INTRODUCTION

In December 2019, an outbreak of a novel coronavirus disease, now known as COVID-19, was reported in Wuhan, China. In total, as of February 21, 2020, there have been 75,467 patients diagnosed with COVID-19 in China. The disease has quickly spread to 29 countries. On January 30, the pathogen was identified to be a novel beta-coronavirus by whole genome sequencing.

Background: In December 2019, the outbreak of coronavirus disease 2019 (COVID-19) started in Wuhan, and is now causing a worldwide pandemic. However, the experience in very elderly patients is very limited, which has important implications for the investigation of hospital infection in medical and health institutions.

Methods: Seven patients with confirmed COVID-19 infection in the Department of Geriatrics at Zhongnan Hospital of Wuhan University were included. Clinical data were retrospectively collected and analyzed. Laboratory tests and chest computed tomography (CT) images from the patients before and after the COVID-19 infection were compared.

Results: The median age of patients was 91 years old (87–96). Six patients had pneumonia in the last 6 months. Dyspnea occurred in one patient 64 h after the onset of the disease. In the other six patients, minor fatigue with low fever were the only other manifestations of the disease. Lymphopenia and a significant reduction in plasma globulin level was observed compared with levels before the onset of the disease. None had typical chest CT phenotypes during the early stage, except for critically ill patients. The elderly patients manifested minor clinical symptoms and atypical changes in chest CT images, which usually lead to misdiagnosis or delayed diagnosis.

Conclusions: The ratio of fatal cases in very elderly patients with COVID-19 is no higher than that reported in non-elderly patients. However, the elderly patients manifested minor clinical symptoms and atypical changes in chest CT images, which usually lead to misdiagnosis or delayed diagnosis.

Data collection

The medical data recorded in this study included demographic data, medical history, exposure history, comorbidities, symptoms,
signs, laboratory findings and chest CT scans. Laboratory results and CT images were obtained before and after the onset of the disease. The date of disease onset was recorded as the day when the patient reported a fever. Throat swab samples were collected for the detection of SARS-CoV2. All samples were tested using quantitative RT-PCR with the CDC recommended kit (BioGerm, Shanghai, China) following WHO guidelines for quantitative RT-PCR. The results were assessed according to the diagnostic criteria based on the recommendations of the National Institute for Viral Disease Control and Prevention (China). (http://ivdc.chinacdc.cn/kyjz/202001/t20200121_211337.html).

**Statistical analysis**

Statistical analysis was performed using Prism GraphPad 6.0c and SPSS 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were directly expressed as a range. Categorical variables were expressed as a number (%). Data were recorded as mean ± SEM and analyzed by Wilcoxon rank-sum test. \( P < 0.05 \) was considered significant.

**Results**

**Clinical characteristics**

In this study, all the patients had been hospitalized before the outbreak of COVID-19. Neither patients nor their recent visitors had direct exposure to the Huanan seafood market. The median age was 91 years (interquartile range [IQR], 89–94; range, 87–96) and five (71.4%) were men (Table 1). All patients were quarantined immediately after the COVID-19 diagnosis had been made. Two of them died, one of acute respiratory distress syndrome (ARDS) 9 days after diagnosis, and the other from ongoing heart failure. One patient was discharged, and the other four were still under quarantine at time of writing. The median time from first symptoms to diagnosis was 10 days (IQR 3–18, range 1–22). All patients had more than two comorbidities, such as hypertension (four patients), cerebral infarction (four), coronary heart disease (three), type 2 diabetes (two) and cancer (left ureteral malignancy) (one). All were long-term patients and bedridden, and six had pulmonary infection or pneumonia during the last 6 months. The most

