

The Course of Mild and Moderate COVID-19 Infections—The Unexpected Long-Lasting Challenge

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Background. The course of disease in mild and moderate COVID-19 has many implications for mobile patients, such as the risk of spread of the infection, precautions taken, and investigations targeted at preventing transmission.

Methods. Three hundred thirty-one adults were hospitalized from January 21 to February 22, 2020, and classified as severe (10%) or critical (4.8%) cases; 1.5% died. Two hundred eighty-two (85.2%) mild or moderate cases were admitted to regular wards. Epidemiological, demographic, clinical, chest computed tomography (CT) scan, laboratory, treatment, and outcome data from patient records were analyzed retrospectively.

Results. Patients were symptomatic for 9.82 ± 5.75 (1–37) days. Pulmonary involvement was demonstrated on a chest CT scan in 97.9% of cases. It took 16.81 ± 8.54 (3–49) days from the appearance of the first symptom until 274 patients tested virus-negative in naso- and oropharyngeal (NP) swabs, blood, urine, and stool, and 234 (83%) patients were asymptomatic for 9.09 ± 7.82 (1–44) days. Subsequently, 131 patients were discharged. One hundred sixty-nine remained in the hospital; these patients tested virus-free and were clinically asymptomatic because of widespread persisting or increasing pulmonary infiltrates. Hospitalization took 16.24 ± 7.57 (2–47) days; the time interval from the first symptom to discharge was 21.37 ± 7.85 (3–52) days.

Conclusions. With an asymptomatic phase, disease courses are unexpectedly long until the stage of virus negativity. NP swabs are not reliable in the later stages of COVID-19. Pneumonia outlasts virus-positive tests if sputum is not acquired. Imminent pulmonary fibrosis in high-risk groups demands follow-up examinations. Investigation of promising antiviral agents should heed the specific needs of mild and moderate COVID-19 patients.

Keywords. Cohort study; coronavirus disease 2019 (COVID-19); lopinavir/ritonavir; Shufeng Jiedu; umifenovir.

Beginning at the end of 2019, the new coronavirus pneumonia COVID-19 spread from Wuhan [1, 2] to the rest of Mainland China within 30 days [3]. By March 11, 2020, it was declared a pandemic [4], demonstrating its high infectiousness. The Coronavirus Study Group named it SARS-CoV-2 [5], but Chinese virologists recommended the name HoV-19 because it is distinct from SARS-CoV [6]. Fever, cough, sputum, and fatigue are the most prominent symptoms. Upper respiratory tract symptoms are infrequent [7, 8]. To date, the mortality rate is lower than the prior known coronavirus diseases SARS and MERS [9]. Mild or moderate

COVID-19 represents the majority (81%) of cases [10]. However, the course of infection is severe in 14% and critical in 5% of cases [10]. The classification [11] is shown in Table 1.

Pneumonia is common in COVID-19 and can occur even in patients with few symptoms. Some studies have found viral pneumonia in 100% of all symptomatic patients [12] and even in 50% of asymptomatic cases [13]. On a chest CT scan, COVID-19 is characterized by rapid evolution from focal unilateral to diffuse bilateral ground-glass opacities that progress to or coexist with consolidations within 1–3 weeks [14].

Treatments in this study population were based on recommendations released by the General Office of the Chinese National Health Commission [11]. Lopinavir/ritonavir is an HIV medication that has been effective for both in vitro and clinical studies against SARS [15]. The antimalarial substance chloroquine and the antiviral influenza medication umifenovir were found to be effective in vitro against SARS-COV-2 [16]. ShuFengJieDu (SFJD) is the first choice herbal medicine against influenza in China. It can alleviate acute lung inflammatory injury [17] and protect against it by suppressing the MAPK/NF- κ B pathway [18] in rodents.

Received 24 April 2020; editorial decision 1 July 2020; accepted 5 July 2020.

