique is also useful to evaluate illness severity and guide treatment. The majority of chest CT images in our study showed multifocal GGOs, consolidations or both that usually appeared peri-bronchially and peripherally in the lung. These patterns have been identified previously.^[10, 11, 16, 21] We found that most

Figure 6. Thin-slice CT images in two patients with COVID-19. A. Afebrile 39-year-old woman (case 15, wife of case 17). CT image obtained on day 9 after onset of symptoms shows scattered pure GGO nodule (arrow) or part-solid nodule (arrowhead) distributed along the bronchovascular bundle in the bilateral lower lobes. B. 40-year-old man (case 17). CT image obtained on day 5 after onset of symptoms shows subpleural scattered GGOS with crazy paving sign in left lower lobe (box).

Figure 7. Thin-slice CT images in three patients with COVID-19. A. 35-year-old man (case 2). CT image obtained on day 10 after onset of symptoms shows large segmental distribution GGO (arrowhead) in the lateral segment of right middle lobe. B. 42-year-old man (case 1). CT image obtained on day 4 after onset of symptoms shows large segmental distribution GGO (arrowhead) in the dorsal segment of left lower lobe. C. 63-year-old woman (case 9). CT image obtained on day 3 after onset of symptoms shows large segmental distribution GGO (arrowhead) in the right middle lobe and multiple subpleural little patchy GGOS (arrow) in the right lower lobe and the left lung.

lesions on CT scans (84.2%) had vascular dilation that may be caused by the increased blood supply to the inflamed area. Additionally, we noted that the initial CT images of 6 (31.6%) patients showed architectural

Figure 8. Serial CT images in a 62-year-old male with COVID-19. A. The initial CT image obtained on day 3 after onset of symptoms shows round GGO in left lower lobe. B. After 3 days, the first repeat CT shows irregular GGO with heterogeneous density and increasing in extent and density. C, D. Subsequently, lesions absorb gradually with decrease of extent and density (C, 11 days later), and only leaves a small amount of faint GGO on the latest CT scan (D, 16 days later).

deformation with bronchial distortion which suggests fibrosis formation and pathological pulmonary changes may occur prior to symptom onset; thus, CT scan can reveal biological changes related to COVID-19 at an early stage. However, these imaging characteristics are nonspecific and bear resemblance to those of SARS-CoV^[22] and MERSCoV infections.^[23] Noticeably, unlike SARS patients, some patients in our study presented with pleural effusion and vacuole signs on CT images. The vacuole signs may be caused by pneumatoceles due to the infection-induced damage to alveolar walls.

CT scan is valuable to evaluate the status of COVID-19 but ordering CT scan for COVID-19 screening should be carried out with adequate caution. Firstly, the imaging characteristics were non-specific. In addition, we found that the presence of CT abnormality and the clinical symptom may occur at different time points. This temporal inconsistency may be caused by delayed visits to hospitals. Similar findings were also reported.^[12, 24] Moreover, the absence of CT abnormalities did not entirely exclude the COVID-19 for that we identified three COVID-19 patients had no CT abnormalities. Similarly, Chung *et al.*^[20] reported that 3 of 21 COVID-19 patients (14%) outside Wuhan had normal CT interpretations. The increasing reports of

mild COVID-19 cases with no or subtle abnormal CT findings suggest that CT examination is complementary rather than pivotal to the diagnosis of COVID-19 in areas where the pandemic was partly contained.

Moreover, two cases had abnormal radiological characteristics but were not confirmed diagnosis in the first multiple consecutive nucleic acid tests. Laboratory testing is the standard protocol for the diagnosis of COVID-19, but the RT-PCR test for SARS-CoV-2 had high specificity and low sensitivity (60%-70%).^[25] Young *et al.*'s^[16] study showed that the viral load in nasopharyngeal samples from COVID-19 patients peaks within the first few days after symptom onset. The duration of viral shedding from nasopharyngeal aspirates lasted for at least 24 days after symptom onset. Toward the end of this period, the virus is only intermittently detected from nasopharyngeal swabs. Therefore, if suspected cases are excluded based on two consecutively negative respiratory pathogenic nucleic acid tests (sampling times ≥ 24 hours), approximately 16% of infection cases will be missed. This speculation is further demonstrated as we identified one patient who had a positive detection of viral nucleic acid after 30 days from the finding of initial CT abnormality. This is longer than the time reported in two comparable series in Singapore^[16] and China^[26]. The results highlight the significance of longitudinal surveillance *via* viral nucleic acid tests for patients with abnormal CT findings and COVID-19-related epidemiologic history.