**Table 1** Characteristics of patients infected with SARS-Cov2

| Clinical characteristics | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 | Patient 7 | n  |
|--------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----|
| Age (years)              | 90        | 88        | 93        | 96        | 88        | 87        | 94        | 90 (IQR 88–94) |
| Sex                      | Female    | Male      | Female    | Male      | Male      | Male      | Male      | 5  |
| BMI                      | 31.2      | 26.8      | 25.0      | 22.0      | 22.9      | 21.2      | 22.9      | 22.9 (IQR 22.0–26.8) |
| Smoking history          | No        | Yes       | No        | Yes       | No        | Yes       | Yes       | 4  |
| Epidemiological history of visitors | No | No | No | No | No | No | 0 | 0  |
| Barthel ADL Index        | 50        | 35        | 10        | 10        | 20        | 10        | 20        | 20 (IQR 10–35)|
| Comorbidities            |           |           |           |           |           |           |           |    |
| Hypertension             | Yes       | Yes       | Yes       | No        | Yes       | No        | No        | 4  |
| Coronary heart disease   | No        | Yes       | No        | No        | Yes       | Yes       | Yes       | 3  |
| Diabetes                 | No        | Yes       | Yes       | No        | No        | No        | No        | 2  |
| Cerebrovascular disease  | No        | Yes       | Yes       | Yes       | Yes       | Yes       | No        | 4  |
| Dementia                 | No        | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | 6  |
| Pneumonia within 6 months | Yes      | Yes      | Yes      | Yes      | Yes      | Yes      | Yes      | 6  |
| Malignancy               | Yes       | No        | No        | No        | No        | No        | No        | 1  |
| Long-term bedridden      | No        | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | 6  |
| Signs and symptoms       |           |           |           |           |           |           |           |    |
| Fever                    | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | 7  |
| Dry cough                | No        | Yes       | Yes       | No        | No        | No        | No        | 2  |
| Expectoration            | Yes       | No        | No        | Yes       | Yes       | Yes       | Yes       | 4  |
| Lethargic                | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | 7  |
| Fatigue                  | Yes       | No        | No        | No        | No        | No        | No        | 1  |
| Shortness of breath      | No        | Yes       | No        | No        | No        | No        | No        | 1  |
| Pharyngalgia             | No        | No        | No        | No        | No        | No        | No        | 0  |
| Vomiting                 | No        | No        | No        | No        | No        | No        | No        | 0  |
| Diarrhea                 | No        | No        | No        | No        | No        | No        | No        | 0  |
| Abdominal pain           | No        | No        | No        | No        | No        | No        | No        | 0  |
| Onset of first symptom to diagnosis (days) | 1       | 6        | 12        | 7         | 16        | 22        | 3        | 7 (IQR 3–18) |
| Respiratory rate (rpm)   | 24        | 35        | 19        | 20        | 24        | 18        | 20        | 20 (IQR 19–27) |
| Heart rate (bpm)         | 102       | 88        | 80        | 89        | 89        | 79        | 84        | 88 (IQR 80–89) |
| PaO2/FiO2                | 310       | 221       | 345       | 323       | 333       | 345       | 310       | 323 (IQR 310–345) |
| Use of non-invasive ventilators | No       | Yes       | No        | Yes       | No        | No        | No        | 2  |

Data are median (IQR) or \( n \), where \( n \) is the total number of patients with positive data. Abbreviations: BMI, body mass index; FiO2, fraction of inspired oxygen; IQR, interquartile range; PaO2, partial pressure of oxygen.
common symptom at the onset of COVID-19 infection was fever, ranging from 37.8 to 39.2°C, while dry cough was only seen in two patients (28.6%). One patient has diarrhea 3 days later, caused by antibiotic treatment; except for this case, all the other patients presented only with upper respiratory tract symptoms. One patient had severe hypoxemia at the onset of the disease, with a PaO2/FiO2 <300 mmHg and died on day 15. The other patients had an average PaO2/FiO2 of 328 mmHg under low-flow mask oxygen treatment. One of seven (14.3%) of the very elderly patients was critically ill during the early stage of infection with COVID-19. Another patient died due to the progress of his ongoing heart failure.

Analysis of laboratory results

The laboratory results were analyzed from the data collected from each patient, 1 month before the COVID-19 infection and 2–5 days after the manifestation of the first symptom (Table 2). A significant decrease in white blood cells, lymphocytes and monocytes was observed after the onset of the disease, while no significant change in neutrophils was noticed (Fig. 1). No changes in creatinine levels were found. In contrast, a remarkable decrease in globulin level was observed without noticeable changes in total protein levels.