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DOI: 10.1093/ofid/ofaa286

Table 1. Classification of Adult Cases With COVID-19 (11)

Classification	Characteristics
Mild	Clinical symptoms mild No sign of pneumonia on imaging
Moderate	Radiological findings of pneumonia fever and respiratory symptoms
Severe	Oxygen saturation $\leq 93\%$ at rest Arterial partial pressure of oxygen (PaO ₂)/fraction of inspired oxygen (FiO ₂) ≤ 300 mmHg (1 mmHg = 0.133 kPa) Obvious lesion progression in chest images within 24–48 h $> 50\%$
Critical	Respiratory failure and requiring mechanical ventilation Shock with another organ failure that requires ICU care

Abbreviation: ICU, intensive care unit.

Many studies have focused on high-risk patients who have higher mortality rates [19]; they have also focused on intensive care management [20], special groups [7], or comorbidities [9]. This study focuses on the course of mild and moderate cases because these represent the majority of mobile patients who have a high risk of transmission of the disease. The analyzed data set of this study is unique because it was acquired in an early phase of the epidemic where there was the capacity to hospitalize patients with low-grade symptoms. With the worldwide spread of the disease, these patients are now candidates for home quarantine. Hence, defining disease stages and the identifying stages' determining factors are instructive for the definition of standards for home quarantine. The necessary clinical and laboratory observations are required, and, for personal safety, adequate protective measures must be implemented to prevent further spread of the disease. So far, less attention has been focused on the follow-up of clinically recovered patients.

METHODS

We collected data from 331 adults with confirmed COVID-19 who were hospitalized at the Shanghai Public Health Clinic Center from January 21 to February 22, 2020. The cohort study protocol was approved by the Shanghai Public Health Clinic Center Ethics Committee (YJ-2020-S015-01), and written informed consent was obtained. Patients were classified as mild, moderate, severe, or critically ill [11]. Thirty-three (10%) of these patients were of the severe type. Sixteen patients (4.8%), of whom 5 patients (1.5%) died, were critically ill and had to be treated in the intensive care unit. The data of 282 (85.2%) patients submitted to regular care inpatient wards with mild ($n = 6$, 1.8%) or moderate ($n = 276$, 83.1%) symptoms on admission were evaluated.

Data Collection

We obtained epidemiological, demographic, clinical, laboratory, chest CT scan, and outcome data from patients' medical

records (Centers for Disease Control and Prevention [CDC] reporting forms). If the epidemiological data were not clear enough, a telephone or face-to-face interview with patients or contacts was conducted. Patients were followed up for clinical outcomes through March 24, 2020. Laboratory confirmation of COVID-19 was done by the Shanghai CDC. Clinical symptoms were monitored daily by the attending physicians. Blood tests, including white blood cell count (WBC), platelets, hemoglobin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, blood urinary nitrogen, creatinine, CD4, CD8, CD4/CD8 ratio, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin (PCT), were taken at admission and before discharge.

COVID-19 Detection

Nasopharyngeal swabs, oropharyngeal swabs, urine, stool (once every 3 days), serum (2 samples on admission and 2–4 weeks after the acute phase) of all patients were collected to do viral nucleic acid analysis by real-time reverse transcriptase polymerase chain reaction (rRT-PCR) until 2 successive (> 24 hours) negative results were obtained in all tests. Procedures were performed in accordance with World Health Organization guidance [21]. Negative rRT-PCR results from at least 2 consecutive sets of nasopharyngeal and throat swabs (collected at least 24 hours apart from a patient with COVID-19) were needed before discontinuing transmission-based precautions. Four negative specimens are needed to meet this requirement [21]. COVID-19 was confirmed by real-time rT-PCR using a protocol based on the recommendation given by the National Institute for Viral Disease Control and Prevention (China).