Most cases in our study were clustered within families, which is consistent with the findings of previous studies.^[3, 11, 14] Additionally, we found that COVID-19 children were more likely to present mild symptoms and normal medical tests compared to adult cases during hospitalization. This phenomenon has been reported in other studies. Xia *et al.*^[15] found milder symptoms in 20 children cases compared to adults. Zhou *et al.*^[27] reported that 5 of 9 studied children had no clinical symptoms. Another family cluster report also showed a lack of symptoms in an infected child.^[3] On the other hand, although rare, deaths of young children with COVID-19 were reported lately in Iran and the United States.^[28, 29] The reasons for their deaths were not revealed except for one that was due to leukemia. Thus prompt nucleic acid testing will be crucial for early identification of COVID-19 in young close contacts. In consideration of radiation dose, CT examination especially repetitive CT follow-up should be prescribed with caution for children.

Another interesting finding is that case 11 had a positive RT-PCR test result two weeks after discharge. A similar phenomenon has also been reported by Lan *et al.*,^[30] who identified positive RT-PCR test results in four recovered patients. These findings suggest that recovered patients can still carry viable SARS-CoV-2, although its pathogenicity and infectivity remain questionable. Further isolation recommendations and continuous nucleic acid tests should be recommended for discharged patients.

Unlike that of SARS-CoV, the transmission of SARS-CoV-2 can occur during the prodromal period and thus may contribute to the spread of infection.^[26] Limited data are available for asymptomatic infections.^[25] Hu *et al.*^[12] reported 24 asymptomatic COVID-19 patients, including 7 CT-negative cases (median age: 14.0 years) during their hospitalizations. Another study on 262 COVID-19 patients in Beijing reported that the proportions of non-pneumonia and asymptomatic cases were 4% and 5%, respectively.^[11] Our study also discovered two asymptomatic cases (case 11 and case 19).^[3, 31] Therefore, prompt identification and proper management of asymptomatic cases are important to prevent transmission of the COVID-19.^[11, 31, 32] Persons with clear exposure history, regardless of clinical symptoms, should be considered for medical observation, home isolation, and further chest CT scanning or viral etiology testing.

Compared with the early cases in Wuhan, COVID-19 cases in Beijing exhibited milder symptoms and had lower proportions of abnormal CT findings. The proportion of pneumonia in the whole lung of our early-onset three family clusters (7.1%-15.5%) was slightly heavier than that of late-onset two family clusters (0.1%-0.3%). In our study, 21% of the patients had no fever, substantially higher than the percentage in patients in previous studies from Wuhan, China,^[1, 2, 14, 16] and similar to the percentages reported in Young *et al.*'s^[16] study in Singapore and Tian *et al.*'s^[11] study in Beijing. The increased proportion of asymptomatic patients outside Wuhan may result from the intensified tracing of contact and travel histories of suspected patients in China.

This study has several limitations. First, this was a single-center study with a relatively small number of cases. Therefore, our findings need to be further verified with large-scale multicenter data. Second, we only summarized pretreatment CT findings and laboratory data of confirmed COVID-19 patients in detail,

and briefly introduced the follow-up CT results. A detailed longitudinal analysis of CT features and blood tests may be more representative of the progression of disease. Third, we did not include the results of immunology tests. At the time of data collection, the IgM/IgG rapid test had not yet been widely used to test for SARS-CoV-2 infection in our institution.

In conclusion, our results highlight the importance of close contact tracing and longitudinal surveillance *via* viral nucleic acid tests. In addition, self-quarantine and follow-up viral nucleic acid detection are also recommended for discharged patients. Most importantly, diagnosis based on a combination of epidemiological history, clinical symptom, radiological and laboratory data is necessary to ensure the early detection of SARS-CoV-2 infection.