Chest computed tomography manifestation

Abnormalities in chest CT images were detected in all patients. Only one patient (patient 2) showed newly emerged ground grass opacity in the left upper lobe, which is a typical change reported in non-elderly patients with COVID-19 (Fig. 2). Another patient showed either minor progression of existing pulmonary disorders or atypical changes, and one patient even showed absorption of the inflammation.

Discussion

To our knowledge, this is the first study to report the clinical features of COVID-19 in very elderly patients. The time from onset to confirmed diagnosis was 10 days on average, which is longer than that reported in non-elderly patients. Wang et al. reported that the median time from first symptoms to hospital admission was 7 days in patients with a median age of 56 years.\(^7\) The reason for the delay in diagnosis of very elderly patients is due to atypical manifestations of clinical symptoms, laboratory tests and chest CT. Most of these patients have comorbidities, particularly chronic pulmonary infection or pneumonia, which interfered with the diagnosis of the disease. Among these seven patients, one was critically ill after the onset of the disease, with PaO2/FiO2 <300 mmHg and received non-invasive ventilator treatment. This patient developed ARDS within 3 days of the first symptoms. Huang et al. also reported the rapid development of ARDS after hospitalization in patients with a median age of 49 years (IQR 41–58 years) with the mortality rate as high as 15%, similar to our findings in very elderly patients.\(^4\) This suggests that the severity and mortality is not as presumed higher in very elderly patients. The cause of death in another patient was very likely because of the progression of his ongoing heart failure but we cannot exclude the injury associated with the viral infection. However, his chest CT only showed minor inflammatory changes.

All the patients in this study were local people whose residence was in Wuchang district near the hospital. None had any direct or indirect exposure to the Huanan Seafood Market, where the initial cases of COVID-19 in Wuhan were reported. However, all these patients had lived in hospital for various periods before the onset of the symptoms for other reasons, such as controlling blood pressure or glucose levels, or dementia. The Barthel ADL Index was used for assessment, with a result of 20 (IQR 10–35), suggesting that the very old patients all need assisted living. One patient had normal cognitive function (patient 1), while the other six had dementia (one had mild dementia, two moderate dementia and three severe dementia). Therefore, this gave rise to difficulties in medical history taking.

All patients had fever, and two had dry cough at the onset of COVID-19. However, as most of the patients had dysphagia and chronic cough, cough could not serve as a typical symptom in these patients. Thus, fever may be an important sign and should be followed up with complete laboratory examinations.

The main mode of transmission has been proven to be person to person by respiratory droplets, and when people are in close physical contact of any contamination, while fecal–oral transmission has also been proposed.\(^13\) Based on early reports between December 10 and January 4, \(R_0\) was estimated to be approximately 2.2, which means each infected patient can spread the infection to 2.2 other people.\(^7\) In a later study with a larger population analysis, \(R_0\) was estimated to be 3.77.\(^8\) The number of infected patients

Table 2  Laboratory data of patients infected with SARS-Cov2 at onset of the disease