Chest CT Scans

All CT scans were performed with a 64-section scanner (SCENARIO, Hitachi Medical, Hitachi, Tokyo, Japan) without using contrast material. The parameters were as follows: tube voltage, 120 kV; automatic tube current, 180 mA–400 mA; iterative reconstruction technique; detector, 64 mm; rotation time, 0.35 seconds; section thickness, 5 mm; collimation, 0.625 mm; pitch, 1.5; matrix, 512×512 ; mediastinal window with a window width of 350 HU and a window level of 40 HU; lung window with a width of 1200 HU and a level of -600 HU. Patients were in the supine position—at full inhalation breath hold—consistent with prior studies on COVID-19 [22]. The chest CT scan pictures were evaluated by 3 radiologists with ~ 6 –32 years' experience in thoracic imaging evaluation, especially in the diagnosis of viral pneumonias, such as H1N1 and H7N9 pneumonia. CT scans were performed at admission and before discharge.

Treatment

Antiviral therapy during the intervention period was as follows: Umifenovir tablets (Arbidol, Ouyi Pharmaceutical Co., Ltd. of Shiyao group, 0.2 g, 3 times daily) or lopinavir/

ritonavir tablets (Abbott, Germany, 2 tablets, twice a day), hydroxychloroquine (Shanghai Zhongxi Sanwei Pharmaceutical Co., Ltd., 4 tablets, once daily) or SFJD capsules (Anhui Jiren Pharmaceutical Co., Ltd., 2.08 g, 3 times daily), darunavir and cobicistat tablets (Janssen Ortho, LLC, 1 tablet, once daily). Supportive medications included vitamin C (Tianjin Lisheng Pharmaceutical Co., Ltd, 2 tablets, 3 times daily).

Data Analysis and Statistics

Statistical analysis was performed using OriginPro 9.0 (OriginLab Corporation, Northampton, USA). Data were presented as mean \pm SD. Significant differences between the means were determined using the Student *t* test and Wilcoxon test. *P* values $<.05$ were considered significant.

RESULTS

Baseline Characteristics

The study consisted of 141 female patients (50%) and 141 males (50%). The mean age was 48.23 ± 15.55 (15–85) years, which was younger in comparison with the severe and critical cases: 59.78 ± 15.42 (25–88) years ($t = 4.8335$; $P < .001$). In addition, 109 (39.7%) patients were suffering from chronic disease: cardiovascular disease ($n = 62$), endocrine disease ($n = 28$), chronic respiratory disease ($n = 5$), cancer ($n = 2$), chronic abdominal disease ($n = 9$), and chronic hepatitis B ($n = 3$). Their course of COVID-19 did not differ statistically from patients without chronic disease in terms of duration of hospitalization or duration of symptoms, nor did patients have a more severe form of pneumonia.

Clinical Symptoms

Patients had a fever ($n = 244$, 86.5 %) with a mean duration of 7.51 ± 3.08 (1–17) days. The mean maximum temperature was $38.23^\circ\text{C} \pm 0.57^\circ\text{C}$ (37.4°C – 40°C). Pulmonary symptoms like cough, shortness of breath, and tightness in the chest ($n = 171$, 60.6%) had a mean duration of 7.24 ± 4.10 (1–20) days. Expectoration of sputum was present in 40.1% of the cases ($n = 113$), with a mean duration of 6.18 ± 4.04 (1–17) days. Fatigue or dizziness ($n = 106$, 36.3%) persisted for 5.93 ± 3.39 (1–14) days. Minor symptoms were headache or muscle pains ($n = 61$, 21.6%), upper respiratory tract symptoms like rhinorrhea and pharyngalgia ($n = 33$, 17%), and abdominal symptoms like diarrhea, constipation, and poor appetite ($n = 50$, 17.7%). In summary, the 282 patients suffered from at least 1 of the above-mentioned symptoms for 9.82 ± 5.75 (1–37) symptomatic days.