The Supporting Information is available free of charge on the CMSJ website at doi: 10.24920/003821.

Supplemental Digital Content 1. The criteria for clinical severity of confirmed COVID-19 and texts that describe the standard of discharge for COVID-19 patients in China.

Supplemental Digital Content 2. Document that explains how the lesion's characteristics in CT images were evaluated in the study.

Acknowledgements

The authors would like to express their appreciation for all of the febrile outpatient services and to all of the doctors, nurses, and other hospital staff for their efforts to combat the COVID-19 outbreak.

Conflicts of Interest Statement

All authors declare no competing interests.

REFERENCES

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5.
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323(11):1061-9. doi: 10.1001/jama.2020.1585.
- Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020; 395(10223):514-23. doi: 10.1016/S0140-6736(20)30154-9.
- Pan Y, Guan H, Zhou S, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. *Eur Radiol* 2020; 30(6):3306-9. doi: 10.1007/s00330-020-06731-x.
- Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382(8):727-33. doi: 10.1056/NEJMoa2001017.
- World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report. 2021; <https://www.who.int/publications/m/item/weekly-epidemiological-update-5-january-2021>. Accessed January 5, 2021.
- Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020; 25(3):2000045. doi: 10.2807/1560-7917.ES.2020.25.3.2000045.
- Wang C, Horby PW, Hayden FG, et al. A novel coronavirus outbreak of global health concern. *Lancet* 2020; 395(10223):470-3. doi: 10.1016/S0140-6736(20)30185-9.
- National Health Commission of China. COVID-19 epidemiological distribution. 2020; <http://2019ncov.chinacdc.cn/2019-nCoV/>. Accessed January 5, 2021.
- Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* 2020; 20(4):425-34. doi: 10.1016/S1473-3099(20)30086-4.
- Tian S, Hu N, Lou J, et al. Characteristics of COVID-19 infection in Beijing. *J Infect* 2020; 80(4):401-6. doi: 10.1016/j.jinf.2020.02.018.
- Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci* 2020; 63(5):706-11. doi: 10.1007/s11427-020-1661-4.
- Lai CC, Liu YH, Wang CY, et al. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): facts and myths. *J Microbiol Immunol Infect* 2020; 53(3):404-12. doi: 10.1016/j.jmii.2020.02.012.
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395(10223):507-13. doi: 10.1016/S0140-6736(20)30211-7.