| Laboratory characteristics | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 | Patient 7 |
|---------------------------|----------|----------|----------|----------|----------|----------|----------|
| White blood cell count, x10^9/L (3.5–9.5) | 8.04 | 3.75 | 2.36 | 4.94 | 2.91 | 2.94 | 4.46 |
| Neutrophil count, x10^9/L (1.8–6.3) | 6.73 | 3.43 | 1.63 | 2.69 | 2.50 | 1.68 | 3.23 |
| Lymphocyte count, x10^9/L (1.1–3.2) | 0.59 | 0.20 | 0.54 | 1.13 | 0.34 | 0.94 | 0.77 |
| Monocyte count, x10^9/L (0.1–0.6) | 0.62 | 0.12 | 0.14 | 0.72 | 0.07 | 0.2 | 0.29 |
| Platelet count, x10^9/L (125–350) | 336 | 101 | 81 | 197 | 140 | 130 | 78 |
| Alamine aminotransferase, U/L (9–50) | 7 | 39 | 8 | 9 | 19 | 32 | 15 |
| Aspartate aminotransferase, U/L (15–40) | 9 | 52 | 36 | 17 | 43 | 14 | 31 |
| Total bilirubin, μmol/L (5–21) | 10.6 | 8.9 | 24.9 | 17.4 | 6 | 13.2 | 8.3 |
| Total protein, g/L (65–85) | 57.7 | 55.7 | 59.9 | 56.9 | 68.9 | 62.8 | 61.5 |
| Albumin, g/L (40–55) | 27.9 | 28.1 | 30 | 25.5 | 32.3 | 32 | 32.2 |
| Globulin, g/L (20–30) | 29.8 | 27.6 | 29.9 | 31.4 | 36.6 | 30.8 | 29.3 |
| Albumin/globulin (1.5–2.5) | 0.94 | 1.02 | 1 | 0.81 | 0.88 | 1.04 | 1.1 |
| Blood urea nitrogen, mmol/L (2.8–7.6) | 5.5 | 7.69 | 10.72 | 6.03 | 22.13 | 4.52 | 5.78 |
| Creatinine, μmol/L (64–104) | 34 | 112.3 | 48.5 | 57.9 | 137.8 | 24.1 | 63.3 |

Normal range of test results is showed in parentheses. \(^1\) Indicates that the result is above the normal range, and vice versa.
stopped increasing in our department 7 days after shutting down the central air-conditioning system and preventing visits from patients’ relatives. In this study, person-to-person transmission was considered the most important approach although airborne transmission during the early stage could not be ruled out.

The most common laboratory abnormalities in patients reported with COVID-19 include decreases in total lymphocytes, prolonged prothrombin time, elevated D-dimers and lactate dehydrogenase. In our very elderly patients, we found decreased levels of white blood cells (three patients), total lymphocytes (six) and monocytes (one), as well as reduced globulin levels after the viral infection. This may indicate a reduced immune and inflammatory activity.

The chest CT scan is the most important approach to diagnose pulmonary lesions caused by COVID-19. The most common abnormality was bilateral ground-glass opacities. However, only one of these patients (14.3%) presented with typical CT signs. The atypical changes in chest CT images suggest that in this

Figure 1 Analysis of laboratory tests before and after the onset of illness. Scatter plots illustrate the laboratory parameters in seven patients before and after the onset of illness. $P < 0.05$ for each parameter collected before and after the illness, by the two-tailed paired Student’s $t$-test.

Figure 2 Representative images of chest computed tomography (CT) before and after the onset of illness. Patient 2 showed typical changes of newly emerged ground grass opacity in the left upper lobe compared with the CT taken 3 months before. Patient 7 showed mild changes of ground grass opacity compared with CT taken 4 months before. Patient 3 showed bronchiectasis in the right upper lobe, and absorption of peripheral inflammation compared with the image taken 5 months before.
particular population, CT scans cannot be used as an exclusive diagnostic tool. Early detection of SARS-CoV2 with RT-PCR could be helpful although the false negative rate has been considered high.

No specific treatment has been officially recommended for the SARS-CoV2 infection. As the combination of lopinavir and ritonavir has been studied in patients with SARS-CoV with positive clinical outcomes,\textsuperscript{14} a clinical trial is ongoing in patients with COVID-19 to test these two drugs. However, so far no antiviral treatment showed clear effectiveness in patients with COVID-19. The most effective approach to control this disease is early diagnosis, effective quarantine and life support treatments.

Our study has some limitations. First, this is only a single center clinical study and the number of patients is limited. Second, the diagnosis was made mainly based on the detection of viral RNA by nasopharyngeal swabs and chest CT scan. No blood or lower respiratory tract specimens were obtained and detected for viral load. Thus, patients with undetectable viral RNA with swabs might exist.

Disclosure statement
The authors declare no conflict of interest.

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