Laboratory Results

The mean CRP was 16.91 ± 21.40 (0.5–112) mg/L (normal value, <3 mg/L) with a value >50 mg/L in 25 cases on admission. CRP decreased in all cases to 1.39 ± 2.63 (0.5–30.74) mg/L

at discharge ($t = 4.4867$; $P < .001$). The ESR (normal level ≥ 15 male, ≥ 20 female) was pathological in 238 (84.4%) patients on admission (62.37 ± 37.68 ; 4–140) and in 197 (68.8%) patients on discharge (50.23 ± 35.11 ; 2–140). All other blood parameters (WBC, platelets, hemoglobin, PCT, ALT, AST, total bilirubin, direct bilirubin, blood urinary nitrogen, creatinine, CD4, CD8, CD4/CD8 ratio) showed no significant mean difference from admission to discharge.

Chest CT Scan

On a chest CT scan, 275 patients (97.5%) showed COVID-19-associated pneumonia; 57 patients (20.2%) had infiltrates in 1 lobe of 1 lung, 9 patients (3.2%) had infiltrates in 2 lobes of 1 lung, 25 patients (8.9%) had infiltrates in 2 lobes in both lungs, and 30 patients (10.6%) had infiltrates in 3 or more lobes in 2 lungs; 154 (54.6%) patients had diffuse infiltrations of both lungs. Seven patients (2.5%) showed no infiltrates.

The lesions were characterized as bullae ($n = 1$), patch shadow ($n = 8$, 2.8%), or nodules ($n = 9$, 3.2%). Typical ground-glass opacities were seen in 256 patients (90.8%); in 215 (76.2%) as the only characteristic lesion; in 3 (1.1%) cases with beginning consolidation fibrosis; in 2 (0.7%) patients in combination with pleural effusion; and in 36 (12.8%) in combination with consolidation fibrosis and pleural effusion. Two (0.7%) patients had pleural effusion alone. Six (2.1%) patients had no lesions.

In 162 patients, a prolonged hospitalization (7.38 ± 3.42 ; 3–26) was needed; 143 patients still had signs of widespread pneumonia with only minimal signs of absorption on chest CT scan, and 20 patients had increasing pulmonary infiltrates. On discharge, 272 patients still had detectable lesions on chest CT scans, though the absorption of pulmonary lesions had started. [Table 2](#) summarizes the chest CT scan findings. [Supplementary Figures 1](#) and [2](#) show chest CT scans in the course of the disease in 2 cases.

Stages of the Disease

All patients had symptoms for a mean time of 5.13 ± 3.66 (1–23) days before hospital admission. In the hospital, their clinical symptoms persisted for another 4.69 ± 4.15 (0–28) days. Together, the patients had clinical symptoms for 9.82 ± 5.75 (1–37) days. The time of admission to negative results in nasoand oropharyngeal (NP) swabs was 8.18 ± 6.86 (2–35) days. The time of first symptom to negative NP swabs was 13.14 ± 7.45 (2–41) days. When the NP swabs were negative, 193 patients (68.4%) had been asymptomatic for a mean time of 7.84 ± 6.96 (1–32) days; 89 (31.6%) patients had been symptomatic for 2.15 ± 2.92 (1–17) days. Despite negative NP swabs, the virus was still present in stool, blood, or urine for another 3.40 ± 4.85 (0–40) days. It took a mean time of 11.58 ± 7.99 (2–47) days from admission before 274 (97.2%) patients showed negative results in all virus tests, which was 16.81 ± 8.54 (3–49) days from the time of the first symptoms. When all tests

Table 2. Chest CT Scan Findings of 282 COVID-19 Patients With Mild and Moderate Course

Chest CT Scan Findings	No.	%
Location of infiltrates		
No infiltrates	7	2.5
One lobe in 1 lung	57	20.2
Two lobes in 1 lung	9	3.2
Two lobes in both lungs	25	8.9
Three lobes in both lungs	30	10.6
Diffuse infiltrations in both lungs	154	54.6
Characteristics of lesions		
None	6	2.1
Bullae	1	0.4
Patch shadow	8	2.8
Nodules	9	3.2
Ground-glass opacity	215	76.2
Ground-glass opacity, and consolidation fibrosis	3	1.1
Ground-glass opacity, and pleural effusion	2	0.7
Ground-glass opacity, pleural effusion, and consolidation fibrosis	36	12.8
Pleural effusion	2	0.7
Outcome		
No pneumonia during the whole course of infection	6	2.1
Completely cured on discharge	4	1.4
Residual infiltrates without fibrosis	233	82.6
Residual infiltrates and, consolidation fibrosis	39	13.8