15. Xia W, Shao J, Guo Y, et al. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol* 2020; 55(5):1169-74. doi: 10.1002/ppul.24718.
16. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA* 2020; 323(15):1488-94. doi: 10.1001/jama.2020.3204.
17. China National Health Commission. Diagnosis and treatment of pneumonia caused by novel coronavirus (trial version 7). 2020; <http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eaae415350a8ce964.pdf>
18. Li ZH, Zhang S, Zhang JG, et al. MVP-Net: multi-view FPN with position-aware attention for deep universal lesion detection. In: Shen D, et al. (eds) *Medical Image Computing and Computer Assisted Intervention-MICCAI 2019*. MICCAI 2019. Lecture Notes in Computer Science, vol 11769. Springer, Cham. https://doi.org/10.1007/978-3-030-32226-7_2
19. Chang D, Lin M, Wei L, et al. Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. *JAMA* 2020; 323(11):1092-3. doi: 10.1001/jama.2020.1623.
20. Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). *Radiology* 2020; 295(1):202-7. doi: 10.1148/radiol.2020200230.
21. Pan F, Ye T, Sun P, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. *Radiology* 2020; 295(3):200370. doi: 10.1148/radiol.2020200370.
22. Wong KT, Antonio GE, Hui DS, et al. Thin-section CT of severe acute respiratory syndrome: evaluation of 73 patients exposed to or with the disease. *Radiology* 2003; 228(2):395-400. doi: 10.1148/radiol.2283030541.
23. Das KM, Lee EY, Enani MA, et al. CT correlation with outcomes in 15 patients with acute Middle East respiratory syndrome coronavirus. *AJR Am J Roentgenol* 2015; 204(4):736-42. doi: 10.2214/AJR.14.13671.
24. Li Y, Xia L. Coronavirus disease 2019 (COVID-19): role of chest CT in diagnosis and management. *AJR Am J Roentgenol* 2020; 214(6):1280-6. doi: 10.2214/AJR.20.22954.
25. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology* 2020; 296(2):E32-E40. doi: 10.1148/radiol.2020200642.
26. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med* 2020; 382(12):1177-9. doi: 10.1056/NEJMc2001737.
27. Zhou Y, Yang GD, Feng K, et al. Clinical features and chest CT findings of coronavirus disease 2019 in infants and young children. *Zhongguo Dang Dai Er Ke Za Zhi* 2020; 22(3):215-20. doi: 10.7499/j.issn.1008-8830.2020.03.007.
28. Lytvynenko J. The first infant has died in the US after testing positive for the coronavirus. 2020; <https://www.buzzfeednews.com/article/janelytyvnenko/baby-us-dies-covid19-coronavirus>. Accessed March 30, 2020.
29. Dursun A. Iran: 6-year-old child dies from coronavirus. 2020; <https://www.aa.com.tr/en/latest-on-coronavirus-outbreak/iran-6-year-old-child-dies-from-coronavirus/1777045#>. Accessed March 30, 2020.
30. Lan L, Xu D, Ye G, et al. Positive RT-PCR test results in patients recovered from COVID-19. *JAMA* 2020; 323(15):1502-3. doi: 10.1001/jama.2020.2783.
31. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med* 2020; 382(10):970-1. doi: 10.1056/NEJMc2001468.
32. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020; 395(10225):689-97. doi: 10.1016/S0140-6736(20)30260-9.

中文摘要

北京市单中心 19 例 COVID-19 患者的流行病学特征、影像学表现及临床转归

宋兰^{1#}, 朱振宸^{1,2#}, 赵瑞杰¹, 李鹏昌³, 田杜雪¹, 杜铁宽⁴,

徐燕⁵, 杨启文³, 曹玮⁶, 宋伟^{1*}, 金征宇^{1*}

中国医学科学院 北京协和医学院 北京协和医院¹放射科,³检验科,⁴急诊科,⁵呼吸与危重症医学科,⁶感染内科, 北京 100730

² 中国医学科学院 北京协和医学院 临床医学专业, 北京 100730

摘要

目的 描述北京协和医院新型冠状病毒肺炎 (COVID-19) 确诊患者的流行病学史、临床特征、实验室检查和影像学特征及预后。

方法 回顾性分析我院自 2020 年 1 月 20 日至 3 月 5 日收诊的 19 例经核酸检测确诊的 SARS-CoV-2 感染的患者, 最终随访时间为 2020 年 3 月 14 日。通过与患者或家属直接沟通获得流行病学和临床预后资料, 从电子病历中检索实验室检查结果, 胸部 CT 图像由两位高年资胸部影像医师进行定性分析, 并通过人工智能软件进行定量分析。

结果 我们从研究队列中确定了 5 个家族簇 (13/19, 68.4%)。所有患者预后良好, 临床分型为轻度 (3/19) 或中度 (16/19)。常见症状为发热 (15/19, 78.9%) 和干咳 (11/19, 57.9%)。两位患者连续 3 次以上病毒核酸检测结果均为阴性。从发现 CT 异常到确诊 COVID-19 的最长时间间隔为 30 天。出院后随访, 1 例患者核酸检测复查呈阳性。影像异常表现对于 COVID-19 的诊断是非特异性的。

结论 北京地区 COVID-19 患者的临床症状多轻微或者无症状。CT 影像表现多为非特异性, 应避免对 COVID-19 患者进行大规模 CT 筛查。调查分析患者的流行病学接触史, 并结合临床、影像及实验室检查结果, 对 COVID-19 的早期诊断至关重要。出院后亦建议密切随访监测。

关键词: 冠状病毒; 严重急性呼吸窘迫综合征冠状病毒 2 型; 新型冠状病毒肺炎; 体层摄影术, X 线计算机; 随访