Abbreviation: CT, computed tomography.

were negative, 234 patients (83%) had been asymptomatic for a mean time of 9.09 ± 7.82 (1–44) days. When negative test results were confirmed, 113 (40.1%) patients were discharged from the hospital. Eight patients, however, still showed positive

results for the virus in stool, and 169 (59.9%) patients, though virus-free, remained in the hospital for another 7.33 ± 3.39 (3–26) days. This decision was made for pulmonary reasons in 162 cases and was based on the evaluation of chest CT scans. At this point, 48 (17%) patients were still symptomatic for another 1.81 ± 2.46 (1–11) days. Seven patients, whose treatment regime had been modified, stayed in the hospital to complete the course of treatment.

In summary, it took a mean time of 16.81 ± 8.43 (3–49) days from detection of the first symptom(s) to virus-negative results in all fluids. The mean length of hospitalization was 16.24 ± 7.57 (2–47) days, and the mean time from first symptom to discharge was 21.37 ± 7.85 (3–52) days. Figure 1 describes the course of COVID-19 infection, and Table 3 compares the duration of each period.

Treatment

One hundred forty-eight patients received antiviral monotherapy (umifenovir $n = 50$, lopinavir/ritonavir tablets $n = 63$, hydroxychloroquine $n = 16$, darunavir $n = 13$ SFJD $n = 6$). In 48 cases, 2 therapies were combined (umifenovir plus SFJD $n = 17$, lopinavir/ritonavir tablets plus umifenovir $n = 18$, umifenovir plus hydroxychloroquine $n = 7$, lopinavir/ritonavir plus SFJD $n = 5$, darunavir plus lopinavir/ritonavir $n = 1$). In 20 cases, 3 drugs were combined (lopinavir/ritonavir plus SFJD plus umifenovir $n = 19$, umifenovir plus hydroxychloroquine plus SFJD $n = 1$). Combinations of medications were not used from the beginning, but depending on a patient's condition, an escalation of therapy could result in a very heterogeneous picture. No statistical difference was found by comparison of the antiviral therapies; 66 patients received no specific antiviral medication. Supportive therapy with vitamin C was used in 59 cases.

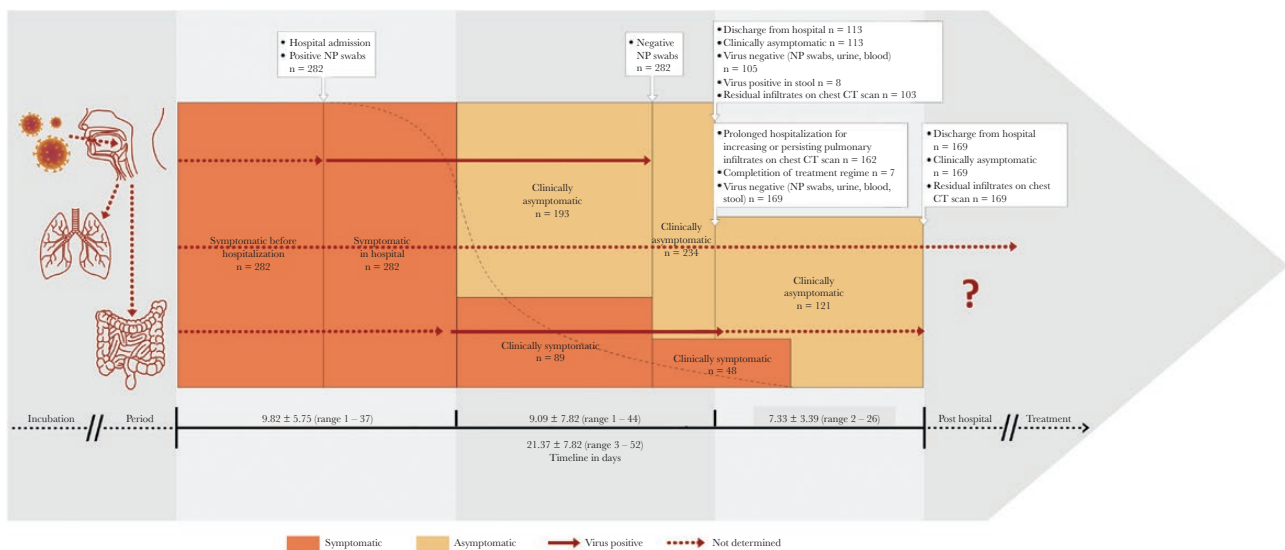


Figure 1. Timeline of the course of mild and moderate COVID-19 cases. Abbreviations: CT, computed tomography; NP, naso- and oropharyngeal swab.

Table 3. Time Course of Coronavirus Infection in Mild and Moderate Cases

Period	No.	Days	±	Range
Incubation period		Unknown		
Symptomatic period	282	9.82	5.75	1–37
Asymptomatic period before virus-negative in NP swabs	192	7.84	6.96	1–33
Asymptomatic period before virus-negative in NP swabs, blood, urine, and stool	234	9.09	7.82	1–44
From first symptom to virus-negative NP swabs	282	13.14	7.45	2–41
From first symptom to virus-negative in NP swabs, blood, urine, and stool	274	16.81	8.43	3–49
Virus still positive in stool after dismissal day	8	Unknown		
Hospitalization	282	16.24	7.57	2–47
Prolonged hospitalization after virus was negative	169	7.33	3.39	3–26
From first symptom to hospital dismissal	282	21.37	7.85	9–52
Treatment necessity after hospital discharge		Unknown		

Abbreviation: NP, naso- and oropharyngeal swab.

DISCUSSION

The results of this study confirm prior reports in relation to symptomatology [8] and case severity as related to age [7]. However, patients had a lower frequency of severe infection (9.9%), and less deadly cases (1.5%) occurred in comparison with prior reports [10]. In contrast to mild and moderate symptomatology, 276 of 282 (97.7%) patients had typical ground-glass opacification with or without consolidative abnormalities on chest CT scans, representing viral pneumonia [12, 14, 23]. However, pleural effusions were common (13.5%), which had been previously described as rare (4%) [11, 24].

The course of COVID-19 is determined by the following characteristics: the incubation period, the symptomatic phase, an asymptomatic phase until virus detection becomes negative, and by the features of disease activity on chest CT scans. Despite the low severity of the described cases, the course of the disease was remarkably long.

The incubation period was not determined, but other studies estimated it to be from 2 to 24 days [25–27].

The symptomatic phase was 9.82 ± 5.75 (1–37) days. Most cases showed mild symptoms, so COVID-19 may be misdiagnosed as a common cold. Furthermore, virus transmission by asymptomatic [13, 25] or presymptomatic persons is possible [28]. Hence, the threshold for suspicious cases should be low, and virus testing should become extensive.

When NP swabs were reported as virus-negative, 68.4% of the patients were already asymptomatic for 7.84 ± 6.96 (1–32) days. So far, this observation has only been reported in a few cases [29]. This raises the question of whether patients can still transmit the disease in this long asymptomatic phase. Transmission mainly occurs via respiratory droplets when a person with infection coughs or sneezes [30]. Hence, the risk of transmission should be lower in the asymptomatic phase. However, as long as NP swabs are still positive, patients' secretions from mouth and nose are still potentially infectious and a patient can by touching contaminate their immediate surroundings. Similar to primary asymptomatic transmission [25],

secondary asymptomatic patients whose NP swabs are virus-positive can transmit the virus from their breath while talking [30]. The virus is stable in aerosols for many hours [31], but most likely can be impeded by simple surgical masks, as shown for other viruses [32].

In contrast, 31.6% of the patients still showed symptoms despite negative tests, which might be explained by nondetected viral activity in the lungs.

Generally, the virus is first detected in NP swabs. Later it passes to the lungs, where virus concentration is generally higher [28]. None of the classic laboratory tests reliably determine the actual state of the disease. CRP was mildly elevated and compatible with a virus infection on admission, which decreased until discharge as expected. ESR, an unspecific marker of inflammation, was high on admission and persisted until discharge in 68.8% patients, despite virus negativity as a possible sign of ongoing inflammation. However, typical chest CT scan features can be found even before positive NP swabs [33]. Furthermore, 162 patients showed persisting signs of widespread pneumonia in chest CT scans after 16.84 ± 8.43 days, in spite of negative virus tests. In 20 (12%) virus-negative patients, their infiltrates even increased at this point, which was observed in only 3.5% previously [34]. These features can be signs of postinfectious lung damage. However, these infiltrates can also represent signs of persisting active viral pneumonia, because some NP-negative patients can still have positive sputum findings even after inducing expectoration [35]. Hence, patients should wear masks, especially when expectorants are prescribed. Thus, negative NP swabs do not mark the end of the disease.

A shift from a positive NP swab to positivity in feces during late infection was observed. Hence, NP swabs become unreliable during the course of the disease; 274 patients were asymptomatic for 9.98 ± 7.68 (1–30) days until discharge, before the virus became negative in stool. However, 8 patients had positive virus tests in stool on discharge. Viral loads in feces are generally lower compared with respiratory samples [36]. However, the level of infection in feces is not clear [37]; furthermore, live viruses have been detected in the feces of asymptomatic patients

[38]. Hence, it is important to base the decision of ending hospitalization only on negative NP swabs, because patients may still shed the virus by the oral–fecal route [38]. Asymptomatic virus-positive patients should wear medical masks. In addition, the practice of rigorous hygiene [39] is mandatory during home quarantine until all virus tests are negative to protect household members.

Consolidation fibrosis was seen in 13.8% of patients on discharge, with an unknown risk of chronic lung disease. COVID-19 imaging features overlap with SARS and MERS [40]. Transient reticular opacities were observed in SARS and MERS lasting for months [40]. In some cases, recovery and consolidation of lung fibrosis took up to 2 years in SARS [41], and fibrosis often became a chronic problem in MERS [42]. Hence, follow-up chest CT scans in patients recovering from COVID-19 should be considered, especially in patients who remain symptomatic or had severe disease, in order to evaluate disease activity and long-term or even permanent pulmonary damage, including fibrosis, as seen in SARS and MERS.

The development and approval of new agents can take time, so it is essential to assess the effectiveness of approved existing drugs. The therapies used in this study [11] were grounded on basic research data and experience with drugs in other infectious diseases. Physicians chose polypragmatic treatments, partly combining drugs for clinical reasons. Hence, the collected data do not allow therapeutic recommendations. Meanwhile, the drugs used have to be evaluated. Lopinavir/ritonavir and umifenovir did not show clinical effectiveness [43, 44]. Clinical pilot studies showed that SFJD might, on its first appearance, positively influence symptoms and time to virus negativity [45, 46], and 1 ingredient of SFJD taxifolin [47] showed high positive binding at the main protease of the virus. The role of hydroxychloroquine remains a matter of debate. A single study showed positive results [48], while large observational studies showed no effectiveness [49], indicating the need for further confirmation. Furthermore, the drug has potential detrimental effects [50].

While moderate and mild cases represent the absolute majority of cases, studies should also focus on the development of well-tolerated drugs that influence symptoms and the disease course of mild and moderate patients in order to avoid long-term pulmonary damage.

This study had certain limitations. Data analysis was retrospective and did not fulfill the criteria of a randomized controlled study. However, all patients had similar severity of the disease, so examination of real-life situations provided useful information. Furthermore, we did not get results from bronchoalveolar fluids. Testing was usually limited to patients with severe illness or those undergoing mechanical ventilation [51].

In conclusion, the 21.37±7.85 (3–52)-day-long course from first symptom(s) to hospital dismissal of mild and moderate

cases of COVID-19 is unexpectedly long and has potential pitfalls. The asymptomatic phase until virus negativity is problematic, with an associated unclear level of infection. While the virus moves quickly from the NP region to the lungs and intestines, detection in NP swabs is not reliable in later stages of the disease, and potential infectiousness from stool or expectoration has to be further evaluated. Relatively mild symptoms obscure the fact that these patients mostly suffer from viral pneumonia. Increased pulmonary infiltrates in 12.3% of asymptomatic patients detected in chest CT scans after virus negativity can be signs of either postinfectious lung damage or a nondetected continuation of pulmonary virus activity. This underlines the relevance of chest CT scan follow-up examinations, because disease activity can otherwise only be determined by invasive sample collections of sputum. In times of an exploding pandemic, mild and moderate cases of COVID may be sent home to quarantine. However, evaluation and close monitoring, the definition of parameters for hospitalization, hygienic measures, and testing frequencies are also essential. Furthermore, possible long-term pulmonary damage like fibrosis demands follow-up examinations. Promising antiviral agents should be investigated in clinical trials as soon as possible. These trials should consider the concerns of patients affected by mild and moderate COVID-19.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases online*. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

We thank Lenja Schröder for figure editing; Elisabeth Buhlmann, MD, Gesa Meyer-Hamme, MD, Ulrike Baumann-Schröder, MD, Joana Schröder, cand. med., for the data analysis discussion; Nils Muiznieks, PhD, for language editing. They were not compensated for their contributions.

Financial support. “Novel Coronavirus Pneumonia Innovative Treatment Regimen Research of Shanghai Science and Technology Commission Second Batch of Emergency Science and Technology Tackling Key Project” (20411950200); “Chinese Medicine Administration of Shanghai Health Protection Committee, Chinese Medicine Prevention and Treatment of Novel Coronavirus Pneumonia Emergency Special Subject, Chinese Medicine Treatment New Coronavirus Pneumonitis Real World Clinical Observation Research” (2020NCP001); “Shanghai Major Projects on Infectious Diseases” (shslczdzk01102); “Shanghai ‘Rising Stars of Medical Talent’ Youth Development Program, Specialist Program” (No. 2019–72); “HanseMercur Insurance Group (HMZTCM-C19-2020-1).”

Role of the funder/sponsor. The funders had no role in the design or conduct of the study; in the collection, management, analysis, or interpretation of the data; in the preparation, review, or approval of the manuscript; or in the decision(s) to submit the manuscript for publication.

Potential conflicts of interest. None reported. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Author contributions. Lu Xia and Jun Chen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Hongzhou Lu and Sven Schröder are co-senior authors, Lu Xia and Jun Chen are co-first authors. Concept and

design: Hongzhou Lu, Sven Schröder. Acquisition, analysis, or interpretation of data: Lu Xia, Jun Chen, Thomas Friedemann, Zongguo Yang, Yun Ling, Xuhui Liu, Shuihua Lu, Tao Li, Zhigang Song, Wei Huang, Yunfei Lu, Sven Schröder, Hongzhou Lu. Drafting of the manuscript: Sven Schröder, Thomas Friedemann, Lu Xia. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Friedemann. Obtained funding: Hongzhou Lu, Sven Schröder. Administrative, technical, or material support: Hongzhou Lu, Sven Schröder. Supervision: Hongzhou Lu and Sven Schröder.

Ethical approval. The study protocol was approved by the SPHCC Ethics Committee (YJ-2020-S015-01).

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